**Table S1.** *International Classification of Disease, Tenth Revision* (ICD-10) codes for the study outcomes.

| Outcomes | | ICD-10 codes |
|---|---|---|
| Stroke or systemic embolism | Ischemic stroke* | G45.9, I63, and I69.3 |
| | Haemorrhagic stroke* | I60, I61, I62, I69.0, I69.1, and I69.2 |
| | Systemic embolism** | I74 |
| Major bleeding*** | Intracranial hemorrhage* | I60, I61, I62, I69.0, I69.1, I69.2, S06.4, S06.5, S06.6, and S06.8 |
| | Gastrointestinal bleeding | I85.0, I98.3, K22.11, K22.6, K22.8, K25.0, K25.2, K25.4, K25.6, K26.0, K26.2, K26.4, K26.6, K27.0, K27.2, K27.4, K27.6, K28.0, K28.2, K28.4, K28.6, K29.0, K31.81, K55.21, K62.5, K92.0, K92.1, and K92.2 |
| | Bleeding from other sites | D62, H44.8, H35.72, H35.6, H31.3, H21.0, H11.3, H05.2, H47.0, H43.1, I31.2, N02.0–N02.9, N42.1, N83.1, N85.7, N92.0, N92.3, N93.0, N93.8, N93.9, M25.0, R23.3, R04.0, R04.1, R04.2, R04.8, R04.9, T79.2, T81.0, N95.0, R31.0, R31.1, R31.8, R58, T45.5, Y44.2, and D68.3 |

* Brain CT/MRI procedure codes and hospitalization were also required to define ischemic stroke, hemorrhagic stroke or intracranial hemorrhage

** Any CT/MRI procedure codes and hospitalization were also required to define systemic embolism

*** Hospitalization was also required to define major bleeding (i.e., intracranial hemorrhage, gastrointestinal bleeding and bleeding from other sites)

**Table S2.** Scoring and *International Classification of Disease, Tenth Revision* (ICD-10) codes for the factors included in the CHA$_2$DS$_2$-VASc score.

| Condition | ICD-10 codes | Point |
|---|---|---|
| Congestive heart failure | I50 | 1 |
| Hypertension | I10-I15 | 1 |
| Age | ≥75 years | 2 |
| Diabetes | E10–E14 | 1 |
| Stroke | I63, I69.3, and G45.9 | 2 |
| Vascular disease | I21, I25.2, and I70–I73 | 1 |
| Age | 65–74 years | 1 |
| Sex | Female | 1 |

**Table S3.** Scoring and *International Classification of Disease, Tenth Revision* (ICD-10) codes for the factors include in the HAS-BLED score.

| Condition | ICD-10 codes | Point |
|---|---|---|
| Hypertension | I10–I15 | 1 |
| Abnormal renal disease | N18.3 and N18.4 | 1 |
| Abnormal liver function | B15–B19, C22, D68.4, I98.2, I98.3, K70–K77, and Z94.4 | 1 |
| Stroke | I63, I69.3, and G45.9 | 1 |
| Bleeding history or predisposition* | I60, I61, I62, I69.0, I69.1, I69.2, S06.4, S06.5, S06.6, S06.8, I85.0, I98.3, K22.11, K22.6, K22.8, K25.0, K25.2, K25.4, K25.6, K26.0, K26.2, K26.4, K26.6, K27.0, K27.2, K27.4, K27.6, K28.0, K28.2, K28.4, K28.6, K29.0, K31.81, K55.21, K62.5, K92.0, K92.1, K92.2, D62, H44.8, H35.72, H35.6, H31.3, H21.0, H11.3, H05.2, H47.0, H43.1, I31.2, N02.0-N02.9, N42.1, N83.1, N85.7, N92.0, N92.3, N93.0, N93.8, N93.9, M25.0, R23.3, R04.0, R04.1, R04.2, R04.8, R04.9, T79.2, T81.0, N95.0, R31.0, R31.1, R31.8, R58, T45.5, Y44.2, and D68.3 | 1 |
| Elderly | ≥65 years | 1 |
| Drug therapy | Antiplatelets and NSAIDs | 1 |
| Alcoholism | E24.4, F10, G31.2, G62.1, G72.1, I42.6, K29.2, K70, K86.0, O35.4, P04.3, Q86.0, T51.0, X45, X65, Y15, Y90-Y91, Z50.2, Z71.4, and Z72.1 | 1 |

