Appendices

Appendix A: Parameters used in model

	Category	Description	References
Risks/Probabilities	Death from other causes	Nonparametric	UK Lifetables. [18]
	Sensitivity and Specificity of TTE in detecting ABN	Jointly estimated from Dirichlet distribution (FN, TP, TN, FP) = (5, 87, 83, 159)	Table 2 of Providencia et al 2012 [6]
	Proportion of patients with ABN	Beta(2.5, 22.5) for $CHADS_2$ Beta(0.5, 11.5) for CHA_2DS_2-VASc (Both with prior of 0.5 added to both cell counts.)	Table 2 of Providencia et al 2012 [6]
	Annual stroke risk by $CHADS_2$ score	Annual risks (95% Credible intervals) by $CHADS_2$ were reported as follows: 0.6% (0.5% to 0.7%) for $CHADS_2$=0 3.0% (2.9% to 3.2%) for $CHADS_2$=1 4.2% (4.0% to 4.4%) for $CHADS_2$=2 7.1% (6.7% to 7.5%) for $CHADS_2$=3 11.1% (10.4% to 11.8%) for $CHADS_2$=4	Friberg 2012[21]
	Annual stroke risk in those with ABN	In the initial study four out of 50 patients with identified ABN had a stroke. This was used to produce a mean stroke rate of 8.0% and bootstrapped 95% CrIs of 7.2% to 8.2%	Stroke Prevention 1988 [5]

	Relative risk (RR) of stroke in patients receiving dabigatran.	Indirect comparison simulation approach. One thousand simulated values from a lognormal distribution representing the RR of warfarin compared with placebo were multiplied by 1000 simulated values from a lognormal distribution comparing dabigatran with warfarin, to produce 1000 estimates of the RR of dabigatran compared with placebo. Mean RRs and 95% CIs/CrIs are shown below: Reported RR warfarin vs. placebo: 0.33 (0.24 to 0.45) Reported RR dabigatran vs. warfarin: 0.66 (0.53 to 0.82) Derived RR dabigatran vs. placebo: 0.22 (0.15 to 0.32)	Lip et al 2006 for RR of warfarin compared with placebo [22] Eikelboom et al 2011 for RR of dabigatran compared with warfarin[14]
	Annual major bleeding risk for patients receiving dabigatran	Stratified by age. Credible interval calculated using simulation approach. Annual risk reported separately for people under 75 years, and people aged 75 years or older. Credible intervals were calculated by assuming sample sizes of 3618 for people aged under 75 years and 2419 for people aged 75 years or older, then sampling repeatedly and taking the values 2.5% and 97.5% of the way along the distributions. The central estimates	Eikelboom et al 2011 [14]

		(95% CrIs) are as follows: Under 75: 2.1% (1.7 to 2.6%) 75 and older: 5.1% (4.2% to 6.0%)	
	Relative risk (RR) of stroke in patients receiving warfarin	Reported RR warfarin vs. placebo: 0.33 (0.24 to 0.45)	Lip et al 2006 [22]
	Annual major bleeding risk for patients receiving warfarin	Stratified by age. Credible interval calculated using simulation approach. Annual risk reported separately for people under 75 years, and people aged 75 years or older. Credible intervals were calculated by assuming sample sizes of 3618 for people aged under 75 years and 2419 for people aged 75 years or older, then sampling repeatedly and taking the values 2.5% and 97.5% of the way along the distributions. The central estimates (95% CrIs) are as follows: Under 75: 3.4% (2.5 to 3.6%) 75 and older: 4.4% (3.6% to 5.2%)	Eikelboom et al 2011 [14]
	Relative risk (RR) of stroke in patients receiving rivaroxaban	Indirect comparison simulation approach. One thousand simulated values from a lognormal distribution representing the RR of warfarin compared with placebo were multiplied by 1000 simulated values from a lognormal distribution comparing dabigatran with warfarin, to produce 1000 estimates of the RR of dabigatran compared	Lip et al 2006 for RR of warfarin compared with placebo [22] Patel et al 2011 for RR of rivaroxaban compared with warfarin [23]

