Supplementary material

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Table S1. Overview of external validation studies of prediction models for recurrent VTE

Author	Study design and setting	Population	N (events/total)	Follow-up time (median)	Outcome	Model	Discrimination (c-statistic)	Calibration
Timp et al. 2019 [S1]	Prospective population-based cohort (Tromsø study), Norway between 1994 and 2016	First VTE without malignancy	73/587	5.0 years	Certain recurrent DVT or PE	L-TRRiP model C and D	0.64 (model c) 0.65 (model d)	Calibration plots show good calibration, for the highest risk quintile of model c the predicted risk was overestimated
Ensor et al. 2016 [S2]	Data of patients with unprovoked VTE from MEGA study, see development of L-TRRiP score	First unprovoked VTE, who discontinued AC	278/1218	5.7 years	Certain recurrent DVT or PE	*Pre D-dimer*	0.56	Overall calibration reasonable, underestimation at lower predicted risk categories
Winter et al. 2023 [S3]	Individual patient data from 2 trials (EINSTEIN-CHOICE, GARFIELD-VTE) and 3 cohort studies (Danish registries, MEGA and Tromsø study), worldwide, between 1977 and 2017	PE or DVT without malignancy	2283/59 257	Ranging from 1 to 5.6 years	Objectively confirmed recurrent DVT or PE	Men and HERDOO2	0.57 (0.56 in untreated patients)	Not reported
						DASH	0.55 (0.52 in untreated patients)	Not reported
						L-TRRiP model C	0.59 (0.56 in untreated patients)	Not reported
						VTE-PREDICT	Ranging from 0.48 to 0.71, overall 0.59	Varying between individual studies and prediction horizon. In cohort studies the risk is underestimated, whereas in trials it was overestimated. Calibration slope ranging from -0.02 to 1.05
Marcucci et al. 2015 [S4]	Individual patient data from 5 prospective cohort studies, published between 2003 and 2008	First unprovoked VTE	123/904 (84 events in 1st year)	1.8 years	Objectively confirmed recurrent DVT or PE	Vienna	0.63	Calibration plot indicates predicted risks at 1 year were underestimated, calibration slope of 1.17
Hylckama Vlieg et al. 2015 [S5]	Cohort of cases from the THE-VTE study, Netherlands and UK, between 2003 and 2008	First unprovoked VTE, aged 18-75 years, without malignancy	54/363	NR for unprovoked VTE, entire cohort: mean 4.8 years	Symptomatic certain contralateral DVT or PE in different vein	DASH	Not reported, KM-plots suggest discrimination	Not reported
Tritschler et al. 2015 [S6]	Prospective cohort (SWITCO65+), 9 hospitals, Switzerland, between 2009 and 2013	Unprovoked VTE, age ≥65 years, treated with AC for 3 to 12 months with D-dimer measurement at 12 months	26/156	Not reported	Objectively confirmed recurrent DVT or PE	Vienna update	0.39 (12 months), 0.43 (24 months)	Calibration plot not reported, Hosmer Lemeshow p-value 0.03 (12 months) and 0.06 (24 months)
Tosetto et al. 2017 [S7]	Retrospective cohort (TRIP study), several hospitals in Italy, between 2007 and 2016	First unprovoked proximal DVT or PE; unprovoked definition according to development study	100/827	2.1 years	Objectively confirmed recurrent DVT or PE	DASH	0.65	Calibration slope of 0.71 suggesting overfitting
Moreno et al. 2017 [S8]	Retrospective cohort, 1 hospital in Spain, between 2012 and 2015	Unprovoked VTE, treated with AC for ≥ 3 months	8/121	1.5 years	Recurrent VTE	DAMOVES	0.83	Calibration plot not reported, good calibration according to authors, Hosmer-Lemeshow p-value 0.125
Timp et al. 2019 [S9]	See development of L-TRRiP score			5.7 years	Certain recurrent DVT or PE	Vienna	0.62 (0.61 for MEGA definition)	No calibration plot, reported observed vs predicted risks correspond reasonable