* A blood transfusion was also required to define a history of bleeding from other sites

**Table S4.** Types of baseline medications.

| Class | Drugs |
| --- | --- |
| NSAIDs | Bromfenac, celecoxib, diclofenac, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, naproxen, meclofenamate, mefenamic acid, meloxicam, nabumetone, oxaprozin, piroxicam, sulindac, and tolmetin |
| Antiplatelets | Aspirin, clopidogrel, prasugrel, ticlopidine, cilostazol, abciximab, tirofiban, dipyridamole, and ticagrelor |
| Proton pump inhibitors | Omeprazole, pantoprazole, lansoprazole, rabeprazole, esomeprazole, and dexlansoprazole |
| $H_2$-receptor antagonists | Cimetidine, ranitidine, famotidine, nizatidine, roxatidine, and lafutidine |
| Antiarrhythmics | Quinidine, procainamide, mexiletine, propafenone, flecainide, amiodarone, bretylium, dronedarone, propranolol, atenolol, esmolol, verapamil, diltiazem, and sotalol |
| Digoxin | Digoxin |
| Statins | Atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, and simvastatin |

NSAID, nonsteroidal antiinflammatory drug

**Table S5.** Scoring and *International Classification of Disease, Tenth Revision* (ICD-10) codes for the factors included in the Charlson Comorbidity Index.

| Condition | ICD-10 codes | Point |
|---|---|---|
| Cerebrovascular disease | G45.x, G46.x, H34.0, and I60.x–I69.x | 1 |
| Congestive heart failure | I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5-I42.9, I43.x, I50.x, and P29.0 | 1 |
| Chronic pulmonary disease | I27.8, I27.9, J40.x–J47.x, J60.x–J67.x, J68.4, J70.1, and J70.3 | 1 |
| Dementia | F00.x–F03.x, F05.1, G30.x, and G31.1 | 1 |
| Diabetes without chronic complication | E10.0, E10.1, E10.6, E10.8, E10.9, E11.0, E11.1, E11.6, E11.8, E11.9, E12.0, E12.1, E12.6, E12.8, E12.9, E13.0, E13.1, E13.6, E13.8, E13.9, E14.0, E14.1, E14.6, E14.8, and E14.9 | 1 |
| Mild liver disease | B18.x, K70.0-K70.3, K70.9, K71.3-K71.5, K71.7, K73.x, K74.x, K76.0, K76.2-K76.4, K76.8, K76.9, and Z94.4 | 1 |
| Myocardial infarction | I21.x, I22.x, and I25.2 | 1 |
| Peripheral vascular disease | I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, and Z95.9 | 1 |
| Peptic ulcer disease | K25.x–K28.x, | 1 |
| Rheumatologic disease | M05.x, M06.x, M32.x–M34.x M31.5M35.1, M35.3, and M36.0 | 1 |
| Diabetes with chronic complication | E10.2–E10.5, E10.7, E11.2–E11.5, E11.7, E12.2-E12.5, E12.7, E13.2–E13.5, E13.7, E14.2–E14.5, and E14.7 | 2 |
| Hemiplegia or paraplegia | G04.1, G11.4, G80.1, G80.2, G81.x, G82.x, G83.0-G83.4, and G83.9 | 2 |
| Any malignancy, including leukemia and lymphoma | C00.x–C26.x, C30.x–C34.x, C37.x–C41.x, C43.x, C45.x–C58.x, C60.x–C76.x, C81.x–C85.x, C88.x, and C90.x–C97.x | 2 |
| Renal disease | I12.0, I13.1, N03.2-N03.7, N05.2-N05.7, N18.x, N19.x, N25.0, Z49.0-Z49.2, Z94.0, and Z99.2 | 2 |
| Moderate or severe liver disease | I85.0, I85.9, I86.4, I98.2, K70.4, K71.1, K72.1, K72.9, K76.5, K76.6, and K76.7 | 3 |
| AIDS/HIV | B20.x–B22.x and B24.x | 6 |
| Metastatic solid tumor | C77.x–C80.x | 6 |

