Supplementary material

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Cost-effectiveness analysis of rivaroxaban plus aspirin compared with aspirin alone in patients with coronary and peripheral artery diseases in Italy

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Table S1. Model Inputs

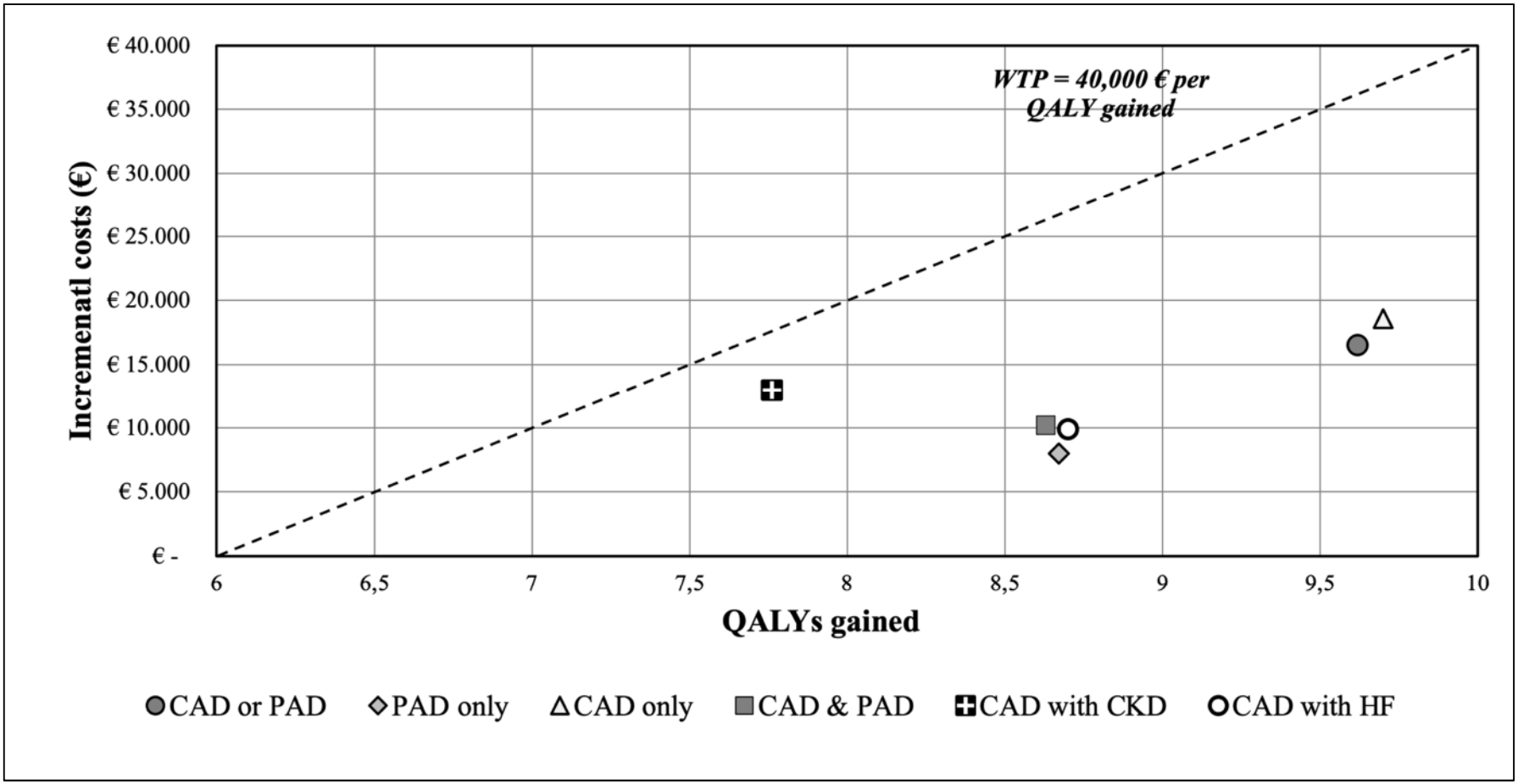
	Base case value	Range used in the DSA [lower case; higher case]	Distribution used in the PSA (distribution parameters)	Source
HRs (rivaroxaban 2.5mg/bid plus ASA vs. ASA alone)				
MI	0.86	[0.70;1.05]	Lognormal (-0.1508, 0.1034)	COMPASS 95% CI for DSA Lognormal distribution for PSA
IS	0.51	[0.38;0.69]	Lognormal (-0.6733;0.1522)	
ICH	1.16	[0.67;2.00]	Lognormal (0.1484;0.2790)	
CV death	0.78	[0.64;0.95]	Lognormal (-0.2485;0.1008)	
Fatal bleeding	1.49	[0.67;3.30]	Lognormal (0.3988;0.4067)	
ASA other events probabilities (3-month probability)				
Major extracranial non-fatal modified ISTH bleeding events	0.00217	[0.00184;0.00253]	Beta (153;70232)	COMPASS 95% CI of a Beta distribution for DSA Beta distribution for PSA
ALI	0.00064	[0.00047;0.00084]	Beta (45;70340)	
Minor amputation	0.00043	[0.00029;0.00059]	Beta (30;70355)	
Major amputation	0.00037	[0.00024;0.00052]	Beta (26;70359)	
VTE	0.00061	[0.00044;0.00081]	Beta (43;70342)	
HRs for other events for rivaroxaban 2.5mg/bid plus ASA vs. ASA alone				
ALI	0.55	[0.32;0.93]	Lognormal (-0.5978;0.2722)	COMPASS 95% CI for DSA Lognormal distribution for PSA
Minor amputation	0.65	[0.35;1.2]	Lognormal (-0.4308;0.3143)	
Major amputation	0.57	[0.30;1.09]	Lognormal (-0.5621;0.3291)	
VTE	0.61	[0.37;1.00]	Lognormal (-0.4943;0.2536)	
Major extracranial non-fatal bleeds	1.79	[1.46;2.19]	Lognormal (0.5822;0.1034)	
Medication costs (daily cost)				
ASA	€0.05	Not included	Not included	

