**Supplementary eTable 1** Definitions of comorbidity (in the order they appear in tables 1-3)

|  |  |
| --- | --- |
| **Covariate** | **ICD-10 or procedure code beginning with** |
| Dementia | F00-03, G051, G300-301, G308-309, G310-312, G318 |
| Heart failure | I50, I110, I130, I132, I255, K761, I42-43 |
| Hypertension | I10-15 |
| Diabetes | E10-14 or use of antidiabetic drug (ATC codes beginning with A10) |
| Stroke/systemic emboli/TIA | I63-64, I693-694, I74, G45 |
| Vascular disease | I21-22, I252, I70-73 (as in CHA2DS2-VASc) |
| Renal disease | N18-19 and/or a procedure code for dialysis DR016, DR024  or transplantation KAS00, KAS10, KAS20 |
| Liver disease | K70-77, procedure codes JJB, JJC |
| Stroke (bleeding or ischaemic) | I61, I63-64, I691, I693-694 |
| Prior bleeding hospitalization | Hospitalization with diagnosis of  intracranial bleed: I60-62, S064-066,  gastrointestinal bleed: K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K284, K286, K290, K625, K661, K920-922 I850, I983  urogenital bleed N02, N501A, N939, N950, R319  other bleed or bleeding anaemia: H113, H131. H356, H431,H450, H422, I312, J942, M250, R04, R58, T810, D500, D629, Z513 or  procedure codes for transfusion DR029, DR033 |
| Alcohol index | E244, F10, G312, G621, G721, I426, K292, K70, K860, O354, P043, Q860, T51, Y90-91, Z502, Z714 (A set of codes used by the Swedish Board of Health and Welfare for annual reporting alcohol related mortality in the population) |
| Ischaemic stroke | I63-64, I693-694 |
| TIA | G45 |
| Systemic embolism | I74 |
| Venous thromboembolism | Pulmonary embolism I26 or deep venous thrombosis I801-802 |
| Intracranial bleed | I60-62, S064-066 , I690-692 |
| Intracerebral bleed | I61, I691 |
| Subarachnoidal bleed | I60, I690 |
| Subdural or traumatic intracranial bleed | I62, S064-066 |
| Myocardial infarction | I21-22, I252 |
| Peripheral artery disease | I70-73 |
| Mitral stenosis | I342, I050, I052, Q232 |
| Mechanical heart valve | Procedure code FGE00, FGJ00, FKD00 or FMD00 |
| Other valvular disease | I34-39, I05-08, Q22-23 |
| Pacemaker or ICD | Z950, Z450 or procedure code FPE |
| Parkinsons disease | G209 |
| Hypothyroidism | E00-03 , E890 |
| Thyrotoxicosis | E05 |
| Chronic obstructive pulmonary disease | J43-46 |
| Cancer | Chapter C except C44 (basalioma) within preceding 3 years |
| Frequent faller | ≥2 hospitalizations with diagnosis W00-19 or R296 |
| Arthrosis | M15-19 |
| Influenza | J10 |
| CHA2DS2-VASc score | 1 point each for : heart failure, hypertension, age 65-74 years, diabetes, vascular disease, female sex and 2 points each for age ≥75 years and stroke/systemic emboli/TIA as defined above |
| HASBLED score  (modified) | 1 point each for : hypertension, renal disease, liver disease, prior stroke (bleeding or ischaemic), prior bleed/anaemia, age>65 years, antiplatelet drugs/NSAIDs, alcohol index as defined above. INR values not available hence no points could be given for labile INRs. |

