

Supplemental Materials

Online Data Supplement

Table s1. ICD-9-CM codes used to define comorbidities.

Condition	ICD-9-CM codes
Anemia	280, 281, 282, 283, 284, 285
Cancer	140-172, 174-195, 200-208, 238.6
Cerebral bleeding	430, 431, 432, 852
Coagulopathy	286, 287.1, 287.3, 287.4, 287.5
Cognitive impairment	331.1-331.9
Diabetes	250
Gastrointestinal bleeding	455.2, 455.5, 455.8, 456.0, 456.20, 530.7, 530.82, 531.0, 531.2, 531.4, 531.6, 532.0, 532.2, 532.4, 532.6, 533.0, 533.2, 533.4, 533.6, 534.0, 534.2, 534.4, 534.6, 535.01, 535.11, 535.21, 535.31, 535.41, 535.51, 535.61, 537.83, 562.02, 562.03, 562.12, 562.13, 568.81, 569.3, 569.85, 578.0, 578.1, 578.9
Heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4, 425.9, 428
Hypertension	401, 402, 403, 404, 405
Prevalent ischemic stroke	433, 434, 435, 436, 437, 438
Incident ischemic stroke*	434, 436
Kidney disease	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582, 583.0,

	583.1, 583.2, 583.3, 583.4, 583.5, 583.6, 583.7, 585, 586, 588.0, V42.0, V45.1, V56
Myocardial infarction	410, 412
Mood disorders	293.83, 296, 311
Other bleeding	423.0, 459.0, 568.81, 593.81, 599.7, 623.8, 626.6, 719.1, 784.7, 784.8, 786.3
Peripheral artery disease	440.0, 440.2, 440.9, 443.9

*Comorbidities were defined by any position from an inpatient or outpatient claim, except for *incident ischemic stroke*, which was defined by primary position from an inpatient claim.

Table s2. Baseline characteristics of patients with atrial fibrillation according to first prescribed oral anticoagulant before propensity score matching: MarketScan, 2007-2015.

	Warfarin	Dabigatran	Rivaroxaban	Apixaban
n	217,087	31,305	39,349	19,358
Age, years, mean (SD)	70 (13)	67 (13)	67 (13)	69 (13)
Women, %	38	35	38	40
CHA ₂ DS ₂ -VASc, mean (SD)	3.3 (2.0)	3.1 (2.0)	3.0 (1.9)	3.4 (2.0)
HAS-BLED, mean (SD)	1.9 (1.2)	1.8 (1.2)	1.7 (1.1)	1.9 (1.2)
Disease history, %				
Heart failure	29	25	24	28
Hypertension	70	75	75	80
Diabetes	30	29	28	30
Myocardial infarction	10	7.9	8.2	9.3
Peripheral artery disease	13	11	11	12
Kidney disease	11	7.4	8.0	12
Ischemic stroke	21	19	17	20
GI bleeding*	7.3	7.4	5.8	6.1
Prior cerebral bleeding	1.0	0.7	0.7	1.0
Other bleeding	9.3	9.5	8.3	8.6
Anemia	20	15	17	18
Coagulopathy	5.9	3.1	3.6	3.8
Cancer	14	12	12	13
Mood disorders	7.7	7.8	8.8	9.2

Cognitive impairment	3.0	2.7	2.5	2.9
COPD†	24	23	23	24
Other medications, %				
Antiplatelet	2.1	2.2	2.0	2.5
Diuretic	44	37	35	38
Antiarrhythmic	6.6	11	11	11
Digoxin	18	14	11	10
ACE inhibitor‡	38	37	34	35
Angiotensin receptor blocker	22	24	23	25
Beta-blocker	69	72	71	74
Calcium channel blocker	38	40	39	41
Lipid lowering medication	57	57	55	59

*GI bleeding: gastrointestinal bleeding; †COPD: chronic obstructive pulmonary disease; ‡ACE inhibitor: angiotensin converting enzyme inhibitor; §SD: standard deviation.

Table s3. Baseline characteristics of patients with atrial fibrillation according to first prescribed oral anticoagulant before propensity score matching: Optum 2009-2015.

