**S8 Table.** Logistic Regression Adaptive LASSO analyses of Major Bleeding Subtype Predictors among OAC new users from 2011 to 2018.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **GI bleeding** | | | **Non-GI extracranial bleeding** | | | | **Major bleeding (all types)** | | |
|  | Warfarin  (n=14,741) | DOAC b (n=21,640) | OACs c (n=36,381) | Warfarin  (n=14,741) | | DOAC b (n=21,640) | OACs c (n=36,381) | Warfarin  (n=14,741) | DOAC b (n=21,640) | OACs c (n=36,381) |
| Age (%) |  |  |  |  | |  |  |  |  |  |
| ≥ 75 | 1.23 | 1.54 | 1.50 | - | | 1.47 | - | - | 1.71 | 1.44 |
| Female (%) | - | - | - | 1.16 | - | | - | 1.11 | - | 1.10 |
| **Co-morbidities within 3 years before cohort entry** | | | | | | | | | |  |
| Hypertension | 1.24 | 1.13 | 1.30 | - | | - | - | 1.13 | 1.08 | 1.18 |
| Coronary artery disease (excl. MI) | - | - | - | - | | 1.22 | - | - | - | - |
| Acute myocardial infarction | - | 1.11 | - | 1.52 | | 1.33 | 1.51 | - | 1.10 | 1.10 |
| Chronic heart failure | 1.13 | 1.13 | 1.19 | - | | - | - | - | 1.18 | 1.12 |
| Cardiomyopathy | - | - | - | 1.46 | | 2.43 | 1.96 | - | 1.34 | 1.25 |
| Other dysrhythmias | - | 0.81 | 0.89 | - | | - | - | - | - | - |
| Valvular heart disease | - | 1.18 | 1.12 | 1.39 | | - | 1.16 | - | 1.11 | 1.12 |
| Stroke/TIA | 0.91 | - | 0.82 | - | | - | - | - | - | - |
| Peripheral vascular (arterial) disease | - | - | 1.07 | 1.20 | | 1.26 | 1.26 | 1.13 | 1.26 | 1.23 |
| Dyslipidemia | - | - | - | - | | - | - | - | - | - |
| History of major bleeding | 1.65 | 1.58 | 1.67 | 1.76 | | 1.76 | 1.83 | 1.58 | 1.66 | 1.61 |
| Chronic renal failure | - | - | - | - | | 1.22 | 1.02 | - | - | - |
| Chronic renal failure ≤ 30 mL/min | - | - | - | 1.32 | | 1.02 | 1.21 | - | - | 1.09 |
| Acute renal failure | - | - | - | 1.07 | | - | - | - | - | - |
| Liver disease | 2.21 | 2.98 | 2.65 | 1.57 | | - | - | 1.97 | 1.41 | 1.75 |
| Chronic obstructive pulmonary disease/asthma | 1.51 | 1.15 | 1.35 | - | | 1.60 | 1.32 | - | 1.23 | 1.15 |
| Infection by Helicobacter pylori | 1.42 | - | - | - | | 1.65 | 1.26 | - | - | - |
| **Concomitant medications (within 2 weeks before cohort entry) (%)** | | | | | | | | | |  |
| Statin | - | - | - | - | | - | - | - | 1.02 | - |
| Antiplatelet | 1.37 | 1.15 | 1.35 | 1.23 | | - | 1.06 | 1.41 | 1.11 | 1.30 |
| Proton pump inhibitors (PPIs) | - | - | 0.91 | 1.07 | | - | - | - | - | 0.94 |
| NSAIDs | - | - | - | 0.22 | | - | 0.83 | 0.87 | - | - |
| Antidepressants | - | - | - | - | | - | - | 1.15 | - | 1.11 |
| Antidiabetics | - | - | - | 1.14 | | 1.51 | 1.34 | 1.16 | 1.10 | 1.21 |
| **OAC used at cohort entry** |  |  |  |  | |  |  |  |  |  |
| DOAC\_type (dabigatran) a | NA | 1.51 | 1.10 | NA | | 1.37 | - | NA | 1.50 | - |
| DOAC\_type (rivaroxaban) a | NA | - | - | NA | | 1.75 | 1.15 | NA | - | - |
| DOAC\_type (apixaban) a | NA | 1.0 (ref) | 0.69 | NA | | 1.0 (ref) | 0.81 | NA | 1.0 (ref) | 0.65 |
|  |  |  |  |  | |  |  |  |  |  |
| **Model statistics** |  | |  | | |  | |  |
| Cross-val. C-Statistic (95% CI) | 0.61 (0.57-0.64) | 0.62 (0.59-0.65) | 0.63 (0.60-0.66) | 0.61 (0.57-0.65) | | 0.65 (0.61-0.69) | 0.65 (0.62-0.68) | 0.60 (0.58-0.62) | 0.62 (0.60-  0.64) | 0.63 (0.61-  0.65) |
| Hosmer-Lemeshow p-value | p>0.05 | p>0.05 | p>0.05 | p>0.05 | | p>0.05 | p>0.05 | p>0.05 | p>0.05 | p>0.05 |

All values are ORs. a In the DOAC group, the rivaroxaban and apixaban variables are compared to dabigatran. In the OAC group, dabigatran, rivaroxaban and apixaban are compared to warfarin. b DOAC users include all doses of dabigatran, rivaroxaban and apixaban. c OAC users include all doses of warfarin, dabigatran, rivaroxaban and apixaban.