

Supplementary table S1

Definition of co-morbidities (according to International Classification of Diseases, 10th revision (ICD10)) and co-medications (Anatomical Therapeutic Chemical (ATC) system). For typical primary care co-morbidities (heart failure, hypertension, diabetes and COPD) a dispensation (using ATC code or reimbursement codes) of drug dispensation was used as a proxy for an underlying condition.

Conditions	Period prior to index*	ICD-10 code from NPR	ATC code or reimbursement code in NorPD
Alcoholism	2008	E244, G312, G621, G721, I426, K860, O354, Z714, Z721, E52, K70, T51	
Chronic kidney disease	2008	N183, N184	
Congestive Heart Failure	2008		Reimbursement codes: I50 (ICD10) or K77 (ICPC)
Dementia	2008	F00-F04, G30	
Diabetes	2008		ATC code A10A or A10B
History of stroke, TIA or thromboembolism	2008	I64, I630, I631, I632, I633, I634, I635, I636, I638, G450, G451, G452, G453, G454, G458, G459, I690, I691, I692, I60, I61, I62	
Hypertension	2008		Reimbursement codes: I10-I13, I15 (ICD10) or K86, K87 (ICPC)
Peripheral Artery Disease	2008	I739	
Ischemic heart disease	2008	I20, I23, I24, I25	
Previous bleeding hospitalisation	2008	See supplementary table I for bleeding definitions	
Prior OAC use	2008		B01AA03, B01AE, B01AF
Viral hepatitis	2008	B15 to B19	
COPD	Last year		Reimbursement codes: J44 (ICD10) or R95 (ICPC)
Active cancer	Last year	C00-C97	
Thrombocytopenia	Last year	D692, D693, D694, D695, D696, D698, D699	
Anaemia	Last year	D65-D67, D680, D681, D682, D683, D684, D685, D686, D688, D689, D50-D53, D55-D59, D60-D64	
NSAID	Last year		M01A
Low-dose aspirin as anti-thrombotic	Last year		B01A C06
Non-aspirin anti-platelet inhibitors	Last year		B01AC (not B01A C06)

Supplementary table S2

ICD10 and procedure codes applied to define first bleeding event. Here presented according to severity of bleeding.

All bleeds
<p>Major bleeding:</p> <ul style="list-style-type: none"> - I60 subarachnoid haemorrhage - I61 intracerebral haemorrhage - I62 other non-traumatic intracranial haemorrhage - K920 hematemesis - K921 melena - I690 sequelae of subarachnoid haemorrhage - I691 sequelae of intracerebral haemorrhage - I692 sequelae of other non-traumatic intracranial haemorrhage - I230 haemopericardium as complication of MI - I312 haemopericardium, not elsewhere classified - M250 haemathrosis - H431 vitreous haemorrhage - H356 retinal haemorrhage - H313 choroidal haemorrhage and rupture - H450 vitreous haemorrhage in diseases classified elsewhere - H448 other disorders of the globe, haemophtlamos - J942 haemothorax - K661 haemoperitoneum - A CRNM bleeding was re-classified to major bleeding if blood transfusion (procedure codes; REGG00 (transfusion of allogeneic erythrocytes) or RXGG02 (transfusion with full blood, allogeneic)) occurred ≤ 10 days after admission date for CRNM bleeding. <p>Clinically relevant non-major bleeding (CRNM):</p> <ul style="list-style-type: none"> - R04 haemorrhage from respiratory passages - N02 recurrent and persistent haematuria - R31 unspecified haematuria - N92 excessive, frequent and irregular menstruation - N93 other abnormal uterine and vaginal bleeding - R58 bleeding, not elsewhere classified - T14 superficial injury of unspecified region, hematoma - D62 acute posthaemorrhagic anemia - K922 unspecified GI bleeding - K250 gastric ulcer with bleeding - K252 gastric ulcer with both perforation and bleeding - K254 chronic or unspecified gastric ulcer with bleeding - K256 chronic or unspecified gastric ulcer with both perforation and bleeding - K260 duodenal ulcer with bleeding - K262 duodenal ulcer with both perforation and bleeding - K264 chronic or unspecified duodenal ulcer with bleeding - K266 chronic or unspecified gastric ulcer with both perforation and bleeding - K270 unspecified peptic ulcer with bleeding - K272 unspecified peptic ulcer with both perforation and bleeding - K274 chronic or unspecified peptic ulcer with bleeding - K276 chronic or unspecified peptic ulcer with both perforation and bleeding - K280 gastrojejunal ulcer with bleeding - K282 gastrojejunal ulcer with both perforation and bleeding - K284 chronic or unspecified gastrojejunal ulcer with bleeding - K286 chronic or unspecified gastric ulcer with both perforation and bleeding - K625 haemorrhage from anus and rectum - K228 haemorrhage of the oesophagus