		with placebo. Mean RRs and 95% CIs/CrIs are shown below: Reported RR warfarin vs. placebo: 0.33 (0.24 to 0.45) Reported RR Rivaroxaban vs. warfarin: 0.88 (0.74 to 1.03) Derived RR Rivaroxaban vs. placebo: 0.30 (0.20 to 0.41)	
	Annual major bleeding risk for patients receiving rivaroxaban	The annual risk of bleeding given rivaroxaban was estimated indirectly by combining estimates of the risk of bleed given warfarin compared with placebo with estimates of the risk of bleed given rivaroxiban compared with warfarin. The central estimates (95% CrIs) were estimated to be as follows: Under 75: 3.2% (2.5% to 4.0%) 75 or older: 4.6% (3.6% to 5.7%)	Eikelboom et al 2011 [14] Patel et al 2011 [23]
	Outcome following stroke	Simulation & mapping based approach described in an upcoming report. The proportion dying of a stroke (95% CrI) was estimated to be 0.25 (0.23 to 0.27); the proportion in an independent state was estimated to be 0.56 (0.52 to 0.59); and the proportion in an dependent state following a	Method described in report using results published in Rivero-Arias et al 2010 [24]

		stroke was estimated to be 0.19 (0.16 to 0.23).	
	Outcome following a major bleeding event	Previous estimates.	Simpson et al 2010 [25]
Utilities	Baseline utilities by age and gender	Regression based approach, described in full in the reference. HRQoL is estimated as a function of age and gender, using the equation for the general population.	Ara et al 2010 [26]
	Utility multiplier following stroke, utility multiplier following major non-fatal intracranial bleed	Simulation & mapping based approach described in an upcoming report. Utility multipliers (95% CrIs) were estimated to be 0.822 (0.819 to 0.824) for an independent state following a stroke, and 0.482 (0.477 to 0.487) for a dependent state following a stroke.	Method described in report results published in Rivero-Arias et al 2010 [24] See Table 2 for assumed mapping between Glasgow Outcome Scale (GOS) states and modified Rankin Scale (mRS) scores, and estimated utility multipliers associated with each state.
Costs	Annual cost of dabigatran	£920. A fixed cost was assumed.	NICE FAD, 2011 [27]
	Annual cost of rivaroxaban	£767. A fixed cost was assumed.	London New Drugs Group [28]
	Annual cost of warfarin	£252 to £259 including monitoring costs. A uniform distribution was assumed.	BNF [29]
	Cost of TTE	£66	NHS Reference Costs [19]
	Cost of death due to stroke	£7,019 (95% CrI £6,975 to £7,064)	Sandercock et al 2002 [30]
	Costs in stroke survivors	Various. Differing according to dependent and independent states. Subdivided into one-off and	NHS Reference Costs [19] NHS Stroke Strategy Impact Assessment [31]

		continuing costs. Estimates (95% CrIs) are as follows: Dependent stroke, one-off costs: £2830 (£2708 to £2952) Dependent stroke, continuing annual cost: £6386 (£5749 to £7023) Independent stroke, one-off costs: £542 (£513 to £571) Independent stroke, continuing annual cost: £3195 (£2871 to £3518)	Unit Costs of Health and Social Care 2010 [32]
	Costs of fatal bleed	Assumed identical to costs of death due to stroke	
	Costs of nonfatal bleed	Major bleeds subdivided into gastrointestinal (GI) and intracranial (IC). GI bleeds were assumed to incur a one-off cost but no continuing costs. The one-off cost (95% CrI) was £1261 (£1212 to £1310). For IC bleeds, the costs depended on the Glasgow Outcome Scale (GOS) level of disability that they cause, from GOS 2 (most severe) to GOS 5 (least severe). The one-off costs (95% CrIs) used were as follows: GOS 2: £46785 (£40895 to £53250) GOS 3: £10096 (£8849 to £11363) GOS 4: £27419 (£22582 to £32964)	NHS Reference Costs [19]

		GOS 5: £1261 (£1211 to £1309) GOS 4 and GOS 5 states were assumed not to have ongoing costs. The ongoing annual costs (95% CrIs) of the other states were as follows: GOS 2: £50047 (£49645 to £50343) GOS 3: £33949 (£33843 to £33969)	

