SUPPLEMENTAL TABLES

**Oral anticoagulation therapy and subsequent risk of venous thromboembolism**

**in atrial fibrillation patients**

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**Supplemental Table 1.** ICD-9-CM Codes used to define pre-defined comorbidities.

|  |  |
| --- | --- |
| **Condition** | **ICD-9-CM codes** |
| Alcoholism | 265.2, 291.1, 291.2, 291.3, 291.5, 291.6, 291.7, 291.8, 291.9, 303.0, 303.9, 305.0, 357.5, 425.5, 535.3, 571.0, 571.1, 571.2, 571.3, 980, V11.3 |
| Chronic pulmonary disease | 416.8, 416.9, 490, 491, 492, 493, 494, 495, 496, 497, 498, 499, 500, 501, 502, 503, 504, 505, 506.4, 508.1, 508.8 |
| Hematological disorders (Anemia, Coagulopathy) | 280, 281, 282, 283, 284, 285,286, 287.1, 287.3, 287.4, 287.5 |
| Dementia | 290.x, 294.1, 331.2 |
| Depression | 296.2, 296.3, 296.5, 300.4, 309.x, 311.x |
| 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 |
| Hemorrhagic stroke | 430, 431 |
| Ischemic stroke | 434, 436 |
| Renal 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 |
| Liver disease | 070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 456.0, 456.1, 456.2, 570, 571, 572.2, 572.3, 572.4, 572.5, 572.6, 572.7, 572.8, 573.3, 573.4, 573.8, 573.9, V42.7 |
| Malignancy | 140-172, 174-195, 200-208, 238.6 |
| Metastatic cancer | 196, 197, 198, 199 |
| Myocardial infarction | 410, 412 |
| Other bleeding | 360.43, 423.0, 432.0, 432.1, 432.9, 459.0, 568.81,593.81, 599.7, 623.8, 626.2, 626.6, 719.1, 729.92, 784.7, 784.8, 786.3, 998.11 |
| Peripheral artery disease | 440.0, 440.2, 440.9, 443.9 |

**Supplemental Table 2.** Adjusted hazard ratios (95% confidence intervals) for incident pulmonary embolism\* and deep vein thrombosis comparing new users of specific oral anticoagulants among patients with non-valvular atrial fibrillation: MarketScan databases, 2010 to September 30, 2015.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Warfarin | Dabigatran | Rivaroxaban | Apixaban |
| N | 27,065 | 27,065 |  |  |
| # PE events | 178 (0.66%) | 100 (0.37%) |  |  |
| HR (95% CI) | 1.00 (reference) | 0.59 (0.46-0.76) |  |  |
| # DVT events | 235 (0.87%) | 114 (0.42%) |  |  |
| HR (95% CI) | 1.00 (reference) | 0.52 (0.42-0.66) |  |  |
|  |  |  |  |  |
| N | 22,581 |  | 22,581 |  |
| # PE events | 126 (0.56%) |  | 160 (0.71%) |  |
| HR (95% CI) | 1.00 (reference) |  | 1.26 (1.00-1.62) |  |
| # DVT events | 210 (0.93%) |  | 172 (0.76%) |  |
| HR (95% CI) | 1.00 (reference) |  | 0.86 (0.70-1.05) |  |
|  |  |  |  |  |
| N | 11,632 |  |  | 11,362 |
| # PE events | 64 (0.55%) |  |  | 30 (0.26%) |
| HR (95% CI) | 1.00 (reference) |  |  | 0.50 (0.32-0.77) |
| # DVT events | 93 (0.80%) |  |  | 43 (0.37%) |
| HR (95% CI) | 1.00 (reference) |  |  | 0.52 (0.36-0.75) |

\* If a participant had codes for both PE and DVT, they were coded as PE.

CI, confidence interval; HR, hazard ratio; N, number; PE, pulmonary embolism; DVT, deep vein thrombosis**.**

**Supplemental Table 3.** Adjusted hazard ratios (95% confidence intervals) for incident venous thromboembolism comparing new users of specific oral anticoagulants among patients with non-valvular atrial fibrillation stratified by whether the VTE was initially treated in an inpatient or outpatient setting\*: MarketScan databases, 2010 to September 01, 2015.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Warfarin** | **Dabigatran** | **Rivaroxaban** | **Apixaban** |
| Inpatient  |  |  |  |  |
| N | 16,231 | 15,900 |  |  |
| # VTE events | 366 (2.3%) | 193 (1.2%) |  |  |
| Person-years | 27,994 | 29,381 |  |  |
| HR (95% CI) | 1.00 (reference) | 0.57 (0.47-0.68) |  |  |
| Outpatient |  |  |  |  |
| N | 10,834 | 11,165 |  |  |
| # VTE events | 47 (0.43%) | 21 (0.19%) |  |  |
| Person-years | 16,176 | 18,004 |  |  |
| HR (95% CI) | 1.00 (reference) | 0.47 (0.28-0.80) |  |  |
|  |  |  |  |  |
| Inpatient |  |  |  |  |
| N | 13,559 |  | 13,310 |  |
| # VTE events | 297 (2.2%) |  | 300 (2.3%) |  |
| Person-years | 16,203 |  | 16,299 |  |
| HR (95% CI) | 1.00 (reference) |  | 1.00 (0.85-0.17) |  |
| Outpatient |  |  |  |  |
| N | 9,022 |  | 9,271 |  |
| # VTE events | 39 (0.43%) |  | 32 (0.35%) |  |
| Person-years | 9,883 |  | 10,233 |  |
| HR (95% CI) | 1.00 (reference) |  | 0.99 (0.61-1.61) |  |
|  |  |  |  |  |
| Inpatient |  |  |  |  |
| N | 6,749 |  |  | 6,310 |
| # VTE events | 142 (2.1%) |  |  | 70 (1.1%) |
| Person-years | 5,905 |  |  | 5,283 |
| HR (95% CI) | 1.00 (reference) |  |  | 0.55 (0.41-0.73) |
| Outpatient |  |  |  |  |
| N | 4,883 |  |  | 5,322 |
| # VTE events | 15 (0.31%) |  |  | 3 (0.06%) |
| Person-years | 4,018 |  |  | 4,271 |
| HR (95% CI) | 1.00 (reference) |  |  | 0.25 (0.07-0.87) |

