

Supplementary Online Content

Graham DJ, Reichman ME, Wernecke M, et al. Stroke, bleeding, and mortality risks in elderly Medicare beneficiaries treated with dabigatran or rivaroxaban for nonvalvular atrial fibrillation. *JAMA Intern Med*. Published online October 3, 2016.
doi:10.1001/jamainternmed.2016.5954

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. International Classification of Disease, 9th edition, Clinical Modification (ICD 9-CM) codes used to define study outcomes

Outcome	ICD-9 Codes	Position	Setting	PPV
AMI	410 (all)	1st or 2nd	IP only	89%-97% ³¹⁻³⁵
Ischemic stroke	433.x1, 434.x (except subcode: x0), 436	1st	IP only	88%-95% ²⁵⁻²⁷
Extracranial bleeding events	A bleeding event is defined as a definite bleeding code, or a possible bleeding code (primary) supported by a definite bleeding code (secondary); without a corresponding trauma (as defined in Cunningham et al ²⁸) Definite bleeding: 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, 456.0, 456.20, 530.7, 530.82, 578.0, 455.2, 455.5, 455.8, 562.02, 562.03, 562.12, 562.13, 568.81, 569.3, 569.85, 578.1, 578.9, 593.81, 599.7, 623.8, 626.2, 626.6, 423.0, 459.0, 568.81, 719.1x, 784.7, 784.8, 786.3 Possible bleeding: 531.1, 531.3, 531.5, 531.7, 531.9, 532.1, 532.3, 532.5, 532.7, 532.9, 533.1, 533.3, 533.5, 533.7, 533.9, 534.1, 534.3, 534.5, 534.7, 534.9, 535.00, 535.10, 535.20, 535.30, 535.40, 535.50, 535.60, 455.x, 562.00, 562.01, 562.10, 562.11, 530.1, 280.0, 285.1, 285.9, 790.92	1st	IP only	87% ²⁸
Major bleeding events	Major bleeding is defined as a bleeding event with (i) a critical site code, (ii) a transfusion, or (iii) death, as described in Cunningham et al. ²⁸ Critical site: Intracranial: 430, 431, 432, 852.0, 852.2, 852.4, 853.0; Extracranial: 336.1, 363.6, 372.72, 376.32, 377.42, 379.23, 719.1, 729.92, 729.97, 423.0, 593.81, 772.5, 866.01, 866.02, 866.11, 866.12 Transfusions: a) ICD-9 PRC: 9903, 9904, 9905, 9906, 9907, 9909, b) HCPC: P9010, P9011, P9016, P9017, P9019, P9020,	N/A	IP only	

	P9021, P9022, P9023, P9031-P9040, P9044, P9051 - P9060, c) Revenue Center Codes: 0380-0392, 0399, d) Additional Value Codes: 37, 38, 39			
Major GI bleeding events	Major GI bleeding is defined as a major bleeding event at a GI site	N/A	IP only	86%-88% ^{28,30}
Intracranial hemorrhage	430, 431, 432, + (852.0, 852.2, 852.4, 853.0) [†]	1st	IP only	89%-97% ^{25,27,28}
[†] Intracranial hemorrhage was defined using codes for atraumatic hemorrhage (430-432), with a PPV of 89%-97%, ^{25,27,28} and codes for hemorrhage with closed head trauma (852-853), which have not been validated. We included these latter codes to capture situations where a bleeding event preceded by a fall may have been coded as trauma-related				

eTable 2. Distribution of additional baseline sociodemographic and medical factors included in unweighted (baseline) and weighted (adjusted) cohorts of Medicare beneficiaries initiating dabigatran or rivaroxaban for atrial fibrillation from 2011-2014