	Warfarin	Dabigatran	Rivaroxaban	Apixaban
n	112,051	15,185	22,480	11,786
Age, years, mean (SD)	73 (11)	69 (12)	70 (12)	73 (11)
Women, %	42	37	40	45
Race, %				
Asian	1.8	2.3	2.2	2.1
Black	7.4	6.6	6.4	7.0
Hispanic	6.8	5.7	6.5	6.3
White	77	79	78	77
Unknown	6.9	6.8	7.5	8.0
Education level, %				
Less than 12 th Grade	0.6	0.3	0.4	0.5
High School Diploma	29	26	25	27
Less than Bachelor Degree	54	53	54	53
Bachelor Degree Plus	12	17	16	15
Unknown	4.0	3.7	4.3	5.3
Household income range, %				
<\$40 K	34	24	24	27
\$40 K- \$49 K	9.0	7.5	8.0	8.5
\$50 K- \$59 K	7.7	7.3	7.5	7.3
\$60 K- \$74 K	9.2	9.9	10	9.1

\$75 K- \$99 K	11	13	13	12
\$100 K+	16	27	25	23
Unknown	14	12	12	13
CHA ₂ DS ₂ -VASc, mean (SD)	4.2 (2.0)	3.6 (2.0)	3.8 (2.1)	4.2 (2.1)
HAS-BLED, mean (SD)	2.5 (1.3)	2.3 (1.3)	2.4 (1.3)	2.7 (1.3)
Disease history, %				
Heart failure	38	30	31	36
Hypertension	84	85	85	88
Diabetes	37	34	35	37
Myocardial infarction	14	11	12	14
Peripheral artery disease	21	17	21	23
Kidney disease	21	14	17	22
Ischemic stroke	26	23	25	29
GI bleeding*	9.2	9.2	11	12
Prior cerebral bleeding	1.3	0.9	1.0	1.5
Other bleeding	12	12	15	16
Anemia	30	23	28	30
Coagulopathy	8.2	4.5	5.7	5.9
Cancer	16	14	16	16
Mood disorders	12	12	14	15
Cognitive impairment	4.8	3.8	4.2	5.3
COPD†	31	28	31	33
Other medications, %				

Antiplatelet	13	13	14	16
Diuretic	47	39	41	47
Antiarrhythmic	18	26	23	26
Digoxin	17	13	11	10
ACE inhibitor‡	44	42	43	45
Angiotensin receptor blocker	19	22	25	27
Beta-blocker	68	72	72	76
Calcium channel blocker	41	44	45	48
Lipid lowering medication	59	59	60	64

*GI bleeding: gastrointestinal bleeding; †COPD: chronic obstructive pulmonary disease; ‡ACE inhibitor: angiotensin converting enzyme inhibitor; §SD: standard deviation.

Table s4. Distribution of patients by sex and anticoagulant dosage. Standard dose is 150 mg for dabigatran, 20 mg for rivaroxaban, 5 mg for apixaban. Reduced dose is 75 mg for dabigatran, 10 or 15 mg for rivaroxaban, 2.5 mg for apixaban.

Women - MarketScan						
	Warfarin	Dabigatran	Warfarin	Rivaroxaban	Warfarin	Apixaban
Standard	N/A	9,549 (87%)	N/A	10,350 (70%)	N/A	6,007 (77%)
Reduced	N/A	1,437 (13%)	N/A	4,503 (30%)	N/A	1,798 (23%)
	Rivaroxaban	Dabigatran	Apixaban	Dabigatran	Rivaroxaban	Apixaban
Standard	4,443 (72%)	5,350 (85%)	2,059 (81%)	2,121 (85%)	5,316 (68%)	6,025 (77%)
Reduced	1,735 (28%)	944 (15%)	469 (19%)	387 (15%)	2,499 (32%)	1,799 (23%)
Optum						
	Warfarin	Dabigatran	Warfarin	Rivaroxaban	Warfarin	Apixaban
Standard	N/A	4,815 (86%)	N/A	6,114 (68%)	N/A	3,929 (74%)
Reduced	N/A	806 (14%)	N/A	2,880 (32%)	N/A	1,375 (26%)
	Rivaroxaban	Dabigatran	Apixaban	Dabigatran	Rivaroxaban	Apixaban
Standard	2,585 (69%)	3,187 (84%)	1,427 (79%)	1,485 (82%)	3,427 (65%)	3,928 (74%)
Reduced	1,155 (31%)	622 (16%)	379 (21%)	336 (18%)	1,881 (35%)	1,375 (26%)
Men - MarketScan						
	Warfarin	Dabigatran	Warfarin	Rivaroxaban	Warfarin	Apixaban
Standard	N/A	19,059 (94%)	N/A	19,837 (81%)	N/A	10,255 (89%)
Reduced	N/A	1,259 (6%)	N/A	4,512 (19%)	N/A	1,245 (11%)
	Rivaroxaban	Dabigatran	Apixaban	Dabigatran	Rivaroxaban	Apixaban
Standard	9,892 (83%)	10,919 (93%)	4,201 (91%)	4,240 (92%)	9,192 (80%)	10,289 (89%)

