

## Comparison of risk prediction scores for venous thromboembolism in cancer patients: a prospective cohort study

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**Appendix 1. Characteristics of derivation cohorts**

<b>Score</b>	<b>Study design</b>	<b>Centers</b>	<b>Country</b>	<b>Cancer types</b>	<b>Follow-up duration</b>	<b>Sample size</b>	<b>Events</b>
Khorana	Prospective cohort	Multi	USA	Various	Median 2.5 months	2,701	60
Vienna CATS	Prospective cohort	Single	Austria	Various	Median 656 days	819	61
PROTECHT	Randomized controlled trial	Multi	Italy	Various	4 months	378	15
CONKO	Randomized controlled trial	Multi	Germany	Pancreatic cancer	3 months	152	15

## Appendix 2. Distribution of scores

<i>Characteristic</i>	<i>Prior to chemotherapy (N=260)</i>	<i>Missing</i>	<i>All patients (N=876)</i>	<i>Missing</i>
Khorana score, n (%)		9 (3.5)		33 (3.8)
0 points	67 (26)		265 (30)	
1 point	80 (31)		249 (28)	
2 points	72 (28)		224 (26)	
3 points	25 (9.6)		83 (10)	
4 points	7 (2.7)		22 (2.5)	
Vienna CATS score		51 (20)		134 (15)
0 points	38 (15)		167 (19)	
1 point	46 (18)		181 (21)	
2 points	58 (22)		204 (23)	
3 points	41 (16)		112 (13)	
4 points	14 (5.4)		57 (6.5)	
5 points	6 (2.3)		15 (1.7)	
6 points	1 (0.4)		6 (0.7)	
PROTECHT score		12 (4.6)		38 (4.3)
0 points	28 (11)		109 (12)	
1 point	51 (20)		224 (26)	
2 points	84 (32)		217 (25)	
3 points	56 (22)		182 (21)	
4 points	23 (8.8)		81 (9.2)	
5 points	5 (1.9)		23 (2.6)	
6 points	1 (0.4)		2 (0.2)	
CONKO score		14 (5.4)		47 (5.4)
0 points	58 (22)		245 (27)	
1 point	76 (29)		240 (27)	
2 points	76 (29)		221 (25)	
3 points	27 (10)		89 (10)	
4 points	9 (3.5)		29 (3.3)	
5 points	0 (0)		5 (0.6)	