Characteristic	Unweighted cohorts			Weighted cohorts		
	Dabigatran (%; n=52,240)	Rivaroxaban (%; n=66,651)	SMD ¹	Dabigatran (%; n=52,264) ²	Rivaroxaban (%; n=66,630) ²	SMD ¹
Low income	19	17	0.06	18	18	0.00
Geographic region						
Northeast	21	18	0.07	19	19	0.00
South	40	45	0.09	43	43	0.00
Midwest	21	21	0.02	21	21	0.00
West	17	16	0.02	17	17	0.00
Rural metropolitan statistical area	24	22	0.04	23	23	0.00
Medical history						
Alcohol abuse	2	2	0.00	2	2	0.00
Anemia	20	19	0.01	20	20	0.00
Chronic liver disease	2	2	0.00	2	2	0.00
COPD	19	19	0.01	19	19	0.00
Dementia	4	4	0.01	4	4	0.00
Gout	5	5	0.01	5	5	0.00
Malignancy	22	23	0.03	23	23	0.00
Peripheral vascular disease	13	13	0.01	13	13	0.00
Other medical conditions						
Home health care	9	9	0.01	9	9	0.00
Home oxygen	7	7	0.01	7	7	0.00
Wheelchair use	1	1	0.02	1	1	0.00
Hospitalizations	36	38	0.04	38	38	0.00
Emergency department visits in past 0-30 days						
0	88	86	0.07	87	87	0.00
1	11	13	0.06	12	12	0.00
≥ 2	1	1	0.03	1	1	0.00
Emergency department visits in past 31-183 days						
0	85	85	0.01	85	85	0.00
1	12	12	0.00	12	12	0.00
≥ 2	3	3	0.01	3	3	0.00
Medication use						
General						0.00
Corticosteroids	15	16	0.03	16	16	0.00
Thyroid replacement	19	19	0.00	19	19	0.00
Prescriber characteristics						

Age group, y						
<40	14	15	0.01	14	14	0.00
40-59	58	58	0.01	58	58	0.00
≥60	18	18	0.02	18	18	0.00
Unknown	10	10	0.01	10	10	0.00
Female	11	10	0.02	11	11	0.00

Footnotes to eTable 2

¹ SMD: standardized mean difference

² Weighted cohort sample size is calculated by summing the stabilized inverse probability of treatment weights from each patient in the cohort. The size of this fully-adjusted pseudo-population can differ slightly from that of the unadjusted actual population.

eTable 3. Outcome event counts and adjusted hazard ratios with 95% confidence intervals comparing inverse probability of treatment weighted new user cohorts treated with lower (renal) doses of dabigatran (75 mg twice-daily) and rivaroxaban (15 mg once-daily) for nonvalvular atrial fibrillation. Dabigatran served as the reference group.

	Crude (unadjusted) incidence rate per 1000 years (No. events)		Adjusted hazard ratio (95% CI)
	Dabigatran (n=12,730)	Rivaroxaban (n=24,435)	
Thromboembolic stroke	17.5 (66)	15.6 (115)	0.88 (0.65-1.20)
Intracranial hemorrhage	5.3 (20)	8.4 (62)	1.58 (0.94-2.66)
Major extracranial bleed	41.9 (158)	67.9 (502)	1.58 (1.32-1.90)
Major gastrointestinal bleed	35.0 (132)	57.7 (426)	1.62 (1.33-1.98)
Death	53.3 (201)	51.3 (382)	1.05 (0.88-1.25)

eTable 4. Hazard ratios with 95% confidence intervals (CI) for mortality in patients treated with dabigatran or rivaroxaban, in subgroups defined by age and CHADS₂ score, with corresponding tests for interaction. Dabigatran served as the reference group.

	Hazard ratio (95% CI)	p-value for interaction
Age < 75 years	0.95 (0.77-1.19)	0.028
Age ≥ 75 years	1.31 (1.10-1.57)	
CHADS ₂ ≤ 2	0.99 (0.83-1.19)	0.016
CHADS ₂ > 2	1.41 (1.13-1.77)	
CHA ₂ DS ₂ -VASc ≤ 3	0.92 (0.73-1.16)	0.021
CHA ₂ DS ₂ -VASc > 3	1.30 (1.09-1.54)	

eTable 5. Hazard ratios with 95% confidence intervals for study outcomes in elderly patients treated with the standard dose of dabigatran or rivaroxaban for stroke prevention with atrial fibrillation, by time on oral anticoagulant therapy. Dabigatran served as the reference group.