Table 1 Parameters used in model

GOS state	Assumed equivalent to	Utility multiplier
GOS 2: vegetative state	mRS 6: dead	0
GOS 3: severely disabled	mRS 4: moderately severely disabled; and mRS 5: severely disabled	0.226 (95% CI 0.221 to 0.231)
GOS 4: moderately disabled	mRS 2: slight disability *and* mRS 3: moderate disability	0.642 (95% CI 0.638 to 0.645)
GOS 5: good recovery	mRS 0: no symptoms *and* mRS 1: no significant disability	0.895 (95% CI 0.892 to 0.898)

Table 2 Assumed relationship between GOS and mRS, and estimated utility multipliers for each GOS state

Appendix B: Sensitivity and Specificity tables

The tables below show how the mean ICER of the TTE compared with the No TTE strategy varies for each of 121 joint configurations of TTE sensitivity and specificity. D indicates that the TTE strategy is dominated by the No TTE strategy. Numbers show the ICER to the nearest £1000 (i.e. 19.2 refers to an ICER of £19 200/QALY). The code in the top left of each table refers to the patient population and OAC strategy under evaluation. (For example, W_65_0_M refers to 65 year old males with warfarin as the OAC of choice.)

W_50 0_M		*Specificity*										
		0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
Sensitivity	**0**	D	D	D	D	D	D	D	D	D	D	∞
	0.1	D	D	D	D	D	D	D	D	D	D	8.4
	0.2	D	D	D	D	D	D	D	D	D	D	5.7
	0.3	D	D	D	D	D	D	D	D	D	70.7	4.9
	0.4	D	D	D	D	D	D	D	D	D	26.2	4.4
	0.5	D	D	D	D	D	D	D	D	>99	17.1	4.2
	0.6	D	D	D	D	D	D	D	D	65.6	13.1	4.0
	0.7	D	D	D	D	D	D	D	D	35.0	10.9	3.8
	0.8	D	D	D	D	D	D	D	>99	24.5	9.5	3.8
	0.9	D	D	D	D	D	D	D	63.9	19.2	8.5	3.7
	1	D	D	D	D	D	D	>99	40.2	16.0	7.8	3.6

a) W_50_0_M

W_65 0_M		*Specificity*										
		0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
Sensitivity	**0**	D	D	D	D	D	D	D	D	D	D	∞
	0.1	D	D	D	D	D	D	D	D	D	D	8.9
	0.2	D	D	D	D	D	D	D	D	D	29.8	4.9
	0.3	D	D	D	D	D	D	D	D	62.8	13.9	3.6
	0.4	D	D	D	D	D	D	D	>99	25.0	9.3	2.9
	0.5	D	D	D	D	D	D	>99	38.8	15.9	7.1	2.5
	0.6	D	D	D	D	D	>99	56.6	23.4	11.8	5.8	2.3
	0.7	D	D	D	D	D	80.4	32.1	16.9	9.4	5.0	2.1
	0.8	D	D	D	D	>99	42.3	22.6	13.3	7.9	4.4	1.9
	0.9	D	D	D	>99	54.5	28.9	17.5	11.0	6.9	4.0	1.8
	1	D	D	>99	69.3	36.1	22.1	14.4	9.5	6.1	3.6	1.7

b) W_65_0_M

W_65 0_F		Specificity										
		0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
Sensitivity	**0**	D	D	D	D	D	D	D	D	D	D	∞
	0.1	D	D	D	D	D	D	D	D	D	>99	8.1
	0.2	D	D	D	D	D	D	D	D	>99	24.4	4.6
	0.3	D	D	D	D	D	D	D	>99	39.8	12.9	3.4

	0.4	D	D	D	D	D	D	>99	54.5	21.0	9.0	2.8
	0.5	D	D	D	D	D	>99	68.6	28.8	14.4	7.0	2.5
	0.6	D	D	D	D	>99	82.0	36.5	19.8	11.1	5.8	2.3
	0.7	D	D	D	>99	94.7	44.1	25.1	15.2	9.1	5.0	2.1
	0.8	D	D	>99	>99	51.4	30.3	19.2	12.4	7.8	4.5	2.0
	0.9	D	>99	>99	58.4	35.4	23.2	15.7	10.6	6.9	4.1	1.9
	1	>99	>99	65.4	40.4	27.1	18.9	13.3	9.2	6.1	3.7	1.8