**Supplementary eTable 2** Baseline characteristics before and after propensity score matching for the likelihood of receiving OAC tretment.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Propensity score matched | | | All patients | | |
| OAC  (n=80,948) | No OAC  (n=80,948) | p | OAC  (n=202,946) | No OAC  (n=241,160) | p |
| Age, mean | | 73.3 years | 73.8 years | <0.001 | 73.7 years | 75.7 years | <0.001 |
| Female sex | | 42.1% | 42.0% | 0.654 | 40.6% | 48.1% | <0.001 |
| Years since first AF diagnosis, mean | | 1.02 years | 1.00 years | 0.050 | 1.88 years | 1.50 years | <0.001 |
| CHA2DS2-VASc | score , mean | 3.07 p | 3.01 p | <0.001 | 3.43 p | 3.49 p | <0.001 |
| Heart failure | 19.6% | 19.6% | 0.802 | 31.0% | 29.2% | <0.001 |
| Hypertension | 49.7% | 49.6% | 0.808 | 53.2% | 48.1% | <0.001 |
| Age 65-74 years | 26.0% | 26.0% | 0.955 | 30.2% | 19.4% | <0.001 |
| Diabetes | 13.7% | 13.7% | 0.756 | 19.2% | 17.3% | <0.001 |
| Stroke/systemic emboli/TIA | 16.6% | 13.6% | <0.001 | 21.1% | 24.8% | <0.001 |
| Vascular disease | 16.8% | 16.8% | 0.968 | 24.8% | 21.1% | <0.001 |
| Age≥75 years | 52.9% | 52.9% | 0.909 | 52.0% | 61.0% | <0.001 |
| HASBLED | score, mean | 2.08 p | 2.08 p | 0.715 | 2.09 p | 2.43 p | <0.001 |
| Renal disease | 1.6% | 1.7% | 0.571 | 3.4% | 5.4% | <0.001 |
| Liver disease | 0.3% | 0.3% | 0.964 | 0.9% | 1.8% | <0.001 |
| Any stroke  (bleeding or ischaemic) | 10.9% | 10.7% | 0.142 | 16.1% | 16.7% | <0.001 |
| Bleeding hospitalization | 8.1% | 8.0% | 0.609 | 12.2% | 19.3% | <0.001 |
| Age >65 years | 78.9% | 78.9% | 0.841 | 82.1% | 80.4% | <0.001 |
| Antiplatelet drugs/NSAIDs | 57.4% | 57.5% | 0.740 | 39.7% | 67.7% | <0.001 |
| Alcohol | 1.1% | 1.1% | 0.795 | 1.8% | 3.7% | <0.001 |
| Other  comorbidity/  history | Ischaemic stroke | 9.5% | 9.4% | 0.581 | 14.4% | 14.4% | 0.653 |
| TIA | 7.5% | 4.2% | <0.001 | 7.4% | 5.5% | <0.001 |
| Systemic embolism | 0.3% | 0.3% | 0.928 | 1.6% | 1.1% | <0.001 |
| Venous thromboembolism | 2.3% | 2.3% | 0.817 | 6.3% | 3.7% | <0.001 |
| Any intracranial bleed | 0.8% | 0.7% | 0.708 | 1.7% | 3.3% | <0.001 |
| Intracerebral | 0.3% | 0.4% | 0.161 | 0.7% | 1.5% | <0.001 |
| Subarachnoidal | <0.1% | <0.1% | 0.931 | 0.2% | 0.4% | <0.001 |
| Subdural or traumatic | 0.3% | 0.3% | 0.074 | 0.7% | 1.5% | <0.001 |
| Myocardial infarction | 14.4% | 14.4% | 0.723 | 16.5% | 19.8% | <0.001 |
| Peripheral artery disease | 3.4% | 3.4% | 0.762 | 6.8% | 7.7% | <0.001 |
| Mitral stenosis | <0.1% | <0.1% | 0.698 | 0.8% | 0.3% | <0.001 |
| Mechanical heart valve | <0.1% | <0.1% | 0.467 | 1.4% | 0.1% | <0.001 |
| Other valvular disease | 6.0% | 6.0% | 0.698 | 13.2% | 8.3% | <0.001 |
| Pacemaker/ICD | 4.1% | 4.1% | 1.000 | 8.7% | 6.5% | <0.001 |
| Hypothyroidism | 2.9% | 2.9% | 0.929 | 5.0% | 6.0% | <0.001 |
| Thyrotoxicosis | 0.7% | 0.7% | 0.536 | 1.7% | 1.6% | 0.157 |
| Chronic obstructive pulmonary disease | 3.3% | 3.3% | 0.922 | 6.8% | 8.3% | <0.001 |
| Cancer | 8.0% | 7.9% | 0.307 | 9.3% | 13.7% | <0.001 |
| Frequent falls | 2.1% | 2.0% | 0.888 | 3.4% | 8.0% | <0.001 |
| Medicine use  at baseline | ACE inhibitor or ARB | 48.0% | 48.0% | 0.893 | 57.9% | 41.2% | <0.001 |
| Statin | 31.2% | 31.2% | 0.902 | 37.9% | 26.0% | <0.001 |
| Beta blocker | 77.7% | 77.7% | 0.905 | 79.1% | 63.2% | <0.001 |
| Class 1 or 3 antiarrhythmic | 5.3% | 5.3% | 0.457 | 7.9% | 7.2% | <0.001 |
| Digoxin | 11.4% | 11.4% | 0.925 | 22.4% | 15.4% | <0.001 |
| Diuretic | 40.6% | 40.6% | 0.948 | 50.6% | 47.0% | <0.001 |