**Table S6.** Baseline characteristics of patients receiving reduced-dose nonvitamin K antagonist oral anticoagulants and warfarin before propensity score matching.

| | Propensity score matching | | | | | |
| | Before | | | | | |
| | R.Apixaban (n=5249) | Warfarin (n=8648) | R.Dabigatran (n=6033) | Warfarin (n=8648) | R.Rivaroxaban (n=7602) | Warfarin (n=8648) |
|---|---|---|---|---|---|---|
| Age (years), mean | 76.02 | 68.73 | 74.33 | 68.73 | 75.25 | 68.73 |
| Female, % | 52.22 | 37.44 | 46.91 | 37.44 | 49.83 | 37.44 |
| CHA$_2$DS$_2$-VASc, mean | 5.04 | 4.06 | 4.68 | 4.06 | 4.80 | 4.06 |
| HAS-BLED, mean | 3.74 | 3.34 | 3.59 | 3.34 | 3.62 | 3.34 |
| CCI, mean | 4.53 | 4.04 | 4.01 | 4.04 | 4.18 | 4.04 |
| Insurance, % | | | | | | |
| National health insurance | 92.55 | 92.45 | 91.63 | 92.45 | 92.50 | 92.45 |
| Medical aid | 7.45 | 7.55 | 8.37 | 7.55 | 7.50 | 7.55 |
| Medical history, % | | | | | | |
| Heart failure | 46.47 | 41.00 | 42.91 | 41.00 | 46.70 | 41.00 |
| Hypertension | 88.59 | 80.80 | 90.37 | 80.80 | 91.12 | 80.80 |
| Diabetes | 57.13 | 51.57 | 52.35 | 51.57 | 54.74 | 51.57 |
| Ischemic stroke | 37.59 | 32.15 | 31.23 | 32.15 | 29.43 | 32.15 |
| Vascular disease | 31.22 | 29.24 | 30.33 | 29.24 | 30.72 | 29.24 |
| Renal disease (CKD3/4) | 2.97 | 2.45 | 1.09 | 2.45 | 2.10 | 2.45 |
| Bleeding | 14.00 | 13.54 | 8.52 | 13.54 | 10.16 | 13.54 |
| Medication history, % | | | | | | |
| NSAIDs | 81.01 | 76.38 | 81.78 | 76.38 | 81.62 | 76.38 |
| Antiplatelets | 75.65 | 70.06 | 75.80 | 70.06 | 77.95 | 70.06 |
| Antiarrhythmics | 49.55 | 48.60 | 46.43 | 48.60 | 42.98 | 48.60 |
| Statins | 60.35 | 51.41 | 58.51 | 51.41 | 55.29 | 51.41 |
| PPI | 46.52 | 42.77 | 42.55 | 42.77 | 42.36 | 42.77 |
| H2RA | 70.58 | 66.27 | 68.41 | 66.27 | 67.73 | 66.27 |
| Digoxin | 26.16 | 27.56 | 26.65 | 27.56 | 27.35 | 27.56 |

CCI, Charlson Comorbidity Index; CHA$_2$DS$_2$-VASc, congestive heart failure, hypertension, age $\geq$ 75 years, diabetes mellitus, stroke, vascular disease, age 65–74 years, and sex; CKD, chronic kidney disease; HAS-BLED, hypertension, abnormal renal and liver function, stroke, bleeding, labile international normalized ratio, elderly, drugs or alcohol; H2RA, H$_2$-receptor antagonists; PPI, proton pump inhibitors; R, reduced dose.