Author	Study design and setting	Population	N (events/total)	Follow-up time (median)	Outcome	Model	Discrimination (c-statistic)	Calibration
		First unprovoked VTE, who discontinued AC, unprovoked definition according to DASH or MEGA definition	156/797 (269/1082 for MEGA definition)			DASH	0.66 (0.56 for MEGA definition)	No calibration plot, observed vs predicted risks show overestimation of predicted risks especially at higher risk categories
Marín-Romero et al. 2019 [S10]	Retrospective cohort, 1 hospital in Spain, between 2006 and 2014	Unprovoked VTE (without active cancer, surgery, immobilization, trauma, prior hospitalization, pregnancy/puerperium, APS or hormonal treatment)	20/159	4 years (mean)	Objectively confirmed symptomatic recurrent DVT or PE	Vienna	0.63	Only observed vs expected stratified by low and high-risk group, correspond reasonable
						DASH	0.63	Only observed vs expected risks stratified by low vs high risk, underestimation of predicted risk for high-risk group
Raj et al. 2020 [S11]	Data from PADIS-PE trial (extended therapy with VKA or placebo), 14 hospitals, France, between 2007 and 2014	First unprovoked PE, treated with VKA for 6 (placebo group) or 24 months, no major thrombophilia, no recurrence or bleeding during initial 6 months, no increased bleeding risk	67/371	2.0 years (warfarin), 3.4 years (placebo)	Objectively confirmed recurrent DVT or PE	Men and HERDOO2	0.61	Not reported
						DASH	0.60	Not reported
						Vienna update	0.58	Not reported

Abbreviations: AC: anticoagulation, DVT: Deep vein thrombosis; NR: not reported; PE: pulmonary embolism; VKA: vitamin-K antagonist; VTE: venous thromboembolism.

Table S2. Overview of external validation studies of prediction models for bleeding