Reduced	1,987 (17%)	844 (7%)	396 (9%)	377 (8%)	2,351 (20%)	1,245 (11%)
Optum						
	Warfarin	Dabigatran	Warfarin	Rivaroxaban	Warfarin	Apixaban
Standard	N/A	8,896 (93%)	N/A	10,823 (81%)	N/A	5,622 (87%)
Reduced	N/A	662 (7%)	N/A	2,622 (19%)	N/A	858 (13%)
	Rivaroxaban	Dabigatran	Apixaban	Dabigatran	Rivaroxaban	Apixaban
Standard	5,295 (82%)	5,863 (92%)	2,647 (90%)	2,665 (91%)	5,009 (77%)	5,622 (87%)
Reduced	1,143 (18%)	506 (8%)	304 (10%)	271 (9%)	1,466 (23%)	858 (13%)

Table s5. Incidence of dementia among patients with atrial fibrillation initially treated with dabigatran, rivaroxaban, or apixaban versus warfarin: MarketScan, 2010-2015.

	Dabigatran	vs	Warfarin
n	31,304		31,304
Dementia, n	419		450
Follow-up in years, mean	1.8		1.6
Incident rate (per 1000 person-years)	7.4		9.0
Hazard ratio (95% confidence interval)			
Model 1*	0.80 (0.70, 0.91)		1
Model 2 †	0.78 (0.68, 0.89)		1

	Rivaroxaban	vs	Warfarin
n	39,202		39,202
Dementia, n	383		552
Follow-up in years, mean	1.1		1.3
Incident rate (per 1000 person-years)	8.7		10.5
Hazard ratio (95% confidence interval)			

Model 1*	0.89 (0.78, 1.02)	1
Model 2†	0.88 (0.77, 1.01)	1

	Apixaban	vs	Warfarin
n	19,305		19,305
Dementia, n	160		264
Follow-up in years, mean	0.7		1.1
Incident rate (per 1000 person-years)	11.3		12.4
Hazard ratio (95% confidence interval)			
Model 1*	0.90 (0.73, 1.09)		1
Model 2†	0.87 (0.71, 1.06)		1

*Model 1 adjusted for age, sex, and prevalent cognitive impairment;

†Model 2 additionally adjusted for comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED score.

Table s6. Incidence of dementia among patients with atrial fibrillation initially treated with dabigatran, rivaroxaban, or apixaban versus warfarin: Optum, 2010-2015

	Dabigatran	vs	Warfarin
n	15,179		15,179
Dementia, n	305		289
Follow-up in years, mean	2.2		2.0
Incident rate (per 1000 person-years)	9.2		9.7
Hazard ratio (95% confidence interval)			
Model 1*	0.92 (0.79, 1.09)		1
Model 2†	0.93 (0.79, 1.09)		1

	Rivaroxaban	vs	Warfarin
n	22,439		22,439
Dementia, n	265		392
Follow-up in years, mean	1.4		1.7
Incident rate (per 1000 person-years)	8.6		10.5
Hazard ratio (95% confidence interval)			

Model 1*	0.81 (0.69, 0.94)	1
Model 2†	0.80 (0.69, 0.94)	1

	Apixaban	vs	Warfarin
n	11,784		11,784
Dementia, n	117		210
Follow-up in years, mean	0.9		1.3
Incident rate (per 1000 person-years)	10.5		13.6
Hazard ratio (95% confidence interval)			
Model 1*	0.70 (0.56, 0.89)		1
Model 2†	0.71 (0.56, 0.90)		1

*Model 1 adjusted for age, sex, race, education level, household income level, and prevalent cognitive impairment;

†Model 2 additionally adjusted for comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED score.