**Covariates used in the logistic regressions for creation of individual propensity scores:**

Age, gender, number of years since first AF diagnosis, previous ischaemic stroke or systemic embolism, intracranial haemorrhage, pulmonary embolism or deep venous thrombosis, myocardial infarction, peripheral artery disease, heart failure, mitral stenosis, mechanical heart valve, other valvular defects, pacemaker or implantable cardioverter/defibrillator (ICD), hypertension, diabetes, renal failure, liver disease, previous hospitalization for major bleeding, Parkinson´s disease, hypothyroidism, thyrotoxicosis, chronic obstructive pumonary disease (COPD), ≥2 hospitalizations for fall accidents, cancer within 3 years, alcohol abuse, baseline use of asprin, clopidogrel or a non-steroidal anti-inflammatory drug (NSAID), ACE-inhibitor or angiotensin-2 blocker (ARB), statin, beta blocker, class 1 or 3 anti-arrhythmic drugs, digoxin or a diuretic.

**Supplementary eTable 3** Baseline characteristics before and after propensity score matching for the likelihood of receiving a NOAC rather than warfarin

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Propensity score matched | | | All patients | | |
| NOAC  (n=7,349) | Warfarin  (n=7,349) | p | NOAC  (n=12,916) | Warfarin  (n=190,030) | p |
| Age, mean years | | 71.7 | 71.3 | 0.060 | 73.2 | 73.7 | <0.001 |
| Female sex | | 42.5% | 42.0% | 0.559 | 45.0% | 40.3% | <0.001 |
| Years since first AF diagnosis, mean | | 0.26 | 0.20 | <0.001 | 0.51 | 1.97 | <0.001 |
| CHA2DS2-VASc | score , mean | 2.75 p | 2.70 p | 0.088 | 3.29 p | 3.44 p | <0.001 |
| Heart failure | 13.6% | 13.6% | 0.923 | 20.6% | 31.7% | <0.001 |
| Hypertension | 53.9% | 53.0% | 0.268 | 60.2% | 52.7% | <0.001 |
| Age 65-74 years | 37.6% | 38.3% | 0.405 | 34.0% | 29.9% | <0.001 |
| Diabetes | 11.2% | 11.4% | 0.774 | 16.5% | 19.4% | <0.001 |
| Stroke/systemic emboli/TIA | 12.2% | 11.6% | 0.222 | 20.4% | 22.0% | <0.001 |
| Vascular disease | 9.5% | 8.6% | 0.070 | 17.0% | 21.4% | <0.001 |
| Age≥75 years | 40.9% | 39.8% | 0.179 | 47.4% | 52.3% | <0.001 |
| HASBLED | score, mean | 1.86 p | 1.83 p | 0.134 | 2.19 p | 2.09 p | <0.001 |
| Renal disease | 0.9% | 0.8% | 0.460 | 2.2% | 3.5% | <0.001 |