Author	Study design and setting	Population	n (events/ total)	Follow-up (median)	Outcome	Model	c-statistic	Calibration
Winter et al. 2023 [S3]	Individual patient data from multiple trials (EINSTEIN-CHOICE, GARFIELD-VTE) and cohort studies (Danish registries and Tromsø study), worldwide, between 1977 and 2017	Adult patients with VTE without cancer	3335/ 59 257	Ranging from 0.5 to 2.5 years.	Composite of MB (ISTH) and CRNMB (ISTH)	Kuijer	0.58 (0.52 in extended therapy)	Not reported
						RIETE	0.63 (0.61 in extended therapy)	Not reported
						ACCP	0.59 (0.54 in extended therapy)	Not reported
						VTE-BLEED	0.63 (0.56 in extended therapy)	Not reported
						Hokusai	0.61 (0.59 in extended therapy)	Not reported
						Martinez	0.58 (0.52 in extended therapy)	Not reported
						VTE-PREDICT	Ranging from 0.61 to 0.68, overall 0.64	Calibration slope ranging from 0.55 to 0.86
Klok et al. 2016 [S12]	See development of VTE-BLEED score	Adult patients with VTE, receiving dabigatran or warfarin	138 (37MB) /2553 dabigatran, 51MB/ 2554 warfarin	0.5 year	MB (ISTH) and CRNMB (ISTH) during AC	Kuijer	0.66 for dabigatran for entire period, 0.60 (dabigatran) and 0.68 (warfarin) for MB beyond first month	Not reported
						RIETE	0.65 for dabigatran for entire period, 0.73 (dabigatran) and 0.65 (warfarin) for MB beyond first month	Not reported
						OBRI	0.64 for dabigatran for entire period, 0.69 (dabigatran) and 0.72 (warfarin) for MB beyond first month	Not reported
						HEMORR2-HAGES	0.63 for dabigatran for entire period, 0.80 (dabigatran) and 0.76 (warfarin) for MB beyond first month	Not reported
						HAS-BLED	0.64 for dabigatran for entire period, 0.76 (dabigatran) and 0.72 (warfarin) for MB beyond first month	Not reported
						ATRIA	0.60 for dabigatran for entire period, 0.75 (dabigatran) and 0.73 (warfarin) for MB beyond first month	Not reported
Di Nisio et al. 2016 [S13]	See development of Einstein score	Adult patients with acute symptomatic DVT or PE, receiving rivaroxaban or VKA	112/8245 (63/8060 after 3 weeks)	0.5 year	MB (ISTH) during AC	Kuijer	0.64 (first 3 weeks), 0.64 (after 3 weeks), 0.64 (entire period)	Not reported
						RIETE	0.63 (first 3 weeks), 0.57 (after 3 weeks), 0.60 (entire period)	Not reported
						OBRI	0.54 (first 3 weeks), 0.53 (after 3 weeks), 0.53 (entire period)	Not reported
						HEMORR2-HAGES	0.64 (first 3 weeks), 0.66 (after 3 weeks), 0.65 (entire period)	Not reported
						HAS-BLED	0.58 (first 3 weeks), 0.62 (after 3 weeks), 0.59 (entire period)	Not reported
Di Nisio et al. 2017 [S14]	See development of Hokusai score	Adult patients with acute symptomatic DVT or PE, receiving edoxaban or warfarin	122/8240	0.75 year	MB (ISTH) and CRNMB (ISTH) during AC	Kuijer	MB: 0.62 (edoxaban), 0.61 (warfarin) CRNMB: 0.61 (edoxaban), 0.59 (warfarin)	Increasing event rate stratified by low, moderate or high-risk group
						Kearon	MB: 0.67 (edoxaban), 0.66 (warfarin) CRNMB: 0.58 (edoxaban), 0.58 (warfarin)	Increasing event rate stratified by low, moderate or high-risk group
						EINSTEIN (entire period)	MB: 0.69 (edoxaban), 0.70 (warfarin) CRNMB: 0.61 (edoxaban), 0.60 (warfarin)	Not reported
						mOBRI	MB: 0.65 (edoxaban), 0.64 (warfarin) CRNMB: 0.57 (edoxaban), 0.57 (warfarin)	Increasing event rate stratified by low, moderate or high-risk group
						HAS-BLED	MB: 0.55 (edoxaban), 0.55 (warfarin) CRNMB: 0.52 (edoxaban), 0.52 (warfarin)	Increasing event rate stratified by low, moderate or high-risk group
						ORBIT	MB: 0.61 (edoxaban), 0.59 (warfarin) CRNMB: 0.54 (edoxaban), 0.54 (warfarin)	Increasing event rate stratified by low, moderate or high-risk group
Seiler et al. 2017 [S15]	See development of Seiler score	Patients aged ≥ 65 years with acute symptomatic DVT or PE, continuing VKA beyond 3 months	66/743	2.3 years (mean)	MB (ISTH) during extended AC	Kuijer	0.67 (3months), 0.61 (6 months), 0.57 (12, 24 and 36 months)	Not reported
						Kearon	0.54 (3 months), 0.55 (6 months), 0.58 (12 months), 0.57 (24 months), 0.59 (36 months)	Not reported