- K221 ulcer of esophagus with bleeding
- K290 acute gastritis with bleeding
- I850 esophageal varices with bleeding
- H113 conjunctival haemorrhage
- N836 haematosalpinx)
- N837 hematoma of the broad ligament
- A985 haemorrhagic fever with renal symptoms
- N421 congestion and haemorrhage of prostate
- N857 hematometra
- O721 other immediate postpartum haemorrhage
- S064 epidural haemorrhage
- S065 traumatic subdural haemorrhage
- S066 traumatic subarachnoid haemorrhage
- S068 other intracranial injuries, traumatic haemorrhage
- D683 haemorrhagic disorder due to circulating anticoagulants
- D698 other specified haemorrhagic conditions
- D699 haemorrhagic condition, unspecified

Time to first bleeding was calculated for the combined endpoint major or CRNM bleeding.

All registered bleeding events were taken into consideration; analyses were not restricted to admissions with bleeding as the primary (first) code.

Supplementary table S3

Univariate Cox proportional hazards regression results

Univariate Cox proportional hazards

Variable	HR (95% CI)	p-value
Gender (male gender)	1.019 (0.911 – 1.139)	0.744
Age	1.043 (1.038 – 1.049)	0.000
Myocardial Infarction	1.386 (1.154 – 1.665)	0.000
Ischaemic Heart Disease	1.478 (1.312 – 1.665)	0.000
Heart failure	1.780 (1.572 – 2.015)	0.000
Vascular disease	1.491 (1.290 – 1.723)	0.000
Peripheral Arterial Disease	1.703 (1.040 – 2.789)	0.034
Cerebrovascular disease (Stroke/TIA)	1.557 (1.355 – 1.790)	0.000
History of Stroke	1.630 (1.380 – 1.925)	0.000
History of Stroke or TIA	1.581 (1.375 – 1.818)	0.000
Diabetes	1.225 (1.041 – 1.442)	0.014
Hypertension	1.447 (1.280 – 1.637)	0.000
CHADSVASc score	1.296 (1.247 – 1.348)	0.000
Chronic Kidney Disease (ICD-10 N18.3&4)	2.316 (1.696 – 3.161)	0.000
Chronic Renal Failure (ICD N18+19)	2.072 (1.701 – 2.524)	0.000
Viral Hepatitis (Liver Failure)	1.107 (0.277 – 4.432)	0.886
NSAID use last 12 mos.	1.002 (0.880 – 1.141)	0.974
Alcoholism	1.856 (0.832 – 4.139)	0.131
Major Bleeding last 12 mos.	4.528 (3.456 – 5.933)	0.000
History of Bleeding	2.591 (2.288 – 2.935)	0.000
Modified HAS-BLED score	1.457 (1.370 – 1.550)	0.000
Dementia	1.700 (1.197 – 2.414)	0.003
COPD	1.421 (1.209 – 1.669)	0.000
Ulcer disease (Bleeding)	2.049 (1.657 – 2.533)	0.000
Cancer, including "cured" patients	1.410 (1.231 – 1.615)	0.000
Comorbidity score	1.267 (1.224 – 1.312)	0.000
OAC use last 12 Mo	1.089 (0.913 – 1.298)	0.343
NSAID use last 12 Mo	1.002 (0.880 – 1.141)	0.974
All antiplatelet use last 12 Mo	1.309 (1.169 – 1.465)	0.000
Low-dose aspirin as antiplatelet therapy	1.238 (1.107 – 1.383)	0.000
Thrombocytopenia	0.965 (0.311 – 2.997)	0.965
Anaemia	2.556 (2.011 – 3.247)	0.000
Hospitalisation last 12 Mo	1.645 (1.452 – 1.864)	0.000
COPD prescription last 12 Mo	1.491 (1.244 – 1.787)	0.000
Active cancer (C-diagnosis last 12 Mo)	1.450 (1.216 – 1.728)	0.000

