

## SUPPLEMENTAL MATERIAL

Supplemental Table I. Predictive risk models for thromboembolic complications and bleeding events in patients with atrial fibrillation.

Risk model	Scoring
CHADS <sub>2</sub> (Gage et al. <sup>1</sup> )	<ul style="list-style-type: none"> <li>• Congestive heart failure – 1 point</li> <li>• Hypertension – 1 point</li> <li>• Age ≥75 – 1 point</li> <li>• Diabetes – 1 point</li> <li>• Stroke, previous history – 2 points</li> </ul>
CHA <sub>2</sub> DS <sub>2</sub> -VASc (Lip et al. <sup>2</sup> )	<ul style="list-style-type: none"> <li>• Congestive heart failure – 1 point</li> <li>• Hypertension – 1 point</li> <li>• Age 65-74 – 1 point</li> <li>• Age 75 or older – 2 points</li> <li>• Diabetes – 1 point</li> <li>• Stroke, previous history – 2 points</li> <li>• Female sex – 1 point</li> <li>• Vascular disease, history – 1 point</li> </ul>
ATRIA (Fang et al. <sup>3</sup> )	<ul style="list-style-type: none"> <li>• Anemia – 3 points</li> <li>• Severe renal disease – 3 points</li> <li>• Age 75+ – 2 points</li> <li>• Prior hemorrhage diagnosis – 1 point</li> <li>• Hypertension history – 1 point</li> </ul>
HEMORR <sub>2</sub> HAGES (Gage et al. <sup>4</sup> )	<ul style="list-style-type: none"> <li>• Hepatic or renal disease – 1 point</li> <li>• Ethanol abuse – 1 point</li> <li>• Malignancy – 1 point</li> <li>• Older age (&gt;75) – 1 point</li> <li>• Reduced platelet count or function – 1 point</li> <li>• Rebleeding risk – 2 points</li> <li>• Hypertension (uncontrolled) – 1 point</li> <li>• Anemia – 1 point</li> </ul>

	<ul style="list-style-type: none"> <li>• Genetic factors – 1 point</li> <li>• Excessive fall risk – 1 point</li> <li>• Stroke – 1 point</li> </ul>
<p>HAS-BLED (Pisters et al.<sup>5</sup>)</p>	<ul style="list-style-type: none"> <li>• Hypertension – 1 point</li> <li>• Abnormal renal function – 1 point</li> <li>• Abnormal liver function – 1 point</li> <li>• Stroke, previous history – 1 point</li> <li>• Bleeding, history of major – 1point</li> <li>• Labile INR – 1 point</li> <li>• Elderly (age 65+) – 1 point</li> <li>• Drug therapy – 1point</li> <li>• Alcohol intake – 1point</li> </ul>

Supplemental Table II. ICD-9-CM codes used to define comorbidities

<b>Condition</b>	<b>ICD-9-CM codes</b>
Heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4x, 425.9x, 428.xx
Hypertension	401.xx-405.xx
Diabetes mellitus	205.xx
Myocardial infarction	410.xx, 412.xx
Kidney disease	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582.xx, 583.0x-583.7x, 585.xx, 586.xx, 588.0x, V42.0x, V45.1x, V56.xx
Liver disease	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6x, 070.9x, 456.0x-456.2x, 570.xx, 571.xx, 572.2x-572.8x, 573.3x, 573.4x, 573.8x, 573.9x, V42.7x
Ischemic stroke	433.xx-438.xx
Gastrointestinal bleeding	455.2x, 455.5x, 455.8x, 456.0x, 456.20, 530.7x, 530.82, 531.0x, 531.2x, 531.4x, 531.6x, 532.0x, 532.2x, 532.4x, 532.6x, 533.0x, 533.2x, 533.4x, 533.6x, 534.0x, 534.2x, 534.4x, 534.6x, 535.01, 535.11, 535.21, 535.31, 535.41, 535.51, 535.61, 537.83, 562.03, 562.03, 562.12, 562.13, 568.81, 569.3x, 569.85, 578.0x, 578.1x, 578.9x
Prior intracranial bleeding	430.xx-432.xx, 852.xx
Other bleeding	423.0x, 459.0x, 568.81, 593.81, 599.7x, 623.8x, 626.6x, 719.1x, 784.7x, 784.8x, 786.3x
Alcohol abuse	265.2x, 291.1x-291.3x, 291.5x-291.9x, 303.0x, 303.9x, 305.0x, 357.5x, 425.5x, 535.3x, 571.0x, 571.1x, 571.2x, 571.3x, 980.xx, V11.3x
Anemia	280.xx-285.xx
Coagulopathy	286.xx, 287.1x, 287.3x-287.5x
Neoplasia	140.xx-172.xx, 174.xx-195.xx, 200.xx-208.xx, 238.6

Supplemental Table III. Risk ratios (95% confidence intervals) of in-hospital death in current users of dabigatran compared to current users of warfarin admitted with intracranial bleeding, MarketScan databases, 2009-2012. For this analysis, current users were defined as those with an active prescription for oral anticoagulation on admission date and those whose oral anticoagulation prescription ended in the 7-day period before the index hospitalization.

	<b>Warfarin</b>	<b>Dabigatran</b>
N	2474	104
In-hospital deaths [n(%)]	560 (22.6)	21 (20.2)
Model 1	1 (ref.)	0.98 (0.67, 1.43)
Model 2	1 (ref.)	0.97 (0.66, 1.41)
Model 3	1 (ref.)	0.97 (0.66, 1.44)

Model 1: Adjusted for age, sex, and hemorrhage subtype

Model 2: Model 1, additionally adjusted for CHA2DS2-VASC score and ATRIA bleeding score

Model 3: Adjusted for age, sex, hemorrhage subtype, and propensity score deciles

Supplemental Table IV. Risk ratios (95% confidence intervals) of in-hospital death in current users of dabigatran compared to current users of warfarin admitted with intracranial bleeding among those with ≤6 months or ≤1 year since initiation of the anticoagulant regime at the time of index hospitalization, MarketScan databases, 2009-2012.