### Appendix 3. Score performance at exploratory positivity thresholds

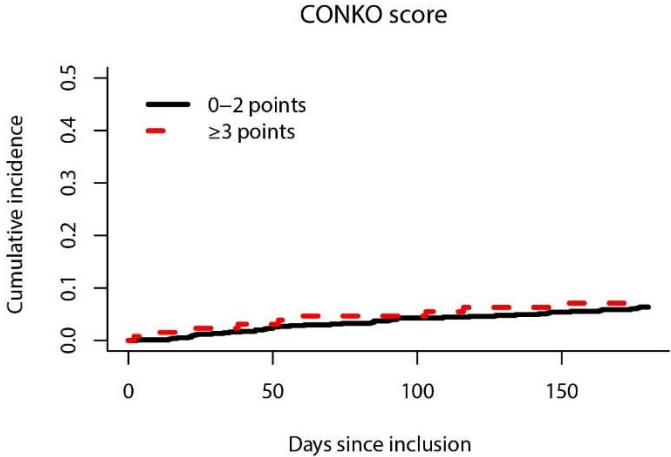
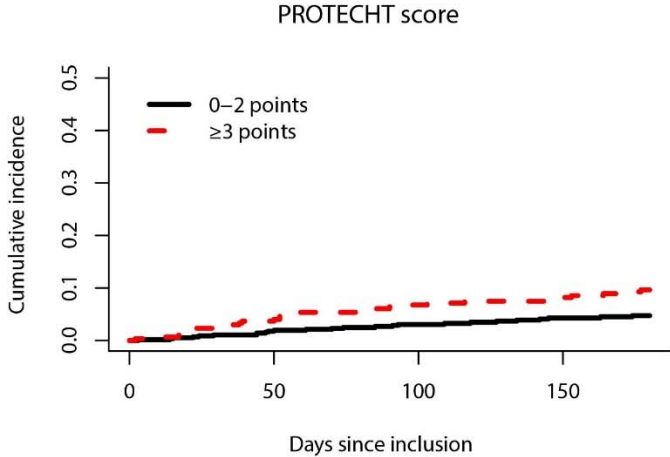
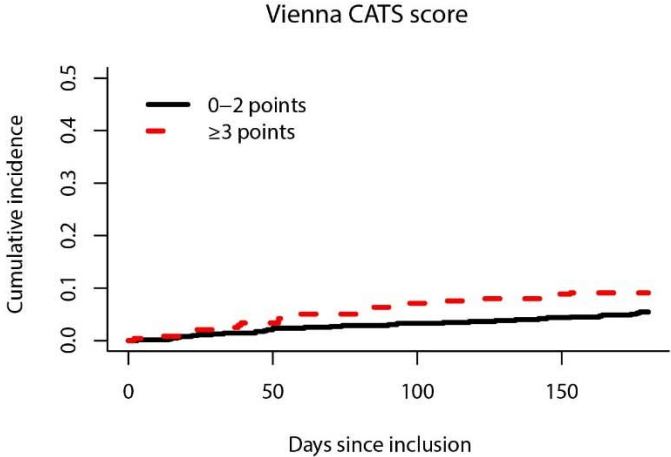
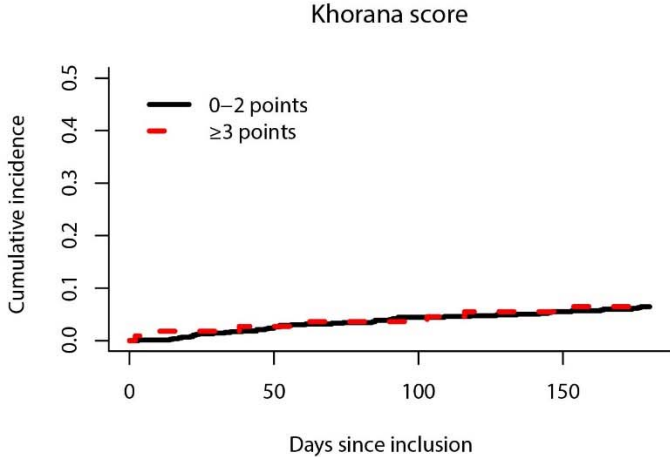
	<b>Khorana score</b>	<b>Vienna CATS score</b>	<b>PROTECHT score</b>	<b>CONKO score</b>
<b>Patients enrolled prior to chemotherapy (N=260)</b>				
<i>Positivity threshold of 2 points</i>				
High risk patients, % (95% CI)	42 (36-48)	60 (54-66)	68 (62-73)	45 (39-51)
6-month VTE risk in low risk patients ( $\leq 1$ point), % (95% CI)	8.4 (4.5-14)	4.6 (1.5-10)	5.1 (1.6-12)	8.9 (4.9-15)
6-month VTE risk in high risk patients ( $\geq 2$ points), % (95% CI)	7.7 (3.6-14)	10 (6.0-16)	9.5 (5.6-14)	7.1 (3.3-13)
Subhazard ratio for high vs low risk patients	0.92 (0.38-2.2)	2.3 (0.76-6.7)	1.9 (0.64-5.6)	0.79 (0.32-1.9)
<i>Positivity threshold of 4 points</i>				
High risk patients, % (95% CI)	2.7 (1.3-5.5)	11 (7.8-16)	12 (8.5-16)	3.9 (2.1-7.1)
6-month VTE risk in low risk patients ( $\leq 3$ points), % (95% CI)	8.3 (5.3-12)	8.7 (5.4-13)	8.7 (5.5-13)	8.4 (5.3-12)
6-month VTE risk in high risk patients ( $\geq 4$ points), %	0	3.5 (0.2-16)	3.3 (0.23-15)	0
Subhazard ratio for high vs low risk patients	Not estimable*	0.39 (0.05-2.8)	0.37 (0.05-2.7)	Not estimable*
<b>All patients (N=876)</b>				
<i>Positivity threshold of 2 points</i>				
High risk patients, % (95% CI)	40 (36-43)	55 (52-58)	61 (58-64)	42 (38-45)
6-month VTE risk in low risk patients ( $\leq 1$ point), % (95% CI)	6.0 (4.1-8.3)	4.4 (2.6-6.9)	4.8 (2.8-7.6)	6.0 (4.1-8.4)
6-month VTE risk in high risk patients ( $\geq 2$ points), % (95% CI)	7.2 (4.7-10)	8.1 (5.8-11)	7.5 (5.4-10)	7.1 (4.7-10)
Subhazard ratio for high vs low risk patients	1.2 (0.72-2.1)	1.9 (1.1-3.5)	1.6 (0.88-2.9)	1.2 (0.71-2.1)
<i>Positivity threshold of 4 points</i>				