	Base case value	Range used in the DSA [lower case; higher case]	Distribution used in the PSA (distribution parameters)	Source
Rivaroxaban	€2.09	Not included	Not included	Formulary of the Italian Agency of Medicine (AIFA)
Health state costs (per 3-month cycle)				
Event-free	€0.0	Not included	Not included	
Acute MI	€7544.70	[5281.30;9808.10]	Gamma (7544.70;496.95)	DRG, Italian diagnosis-related group tariff; Mantovani et al. [1]; Lucchese et al. [2] +/- 30% for DSA Gamma distribution for PSA
Post-acute MI	€979.80	[685.09;1273.70]	Gamma (979.80;41.05)	
Acute IS	€6164.50	[4315.20;8013.90]	Gamma (6164.50;1213.77)	
Post-IS	€1855.50	[1298.90;2412.20]	Gamma (1855.50;237.20)	
Acute ICH	€3891.00	[2723.70;5058.30]	Gamma (3891.00;2241.80)	
Health event costs for the 3 first months				
ALI	€2199.00	[1539.30;2858.70]	Gamma (2199.00;534.13)	DRG, Italian diagnosis-related group tariff; Marone et al. [3]. +/- 30% for DSA Gamma distribution for PSA
Minor amputation	€6056.00	[4239.20;7872.80]	Gamma (6056.00;793.60)	
Major amputation	€13947.70	[9763.40;18132.00]	Gamma (13947.70;2199.32)	
VTE	€2315.00	[1620.50;3009.50]	Gamma (2315.00;154.70)	
Major non-fatal extracranial bleeds	€2091.00	[1463.70;2718.30]	Gamma (2091.00;123.84)	
Utilities				
Event-free	0.835	[0.752;0.919]	Beta (0.835;0.050)	COMPASS EQ-5D +/- 10% for DSA Beta distribution for PSA
Acute MI	0.784	[0.706;0.862]	Beta (0.784;0.043)	
Post MI	0.807	[0.726;0.888]	Beta (0.807;0.047)	
Acute IS	0.647	[0.582;0.712]	Beta (0.647;0.037)	
Post IS	0.743	[0.669;0.817]	Beta (0.743;0.044)	
Acute ICH	0.702	[0.632;0.772]	Beta (0.702;0.037)	

	Base case value	**Range used in the DSA** [lower case; higher case]	**Distribution used in the PSA** (distribution parameters)	**Source**
Post ICH	0.755	[0.680;0.831]	Beta (0.755;0.044)	
Utility decrements				
ALI (1 cycle)	-0.157	[-0.141;-0.173]	-Beta (-0.157;0.009)	COMPASS EQ-5D +/- 10% for DSA Inverted beta (-beta) distribution for PSA
Minor amputation (each cycle)	-0.100	[-0.090;-0.110]	-Beta (-0.100;0.006)	
Major amputation (each cycle)	-0.175	[-0.158;-0.193]	-Beta (-0.175;0.013)	
VTE (1 cycle)	-0.111	[-0.100;-0.122]	-Beta (-0.111;0.006)	
Major extracranial non-fatal bleeds (1 cycle)	-0.019	[-0.017;-0.021]	-Beta (-0.019;0.001)	

DSA, deterministic sensitivity analyses; *PSA*, probabilistic sensitivity analyses; *ASA*, acetylsalicylic acid; *HR*, hazard ratio; *CI*, confidence interval; *CV*, cardiovascular; *ALI*, acute limb ischaemia; *ICH*, intracranial haemorrhage; *IS*, ischaemic stroke; *MI*, myocardial infarction; *VTE*, venous thromboembolism; *EQ-5D*, EuroQol-5D tool

Figure S1. Cost-effectiveness results plane



CAD, coronary artery disease; *PAD*, peripheral arterial disease; *CKD*, chronical kidney disease; *HF*, heart failure; *QALYs*, quality-adjusted life years; WTP; willingness to pay threshold.

References:

1. Mantovani LG, Fornari C, Madotto F, et al. Burden of acute myocardial infarction. International Journal of Cardiology 2011;150(1):111-2.

2. Lucchese M, Borisenko O, Mantovani LG, et al. Cost-Utility Analysis of Bariatric Surgery in Italy: Results of Decision-Analytic Modelling. Obes Facts. 2017; 10(3): 261-72.

3. Marone EM, Cozzolino P, Ciampichini R, et al. Peripheral arterial disease in diabetic patients: a long-term population-based study on occurrence, outcomes and cost. J Cardiovasc Surg (Torino). 2018;59(4):572-579.