c) W_65_0_F

R_50 0_M		*Sensitivity*										
		0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
Specificity	**0**	D	D	D	D	D	D	D	D	D	D	∞
	0.1	D	D	D	D	D	D	D	D	D	D	7.5
	0.2	D	D	D	D	D	D	D	D	D	D	5.1
	0.3	D	D	D	D	D	D	D	D	D	38.2	4.3
	0.4	D	D	D	D	D	D	D	D	D	19.0	3.9
	0.5	D	D	D	D	D	D	D	D	82.0	13.3	3.6
	0.6	D	D	D	D	D	D	D	D	35.4	10.5	3.5
	0.7	D	D	D	D	D	D	D	>99	23.2	8.9	3.3
	0.8	D	D	D	D	D	D	D	54.8	17.7	7.8	3.2
	0.9	D	D	D	D	D	D	>99	34.4	14.5	7.1	3.2
	1	D	D	D	D	D	D	78.5	25.5	12.4	6.5	3.1

d) R_50_0_M

R_50 0_F		*Sensitivity*										
		0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
Specificity	**0**	D	D	D	D	D	D	D	D	D	D	∞
	0.1	D	D	D	D	D	D	D	D	D	D	7.5
	0.2	D	D	D	D	D	D	D	D	D	D	5.2
	0.3	D	D	D	D	D	D	D	D	D	35.2	4.4
	0.4	D	D	D	D	D	D	D	D	D	19.1	4.0
	0.5	D	D	D	D	D	D	D	D	63.0	13.7	3.8
	0.6	D	D	D	D	D	D	D	D	32.9	11.0	3.7
	0.7	D	D	D	D	D	D	D	90.7	22.9	9.4	3.6
	0.8	D	D	D	D	D	D	D	46.8	17.9	8.3	3.5
	0.9	D	D	D	D	D	D	>99	32.2	14.9	7.5	3.4
	1	D	D	D	D	D	D	60.7	24.8	12.9	6.9	3.4

e) R_50_0_F

R_65 0_M		*Sensitivity*										
		0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
Specificity	**0**	D	D	D	D	D	D	D	D	D	D	∞
	0.1	D	D	D	D	D	D	D	D	D	>99	8.0
	0.2	D	D	D	D	D	D	D	D	>99	20.4	4.4
	0.3	D	D	D	D	D	D	D	>99	31.5	10.8	3.1
	0.4	D	D	D	D	D	D	>99	41.5	16.9	7.5	2.5
	0.5	D	D	D	D	D	>99	50.7	22.7	11.7	5.8	2.2

	0.6	D	D	D	D	>99	59.1	28.2	15.7	9.0	4.8	1.9
	0.7	D	D	D	>99	66.7	33.4	19.6	12.1	7.4	4.1	1.7
	0.8	D	D	>99	73.8	38.4	23.4	15.2	9.9	6.3	3.6	1.6
	0.9	D	>99	80.3	43.2	27.1	18.1	12.4	8.4	5.5	3.3	1.5
	1	>99	86.3	47.7	30.6	21.0	14.8	10.5	7.3	4.9	3.0	1.4

f) R_65_0_M

R_65 0_F		*Sensitivity*										
		0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
Specificity	**0**	D	D	D	D	D	D	D	D	D	D	∞
	0.1	D	D	D	D	D	D	D	D	D	77.0	7.3
	0.2	D	D	D	D	D	D	D	D	65.3	17.4	4.1
	0.3	D	D	D	D	D	D	>99	61.4	23.9	10.1	3.0
	0.4	D	D	D	D	D	>99	59.5	28.4	14.8	7.3	2.4
	0.5	D	D	D	D	>99	58.3	31.7	18.6	10.9	5.8	2.1
	0.6	D	D	>99	>99	57.5	34.2	21.8	14.0	8.7	4.8	1.9
	0.7	D	>99	>99	57.0	36.3	24.4	16.7	11.3	7.3	4.2	1.7
	0.8	>99	93.2	56.6	37.9	26.6	19.0	13.6	9.5	6.3	3.7	1.6
	0.9	87.0	56.2	39.3	28.5	21.1	15.6	11.5	8.2	5.6	3.4	1.5
	1	56.0	40.4	30.1	22.9	17.5	13.3	10.0	7.3	5.0	3.1	1.5