Table s7. Meta-analyzed hazard ratios and 95% confidence intervals of incident dementia in oral anticoagulant comparison cohorts with further adjustment of incident ischemic stroke: MarketScan and Optum, 2010-2015.

Hazard ratios (95% confidence intervals)	Warfarin	Dabigatran	Warfarin	Rivaroxaban	Warfarin	Apixaban
Model 1*	1	0.85 (0.74, 0.97)	1	0.85 (0.77, 0.94)	1	0.80 (0.63, 1.03)
Model 2 †	1	0.85 (0.71, 1.01)	1	0.85 (0.76, 0.94)	1	0.80 (0.65, 0.97)
Model 3 ‡	1	0.85 (0.71, 1.02)	1	0.87 (0.78, 0.96)	1	0.80 (0.65, 0.99)

*Model 1 adjusted for age, sex, and prevalent cognitive impairment in study from MarketScan and age, sex, race, education level, household income level, and prevalent cognitive impairment in study from Optum;

†Model 2 additionally adjusted for comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED score;

‡Model 3 additionally adjusted for incident ischemic stroke.

Table s8. Comparisons of incidence of dementia (defined based on inpatient diagnosis) among patients with atrial fibrillation initially treated with dabigatran, rivaroxaban, or apixaban: MarketScan, 2010-2015.

	Dabigatran	vs	Rivaroxaban
n	18,057		18,057
Dementia, n	211		164
Follow-up in years, mean	1.6		1.1
Incident rate (per 1000 person-years)	7.5		8.1
Hazard ratio (95% confidence interval)			
Model 1*	0.94 (0.76, 1.15)		1
Model 2†	0.90 (0.73, 1.10)		1

	Dabigatran	vs	Apixaban
n	7,125		7,125
Dementia, n	60		48
Follow-up in years, mean	1.2		0.7
Incident rate (per 1000 person-years)	6.7		9.0
Hazard ratio (95% confidence interval)			
Model 1*	0.79 (0.54, 1.16)		1

Model 2† 0.76 (0.51, 1.13) 1

	Apixaban	vs	Rivaroxaban
n	19,358		19,358
Dementia, n	160		206
Follow-up in years, mean	0.7		1.0
Incident rate (per 1000 person-years)	11.3		10.7
Hazard ratio (95% confidence interval)			
Model 1*	1.03 (0.83, 1.27)		1
Model 2†	1.03 (0.84, 1.28)		1

*Model 1 adjusted for age, sex, and prevalent cognitive impairment;

†Model 2 additionally adjusted for comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED score.

Table s9. Comparisons of incidence of dementia (defined based on inpatient diagnosis) among patients with atrial fibrillation initially treated with dabigatran, rivaroxaban, or apixaban: Optum, 2010-2015

	Dabigatran	vs	Rivaroxaban
n	10,178		10,178
Dementia, n	188		126
Follow-up in years, mean	1.9		1.4
Incident rate (per 1000 person-years)	9.5		9.1
Hazard ratio (95% confidence interval)			
Model 1*	1.14 (0.90, 1.43)		1
Model 2†	1.17 (0.93, 1.48)		1

	Dabigatran	vs	Apixaban
N	4,757		4,757
Dementia, n	59		39
Follow-up in years, mean	1.5		1.0
Incident rate (per 1000 person-years)	8.3		8.6
Hazard ratio (95% confidence interval)			
Model 1*	1.16 (0.76, 1.75)		1
Model 2†	1.13 (0.75, 1.71)		1

	Apixaban	vs	Rivaroxaban
n	11,785		11,785
Dementia, n	119		154
Follow-up in years, mean	0.9		1.2
Incident rate (per 1000 person-years)	10.6		10.5
Hazard ratio (95% confidence interval)			
Model 1*	0.94 (0.74, 1.20)		1
Model 2†	0.99 (0.77, 1.26)		1

*Model 1 adjusted for age, sex, race, education level, household income level, and prevalent cognitive impairment;

†Model 2 additionally adjusted for comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED score.

