Objectives

The aims of the present analysis were

- To identify independent predictors of the *overall clinical outcome* of patients with atrial fibrillation (AF), including both stroke/thromboembolism and/or major bleeding.

- Given the overlap between stroke and bleeding risk factors, to develop a composite risk stratification score for stroke/thromboembolism or bleeding.
Methods

- We used data from the vitamin K antagonist (VKA) arm (n=2293; 65% men, mean age 70±9) of the AMADEUS trial, which was a multicentre, randomised, open-label non-inferiority study that compared fixed-dose idraparinux with VKA in AF patients.

- We defined two composite endpoints:
  - Endpoint 1 was the sum of stroke/thromboembolism or major bleeding.
  - Endpoint 2 was defined as the sum of stroke, systemic or venous embolism, myocardial infarction, cardiovascular death or major bleeding.

Results

- The independent predictors for composite endpoint 1 were age (p=0.014), previous stroke/TIA (p=0.049), aspirin use (p=0.002) and time in therapeutic range (TTR) (p=0.007).

- For composite endpoint 2, similar predictors were evident, plus LV dysfunction (p=0.011).

- Based on the regression models, two novel composite risk prediction scores were developed and externally validated in a ‘real world’ cohort of 441 anticoagulated outpatients with AF.
Results

Based on the regression models, two novel composite risk prediction scores for stroke (±CV events) or bleeding were developed and compared to existing individual stroke and bleeding risk scores (ie. CHADS₂, CHA₂DS₂-VASc, HAS-BLED) ……

<table>
<thead>
<tr>
<th>Composite score 1</th>
<th>(0.05 x Age)+(0.6 x Previous stroke or TIA)+(0.9 x concomitant aspirin)-(1.8 x TTR)</th>
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<tbody>
<tr>
<td>Composite score 2</td>
<td>(0.05 x Age)+(0.6 x Previous stroke or TIA)+(0.7 x concomitant aspirin)+(0.6 x LV dysfunction)-(1.4 x TTR)</td>
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Summary of findings

Composite score 1 (stroke or major bleeding - the simple one)
- There were no statistically significant differences in the AUCs between composite score 1 and the HAS-BLED, CHA₂DS₂-VASc or CHADS₂ scores, nor to a combined HAS-BLED/CHA₂DS₂-VASc score.
- No statistically significant difference in net reclassification improvement between the scores.

Composite score 2 (the complex one)
- Composite score 2 demonstrated the numerically highest predictive performance (AUC=0.707; 95%CI 0.655-0.758), and positive net reclassification compared to all other scores.
- The differences in AUCs reached the cut-off point of statistical significance only for the comparison of the composite score 2 with HAS-BLED (p=0.032), and CHADS₂ (p=0.032).
- The net reclassification improvement with composite score 2 did not reach statistical significance in all comparisons.
Conclusion

• We have developed and validated 2 novel composite scores for stroke/thromboembolism/bleeding that offer good discriminatory and predictive performance.

• These composite risk scores did not perform much better than the easier and more practical ‘traditional’ stroke and bleeding risk scores that are currently in use, which allow greater practically for everyday clinical practice and more personalised balancing of risks.

Simplicity is best …. assess stroke risk using CHA\textsubscript{2}DS\textsubscript{2}-VASc; assess bleeding risk with HAS-BLED