<b>6 months</b>		
	<b>Warfarin</b>	<b>Dabigatran</b>
N	327	42
In-hospital deaths [n(%)]	88 (26.9)	8 (19.1)
Model 1	1 (ref.)	0.76 (0.40, 1.45)
Model 2	1 (ref.)	0.75 (0.39, 1.43)
Model 3	1 (ref.)	0.71 (0.37, 1.36)
<b>1 year</b>		
	<b>Warfarin</b>	<b>Dabigatran</b>
N	833	80
In-hospital deaths [n(%)]	191 (22.9)	13 (16.3)
Model 1	1 (ref.)	0.78 (0.47, 1.29)
Model 2	1 (ref.)	0.76 (0.46, 1.27)
Model 3	1 (ref.)	0.84 (0.50, 1.39)

Model 1: Adjusted for age, sex, and hemorrhage subtype

Model 2: Model 1, additionally adjusted for CHA2DS2-VASC score and ATRIA bleeding score

Model 3: Adjusted for age, sex, hemorrhage subtype, and propensity score deciles

Supplemental Table V. Risk ratios (95% confidence intervals) of in-hospital death in current users of dabigatran compared to current users of warfarin admitted with intracranial bleeding restricted to non-traumatic intracranial hemorrhages, MarketScan databases, 2009-2012.

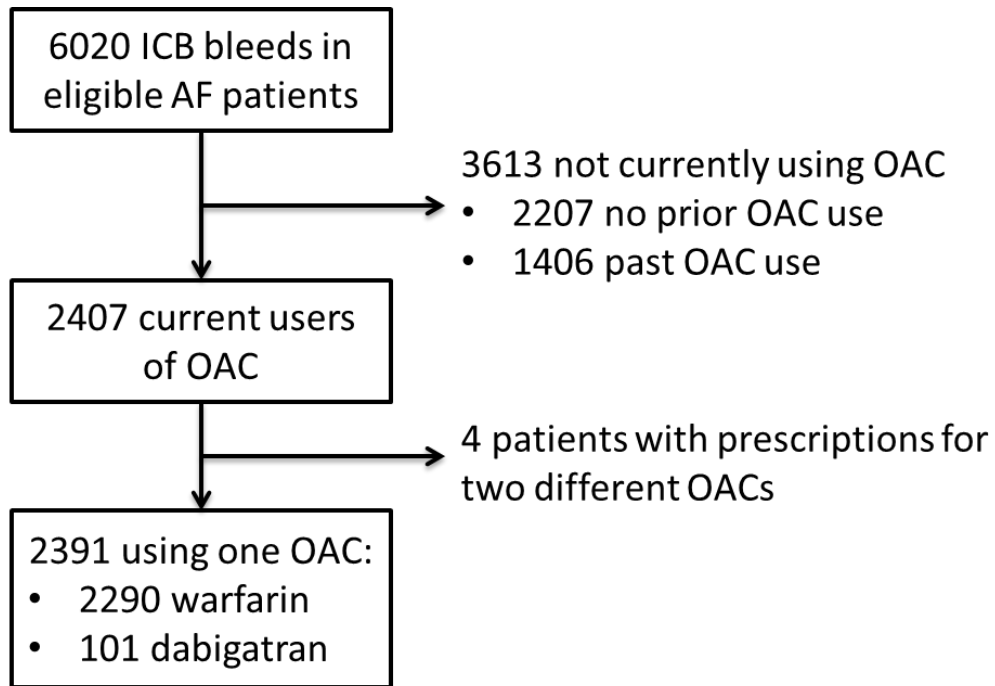
	<b>Warfarin</b>	<b>Dabigatran</b>
N	1396	56
In-hospital deaths [n(%)]	389 (27.9)	14 (25.0)
Model 1	1 (ref.)	0.99 (0.63, 1.55)
Model 2	1 (ref.)	0.98 (0.63, 1.54)
Model 3	1 (ref.)	1.00 (0.62, 1.60)

Model 1: Adjusted for age, sex, and hemorrhage subtype

Model 2: Model 1, additionally adjusted for CHA2DS2-VASC score and ATRIA bleeding score

Model 3: Adjusted for age, sex, hemorrhage subtype, and propensity score deciles

Supplemental Figure I. Flowchart of study patients



## REFERENCES

1. Gage BF, Waterman AD, Shannon W, Boehler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA*. 2001;285:2864-2870
2. Lip GYH, Nieuwlaat R, Pisters R, Lane DA, Crijns HM. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: The Euro Heart Survey on Atrial Fibrillation. *Chest*. 2010;137:263-272
3. Fang MC, Go AS, Chang Y, Borowsky LH, Pomernacki NK, Udaltsova N, et al. A new risk scheme to predict warfarin-associated hemorrhage: the ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation) Study. *J Am Coll Cardiol*. 2011;58:395-401
4. Gage BF, Yan Y, Milligan PE, Waterman AD, Culverhouse R, Rich MW, et al. Clinical classification schemes for predicting hemorrhage: results from the National Registry of Atrial Fibrillation (NRAF). *Am Heart J*. 2006;151:713-719
5. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJGM, Lip GYH. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: The Euro Heart Survey. *Chest*. 2010;138:1093-1100