

Supplementary data file – Table S1

Manuscript title: Cost-effectiveness analysis and budget impact of rivaroxaban in cancer patients at risk of recurrent venous thromboembolism

Table S1. Transition probabilities used in the cost-effectiveness model

	Rivaroxaban (95% CI)	LMWH (95% CI)	Distribution	Reference
Recurrent VTE				
0–6 months	0.040 (0.020 – 0.090)	0.110 (0.070 – 0.160)	Beta	[1]
6–12 months	0.040 (0.031 – 0.050)		Beta	[2]
1–2 years	0.034 (0.027 – 0.042)		Beta	[2]
2–3 years	0.021 (0.014 – 0.029)		Beta	[2]
3–4 years	0.016 (0.009 – 0.026)		Beta	[2]
4–5 months	0.013 (0.006 – 0.024)		Beta	[2]
Type of recurrent VTE				
Symptomatic PE	17.4% ($\alpha = 4, \beta = 19$)		Dirichlet	[1]
Incidental PE	30.4% ($\alpha = 7, \beta = 16$)		Dirichlet	[1]
DVT	43.5% ($\alpha = 10, \beta = 13$)		Dirichlet	[1]
Fatal PE	8.7% ($\alpha = 2, \beta = 21$)		Dirichlet	[1]
MB				
0–6 months	0.060 (0.030 – 0.110)	0.040 (0.020 – 0.080)	Beta	[1]
Beyond 6 months treatment	0.008 (0.006 – 0.010)		Beta	[3]
Type of MB				
ICH	10% ($\alpha = 5, \beta = 45$)		Dirichlet	[3]
Non-ICH MB	86% ($\alpha = 43, \beta = 7$)		Dirichlet	[3]
Fatal MB	4% ($\alpha = 2, \beta = 48$)		Dirichlet	[3]
CRNMB				
0–6 months	0.130 (0.090 – 0.190)	0.040 (0.020 – 0.090)	Beta	[1]
Beyond 6 months treatment	0.008 (0.006 – 0.010)		Beta	[3]
PTS				
0–6 months	0.015 (0.011 – 0.019)		Beta	[4]
6–12 months	0.012 (0.009 – 0.015)		Beta	[4]
12–18 months	0.008 (0.006 – 0.010)		Beta	[4]
18–24 months	0.025 (0.023 – 0.019)		Beta	[4]
24–30 months	0.011 (0.008 – 0.014)		Beta	[4]
30–36 months	0.006 (0.005 – 0.008)		Beta	[4]
3–4 years	0.001 (0.0008 – 0.0013)		Beta	[4]
4–5 years	0.001 (0.0008 – 0.0013)		Beta	[4]
CTEPH (annual risk)	0.0057 (0.0002 – 0.012)		Beta	[5]
Mortality (annual risk)				
0–1 years	0.230 (0.200 – 0.390)		Beta	[6]
1–2 years	0.104 (0.088 – 0.180)		Beta	[6]
2–3 years	0.058 (0.055 – 0.120)		Beta	[6]
3–4 years	0.046 (0.043 – 0.068)		Beta	[6]
4–5 years	0.032 (0.030 – 0.073)		Beta	[6]
Relative risk of recurrent VTE, MB, and CRNMB for LMWH versus placebo, used in scenario 5				
Recurrent VTE (any)	5.170		Fixed	[7]
MB	0.242		Fixed	[7]
CRNMB	1.000		Fixed	[7]