High risk patients, % (95% CI)	2.8 (1.9-4.1)	11 (9.3-14)	13 (11-16)	4.1 (2.9-5.6)
6-month VTE risk in low risk patients ( $\leq 3$ points), % (95% CI)	6.4 (4.8-8.3)	6.2 (4.6-8.1)	6.5 (4.8-8.5)	6.2 (4.7-8.1)
6-month VTE risk in high risk patients ( $\geq 4$ points), %	8.4 (1.4-24)	8.9 (4.2-16)	6.3 (2.8-12)	12 (3.6-25)
Subhazard ratio for high vs low risk patients	1.4 (0.32-5.6)	1.5 (0.70-3.2)	0.98 (0.44-2.2)	2.0 (0.7-5.6)

Abbreviations: CI indicates confidence interval; and VTE, venous thromboembolism.

\* No venous thromboembolism events in patients high risk patients

**Appendix 4. Cumulative VTE incidence in high vs low risk patients for the four scores in all patients (N=876)**



**Appendix 5. Sensitivity analysis restricted to symptomatic venous thromboembolism in all patients (N=876)**

	<b>Khorana score</b>	<b>Vienna CATS score</b>	<b>PROTECT score</b>	<b>CONKO score</b>
Time-dependent c-index at 180 days (95% CI)	0.62 (0.59-0.66)	0.67 (0.64-0.70)	0.60 (0.56-0.63)	0.65 (0.61-0.68)
6-month VTE risk in low risk patients ( $\leq 2$ points), % (95% CI)	4.1 (2.8-5.7)	3.5 (2.2-5.2)	2.8 (1.6-4.5)	3.9 (2.6-5.5)
6-month VTE risk in high risk patients ( $\geq 3$ points), % (95% CI)	3.7 (1.2-8.6)	5.3 (2.9-8.8)	6.2 (3.8-9.4)	4.7 (1.9-9.5)
Subhazard ratio for high ( $\geq 3$ points) vs low risk patients ( $\leq 2$ points)	0.91 (0.32-2.6)	1.6 (0.76-3.2)	2.2 (1.1-4.4)	1.2 (0.51-3.0)

Abbreviations: CI indicates confidence interval; VTE, venous thromboembolism

**Appendix 6. Sensitivity analysis restricted to first 90 days of follow-up in all patients (N=876)**

	<b>Khorana score</b>	<b>Vienna CATS score</b>	<b>PROTECHT score</b>	<b>CONKO score</b>
Time-dependent c-index at 90 days (95% CI)	0.54 (0.45-0.63)	0.60 (0.51-0.70)	0.61 (0.52-0.69)	0.55 (0.46-0.64)
6-month VTE risk in low risk patients ( $\leq 2$ points), % (95% CI)	4.0 (2.8-5.6)	3.1 (1.9-4.6)	2.7 (1.6-4.3)	3.9 (2.6-5.4)
6-month VTE risk in high risk patients ( $\geq 3$ points), % (95% CI)	3.6 (1.2-8.4)	6.4 (3.7-10)	6.4 (4.0-9.6)	4.7 (1.9-9.3)
Subhazard ratio for high ( $\geq 3$ points) vs low risk patients ( $\leq 2$ points)	0.91 (0.32-2.6)	2.1 (1.1-4.2)	2.4 (1.2-4.8)	1.2 (0.51-3.0)