| Liver disease | 0.2% | 0.2% | 0.853 | 1.0% | 0.9% | 0.314 |
| Any stroke  (bleeding or ischaemic) | 8.8% | 8.6% | 0.578 | 14.9% | 16.2% | <0.001 |
| Bleeding hospitalization | 4.3% | 4.2% | 0.595 | 11.2% | 12.2% | <0.001 |
| Age >65 years | 78.6% | 78.1% | 0.535 | 81.4% | 82.2% | 0.027 |
| Antiplatelet drugs/NSAIDs | 38.5% | 37.3% | 0.163 | 45.8% | 39.3% | <0.001 |
| Alcohol | 0.7% | 0.7% | 0.842 | 2.6% | 1.7% | <0.001 |
| Other  comorbidity/  history | Ischaemic stroke | 8.6% | 8.3% | 0.554 | 13.4% | 14.5% | 0.001 |
| TIA | 4.1% | 3.6% | 0.169 | 7.5% | 7.4% | 0.443 |
| Systemic embolism | 0.2% | 0.2% | 0.695 | 0.6% | 1.7% | <0.001 |
| Venous thromboembolism | 2.0% | 1.9% | 0.590 | 4.3% | 6.5% | <0.001 |
| Any intracranial bleed | 0.4% | 0.4% | 0.894 | 1.8% | 1.7% | 0.119 |
| Intracerebral | 0.1% | 0.1% | 1.000 | 0.7% | 0.6% | 0.966 |
| Subarachnoidal | 0.1% | 0.1% | 0.564 | 0.3% | 0.2% | 0.038 |
| Subdural or traumatic | 0.2% | 0.2% | 0.695 | 0.9% | 0.7% | 0.017 |
| Myocardial infarction | 7.8% | 7.3% | 0.275 | 13.2% | 16.7% | <0.001 |
| Peripheral artery disease | 2.1% | 1.8% | 0.149 | 5.4% | 6.9% | <0.001 |
| Mitral stenosis | <0.1% | 0.1% | 0.479 | 0.2% | 0.8% | <0.001 |
| Mechanical heart valve | <0.1%\* | 0.3% | <0.001 | <0.01%\*\* | 1.5% | <0.001 |
| Other valvular disease | 4.5% | 4.4% | 0.809 | 8.1% | 13.6% | <0.001 |
| Pacemaker/ICD | 3.2% | 3.0% | 0.366 | 7.3% | 8.8% | <0.001 |
| Parkinson’s disease | 0.7% | 0.4% | 0.018 | 0.7% | 0.5% | 0.012 |
| Hypothyroidism | 2.8% | 2.3% | 0.105 | 6.2% | 4.9% | <0.001 |
| Thyrotoxicosis | 0.8% | 0.8% | 0.643 | 1.8% | 1.7% | 0.453 |
| Chronic obstructive  pulmonary disease | 2.6% | 2.5% | 0.677 | 6.4% | 6.8% | 0.043 |
| Cancer | 4.4% | 4.4% | 0.936 | 7.8% | 9.4% | <0.001 |
| Frequent falls | 1.0% | 1.0% | 0.802 | 4.0% | 3.3% | <0.001 |
| Medicine use  at baseline | ACE inhibitor or ARB | 52.0% | 51.9% | 0.869 | 55.4% | 58.1% | <0.001 |
| Statin | 30.8% | 29.9% | 0.274 | 37.6% | 37.9% | 0.513 |
| Beta blocker | 85.4% | 85.4% | 0.926 | 81.8% | 78.9% | <0.001 |
| Class 1 or 3 antiarrhythmic | 1.6% | 1.6% | 0.947 | 3.0% | 8.2% | <0.001 |
| Digoxin | 8.6% | 8.6% | 0.930 | 10.9% | 23.2% | <0.001 |
| Diuretic | 30.8% | 30.2% | 0.463 | 36.4% | 51.6% | <0.001 |