Drug-specific distribution of the type of VTE, used in scenario 6				
<i>Symptomatic PE</i>	28.6% ($\alpha = 2, \beta = 5$)	12.5% ($\alpha = 2, \beta = 14$)	Dirichlet	[1]
<i>Incidental PE</i>	14.3% ($\alpha = 1, \beta = 6$)	37.5% ($\alpha = 6, \beta = 10$)	Dirichlet	[1]
<i>DVT</i>	42.9% ($\alpha = 3, \beta = 4$)	43.8% ($\alpha = 7, \beta = 9$)	Dirichlet	[1]
<i>Fatal PE</i>	14.3% ($\alpha = 1, \beta = 6$)	6.3% ($\alpha = 1, \beta = 15$)	Dirichlet	[1]
Drug-specific distribution of the type of MB, used in scenario 6				
<i>ICH</i>	6.1% ($\alpha = 2, \beta = 31$)	17.6% ($\alpha = 3, \beta = 14$)	Dirichlet	[3]
<i>Non-ICH MB</i>	93.9% ($\alpha = 31, \beta = 2$)	70.6% ($\alpha = 12, \beta = 5$)	Dirichlet	[3]
<i>Fatal MB</i>	0% ($\alpha = 0, \beta = 33$)	11.8% ($\alpha = 2, \beta = 15$)	Dirichlet	[3]

Abbreviations: CI, confidence interval; CRNMB, clinically relevant non-major bleeding; CTEPH, chronic thromboembolic pulmonary hypertension; DVT, deep vein thrombosis; ICH, intracranial haemorrhage; LMWH, low-molecular weight heparin; MB, major bleeding; PE, pulmonary embolism; PTS, post-thrombotic syndrome; SE, standard error; VTE, venous thromboembolism

References

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Supplementary data file – Table S2

Manuscript title: Cost-effectiveness analysis and budget impact of rivaroxaban in cancer patients at risk of recurrent venous thromboembolism

Table S2. Costs included in the cost-effectiveness model (Euros, 2019)

	Value (95% CI)	Distribution	Reference
Event costs			
Recurrent VTE			
Symptomatic PE	€4,717 (€2,364 – €7,868)	Gamma	[1]
Incidental PE	€0	Fixed	Assumption
DVT	€663 (€464 – €862)	Gamma	[1]
Fatal recurrent VTE ^a	€4,717 (€2,364 – €7,868)	Gamma	[1]
ICH acute care costs	€22,769 (€11,644 – €31,175)	Gamma	[2]
ICH long-term costs (monthly)	€637 (€319 – €1,063)	Gamma	[1]
Non-ICH MB	€10,685 (€5,356 – €17,824)	Gamma	[1]
Fatal MB	€10,685 (€5,356 – €17,824)	Gamma	[1]
CRNMB	€274 (€137 – €457)	Gamma	[1]
PTS	€1,431 (€717 – €2,387)	Gamma	[1]
CTEPH acute care costs	€7,843 (€3,931 – €16,433)	Gamma	[1]
CTEPH long-term costs (monthly)	€89 (€45 – €149)	Gamma	[1]
Treatment costs			
Drug cost (daily)			
LMWH ^b	€9.93	Fixed	[3]
Rivaroxaban 15 mg	€4.58	Fixed	[3]
Rivaroxaban 20 mg	€2.29	Fixed	[3]
Treatment duration (days)			
LMWH	183 (137 – 228)	Gamma	[4]
Rivaroxaban 15 mg	21 (16 – 26)	Gamma	[4]
Rivaroxaban 20 mg	162 (121 – 202)	Gamma	[4]
LMWH administration costs			
Costs for home caregiver (per hour)	€59.34 (€44.51 – €74.18)	Gamma	[5]
Duration of at home administration (hour)	0.25 (0.19 – 0.31)	Gamma	Assumption
Hospitalisation duration PE (days) ^c	6.6 (5.0 – 8.3)	Gamma	[6]
Renal monitoring ^c	€1.64 (€1.23 – €2.05)	Gamma	[7]
Indirect costs			
Travel costs			
Cost per km	€0.20 (€0.15 – €0.25)	Gamma	[8]
Distance to hospital (km)	7	Fixed	[8]
Distance to GP (km)	1.1	Fixed	[8]
Informal care costs			
PE	€1,515 (€1,136 – €1,894)	Gamma	[5,9]
DVT	€233 (€175 – €291)	Gamma	[5,9]
ICH (acute informal care costs)	€1,515 (€1,136 – €1,894)	Gamma	[5,9]
ICH (long-term informal care costs, monthly)	€626 (€470 – €783)	Gamma	[10]
Non-ICH MB	€758 (€568 – €947)	Gamma	[5,9]
CRNMB	€117 (€87 – €146)	Gamma	[5,9]