Table s10. Incidence of dementia among patients with atrial fibrillation initially treated with dabigatran, rivaroxaban, or apixaban versus warfarin: MarketScan, 2010-2015.

Dementia defined based on inpatient and outpatient diagnoses.

	Dabigatran	vs	Warfarin
n	30,704		30,704
Dementia, n	1,043		1,155
follow-up/year, mean	1.8		1.6
Incident rate (per 1000 person-years)	19.0		24.1
Hazard ratio (95% confidence interval)			
Model 1*	0.77 (0.71, 0.84)		1
Model 2†	0.75 (0.69, 0.82)		1

	Rivaroxaban	vs	Warfarin
n	38,485		38,485
Dementia, n	1,005		1,394
Follow-up/year, mean	1.1		1.3
Incident rate (per 1000 person-years)	23.5		27.4
Hazard ratio (95% confidence interval)			
Model 1*	0.91 (0.83, 0.98)		1

Model 2†	0.88 (0.81, 0.95)	1
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	Apixaban	vs Warfarin
n	18,876	18,876
Dementia, n	415	686
Follow-up/year, mean	0.7	1.1
Incident rate (per 1000 person-years)	30.2	33.4
Hazard ratio (95% confidence interval)		
Model 1*	0.89 (0.78, 1.00)	1
Model 2†	0.86 (0.76, 0.98)	1

*Model 1 adjusted for age, sex, and prevalent cognitive impairment;

†Model 2 additionally adjusted for comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED score.

Table s11. Incidence of dementia among patients with atrial fibrillation initially treated with dabigatran, rivaroxaban, or apixaban versus warfarin: Optum, 2010-2015. Dementia defined based on inpatient and outpatient diagnoses.

	Dabigatran	vs	Warfarin
n	14,735		14,735
Dementia, n	666		722
Follow-up in years, mean	2.2		1.9
Incident rate (per 1000 person-years)	20.9		25.2
Hazard ratio (95% confidence interval)			
Model 1*	0.82 (0.74, 0.92)		1
Model 2†	0.84 (0.75, 0.93)		1

	Rivaroxaban	vs	Warfarin
n	21,693		21,693
Dementia, n	582		958
Follow-up in years, mean	1.4		1.6
Incident rate (per 1000 person-years)	19.8		27.0
Hazard ratio (95% confidence interval)			
Model 1*	0.70 (0.63, 0.78)		1

Model 2†	0.70 (0.63, 0.78)	1
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	Apixaban	vs	Warfarin
n	11,342		11,342
Dementia, n	245		457
Follow-up in years, mean	0.9		1.3
Incident rate (per 1000 person-years)	22.9		31.3
Hazard ratio (95% confidence interval)			
Model 1*	0.62 (0.53, 0.73)		1
Model 2†	0.61 (0.52, 0.72)		1

*Model 1 adjusted for age, sex, race, education level, household income level, and prevalent cognitive impairment;

†Model 2 additionally adjusted for comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED score.

Table s12. Comparisons of incidence of dementia (defined based on inpatient and outpatient diagnosis) among patients with atrial fibrillation initially treated with dabigatran, rivaroxaban, or apixaban: MarketScan, 2010-2015.

	Dabigatran	Vs	Rivaroxaban
n	17,722		17,722
Dementia, n	497		437
Follow-up in years, mean	1.6		1.1
Incident rate (per 1000 person-years)	18.0		21.9
Hazard ratio (95% confidence interval)			
Model 1*	0.85 (0.75, 0.97)		1
Model 2†	0.84 (0.73, 0.95)		1

	Dabigatran	vs	Apixaban
n	6,991		6,991
Dementia, n	168		117
Follow-up in years, mean	1.3		0.7
Incident rate (per 1000 person-years)	19.4		22.6
Hazard ratio (95% confidence interval)			
Model 1*	0.97 (0.76, 1.23)		1

Table s13. Comparisons of incidence of dementia (defined based on inpatient and outpatient diagnosis) among patients with atrial fibrillation initially treated with dabigatran, rivaroxaban, or apixaban: Optum, 2010-2015.