Supplementary table S4

Bootstrapping results, full model

Individual predictors of bleeding in full model

Risk factor	HR (95% CI)	SE	P-value	Bootstrapping, 300 samples HR (95% CI)	SE	P-value
Male sex	1.242 (1.106 – 1.395)	0.059	<0.001	1.242 (1.106 – 1.394)	0.073	<0.001
Age (continuous)	1.036 (1.030 – 1.043)	0.003	<0.001	1.036 (1.029 – 1.043)	0.0035	<0.001
Hypertension	1.197 (1.056 – 1.358)	0.064	0.005	1.197 (1.061 – 1.351)	0.073	0.003
Chronic Kidney Disease	1.257 (1.024 – 1.542)	0.104	0.029	1.257 (1.028 – 1.584)	0.148	0.041
Chronic Heart Failure	1.260 (1.106 – 1.436)	0.067	0.001	1.260 (1.114 – 1.426)	0.079	<0.001
Stroke/TIA in history	1.250 (1.082 – 1.444)	0.074	0.002	1.250 (1.100 – 1.421)	0.081	0.001
COPD	1.276 (1.061 – 1.533)	0.094	0.010	1.276 (1.0579 – 1.538)	0.121	0.011
Anaemia diagnosed last 12 months.	1.400 (1.092 – 1.796)	0.127	0.008	1.400 (1.052 – 1.865)	0.204	0.021
Bleeding in history	1.996 (1.752 – 2.273)	0.067	<0.001	1.996 (1.743 – 2.284)	0.137	<0.001
Hospitalisation (non-bleeding related), last 12 months	1.165 (1.019 – 1.331)	0.068	0.025	1.165 (1.013 – 1.339)	0.082	0.032

HR, hazard ratio; CI, confidence interval.