\* 1 patient, \*\* 3 patients

**Supplementary eTable 4** Odd ratios for likelihood of receiving an oral anticoagulant rather than nothing, and for receiving a NOAC rather than warfarin

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Any oral anticoagulant  rather than nothing | | | NOAC  rather than warfarin | | |
|  | | OR | 95% CI | p | OR | 95% CI | p |
| Age | <65 years | reference | | | reference | | |
| 65-74 years | 1.43 | 1.41-1.46 | <0.001 | 0.41 | 0.40-0.43 | <0.001 |
| ≥75 years | 0.96 | 0.95-0.98 | <0.001 | 0.38 | 0.36-0.39 | <0.001 |
| Female sex | | 0.62 | 0.61-0.63 | <0.001 | 1.03 | 0.99-1.07 | 0.112 |
| Years since first  AF diagnosis | 0-1 years | reference | | | reference | | |
| 1-3 years | 0.90 | 0.87-0.93 | <0.001 | - | - | - |
| 3-5 years | 0.98 | 0.96-1.01 | 0.288 | - | - | - |
| ≤5 years | 1.06 | 1.04-1.08 | <0.001 | 0.17 | 0.15-0.18 | <0.001 |
| CHA2DS2-VASc  risk factors | Heart failure | 0.85 | 0.83-0.86 | <0.001 | 1.03 | 0.98-1.08 | 0.291 |
| Hypertension | 1.03 | 1.02-1.05 | <0.001 | 1.30 | 1.25-1.35 | <0.001 |
| Diabetes | 0.93 | 0.92-0.95 | <0.001 | 0.83 | 0.79-0.87 | <0.001 |
| Stroke/systemic emboli/TIA | 1.39 | 1.37-1.41 | <0.001 | 0.80 | 0.76-0.83 | <0.001 |
| Vascular disease | 0.72 | 0.70-0.73 | <0.001 | 1.04 | 0.97-1.10 | 0.255 |
| Additional  HASBLED  risk factors | Renal disease | 0.60 | 0.58-0.62 | <0.001 | 0.74 | 0.65-0.84 | <0.001 |
| Liver disease | 0.60 | 0.56-0.64 | <0.001 | 0.96 | 0.79-1.16 | 0.683 |
| Stroke (bleeding or ischaemic) | 1.09 | 1.07-1.11 | <0.001 | 0.83 | 0.79-0.87 | <0.001 |
| Bleeding hospitalization | 0.61 | 0.59-0.62 | <0.001 | 1.02 | 0.95-1.08 | 0.628 |
| Antiplatelet drug/NSAID | 0.20 | 0.20-0.20 | <0.001 | 0.90 | 0.86-0.93 | <0.001 |
| Alcohol | 0.37 | 0.36-0.39 | <0.001 | 1.02 | 0.90-1.15 | 0.770 |
| Other  comorbidity/  history | Ischaemic stroke | 1.15 | 1.13-1.18 | <0.001 | 0.83 | 0.78-0.88 | <0.001 |
| TIA | 1.66 | 1.61-1.71 | <0.001 | 0.88 | 0.82-0.94 | <0.001 |
| Systemic embolism | 1.82 | 1.72-1.94 | <0.001 | 0.42 | 0.34-0.53 | <0.001 |
| Venous thromboembolism | 2.01 | 1.95-2.07 | <0.001 | 0.44 | 0.40-0.48 | <0.001 |
| Intracranial bleed | 0.62 | 0.59-0.65 | <0.001 | 1.05 | 0.90-1.22 | 0.529 |
| Intracerebral | 0.48 | 0.45-0.52 | <0.001 | 0.93 | 0.73-1.18 | 0.532 |
| Subarachnoidal | 0.73 | 0.64-0.83 | <0.001 | 1.16 | 0.81-1.66 | 0.415 |
| Subdural or traumatic | 0.82 | 0.76-0.88 | <0.001 | 1.15 | 0.93-1.42 | 0.194 |
| Myocardial infarction | 0.73 | 0.71-0.74 | <0.001 | 1.05 | 0.99-1.12 | 0.079 |
| Peripheral artery disease | 1.04 | 1.01-1.08 | 0.007 | 0.89 | 0.81-0.98 | 0.021 |
| Mitral stenosis | 1.67 | 1.49-1.86 | <0.001 | 0.58 | 0.40-0.84 | 0.004 |
| Mechanical heart valve | 5.09 | 4.51-5.75 | <0.001 | 0.01 | <0.01-0.05 | <0.001 |
| Other valvular disease | 1.43 | 1.40-1.47 | <0.001 | 0.66 | 0.61-0.70 | <0.001 |
| Pacemaker/ICD | 1.23 | 1.20-1.27 | <0.001 | 1.00 | 0.93-1.08 | 0.992 |
| Parkinson’s disease | 0.62 | 0.58-0.68 | <0.001 | 1.09 | 0.87-1.36 | 0.477 |
| Hypothyroidism | 1.00 | 0.97-1.03 | 0.902 | 1.24 | 1.14-1.34 | <0.001 |
| Thyrotoxicosis | 1.02 | 0.97-1.07 | 0.509 | 0.94 | 0.81-1.08 | 0.376 |
| Chronic obstructive  pulmonary disease | 0.82 | 0.80-0.85 | <0.001 | 1.01 | 0.93-1.09 | 0.824 |
| Cancer | 0.58 | 0.57-0.59 | <0.001 | 0.76 | 0.71-0.81 | <0.001 |
| Frequent falls | 0.56 | 0.55-0.58 | <0.001 | 1.25 | 1.13-1.38 | <0.001 |
| Medicine  at baseline | ACE inhibitor or ARB | 1.74 | 1.71-1.76 | <0.001 | 0.71 | 0.68-0.74 | <0.001 |
| Statin | 1.91 | 1.88-1.94 | <0.001 | 0.88 | 0.85-0.92 | <0.001 |
| Beta blocker | 1.94 | 1.92-1.97 | <0.001 | 0.35 | 0.34-0.36 | <0.001 |
| Class 1 or 3 antiarrhythmic | 1.05 | 1.03-1.08 | <0.001 | 0.30 | 0.27-0.33 | <0.001 |
| Digoxin | 1.69 | 1.65-1.72 | <0.001 | 0.45 | 0.43-0.48 | <0.001 |
| Diuretic | 1.15 | 1.13-1.17 | <0.001 | 0.62 | 0.59-0.64 | <0.001 |