Abbreviations: CI, confidence interval; CRNMB, clinically relevant non-major bleeding; CTEPH, chronic thromboembolic pulmonary hypertension; DVT, deep vein thrombosis; GP, general practitioner; ICH, intracranial haemorrhage; LMWH, low-molecular weight heparin; MB, major bleeding; PE, pulmonary embolism; PTS, post-thrombotic syndrome; VTE, venous thromboembolism

^a Assumed to be equal to the costs of non-fatal PE

^bBased on an average weight between 69 and 82 kg.

^cBased on DRG code 070419 and only taken into account for rivaroxaban treated patients

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Supplementary data file – Table S3

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Table S3. Utility values included in the cost-effectiveness model

	Value (95% CI)	Distribution	Reference
Utilities			
Index VTE			
0–1 month	0.565 (0.501 – 0.620)	Beta	[1]
1–2 months	0.655 (0.585 – 0.713)	Beta	[1]
2–3 months	0.674 (0.606 – 0.729)	Beta	[1]
3–4 months	0.698 (0.635 – 0.750)	Beta	[1]
4–5 months	0.707 (0.645 – 0.758)	Beta	[1]
Baseline utility 6 months after index VTE	0.715 (0.646 – 0.770)	Beta	[1]
Recurrent VTE			
DVT	0.605 (0.514 – 0.678)	Beta	[1]
Non-fatal symptomatic PE	0.621 (0.477 – 0.725)	Beta	[1]
Non-fatal incidental PE	0.664 (0.615 – 0.707)	Beta	[1]
Non-ICH MB	0.593 (0.461 – 0.693)	Beta	[1]
CRNMB	0.622 (0.568 – 0.669)	Beta	[1]
Utility decrements			
Recurrent VTE within first six months after index VTE			
DVT	0.040 (0.000 – 0.158)	Beta	[1]
Symptomatic PE	0.024 (0.000 – 0.195)	Beta	[1]
Incidental PE	0.189 (0.021 – 0.404)	Beta	[1]
ICH	0.380 (0.285 – 0.475)	Beta	[2]
Severe PTS (<6 months after diagnosis)	0.186 (0.090 – 0.280)	Beta	[1]
Severe PTS (>6 months after diagnosis)	0.070 (0.053 – 0.088)	Beta	[2]
CTEPH			
0-1 year	0.194 (0.071 – 0.303)	Beta	[3]
1–4 years	0.109 (0.000 – 0.244)	Beta	[3]
4–5 years	0.079 (0.000 – 0.277)	Beta	[3]

Abbreviations: CI, confidence interval; CRNMB, clinically relevant non-major bleeding; CTEPH, chronic thromboembolic pulmonary hypertension; DVT, deep vein thrombosis; ICH, intracranial haemorrhage; MB, major bleeding; PE, pulmonary embolism; PTS, post-thrombotic syndrome; VTE, venous thromboembolism

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Supplementary data file – Figure S1