Supplementary table S5

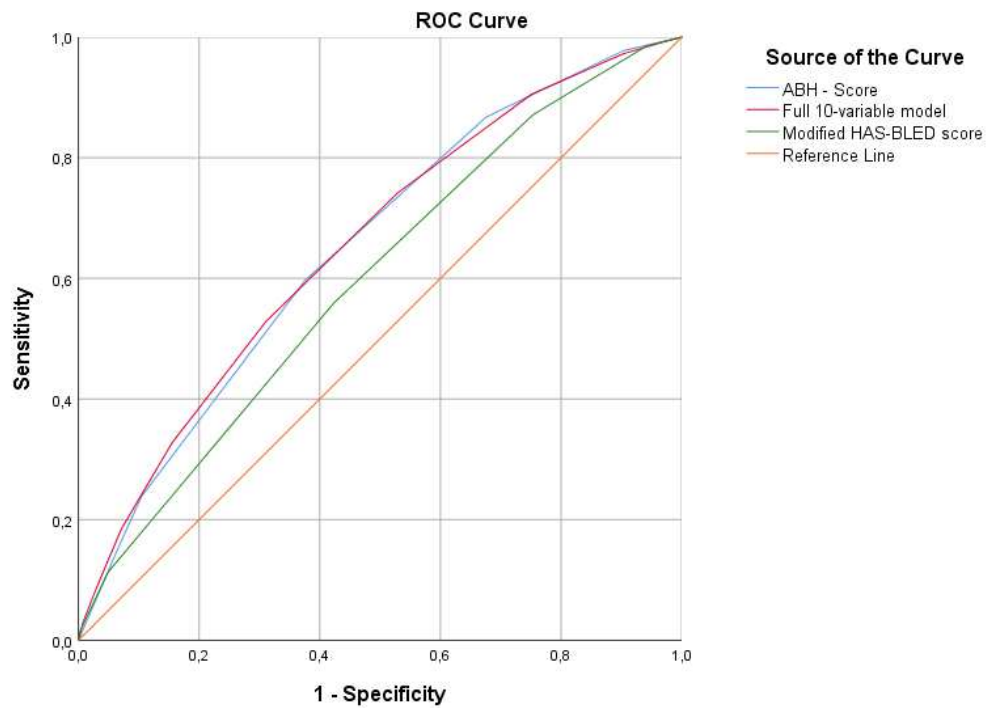
Bootstrapping results, ABH - score

Individual predictors of bleeding in ABH - score

Risk factor	HR adjusted	SE	P-value	Bootstrapping, 300 samples HR (95% CI)	SE	P-value
Age groups						
< 65 yrs.	1.00 (reference)			1.00 (reference)		
65 – 75 yrs.	1.666 (1.337 – 2.077)	0.112	<0.001	1.666 (1.398 – 1.998)	0.114	<0.001
>75 yrs.	2.681 (2.178 – 3.300)	0.106	<0.001	2.681 (2.109 – 3.287)	0.100	<0.001
History of bleeding	2.208 (1.945 – 2.507)	0.065	<0.001	2.208 (1.914 – 2.447)	0.068	<0.001
Hospitalisation (non-bleeding related) last 12 months.	1.365 (1.202 – 1.549)	0.065	<0.001	1.365 (1.215 – 1.486)	0.063	<0.001

Supplementary table S6

Receiver operating characteristic (ROC) – curves with coordinate tables

**Area Under the Curve**

Test Result Variable(s)	Area	Std. Error	Sig.	95% Confidence Interval	
				Lower Bound	Upper Bound
ABH - Score	0,651	0,008	0,000	0,636	0,666
Full 10-variable model	0,655	0,008	0,000	0,640	0,670
Modified HAS-BLED score	0,597	0,008	0,000	0,582	0,613

Supplementary table S7

Definition used for the construction of the modified HAS-BLED risk score. Diagnose codes was according to the International Classification of Disease, 10th edition (ICD10) and medication codes was according to the Anatomical Therapeutic Chemical system (ATC). For hypertension definition a dispensation of a drug for the treatment of hypertension was used as a proxy for the underlying diagnosis.

Factor	Definition in study	Score at index (baseline) Total score 0-8
Hypertension	NorPD reimbursement codes for hypertension: I10-13, I15 (ICD10) or K86, K87 (ICPC)	1 point
Renal impairment	CKD stage 3 and 4 (ICD10 code N183 and N184)	1 point
Liver impairment	ICD10 B15-B19	1 point
Stroke	Stroke ICD10 I60-I64	1 point
Prior major bleeding during last year before index	K920, K921, I600, I601, I602, I603, I604, I605, I606, I607, I608, I609, I610, I611, I612, I613, I614, I615, I616, I618, I619, I620, I621, I629, I230, I312, M250, H431, H356, H313, H450, H448, J942, K661	1 point
Age ≥ 65 years	Age ≥ 65 years at index	1 point
Therapy with either Nonsteroidal Anti-inflammatory Drugs (NSAID) or anti-platelets in the previous year before index date	ATC code M01A or B01AC	1 point
Alcoholism	ICD10: E52, K70, T51, E244, G312, G621, G721, I426, K860, O354, Z714, Z721	1 point