g) R_65_0_F

D_65 0_M		*Sensitivity*										
		0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
Specificity	**0**	D	D	D	D	D	D	D	D	D	D	∞
	0.1	D	D	D	D	D	D	D	D	D	44.1	6.8
	0.2	D	D	D	D	D	D	D	>99	36.0	12.8	3.6
	0.3	D	D	D	D	D	>99	84.7	33.4	16.2	7.6	2.5
	0.4	D	D	D	D	>99	62.0	32.0	18.3	10.5	5.5	1.9
	0.5	D	D	>99	>99	52.3	31.2	19.8	12.7	7.9	4.3	1.6
	0.6	>99	>99	79.3	46.9	30.7	20.9	14.4	9.8	6.3	3.6	1.4
	0.7	>99	66.5	43.5	30.3	21.8	15.8	11.4	8.0	5.3	3.1	1.2
	0.8	58.8	41.1	30.0	22.4	16.9	12.7	9.4	6.7	4.5	2.7	1.1
	0.9	39.3	29.8	22.9	17.8	13.8	10.6	8.0	5.8	4.0	2.4	1.0
	1	29.6	23.4	18.6	14.8	11.7	9.2	7.0	5.2	3.6	2.2	1.0

h) D_65_0_M

D_65 0_F		*Sensitivity*										
		0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1**
Specificity	**0**	D	D	D	D	D	D	D	D	D	D	∞
	0.1	D	D	D	D	D	D	D	D	>99	28.3	6.2
	0.2	D	D	D	D	D	>99	>99	46.8	23.8	11.2	3.3
	0.3	D	D	>99	>99	99.6	57.0	35.4	22.2	13.4	7.1	2.4
	0.4	>99	>99	97.7	63.5	43.6	30.6	21.5	14.7	9.5	5.3	1.9
	0.5	96.6	67.9	49.8	37.2	28.0	21.0	15.5	11.0	7.4	4.3	1.6

		0.6	54.5	42.5	33.5	26.4	20.7	16.1	12.2	8.9	6.1	3.6	1.4
		0.7	38.1	31.0	25.3	20.5	16.5	13.0	10.1	7.5	5.2	3.1	1.3
		0.8	29.3	24.5	20.4	16.8	13.7	11.0	8.6	6.4	4.5	2.8	1.2
		0.9	23.9	20.2	17.1	14.3	11.8	9.5	7.5	5.7	4.0	2.5	1.1
		1	20.1	17.3	14.7	12.4	10.3	8.4	6.7	5.1	3.6	2.3	1.1
i) D_65_0_F													

Table 3 Effect of assumed sensitivity and specificity of device on estimated cost effectiveness. D: dabigatran; W: Warfarin; R: rivaroxaban; M: Male; F: Female; 65: 65 years old; 50: 50 years old

