**Supplemental material**

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| 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. | |

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| 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 |
| CHA2DS2-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

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| 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 12th 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 |
| CHA2DS2-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

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| Table s4. 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% CI) |  |  |  |
| 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% CI) |  |  |  |
| 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% CI) |  |  |  |
| 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. | | | | |

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| Table s5. 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% CI) |  |  |  |
| 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% CI) |  |  |  |
| 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% CI) |  |  |  |
| 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. | | | | |
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| Table s6. Meta-analyzed hazard ratios and 95% confidence intervals of incident dementia in OAC 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.

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| Table s7. Comparisons of incidence of dementia 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% CI) |  |  |  |
| 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% CI) |  |  |  |
| 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% CI) |  |  |  |
| 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. | | | |

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| Table s8. Comparisons of incidence of dementia 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% CI) | |  |  |
| 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% CI) | |  |  |
| 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% CI) | |  |  |
| 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. | | | | |

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| Table s9. 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% CI) |  |  |  |
| 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% CI) |  |  |  |
| Model 1\* | 0.91 (0.83, 0.98) |  | 1 |
| Model 2† | 0.88 (0.81, 0.95) |  | 1 |
|  |  |  |  |
|  | 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% CI) |  |  |  |
| 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. | | | | |

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| Table s10. 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% CI) |  |  |  |
| 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% CI) |  |  |  |
| Model 1\* | 0.70 (0.63, 0.78) |  | 1 |
| Model 2† | 0.70 (0.63, 0.78) |  | 1 |
|  |  |  |  |
|  | 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% CI) |  |  |  |
| 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. | | | | |

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| Table s11. Comparisons of incidence of dementia among patients with atrial fibrillation initially treated with dabigatran, rivaroxaban, or apixaban: MarketScan, 2010-2015. Dementia defined based on inpatient and outpatient diagnoses. | | | |
|  | 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% CI) |  |  |  |
| 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% CI) |  |  |  |
| Model 1\* | 0.97 (0.76, 1.23) |  | 1 |
| Model 2† | 0.94 (0.74, 1.20) |  | 1 |
|  |  |  |  |
|  | Apixaban | vs | Rivaroxaban |
| n | 18,930 |  | 18,930 |
| Dementia, n | 415 |  | 546 |
| Follow-up in years, mean | 0.7 |  | 1.0 |
| Incident rate (per 1000 person-years) | 30.1 |  | 29.2 |
| Hazard ratio (95% CI) |  |  |  |
| Model 1\* | 0.96 (0.85, 1.09) |  | 1 |
| Model 2† | 0.97 (0.85, 1.10) |  | 1 |
|  |  |  |  |
| \*Model 1 adjusted for age, sex, and prevalent cognitive impairment; | | | | |
| †Model 2 additionally adjusted for comorbidities, medications, CHA2DS2-VASc and HAS-BLED score. | | | | |

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| Table s12. Comparisons of incidence of dementia among patients with atrial fibrillation initially treated with dabigatran, rivaroxaban, or apixaban: Optum, 2010-2015. Dementia defined based on inpatient and outpatient diagnoses. | | | |
|  | 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% CI) |  |  |  |
| 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% CI) |  |  |  |
| 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% CI) |  |  |  |
| 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. | | | | |

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| Table s13. 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 | | |
|  | 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 |
| CHA2DS2-VASc <2 | 15,309 | 0.36 (0.10, 1.34) | CHA2DS2-VASc <2 | 9,638 | 0.39 (0.04, 3.57) |
| CHA2DS2-VASc ≥2 | 47,299 | 0.78 (0.69, 0.90) | CHA2DS2-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 |
| CHA2DS2-VASc <2 | 17,587 | 1.00 (0.37, 2.74) | CHA2DS2-VASc <2 |  |  |
| CHA2DS2-VASc ≥2 | 60,817 | 0.89 (0.78, 1.01) | CHA2DS2-VASc ≥2 |  |  |
|  |  | p-value 0.82 |  |  |  |
|  |  |  |  |  |  |
| 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 |
| CHA2DS2-VASc <2 | 6,960 | 0.43 (0.04, 4.60) | CHA2DS2-VASc <2 | 7,463 | 0.36 (0.04, 3.25) |
| CHA2DS2-VASc ≥2 | 31,650 | 0.88 (0.72, 1.08) | CHA2DS2-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. | | | | | |

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| Table s14. 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 | | |
|  | n | Hazard Ratio (95% CI) |  | n | Hazard Ratio (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. | | | | | |

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| Table s15. 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. | | | |