Author	Study design and setting	Population	n (events/ total)	Follow-up (median)	Outcome	Model	c-statistic	Calibration
						RIETE	0.59 (3 and 6 months), 0.63 (12 and 36 months), 0.62 (24 months)	Not reported
						mOBRI	0.54 (3 months), 0.51 (6 months), 0.52 (12 and 24 months), 0.53 (36 months)	Not reported
Martinez et al. 2020 [S16]	See development of Martinez score	Patients with a first VTE, given VKA within 30 days after initial VTE	167/10 010	0.25 year	MB (fatal, at a critical site; with hematoma, compartment syndrome, anemia or transfusion within 7 days; Hb decrease >2g/dL within 14 days) or hospitalization for CRNMB, during VKA treatment	Kuijer	0.56 (0.59 for MB)	Not reported
						RIETE	0.62 (0.64 for MB)	Not reported
						VTE-BLEED	0.66 (0.69 for MB)	Not reported
Alonso et al. (2021) [S17]	See development of Alonso score	Adult patients with VTE, using OAC	2294/165 434	0.4 year (mean)	Hospitalization for intracranial hemorrhage, gastrointestinal bleeding or other MB	VTE-BLEED	0.65 (0.61 for dichotomized score)	Not reported
						HAS-BLED	0.62	Not reported
Chopard et al. 2021 [S18]	See development of PE-SARD score	Adult patients with acute PE	82/2754	2.8 days	MB (ISTH)	RIETE	0.69	$\chi 2$ Hosmer-Lemeshow test 13.9 (indicating p-value >0.05)
						VTE-BLEED	0.63	$\chi 2$ Hosmer-Lemeshow test 10.4 (indicating p-value > 0.05)
Wells et al. 2022 [S19]	See development of CHAP model	Adult patients an unprovoked or weakly provoked DVT or PE, requiring extended anticoagulant therapy beyond 3 months	118/2516	2.6 years	MB (ISTH)	RIETE	0.51	Event rate stratified by total score is fluctuating, indicating poor calibration
						ACCP	0.65	Increasing event rate with increasing score except for highest total score (probably due to low nr of patients)
						VTE-BLEED	0.61	Increasing event rate with increasing score except for highest total score (probably due to low nr of patients)
						mOBRI	0.51	Increasing event rate with increasing score except for highest total score (probably due to low nr of patients)
						HAS-BLED	0.57	Increasing event rate with increasing score except for highest scores (probably due to low nr of patients)
Scherz et al. 2013 [S20]	Prospective cohort (SWITCO65+), nine hospitals, Swiss, between 2009 and 2011	Acute symptomatic DVT or PE, age ≥ 65 years	28/663	0.25 year	MB (fatal; in a critical organ; ≥2 units of blood; causing >2 g/dL decrease in Hb) within 90 days of index VTE	Kuijer	0.49	P-value Pearson's chi-square goodness of fit 0.84
						Kearon	0.59	P-value Pearson's chi-square goodness of fit 0.53
						RIETE	0.60	P-value Pearson's chi-square goodness of fit 0.87
						OBRI	0.54	P-value Pearson's chi-square goodness of fit 0.82
Poli et al. 2013 [S21]	Prospective cohort (EPICA study), 27 centers in Italy, study period not reported	Patients ≥ 80 years treated for secondary prevention of VTE with VKA	47/1078	1.8 years (mean)	MB (fatal, intracranial, ocular causing blindness, retroperitoneal; requiring surgery, invasive maneuvers or ≥2 units of blood; causing >2 g/dL decrease in Hb) during AC	RIETE	0.61 for continuous and 0.51 for categorical variables	Not reported
						ACCP	0.55 for continuous and 0.52 for categorical variables	Not reported
						mOBRI	0.58 for continuous and 0.51 for categorical variables	Not reported
						HEMORR2-HAGES	0.60 for continuous and 0.60 for categorical variables	Not reported
						HAS-BLED	0.55 for continuous and 0.58 for categorical variables	Not reported
						ATRIA	0.58 for continuous and 0.56 for categorical variables	Not reported
Riva et al. 2014 [S22]	Retrospective cohort, five hospitals in Italy, between 2010 and 2012	Patients on VKA treatment for VTE	50/681	0.73 year (mean)	MB (ISTH) and CRNMB (ISTH)	Kuijer	0.51 (MB), 0.56 (MB and CRNMB)	Not reported
						RIETE	0.54 (MB), 0.58 (MB and CRNMB)	Not reported
						ACCP	0.59 (MB), 0.63 (MB and CRNMB)	Not reported
						mOBRI	0.59 (MB), 0.59 (MB and CRNMB)	Not reported