Appendix C: Simulated clinical outcomes

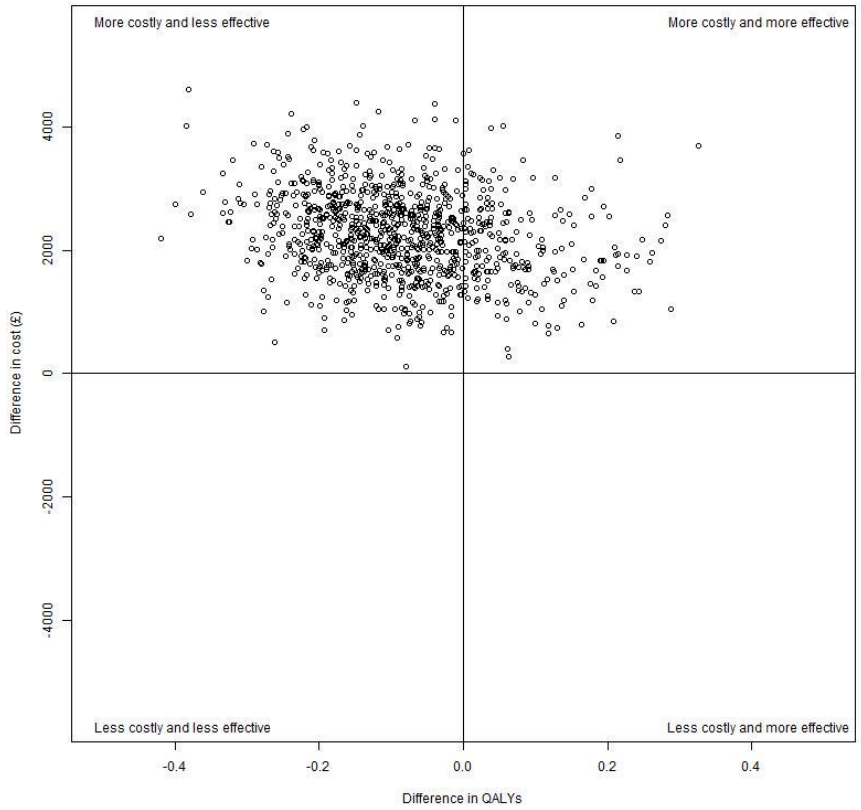
Introduction

This appendix shows the simulated clinical outcomes for each of the patient, OAC and TTE strategies which were simulated. Values are presented to as many decimal places as are required to show differences in outcomes. Two different ages at diagnosis were simulated: aged 65 at diagnosis, and aged 50 years at diagnosis. All patients were assumed to have a $CHADS_2$ score of zero at diagnosis.

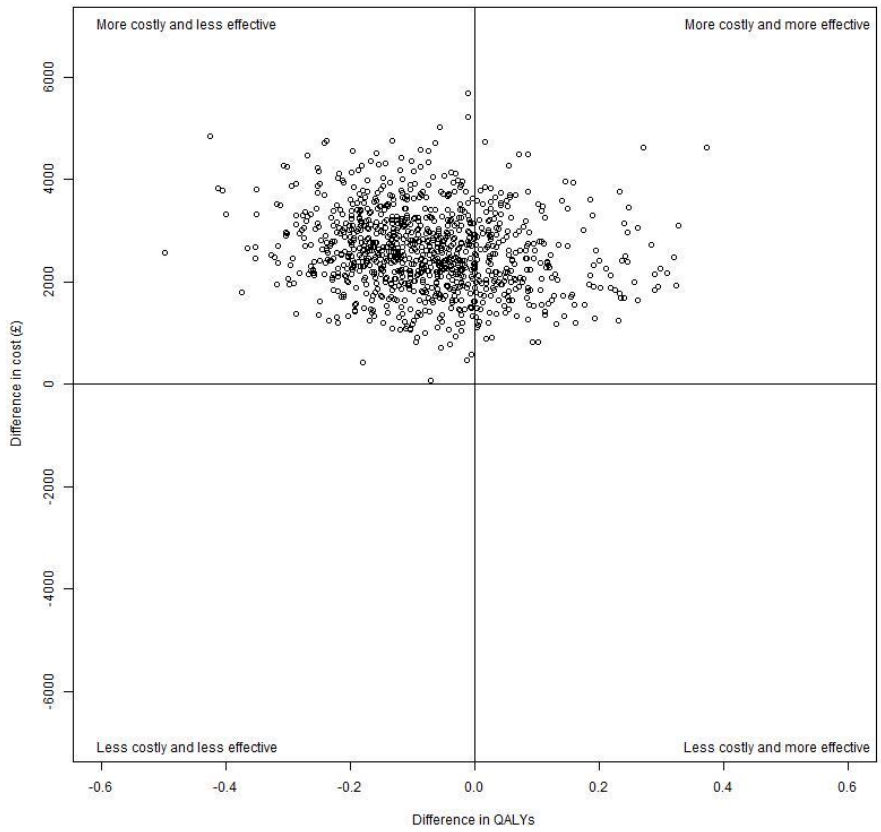
				Cause of Death (%)			*Average Number of Events*			
OAC	*Patient population*	*Strategy*	Life Years	Stroke	Bleed	Other	Dependent Strokes	Independent Strokes	ICH	NICH
Warfarin	Male, 50 years old	Without TTE	28.840	11.7	1.3	87.1	0.120	0.242	0.010	0.075
		With TTE	28.928	10.8	1.8	87.4	0.111	0.223	0.014	0.112
	Female, 50 years old	Without TTE	31.633	13.5	1.6	84.9	0.139	0.278	0.012	0.091
		With TTE	31.734	12.6	2.1	85.2	0.130	0.259	0.017	0.130
	Male, 65 years old	Without TTE	17.131	9.0	0.9	90.2	0.087	0.192	0.007	0.052
		With TTE	17.204	8.0	1.3	90.7	0.078	0.172	0.010	0.079
	Female, 65 years old	Without TTE	19.447	10.6	1.1	88.3	0.105	0.225	0.009	0.065
		With TTE	19.531	9.6	1.6	88.8	0.096	0.205	0.012	0.095
Rivaroxaban	Male, 50 years old	Without TTE	28.861	11.5	1.3	87.2	0.117	0.239	0.010	0.075
		With TTE	28.963	10.5	1.8	87.6	0.108	0.219	0.014	0.113
	Female, 50 years old	Without TTE	31.657	13.3	1.6	85.1	0.136	0.275	0.012	0.091
		With TTE	31.772	12.4	2.1	85.5	0.127	0.255	0.017	0.130
	Male, 65 years old	Without TTE	17.141	8.8	0.9	90.3	0.085	0.190	0.007	0.052
		With TTE	17.221	7.8	1.3	90.9	0.076	0.169	0.010	0.080
	Female, 65 years old	Without TTE	19.460	10.5	1.1	88.4	0.103	0.223	0.009	0.066
		With TTE	19.554	9.4	1.6	89.0	0.093	0.201	0.012	0.096
Dabigatran	Male, 65 years old	Without TTE	17.158	8.6	0.9	90.5	0.081	0.188	0.007	0.053
	Female, 65 years old	With TTE	17.251	7.5	1.3	91.2	0.072	0.163	0.010	0.081