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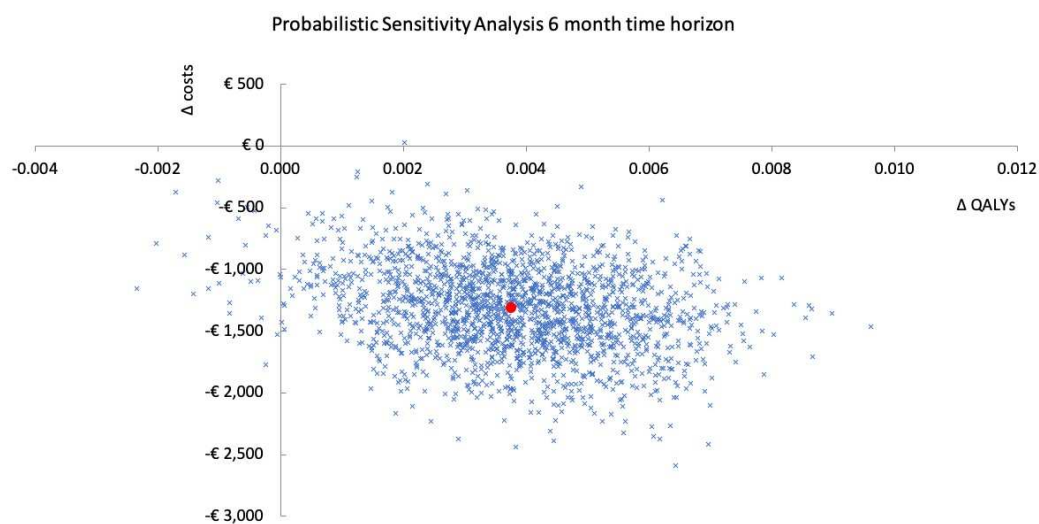


Figure S1. Probabilistic sensitivity analysis with six-month time horizon (scenario 1). The red mark represents the deterministic incremental cost-effectiveness ratio. Abbreviation: QALY, quality adjusted life-year

Supplementary data file – Figure S2

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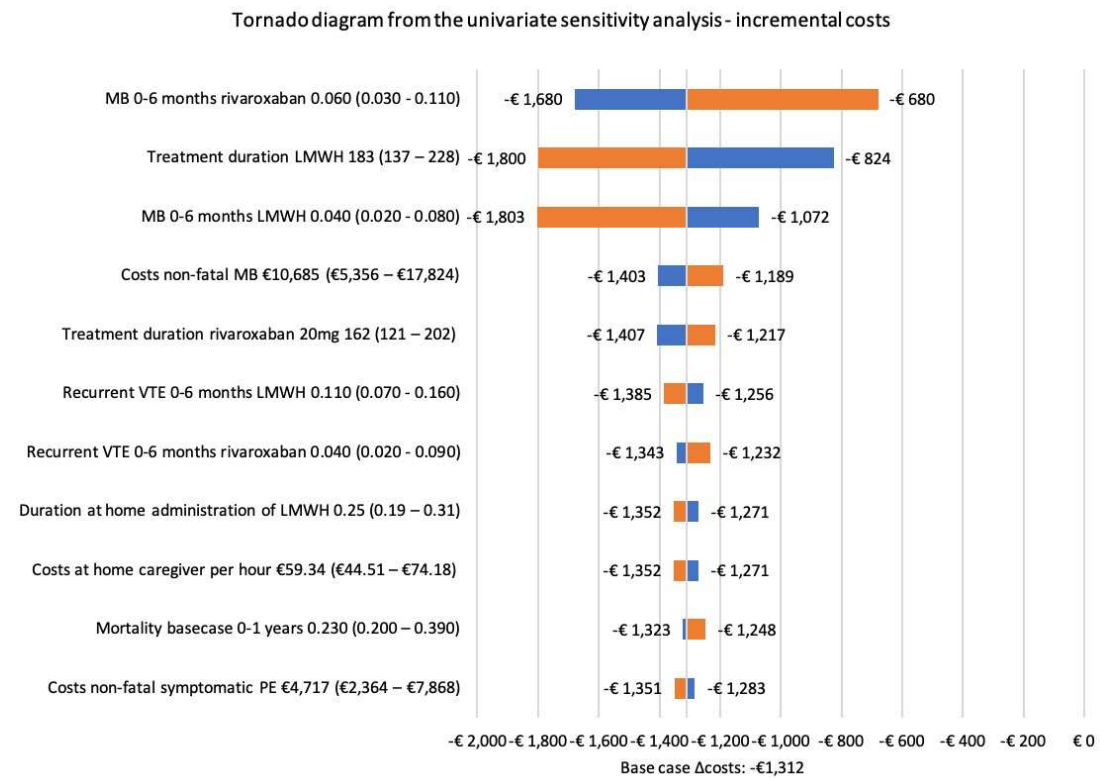