	Dabigatran	vs	Rivaroxaban
n	9,874		9,874
Dementia, n	403		253
Follow-up in years, mean	1.9		1.4
Incident rate (per 1000 person-years)	21.2		19.0
Hazard ratio (95% confidence interval)			
Model 1*	1.20 (1.03, 1.41)		1
Model 2†	1.20 (1.02, 1.41)		1

	Dabigatran	vs	Apixaban
n	4,591		4,591
Dementia, n	153		69
Follow-up in years, mean	1.5		0.9
Incident rate (per 1000 person-years)	22.6		15.9
Hazard ratio (95%			

confidence interval)

Model 1* 1.55 (1.16, 2.08) 1

Model 2† 1.53 (1.14, 2.05) 1

	Apixaban	vs	Rivaroxaban
n	11,341		11,341
Dementia, n	245		323
Follow-up in years, mean	0.9		1.2
Incident rate (per 1000 person-years)	22.9		23.0
Hazard ratio (95% confidence interval)			
Model 1*	0.91 (0.77, 1.08)		1
Model 2†	0.93 (0.78, 1.10)		1

*Model 1 adjusted for age, sex, race, education level, household income level, and prevalent cognitive impairment;

†Model 2 additionally adjusted for comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED score.

Table s14. Database-specific and meta-analyzed hazard ratios and 95% confidence intervals of incident dementia in oral anticoagulant comparison cohorts using refined baseline cognitive impairment adjustment: MarketScan and Optum, 2010-2015

	Warfarin	Dabigatran	Warfarin	Rivaroxaban	Warfarin	Apixaban
MarketScan	1 (ref.)	0.78 (0.68, 0.89)	1 (ref.)	0.88 (0.77, 1.01)	1 (ref.)	0.88 (0.72, 1.07)
Optum	1 (ref.)	0.92 (0.78, 1.09)	1 (ref.)	0.80 (0.68, 0.94)	1 (ref.)	0.71 (0.56, 0.89)
Pooled	1 (ref.)	0.83 (0.75, 0.92)	1 (ref.)	0.85 (0.76, 0.94)	1 (ref.)	0.80 (0.69, 0.93)
	Rivaroxaban	Dabigatran	Apixaban	Dabigatran	Rivaroxaban	Apixaban
MarketScan	1 (ref.)	0.89 (0.73, 1.10)	1 (ref.)	0.74 (0.50, 1.10)	1 (ref.)	1.04 (0.84, 1.28)
Optum	1 (ref.)	1.17 (0.92, 1.47)	1 (ref.)	1.13 (0.74, 1.71)	1 (ref.)	0.92 (0.72, 1.18)
Pooled	1 (ref.)	1.00 (0.86, 1.17)	1 (ref.)	0.90 (0.68, 1.20)	1 (ref.)	0.99 (0.84, 1.16)

Results from Cox models adjusted for age, sex, prevalent cognitive impairment in inpatient claims, prevalent cognitive impairment in outpatient claims, comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED scores, and, in the Optum dataset, race, education level, and household income.

Table s15. Database-specific and meta-analyzed hazard ratios and 95% confidence intervals of incident dementia in oral anticoagulant comparison cohorts censoring patients at the time of oral anticoagulant discontinuation or switching: MarketScan and Optum, 2010-2015