Author	Study design and setting	Population	n (events/ total)	Follow-up (median)	Outcome	Model	c-statistic	Calibration
						Shireman	0.63 (MB), 0.50 (MB and CRNMB)	Not reported
						HEMORR2-HAGES	0.51 (MB), 0.59 (MB and CRNMB)	Not reported
						HAS-BLED	0.60 (MB), 0.63 (MB and CRNMB)	Not reported
						ATRIA	0.47 (MB), 0.59 (MB and CRNMB)	Not reported
Piovella et al. 2014[S23]	Data from registry (RIETE) of patients with acute VTE, >100 hospitals, mainly Spain, study period not reported	Patients with acute VTE of whom data of variables in scores were complete	82/8717	0.25 year	MB (clinically overt, ≥2 units of blood, retroperitoneal or intracranial, requiring discontinuation of AC, fatal)	Kuijer	0.55	P-value goodness of fit not reported
						RIETE	0.56	P-value goodness of fit not reported
						OBRI	0.59	P-value goodness of fit not reported
						mOBRI	0.60	P-value goodness of fit not reported
Klok et al. 2015 [S24]	Prospective cohort (PERGO), 1 hospital, Germany, between 2005 and 2014	Patients with acute symptomatic PE treated with VKA or LMWH	20/448	30 days	MB (ISTH)	Kuijer	0.57	Not reported
						RIETE	0.58	Not reported
						HEMORR2-HAGES	0.60	Not reported
						HAS-BLED	0.59	Not reported
						ATRIA	0.64	Not reported
Kline et al. 2016 [S25]	Data from 2 trials (EINSTEIN-PE and EINSTEIN-DVT; rivaroxaban vs VKA), 38 countries, between 2007 and 2011	Adult patients with acute symptomatic DVT or PE	40/ 4130 (rivaroxaban) 72/4116 (VKA)	0.6 year (mean)	MB (ISTH) during AC	Kuijer	Not reported, incidence of MB low vs. high risk 0.3% vs 1.4% rivaroxaban, 0.7% vs 4.4% VKA	Not reported
						RIETE	Not reported, incidence of MB low vs. high risk 0.5% vs 2.1% rivaroxaban, 0.9% vs 3.7% VKA	Not reported
						OBRI	Not reported, incidence of MB low vs. high risk 0.5% vs. NA (0 events in high-risk group) rivaroxaban, 0.7% vs 12.0% VKA	Not reported
						mOBRI	Not reported, incidence of MB low vs. high risk 0.4% vs NA% (no events in high-risk group) rivaroxaban, 0.8% vs 7.7% VKA	Not reported
Klok et al. 2017 [S26]	Data from Hokusai VTE study (RCT investigating edoxaban vs warfarin), worldwide, between 2010 and 2012	Adult patients with VTE, receiving edoxaban or warfarin	66/4122 (warfarin), 56/4118 (edoxaban)	0.75 year	MB (ISTH) during stable anticoagulation (>30 days)	VTE-BLEED	0.66 (0.63 for edoxaban and 0.69 for warfarin arm)	Not reported
Rief et al. 2018 [S27]	Prospective cohort, 1 hospital, Austria between 2014 and 2016	Adult patients with VTE treated with AC	4/111	1 year	MB (ISTH) during AC	VTE-BLEED	Not reported, OR of MB in high-risk group 6.4 95%CI 0.5-342	Not reported
						HAS-BLED	Not reported, OR of MB in high-risk group 13.0 95%CI 0.9-692	Not reported
Klok et al. 2018 [S28]	Data from the XALIA study (cohort of patients treated with rivaroxaban or VKA) worldwide, between 2012 and 2014	Adult patients with DVT, and indication for anticoagulant treatment for ≥3 months, excluding early switchers from VKA to DOAC	39/4457	0.5 year	MB (ISTH) during AC	VTE-BLEED	0.68 (0.69 in rivaroxaban and 0.64 in VKA group)	Not reported
Palareti et al. 2018 [S29]	Cohort from the START2 Register, Italy, until 2017	Adult patients on long-term anticoagulation for a first PE or DVT	48 (28 MB)/2263	1 year	MB (ISTH) and CRNMB (ISTH) during AC	ACCP	0.56	Overestimation of risk above 3rd decile of predicted risk.
Zhang et al. 2019 [S30]	Prospective cohort, 1 hospital, China between 2009 and 2013	Adult patients with acute symptomatic PE	16 MB, 73CRNMB/ 563	0.25 year	MB (ISTH) or CRNMB (spontaneous hematoma ≥ 25 cm, spontaneous nosebleed or gingival bleeding >5 minutes, macroscopic hematuria, spontaneous rectal bleeding, bleeding requiring hospitalization or surgical intervention, transfusion of 1 units of blood or any other bleeding considered clinically relevant)	Kuijer	0.57 (MB), 0.60 (all bleeding)	P-value Pearson's chi-square goodness of fit 0.31(MB), 0.44 (all bleeding)
						Kearon	0.75 (MB), 0.62 (all bleeding)	P-value Pearson's chi-square goodness of fit 0.72(MB), 0.56 (all bleeding)
						RIETE	0.56 (MB), 0.53 (all bleeding)	P-value Pearson's chi-square goodness of fit 0.52(MB), 0.53 (all bleeding)

