

## **Supplementary Appendix**

### **Ethics committees involved in the respective countries**

#### Austria

Ethikkommission der Medizinischen Universität Wien  
Borschkegasse 8b/E06, Vienna

#### Germany

Geschäftsstelle der Ethik-Kommission, Ärztekammer Berlin  
Friedrichstrasse 16, Berlin

#### Switzerland

EKOS – Ethikkommission Ostschweiz, St. Gallen  
Ethikkommission Nordwest- und Zentralschweiz, Basel  
Kantonale Ethikkommission Zürich, Zürich  
Comitato etico cantonale, Bellinzona

#### Spain

CEIC Hospital Clínico San Carlos; Doctor Martín Lagos, s/n. Madrid 28040  
Madrid  
EC Valencia

#### France

Ministere De L'enseignement superieur Et de la recherché  
Paris, France

#### Italy

EC Chieti, Ospedali Riuniti SS Annunziata-Chieti  
EC Spezia  
EC Salerno  
EC Taranto  
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#### United Kingdom

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**Supplementary table 1: C-statistics for validated risk scores and the clusters of risk factors for thromboembolic and bleeding events (PREFER in AF derivation cohort)**

Score	AUC	95% CI	p-value vs. cluster - stroke	p-value vs. HAS-BLED
<b>Stroke or SEE</b>				
Cluster - stroke*	0.7402	0.6868 - 0.7935	-	<0.01
HAS-BLED	0.6871	0.6320 - 0.7422	<0.01	-
Cluster – bleeding	0.6639	0.6070 - 0.7209	<0.01	0.581
CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.6464	0.5932 - 0.6995	<0.01	0.408
			p-value vs. cluster - bleeding	p-value vs. HAS-BLED
<b>Major Bleeding</b>				
Cluster – bleeding*	0.6982	0.6529 - 0.7469	-	<0.01
HAS-BLED	0.6314	0.5846 - 0.6782	<0.01	-
Cluster – stroke	0.5956	0.5469 - 0.6443	<0.01	0.178
CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.5855	0.5403 - 0.6307	<0.01	0.018

Legend: AUC: area under the curve, CI: confidence interval

**Supplementary table 2: C-statistics for ischemic stroke and systemic embolic events without TIA (derivation cohort)**

	<b>AUC</b>	<b>p-value*</b>	<b>95% CI</b>	
New Cluster – stroke	0.6802	<0.0001	0.6074	0.7536
CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.6562	<0.0001	0.5888	0.7235
HAS-BLED	0.6337	<0.0001	0.5549	0.7125
Cluster – bleeding	0.6259	<0.0001	0.5400	0.7117

Legend: AUC: area under the curve, CI: confidence interval

\* testing of difference from AUC=0.5000

**Supplementary table 3: C-statistics for TIA only (derivation cohort)**

	<b>AUC</b>	<b>p-value*</b>	<b>95% CI</b>	
New Cluster – stroke	0.7850	<0.0001	0.7197	0.8504
HAS-BLED	0.7473	<0.0001	0.6775	0.8172
Cluster – bleeding	0.7105	<0.0001	0.6407	0.7802
CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.6340	<0.0001	0.5570	0.7109

Legend: AUC: area under the curve, CI: confidence interval

\* testing of difference from AUC=0.5000

**Supplementary table 4: Validation of the identified clusters of risk factors for thromboembolic and bleeding events in the PREFER in AF Prolongation Study (labile INR disregarded)**

<b>Score</b>	<b>AUC</b>	<b>95% CI</b>	<b>p-value vs. cluster - stroke</b>
<b>Stroke or SEE</b>			
Cluster - stroke	0.6197	0.5219 - 0.7175	-
CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.5600	0.4777 - 0.6423	0.3029
Cluster – bleeding	0.5399	0.4345 - 0.6453	0.1023
HAS-BLED	0.5371	0.4487 - 0.6255	0.2433
<b>p-value vs. cluster – bleeding</b>			
<b>Major Bleeding</b>			
Cluster – bleeding	0.6334	0.5548 - 0.7119	-
HAS-BLED	0.6252	0.5611 - 0.6892	0.8764
CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.5607	0.4910 - 0.6305	0.2898
Cluster - stroke	0.5567	0.4712 - 0.6423	0.0092

Legend: AUC: area under the curve, CI: confidence interval, SEE: systemic embolic event

**Supplementary table 5: Validation of the identified clusters of risk factors for thromboembolic and bleeding events in the PREFER in AF Prolongation Study** (labile INR accounted for as reported in 6.9% of patients)

Score	AUC	95% CI	p-value vs. cluster - stroke
<b>Stroke or SEE</b>			
Cluster - stroke	0.6095	0.5153 - 0.7037	-
CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.5600	0.4777 - 0.6423	0.3307
Cluster – bleeding	0.5390	0.4342 - 0.6438	0.1527
HAS-BLED	0.5371	0.4487 - 0.6255	0.2782
			p-value vs. cluster – bleeding
<b>Major Bleeding</b>			
Cluster – bleeding	0.6476	0.5668 - 0.7283	-
HAS-BLED	0.6252	0.5611 - 0.6892	0.9066
Cluster - stroke	0.5758	0.4850 - 0.6665	0.0132
CHA <sub>2</sub> DS <sub>2</sub> -VASc	0.5607	0.4910 - 0.6305	0.1423

Legend: AUC: area under the curve, CI: confidence interval, SEE: systemic embolic event