	Warfarin	Dabigatran	Warfarin	Rivaroxaban	Warfarin	Apixaban
MarketScan	1 (ref.)	0.79 (0.64, 0.96)	1 (ref.)	0.89 (0.75, 1.06)	1 (ref.)	0.85 (0.67, 1.08)
Optum	1 (ref.)	0.83 (0.64, 1.06)	1 (ref.)	0.85 (0.69, 1.04)	1 (ref.)	0.66 (0.50, 0.87)
Pooled	1 (ref.)	0.81 (0.69, 0.94)	1 (ref.)	0.87 (0.76, 1.00)	1 (ref.)	0.76 (0.64, 0.91)
	Rivaroxaban	Dabigatran	Apixaban	Dabigatran	Rivaroxaban	Apixaban
MarketScan	1 (ref.)	0.86 (0.65, 1.13)	1 (ref.)	0.65 (0.40, 1.07)	1 (ref.)	1.02 (0.80, 1.30)
Optum	1 (ref.)	1.00 (0.73, 1.38)	1 (ref.)	1.00 (0.61, 1.65)	1 (ref.)	0.87 (0.65, 1.16)
Pooled	1 (ref.)	0.92 (0.74, 1.13)	1 (ref.)	0.80 (0.57, 1.14)	1 (ref.)	0.96 (0.79, 1.15)

Results from Cox models adjusted for age, sex, prevalent cognitive impairment in inpatient claims, prevalent cognitive impairment in outpatient claims, comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED scores, and, in the Optum dataset, race, education level, and household income.

Table s16. Adjusted hazard ratios (HRs) and 95% confidence intervals (CIs)* of dementia in matched cohort stratified by age, gender, and CHA₂DS₂-VASc score: MarketScan, 2010-2015.

Comparison of DOACs with Warfarin		Comparison among Dabigatran, Rivaroxaban, and Apixaban			
		Dabigatran vs Rivaroxaban		Apixaban	
	n	Hazard Ratio (95% CI)		n	Hazard Ratio (95% CI)
Dabigatran vs Warfarin			Dabigatran vs Rivaroxaban		
Age≤75	44,714	0.84 (0.61, 1.15)	Age≤75	26,744	0.90 (0.57, 1.44)
Age>75	17,894	0.77 (0.66, 0.89)	Age>75	9,370	0.90 (0.71, 1.13)
		p-value 0.56			p-value 0.87
Men	40,729	0.80 (0.66, 0.97)	Men	23,642	0.90 (0.66, 1.24)
Women	21,879	0.76 (0.63, 0.91)	Women	12,472	0.87 (0.66, 1.14)
		p-value 0.59			p-value 0.65
CHA ₂ DS ₂ -VASc <2	15,309	0.36 (0.10, 1.34)	CHA ₂ DS ₂ -VASc <2	9,638	0.39 (0.04, 3.57)
CHA ₂ DS ₂ -VASc ≥2	47,299	0.78 (0.69, 0.90)	CHA ₂ DS ₂ -VASc ≥2	26,476	0.89 (0.73, 1.11)
		p-value 0.37			p-value 0.80
Rivaroxaban vs Warfarin			Dabigatran vs Apixaban		
Age≤75	54,897	0.73 (0.54, 0.98)	Age≤75	10,441	0.68 (0.26, 1.75)
Age>75	23,507	0.94 (0.81, 1.08)	Age>75	3,809	0.82 (0.53, 1.26)
		p-value 0.21			p-value 0.55
Men	48,465	0.77 (0.62, 0.94)	Men	9,214	0.62 (0.34, 1.14)
Women	29,939	0.99 (0.83, 1.18)	Women	5,036	0.90 (0.52, 1.54)

		p-value 0.10			p-value 0.33
CHA ₂ DS ₂ -VASc <2	17,587	1.00 (0.37, 2.74)	CHA ₂ DS ₂ -VASc <2		
CHA ₂ DS ₂ -VASc ≥2	60,817	0.89 (0.78, 1.01)	CHA ₂ DS ₂ -VASc ≥2		
		p-value 0.82			
<hr/>			<hr/>		
Warfarin vs Apixaban			Apixaban vs Rivaroxaban		
Age≤75	25,070	0.81 (0.50, 1.30)	Age≤75	25,552	1.08 (0.65, 1.81)
Age>75	13,540	0.90 (0.72, 1.12)	Age>75	13,164	1.03 (0.82, 1.30)
		p-value 0.60			p-value 0.71
Men	23,075	0.90 (0.66, 1.21)	Men	23,077	1.18 (0.86, 1.64)
Women	15,535	0.85 (0.65, 1.11)	Women	15,639	0.91 (0.69, 1.20)
		p-value 0.69			p-value 0.19
CHA ₂ DS ₂ -VASc <2	6,960	0.43 (0.04, 4.60)	CHA ₂ DS ₂ -VASc <2	7,463	0.36 (0.04, 3.25)
CHA ₂ DS ₂ -VASc ≥2	31,650	0.88 (0.72, 1.08)	CHA ₂ DS ₂ -VASc ≥2	31,253	1.05 (0.85, 1.30)
		p-value 0.28			p-value 0.24