Author	Study design and setting	Population	n (events/ total)	Follow-up (median)	Outcome	Model	c-statistic	Calibration
Kresoja et al. 2019 [S31]	Prospective cohort, 1 hospital, Germany, between 2008 and 2016	Adult patients with PE	18/552	In-hospital, nr of days not reported	In hospital MB (ISTH)	VTE-BLEED	0.69 (MB in hospital)	Not reported
						HAS-BLED	0.58 (MB in hospital)	Not reported
Skowrońska et al. 2019 [S32]	Prospective cohort (PE-aWARE registry), 1 hospital, between 2014 and 2017	Patients hospitalized with acute PE	17MB, 18 CRNMB/310	6.5 days	First in hospital bleeding (MB or CRNMB)	RIETE	0.77	Not reported
						VTE-BLEED	0.75	Not reported
						HEMORR2-HAGES	0.76	Not reported
						HAS-BLED	0.51	Not reported
Vedovati et al. 2020 [S33]	Prospective cohort, five hospitals in Italy, between 2014 and 2017	Adult patients starting DOACs for PE or DVT	26/1034	0.72 year	MB (ISTH) during AC	Kuijer	0.55	Increasing event rate stratified by low, moderate or high-risk group
						RIETE	0.60	Increasing event rate stratified by low vs moderate group, high risk group is small
						VTE-BLEED	0.67	Increasing event rate stratified by low vs high risk group
						HAS-BLED	0.55	Increasing event rate stratified by low vs high risk group
						ATRIA	0.62	Increasing event rate stratified by low, moderate or high-risk group
						ORBIT	0.65	Increasing event rate stratified by low, moderate or high-risk group
Nishimoto et al. 2019 [S34]	Retrospective cohort (COMMAND VTE), 29 centers, Japan, between 2010 and 2014	Adult patients with VTE, with prolonged anticoagulant therapy beyond 30 days	121/2124	1.8 years	MB (ISTH) beyond 30 days during AC	VTE-BLEED	0.63	Observed incidences stratified by total score fluctuate, but on average increase by increasing total score
Lecumberri et al. 2021 [S35]	Data from registry (RIETE) of patients with acute VTE, >100 hospitals, mainly Spain, between 2001 and 2019	Patients receiving anticoagulant therapy for acute VTE	1979/82 239	< 0.5 year	MB (overt and requiring ≥2 units of blood; retroperitoneal, spinal, intracranial; fatal)	RIETE	0.71 (day 1-30), 0.69 (day 31-90), 0.80 (day 91-180), 0.72 (day 181-360)	Not reported
						VTE-BLEED	0.69 (day 1-30), 0.70 (day 31-90), 0.80 (day 91-180), 0.71 (day 181-360)	Not reported
Keller et al. 2021 [S36]	Data from German nationwide inpatient statistics, Germany 2005 and 2017	Patients with VTE based on ICD-10 codes	1288 intracerebral, 7209 gastro-intestinal/ 1 204 895	In hospital, duration not reported	Serious bleeding events (intracerebral bleeding, gastro-intestinal bleeding, necessity of transfusion)	Kuijer	C-statistic not reported, statistically significant difference in risk of intracerebral bleeding and gastro-intestinal bleeding between patients with high-risk category, indicate discrimination	Not reported
Frei et al. 2021 [S37]	Prospective cohort (SWITCO65+), nine hospitals, Swiss, between 2009 and 2013	Patients aged ≥ 65 years with acute symptomatic DVT or PE, continuing VKA beyond 3 months	45 MB, 127 CRNMB/ 743	0.8 year	MB (ISTH) and CRNMB (ISTH) during extended anticoagulation	Kuijer	0.55 (MB), 0.54 (CRNMB)	P-value Pearson's chi-square goodness of fit 0.71 (MB), 0.52 (CRNMB)
						Kearon	0.53 (MB), 0.58 (CRNMB)	P-value Pearson's chi-square goodness of fit 0.93 (MB), 0.63 (CRNMB)
						RIETE	0.63 (MB), 0.62 (CRNMB)	P-value Pearson's chi-square goodness of fit 0.95 (MB), 0.49 (CRNMB)
						ACCP	0.59 (MB), 0.65 (CRNMB)	P-value Pearson's chi-square goodness of fit 0.14 (MB), 0.26 (CRNMB)
						VTE-BLEED	0.57 (MB), 0.58 (CRNMB)	P-value Pearson's chi-square goodness of fit 0.11 (MB), 0.64 (CRNMB)
						Seiler	0.70 (MB), 0.66 (CRNMB)	P-value Pearson's chi-square goodness of fit 0.20 (MB), 0.72 (CRNMB)
						OBRI	0.47 (MB), 0.52 (CRNMB)	P-value Pearson's chi-square goodness of fit 0.92 (MB), 0.22 (CRNMB)
						HEMORR2-HAGES	0.57 (MB), 0.67 (CRNMB)	P-value Pearson's chi-square goodness of fit <0.001 (MB), 0.01 (CRNMB)
						HAS-BLED	0.54 (MB), 0.60 (CRNMB)	P-value Pearson's chi-square goodness of fit 0.65 (MB), 0.42 (CRNMB)
						ATRIA	0.61 (MB), 0.60 (CRNMB)	P-value Pearson's chi-square goodness of fit 0.21 (MB), 0.40 (CRNMB)
Mathonier et al. 2021 [S38]	Cohort (BFC-FRANCE), 5 hospitals, France, between 2011 and 2019	Adult patients with PE	82/2754	In hospital, 2.8 days	MB (ISTH)	RIETE	0.69	Calibration plot indicates predicted risks were underestimated especially at higher risks
						VTE-BLEED	0.63	Calibration plot indicates predicted risks were underestimated at higher risks