**Suppl eTable 5** Hazard ratios for risk of dementia with OAC compared to no OAC. Subgroup analyses and interactions for Figure 2

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Multivariable  (n=444,106) | | | "Intention to treat"  Propensity score matched  (n=161,896) | | | "On treatment"  Propensity score matched  (n=99,353) | | |
|  | | HR | 95%CI | p  interaction | HR | 95%CI | p  interaction | HR | 95%CI | p  interaction |
| Age group, years | <65 | 0.72 | 0.58-0.90 | 0.803 | 0.73 | 0.49-1.07 | 0.408 | 0.71 | 0.44-1.15 | 0.621 |
| 65-74 | 0.71 | 0.66-0.76 | 0.75 | 0.67-0.84 | 0.53 | 0.46-0.62 |
| 75-85 | 0.64 | 0.62-0.67 | 0.63 | 0.59-0.69 | 0.44 | 0.41-0.47 |
| ≥85 | 0.63 | 0.60-0.67 | 0.61 | 0.56-0.66 | 0.43 | 0.38-0.48 |
| Gender | Male | 0.74 | 0.71-0.77 | 0.508 | 0.70 | 0.66-0.75 | 0.347 | 0.53 | 0.49-0.58 | 0.419 |
| Female | 0.71 | 0.68-0.74 | 0.70 | 0.66-0.75 | 0.51 | 0.47-0.55 |
| CHA2DS2\_VASc score | 0-1 p | 0.79 | 0.67-0.94 | 0.022 | 0.85 | 0.67-1.06 | 0.437 | 0.63 | 0.46-0.85 | 0.699 |
| 2-3 p | 0.73 | 0.69-0.77 | 0.72 | 0.67-0.78 | 0.52 | 0.48-0.58 |
| 4-9 p | 0.66 | 0.63-0.68 | 0.64 | 0.60-0.68 | 0.45 | 0.42-0.49 |
| Years since first  AF diagnosis | 0-1 | 0.66 | 0.64-0.69 | <0.001 | 0.66 | 0.63-0.70 | <0.001 | 0.51 | 0.48-0.54 | 0.039 |
| 1-3 | 0.89 | 0.79-1.00 | 0.80 | 0.64-0.99 | 0.57 | 0.42-0.77 |
| 3-5 | 0.87 | 0.79-0.97 | 1.12 | 0.92-1.37 | 0.81 | 0.61-1.07 |
| ≤5 | 0.83 | 0.78-0.89 | 0.83 | 0.74-0.94 | 0.54 | 0.46-1.31 |
| Heart failure | Yes | 0.69 | 0.66-0.73 | <0.001 | 0.72 | 0.66-0.79 | 0.006 | 0.58 | 0.52-0.65 | <0.001 |
| No | 0.73 | 0.70-0.75 | 0.69 | 0.66-0.73 | 0.50 | 0.47-0.53 |
| Hypertension | Yes | 0.71 | 0.68-0.74 | 0.033 | 0.68 | 0.64-0.72 | 0.231 | 0.49 | 0.45-0.53 | 0.303 |
| No | 0.74 | 0.71-0.77 | 0.74 | 0.70-0.79 | 0.57 | 0.52-0.61 |
| Diabetes | Yes | 0.69 | 0.65-0.74 | 0.325 | 0.69 | 0.62-0.77 | 0.913 | 0.51 | 0.44-0.59 | 0.788 |
| No | 0.73 | 0.71-0.76 | 0.71 | 0.68-0.74 | 0.53 | 0.50-0.56 |
| Ischaemic stroke | Yes | 0.66 | 1.06-1.07 | <0.001 | 0.58 | 0.52-0.65 | 0.025 | 0.42 | 0.37-0.49 | 0.576 |
| No | 0.74 | 0.71-0.76 | 0.72 | 0.69-0.76 | 0.53 | 0.50-0.59 |
| Intracranial bleed | Yes | 0.70 | 0.59-0.83 | 0.374 | 0.87 | 0.57-1.32 | 0.153 | 0.53 | 0.28-1.03 | 0.624 |
| No | 0.73 | 0.71-0.75 | 0.70 | 0.67-0.74 | 0.52 | 0.50-0.56 |
| Prior bleed hospitalization | Yes | 0.74 | 0.69-0.80 | <0.001 | 0.72 | 0.63-0.83 | 0.201 | 0.54 | 0.45-0.66 | 0.141 |
| No | 0.72 | 0.70-0.75 | 0.70 | 0.67-0.74 | 0.52 | 0.49-0.55 |
| Myocardial infarction | Yes | 0.70 | 0.65-0.74 | 0.022 | 0.73 | 0.65-0.81 | 0.338 | 0.61 | 0.53-0.71 | 0.006 |
| No | 0.73 | 0.71-0.75 | 0.70 | 0.67-0.74 | 0.51 | 0.48-0.54 |
| Renal disease | Yes | 0.63 | 0.54-0.75 | 0.987 | 0.72 | 0.50-1.04 | 0.680 | 0.55 | 0.34-0.88 | 0.585 |
| No | 0.73 | 0.71-0.75 | 0.71 | 0.68-0.74 | 0.52 | 0.49-0.56 |
| Alcohol | Yes | 0.63 | 0.51-0.79 | 0.199 | 0.73 | 0.39-1.38 | 0.760 | 0.67 | 0.26-1.74 | 0.674 |
| No | 0.73 | 0.71-0.75 | 0.71 | 0.68-0.74 | 0.52 | 0.49-0.55 |
| Frequent falls | Yes | 0.62 | 0.56-0.69 | 0.280 | 0.52 | 0.41-0.66 | 0.317 | 0.48 | 0.35-0.66 | 0.243 |
| No | 0.72 | 0.70-0.75 | 0.71 | 0.68-0.74 | 0.52 | 0.50-0.56 |
| Treatment | VKA | 0.73 | 0.70-0.75 | n/a | 0.71 | 0.68-0.74 | n/a | 0.53 | 0.50-0.56 | n/a |
| NOAC | 0.47 | 0.39-0.57 | 0.40 | 0.30-0.54 | 0.30 | 0.22-0.42 |
| All patients | | 0.73 | 0.71-0.75 |  | 0.71 | 0.68-0.74 |  | 0.52 | 0.50-0.55 |  |