\* If a participant had codes for both inpatient and outpatient, they were coded as inpatient.

CI, confidence interval; HR: hazard ratio; N, number; VTE: venous thrombo­embolism**.**

**Supplemental Table 4.** Characteristics\* of atrial fibrillation patients by warfarin use or rivaroxaban dose, MarketScan databases, 2010 to September 30, 2015.

|  |  |  |
| --- | --- | --- |
|  | Warfarin (n=22,581) | Rivaroxaban |
|  |  | Reduced dose (10 mg) | Reduced dose (15 mg) | Standard dose(20 mg) |
| Age, years | 72.2 ± 11.5 | 72.5 ± 11.6 | 79.9 ± 9.3 | 68.1 ± 10.5 |
| Female, % | 41 | 51 | 53 | 36 |
| Comorbidities,† % |  |  |  |  |
| Hypertension | 80 | 82 | 86 | 76 |
| Diabetes | 33 | 30 | 35 | 30 |
| Myocardial infarction | 12 | 11 | 14 | 9 |
| Heart failure | 33 | 29 | 42 | 25 |
| Ischemic stroke/TIA | 25 | 24 | 32 | 18 |
| Hemorrhagic stroke | 1.3 | 1.1 | 1.4 | 0.9 |
| Peripheral artery disease | 20 | 21 | 27 | 14 |
| Dementia | 2.1 | 3.2 | 3.5 | 1.0 |
| Renal Disease | 14 | 15 | 27 | 6 |
| Chronic pulmonary disease | 31 | 33 | 37 | 25 |
| Liver disease | 6 | 6 | 5 | 5 |
| Malignancy | 15 | 16 | 19 | 13 |
| Depression | 11 | 17 | 11 | 9 |
| Hematological disorders | 14 | 17 | 16 | 9 |
| Metastatic cancer | 2.5 | 2.5 | 3.1 | 1.9 |
| Alcohol abuse | 0.6 | 0.7 | 0.4 | 0.6 |
| Gastrointestinal bleed | 8 | 10 | 10 | 6 |
| Other bleed | 6 | 7 | 7 | 4 |
| CHA2DS2-VASC score | 3.8 ± 2.0 | 3.8 ± 2.0 | 4.8 ± 1.8 | 3.1 ± 1.9 |
| Prior procedures, % |  |  |  |  |
| Cardiac | 68 | 74 | 64 | 67 |
| Vascular | 8 | 8 | 8 | 5 |
| Gastrointestinal | 33 | 42 | 35 | 29 |
| Neurological | 19 | 52 | 17 | 15 |
| Medications, % |  |  |  |  |
| Digoxin | 11 | 10 | 11 | 9 |
| Clopidogrel | 13 | 13 | 18 | 11 |
| Antiplatelets | 2 | 2 | 4 | 2 |
| Angiotensin-converting enzyme inhibitors | 36 | 35 | 36 | 32 |
| Angiotensin receptor blockers | 24 | 23 | 29 | 23 |
| Beta-blockers | 65 | 62 | 65 | 60 |
| Calcium channel blockers | 40 | 36 | 45 | 36 |
| Anti-arrhythmias | 19 | 18 | 16 | 18 |
| Statins | 54 | 50 | 58 | 51 |
| Diabetes medications | 24 | 19 | 25 | 21 |

**Supplemental Table 5.** Adjusted hazard ratios (95% confidence intervals) for incident venous thromboembolism comparing new users of specific oral anticoagulants among patients with non-valvular atrial fibrillation, requiring ≥6 months of continuous enrollment before the 1st OAC prescription: MarketScan databases, 2010 to September 30, 2015

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Warfarin** | **Dabigatran** | **Rivaroxaban** | **Apixaban** |
| N | 22,253 | 22,469 |  |  |
| # VTE events | 343 (1.5%) | 182 (0.81%) |  |  |
| Person-years | 37,160 | 40,318 |  |  |
| HR (95% CI) | 1 (ref) | 0.55 (0.46-0.66) |  |  |
|  |  |  |  |  |
| N | 16,181 |  | 17,118 |  |
| # VTE events | 241 (1.5%) |  | 255 (1.5%) |  |
| Person-years | 18,166 |  | 19,856 |  |
| HR (95% CI) | 1 (ref) |  | 1.03 (0.86-1.23) |  |
|  |  |  |  |  |
| N | 8,449 |  |  | 8,910 |
| # VTE events | 117 (1.4%) |  |  | 62 (0.70%) |
| Person-years | 7,040 |  |  | 7,305 |
| HR (95% CI) | 1 (ref) |  |  | 0.55 (0.40-0.75) |

CI, confidence interval; HR: hazard ratio; N, number; OAC: oral anticoagulants; VTE: venous thrombo­embolism**.**