Author	Study design and setting	Population	n (events/ total)	Follow-up (median)	Outcome	Model	c-statistic	Calibration
						HEMORR2-HAGES	0.67	Calibration plot indicates predicted risks were underestimated at higher risks
						HAS-BLED	0.57	Calibration plot indicates predicted risks were underestimated
						ATRIA	0.67	Calibration plot indicates predicted risks were underestimated
						ORBIT	0.68	Calibration plot indicates predicted risks were underestimated at median risks
Wells et al. 2003 [S39]	Prospective cohort, 1 hospital, Canada, study period not reported	Patients with objectively confirmed DVT or PE	10 MB, 18 minor/222	1.5 year	MB (loss of 2 units of blood within 1 week, or otherwise life threatening), minor (all other bleedings)	mOBRI	Not reported, statistically significant difference between low- and moderate-risk groups	Not reported
Kooiman et al 2015 [S40]	Retrospective cohort, anticoagulation clinic Leiden, the Netherlands, between 2006 and 2007	Patients with acute VTE, starting VKA	11/537	0.5 year	MB (ISTH) during AC	HAS-BLED	0.78 (0.81 if excluding labile INR and alcohol use)	Not reported
Brown et al. 2018 [S41]	Retrospective cohort, using data from medical claims, USA, between 2010 and 2013	Adult patients with VTE	4789 (1847 MB)/132 280	0.4 year	MB (during inpatient stay, at critical site, need for transfusion or fatal) and all bleeding	HAS-BLED	Ranging from 0.66 to 0.73	Not reported