\*From the propensity score matched cohorts, non-OAC patients who later recieved OAC treatment, and OAC patients with access to less OAC than needed to cover 80% of time at risk were excluyded, which left 48,947 non-OAC patients and 50,406 OAC-patients for the analysis.

**Supplementary eTable 6** Hazard ratios for risk of dementia with NOAC compared to warfarin.

Subgroup analyses and interactions for the Forest plot in Figure 4

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | Multivariable  (n=205,045) | | | PS matched  (n=14,698) | | |
|  | | HR | 95%CI | p  interaction | HR | 95%CI | p  interaction |
| Age group | <65 years | 1.40 | 0.34-5.85 | 0.086 | - | - | 0.339 |
| 65-74 years | 0.59 | 0.30-1.14 | 0.66 | 0.24-1.79 |
| 75-85 years | 1.03 | 0.78-1.36 | 0.88 | 0.53-1.44 |
| ≥85 years | 1.21 | 0.89-1.65 | 1.55 | 0.76-3.15 |
| Gender | Male | 1.02 | 0.77-1.34 | 0.460 | 0.96 | 0.56-1.64 | 0.686 |
| Female | 0.93 | 0.70-1.22 | 0.97 | 0.58-1.62 |
| CHA2DS2\_VASc score | 0-1 p | 0.30 | 0.04-2.11 | 0.048 | 0.56 | 0.06-5.34 | 0.575 |
| 2-3 p | 0.49 | 0.33-0.72 | 0.83 | 0.45-1.52 |
| 4-9 p | 0.68 | 0.55-0.85 | 1.12 | 0.69-1.81 |
| Heart failure | Yes | 1.17 | 0.83-1.63 | 0.112 | 0.68 | 0.31-1.49 | 0.837 |
| No | 0.90 | 0.71-1.14 | 1.07 | 0.70-1.64 |
| Hypertension | Yes | 1.09 | 0.86-1.37 | 0.282 | 0.92 | 0.58-1.49 | 0.546 |
| No | 0.77 | 0.54-1.11 | 1.06 | 0.58-1.92 |
| Diabetes | Yes | 0.94 | 0.60-1.46 | 0.921 | 0.24 | 0.05-1.09 | 0.064 |
| No | 0.97 | 0.78-1.20 | 1.12 | 0.76-1.66 |
| Ischaemic stroke | Yes | 1.21 | 0.83-1.76 | 0.154 | 1.35 | 0.62-2.97 | 0.152 |
| No | 0.90 | 0.72-1.13 | 0.89 | 0.59-1.37 |
| Bleeding hospitalization | Yes | 0.90 | 0.56-1.45 | 0.829 | 1.56 | 0.35-7.00 | 0.836 |
| No | 0.98 | 0.79-1.21 | 0.95 | 0.65-1.39 |
| Myocardial infarction | Yes | 1.38 | 0.92-2.07 | 0.064 | 1.89 | 0.62-5.79 | 0.191 |
| No | 0.89 | 0.71-1.11 | 0.89 | 0.60-1.33 |
| All patients | | 0.96 | 0.79-1.17 |  | 0.97 | 0.67-1.40 |  |