Figure S2. Tornado diagram from the univariate sensitivity analysis for scenario 1 showing the impact of parameters on the incremental costs. Abbreviations: MB, major bleeding; PE, pulmonary embolism; VTE, venous thromboembolism

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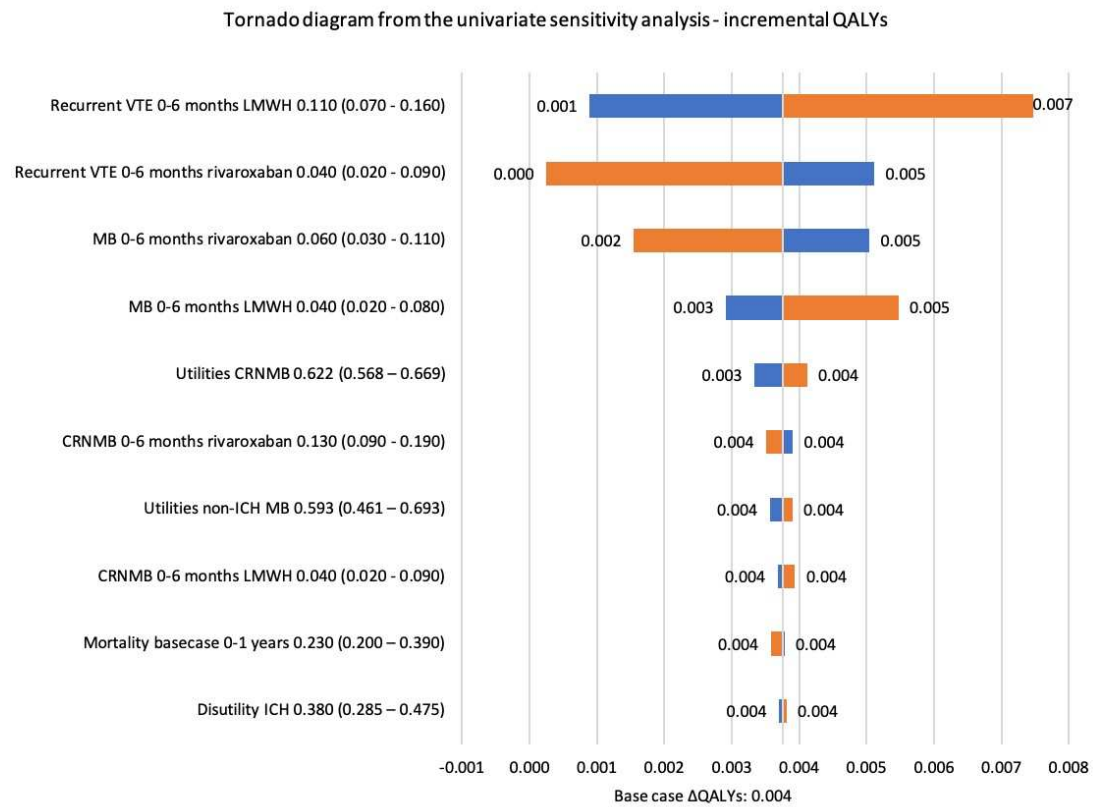


Figure S3. Tornado diagram from the univariate sensitivity analysis for scenario 1 showing the impact of parameters on the incremental QALYs. Abbreviations: CRNMB, clinically relevant non-major bleeding; ICH, intracranial haemorrhage; MB, major bleeding; PE, pulmonary embolism; VTE, venous thromboembolism