Table S3. Overview of variables included in other bleeding models validated in VTE patients

	OBRI [S42]	mOBRI [S43]	Shireman et al. [S44]	HEMORR2HAGES [S45]	HAS-BLED [S46]	ATRIA [S47]	ORBIT [S48]
Clinical variables							
General characteristics							
Age	x	x	x	x	x	x	x
Sex			x				
Medical history/comorbidities							
Active malignancy				x			
History of malignancy							
(Major) bleeding			x	x	x	x	x
Gastrointestinal bleeding	x	x					
Peptic ulcer disease							
Stroke	x	x		x	x		
Atrial fibrillation	x						
Myocardial infarction	x*	x*					
Hypertension				x		x	
Diabetes	x*	x*	x				
Liver disease				x*	x		
Anemia							x*
Medication use							
NSAIDs					x*		
Antiplatelet therapy			x	x#	x*		x
Poor INR control					x		
Other variables							
Fall risk				x			
Alcohol abuse			x*	x	x		
Drugs abuse			x*				
Physical examination							
Systolic blood pressure					x		
Laboratory variables							
Hemoglobin (anemia)			x	x		x	x*
Hematocrit	x*	x*					x*
Creatinine (renal insufficiency)	x*	x*		x*	x	x	x
Platelet count (thrombocytopenia)				x#			
Platelet function				x#			
Genetic variables							
CYP2C9 variant				x			

Table S4. Model characteristics of other bleeding models validated in VTE patients

Model	Author, year	Time horizon	Prediction outcome
OBRI	Landefeld et al. 1989 [S42]	Not specified	Score of 0-7; low risk: 0, intermediate risk: 1-2, high risk: ≥3
mOBRI	Beyth et al. 1998 [S43]	Not specified	Score of 0-5; low risk: 0, intermediate risk 1-2, high risk: 3-4
Shireman et al.	Shireman et al. 2006 [S44]	90 days	Score of 0-4.17; low risk: ≤1.07; intermediate risk: >1.07, but <2.19; high risk: ≥2.19
HEMORR2 HAGES	Gage et al. 2006 [S45]	Until next hospitalization or 1000 days	Score of 0-12 with corresponding risk estimates
HAS-BLED	Pisters et al. 2010 [S46]	1 year	Score of 0-9; low risk: 0-1, intermediate risk: 2, high risk: 3-5, very high risk: >5
ATRIA	Fang et al. 2011 [S47]	Not specified	Score of 0-10; low risk: 0-3, intermediate risk: 4, high risk: >4
ORBIT	O'Brien et al. 2015 [S48]	2 years	Score of 0-7; low risk: 0-2, intermediate risk: 3, high risk: 4-7

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