*Models adjusted for age, sex, prevalent cognitive impairment, comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED score.

†DOAC: direct oral anticoagulant.

Table s17. Adjusted hazard ratios (HRs) and 95% confidence intervals (CIs)* of dementia in matched cohort stratified by age and gender: Optum, 2010-2015.

Comparison of DOACs with Warfarin		Comparison among Dabigatran, Rivaroxaban, and Apixaban			
		Apixaban		Apixaban	
		Hazard Ratio		Hazard Ratio	
		n	(95% CI)	n	(95% CI)
Dabigatran vs Warfarin			Dabigatran vs Rivaroxaban		
Age≤75	20,530	0.61 (0.41, 0.89)	Age≤75	13,744	0.54 (0.32, 0.91)
Age>75	9,828	1.04 (0.87, 1.25)	Age>75	6,612	1.41 (1.09, 1.84)
		p-value 0.01		p-value 0.002	
Men	19,164	0.93 (0.73, 1.18)	Men	12,807	1.06 (0.77, 1.47)
Women	11,194	0.93 (0.75, 1.16)	Women	7,549	1.30 (0.93, 1.81)
		p-value 0.93		p-value 0.44	
Rivaroxaban vs Warfarin			Dabigatran vs Apixaban		
Age≤75	28,909	0.71 (0.50, 0.99)	Age≤75	6,212	0.65 (0.22, 1.88)
Age>75	15,969	0.86 (0.72, 1.03)	Age>75	3,302	1.27 (0.80, 2.03)
		p-value 0.24		p-value 0.26	
Men	26,866	0.96 (0.76, 1.21)	Men	5,887	1.92 (0.95, 3.87)
Women	18,012	0.70 (0.56, 0.87)	Women	3,627	0.80 (0.47, 1.38)
		p-value 0.04		p-value 0.04	
Apixaban vs Warfarin			Apixaban vs Rivaroxaban		

Age≤75	13,447	0.90 (0.52, 1.54)	Age≤75	13,459	1.20 (0.67, 2.17)
Age>75	10,121	0.69 (0.53, 0.89)	Age>75	10,111	0.94 (0.72, 1.23)
		p-value 0.45			p-value 0.52
Men	12,921	0.55 (0.39, 0.80)	Men	12,976	0.79 (0.54, 1.16)
Women	10,647	0.86 (0.63, 1.17)	Women	10,594	1.17 (0.85, 1.61)
		p-value 0.09			p-value 0.12

*Models adjusted for age, sex, race, education level, household income level, prevalent cognitive impairment, comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED score.

†DOAC: direct oral anticoagulant.

Table s18. Odds ratios (ORs) and 95% confidence intervals (CIs) of having DOAC prescription (versus warfarin) among atrial fibrillation patients with dementia and cognitive impairment before OAC initiation compared with cognitively normal patients: MarketScan, 2007-2015, and Optum, 2009-2015.

		Individuals with dementia and other cognitive impairment	Cognitively normal enrollees
MarketScan	n	13,224	298,333
	OR* (95%CI)	0.99 (0.90, 1.10)	1
Optum	n	11,146	153,874
	OR† (95%CI)	0.91 (0.81, 1.03)	1
Combined		0.96 (0.88, 1.04)	1

*Odds ratio adjusted for age, sex, comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED score in MarketScan;

†Odds ratio adjusted for age, sex, race, education level, household income level, comorbidities, medications, CHA₂DS₂-VASc and HAS-BLED score in Optum.

‡DOAC: direct oral anticoagulant; OAC: oral anticoagulant.