**Supplementary eTable 7** Baseline factors associated with use of an oral anticoagulant among 444,106 AF patients without a diagnosis of dementia at baseline.

|  |  |  |
| --- | --- | --- |
|  | | Odds ratio  (95% CI) |
| Age, mean | <65 years | reference |
| 65-74 yrears | 1.97 (1.94-2.02) |
| ≥75 years | 1.32 (1.29-1.34) |
| Female sex | | 0.67 (0.66-0.68) |
| Years since first  AF diagnosis | 0-1 year | reference |
| 1-3 years | 0.99 (0.96-1.02) |
| 3-5 years | 1.07 (1.04-1.10) |
| >5 years | 1.15 (1.12-1.17) |
| Additional  CHA2DS2-VASc  risk factors | Heart failure | 0.85 (0.83-0.86) |
| Hypertension | 1.06 (1.06-1.08) |
| Diabetes | 0.95 (0.93-0.97) |
| Stroke/systemic emboli/TIA | 1.42 (1.39-1.44) |
| Vascular disease | 0.71 (0.70-0.72) |
| Additional  HASBLED  risk factor | Renal disease | 0.61 (0.59-0.63) |
| Liver disease | 0.63 (0.59-0.67) |
| Stroke (bleeding or ischaemic) | 1.15 (1.13-1.18) |
| Prior bleed or anaemia | 0.62 (0.61-0.64) |
| Antiplatelet drug/NSAID | 0.21 (0.21-0.21) |
| Alcohol | 0.44 (0.42-0.46) |
| Other  comorbidity/  history | Ischaemic stroke | 1.17 (1.15-1.20) |
| Systemic embolism | 1.84 (1.73-1.95) |
| TIA | 1.68 (1.63-1.73) |
| Venous thromboembolism | 2.13 (2.06-2.20) |
| Intracranial bleed | 0.63 (0.60-0.66) |
| Intracerebral | 0.49 (0.45-0.52) |
| Subarachnoidal | 0.75 (0.66-0.85) |
| Subdural or traumatic | 0.83 (0.77-0.89) |
| Myocardial infarction | 0.70 (0.69-0.71) |
| Peripheral artery disease | 0.84 (0.81-0.86) |
| Mitral stenosis | 1.72 (1.54-1.92) |
| Mechanical heart valve | 5.88 (5.20-6.64) |
| Other valvular disease | 1.46 (1.43-1.50) |
| Pacemaker/ICD | 1.28 (1.25-1.31) |
| Hypothyroidism | 0.99 (0.96-1.02) |
| Thyrotoxicosis | 1.05 (0.99-1.11) |
| Chronic obstructive  pulmonary disease | 0.85 (0.83-0.88) |
| Parkinson's disease | 0.67 (0.61-0.72) |
| Cancer | 0.61 (0.60-0.62) |
| Frequent falls | 0.56 (0.54-0.58) |
| Medicine use  at baseline | ACE inhibitor or ARB | 1.84 (1.81-1.87) |
| Statin | 1.97 (1.94-2.00) |
| Beta blocker | 2.47 (2.43-2.51) |
| Class 1 or 3 antiarrhythmic | 1.22 (1.19-1.25) |
| Digoxin | 1.72 (1.69-1.76) |
| Diuretic | 1.15 81.13-1.16) |

The more inclusive diagnoses stroke/systemic emboli/TIA, stroke (bleeding or ischaemic) , intracranial bleed and vascular disease were entered one at a time as cofactors after the withdrawal of their constituent factors.