Abbreviations: CI indicates confidence interval; VTE, venous thromboembolism



## Appendix 7. Complete case analysis

	<b>Khorana score</b>	<b>Vienna CATS score</b>	<b>PROTECHT score</b>	<b>CONKO score</b>
<b>Patients enrolled prior to chemotherapy (N=260)</b>				
Time-dependent c-index at 180 days (95% CI)	0.50 (0.43-0.56)	0.58 (0.52-0.64)	0.54 (0.47-0.60)	0.53 (0.47-0.60)
High risk patients ( $\geq 3$ points), % (95% CI)	13 (9.0-17)	30 (24-37)	34 (28-40)	14 (10-19)
6-month VTE risk in low risk patients ( $\leq 2$ points), % (95% CI)	8.7 (5.3-13)	9.0 (4.9-15)	7.8 (4.2-13)	8.0 (4.8-12)
6-month VTE risk in high risk patients ( $\geq 3$ points), % (95% CI)	6.5 (1.1-19)	9.8 (4.0-19)	9.8 (4.6-17)	5.7 (0.99-17)
Subhazard ratio for high vs low risk patients	0.72 (0.17-3.0)	1.1 (0.41-2.8)	1.3 (0.52-3.1)	0.69 (0.16-3.1)
<b>All patients (N=876)</b>				
Time-dependent c-index at 180 days (95% CI)	0.53 (0.47-0.59)	0.59 (0.53-0.65)	0.59 (0.53-0.66)	0.55 (0.48-0.61)
High risk patients ( $\geq 3$ points), % (95% CI)	12 (10-15)	26 (23-29)	34 (31-37)	14 (12-17)
6-month VTE risk in low risk patients ( $\leq 2$ points), % (95% CI)	6.7 (5.0-8.7)	5.8 (4.0-8.1)	4.9 (3.3-7.1)	6.3 (4.6-8.3)
6-month VTE risk in high risk patients ( $\geq 3$ points), % (95% CI)	7.0 (3.1-13)	9.7 (6.0-15)	10 (6.9-14)	7.5 (3.7-13)
Subhazard ratio for high vs low risk patients	1.1 (0.48-2.4)	1.8 (0.98-3.2)	2.1 (1.3-3.7)	1.2 (0.60-2.6)

Abbreviations: CI indicates confidence interval; VTE, venous thromboembolism

## Appendix 8. Multivariable analysis (N=876)

Item	Khorana score SHR (95% CI)	Vienna CATS score SHR (95% CI)	PROTECHT score SHR (95% CI)	CONKO score SHR (95% CI)
Pancreatic or gastric cancer (very high risk tumors)	1.4 (0.72-2.9)	1.5 (0.72-2.9)	1.1 (0.54-2.2)	1.5 (0.72-2.9)
Lung, ovarian, or bladder cancer (high risk tumors)	1.1 (0.59-2.1)	1.0 (0.53-1.8)	0.66 (0.33-1.3)	1.1 (0.58-2.0)
Prechemotherapy hemoglobin <10 g/dL or use of erythropoietin stimulating agents	0.76 (0.32-1.8)	0.64 (0.27-1.6)	0.70 (0.28-1.7)	0.76 (0.31-1.8)
Prechemotherapy white blood cell count >11 x 10 <sup>9</sup> /L	0.87 (0.42-1.8)	0.82 (0.39-1.8)	0.77 (0.36-1.7)	0.86 (0.41-1.8)
Prechemotherapy platelet count ≥350 x 10 <sup>9</sup> /L	1.4 (0.80-2.4)	1.3 (0.71-2.2)	1.3 (0.74-2.3)	1.4 (0.8-2.4)
Body mass index >35 kg/m <sup>2</sup>	Not estimable*	Not estimable*	Not estimable*	-
D-dimer >1.44 g/L	-	2.4 (1.3-4.4)	-	-
Soluble P-selectin >53.1 g/L	-	1.5 (0.69-3.0)	-	-
Gemcitabine chemotherapy	-	-	3.7 (1.8-7.6)	-
Platinum-based chemotherapy	-	-	2.8 (1.4-5.6)	-
WHO-score ≥2	-	-	-	1.2 (0.5-2.9)

Abbreviations: CI, confidence interval; SHR, subdistribution hazard ratio; WHO, World Health Organization.

\* No events in patients with body mass index >35 kg/m<sup>2</sup>