	1-90 days	91+ days	p-value (interaction)
Primary outcomes			
Thromboembolic stroke	0.71 (0.55-0.93)	1.14 (0.74-1.75)	0.074
Intracranial hemorrhage	1.41 (0.94-2.13)	2.04 (1.25-3.34)	0.26
Major extracranial bleed	1.52 (1.32-1.75)	1.39 (1.11-1.74)	0.52
Gastrointestinal	1.47 (1.26-1.71)	1.25 (0.98-1.58)	0.26
Mortality	1.18 (1.00-1.39)	1.08 (0.83-1.40)	0.57
Secondary outcomes			
All hospitalized extracranial bleeds	1.38 (1.23-1.55)	1.40 (1.15-1.69)	0.92
Acute myocardial infarction	0.90 (0.72-1.13)	0.81 (0.56-1.18)	0.64

eTable 6. Sensitivity analyses showing hazard ratios with 95% confidence intervals for study outcomes in elderly patients treated with the standard dose of dabigatran or rivaroxaban for stroke prevention with atrial fibrillation. Dabigatran served as the reference group.

	14-day gap	≥ 2 prescription fills	Multivariate	CHA ₂ DS ₂ -VASc instead of CHADS ₂	Modified censoring criteria ²	Competing risks model
Primary outcomes						
Thromboembolic stroke	0.75 (0.62-0.91)	0.88 (0.63-1.24)	0.83 (0.66-1.04)	0.81 (0.65-1.02)	0.82 (0.65-1.02)	0.81 (0.65-1.01)
Intracranial hemorrhage	1.40 (1.08-1.81)	2.00 (1.32-3.01)	1.66 (1.21-2.28) ¹	1.65 (1.20-2.26)	1.62 (1.19-2.22)	1.64 (1.20-2.25)
Major extracranial bleed	1.42 (1.29-1.58)	1.50 (1.27-1.78)	1.49 (1.32-1.68)	1.48 (1.32-1.67)	1.47 (1.31-1.66)	1.48 (1.32-1.67)
Gastrointestinal	1.32 (1.18-1.47)	1.45 (1.21-1.74)	1.41 (1.24-1.60)	1.40 (1.23-1.60)	1.39 (1.22-1.58)	1.40 (1.23-1.59)
Mortality	1.11 (0.99-1.24)	1.16 (0.95-1.41)	1.14 (1.00-1.32)	1.15 (1.00-1.32)	1.18 (1.05-1.33)	---
Secondary outcomes						
All hospitalized extracranial bleeds	1.33 (1.22-1.45)	1.41 (1.22-1.63)	1.39 (1.26-1.54)	1.39 (1.25-1.53)	1.37 (1.24-1.52)	1.38 (1.25-1.53)
Acute myocardial infarction	0.87 (0.74-1.03)	0.80 (0.61-1.06)	0.89 (0.73-1.08)	0.88 (0.72-1.06)	0.86 (0.71-1.05)	0.88 (0.72-1.06)

¹ Regression model results are not optimized since some covariate estimates did not converge due to large number of covariates and relatively low number of outcome events.

² Patient were not censored for initiation of dialysis or kidney transplantation, or for admission to a nursing home, skilled nursing facility, or hospice care.

eTable 7. Number of elderly Medicare patients with atrial fibrillation included in new-user cohorts of dabigatran or rivaroxaban, stratified by dose (standard or lower (renal) dose)

	Dabigatran	Rivaroxaban
Standard dose	52,240 (80.4%)	66,651 (73.2%)
Lower (renal) dose	12,730 (19.6%)	24,435 (26.8%)
Total	64,970	91,086