Table 4 Simulated Clinical Outcomes

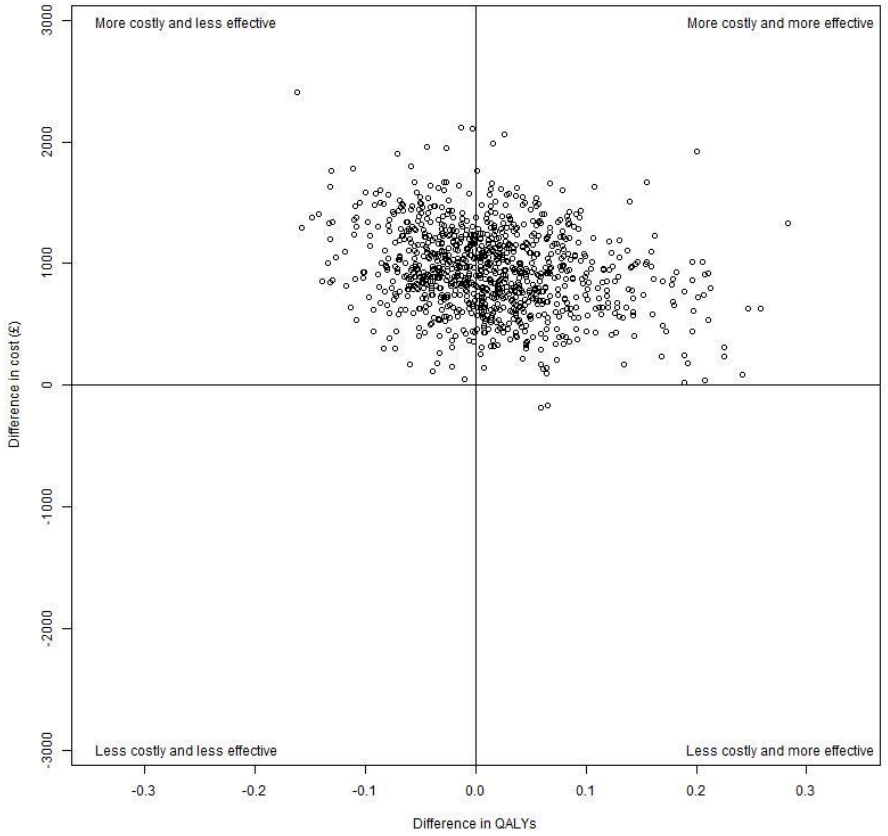
Appendix D: Scatterplots of estimated difference in costs and health outcomes from probabilistic sensitivity analysis



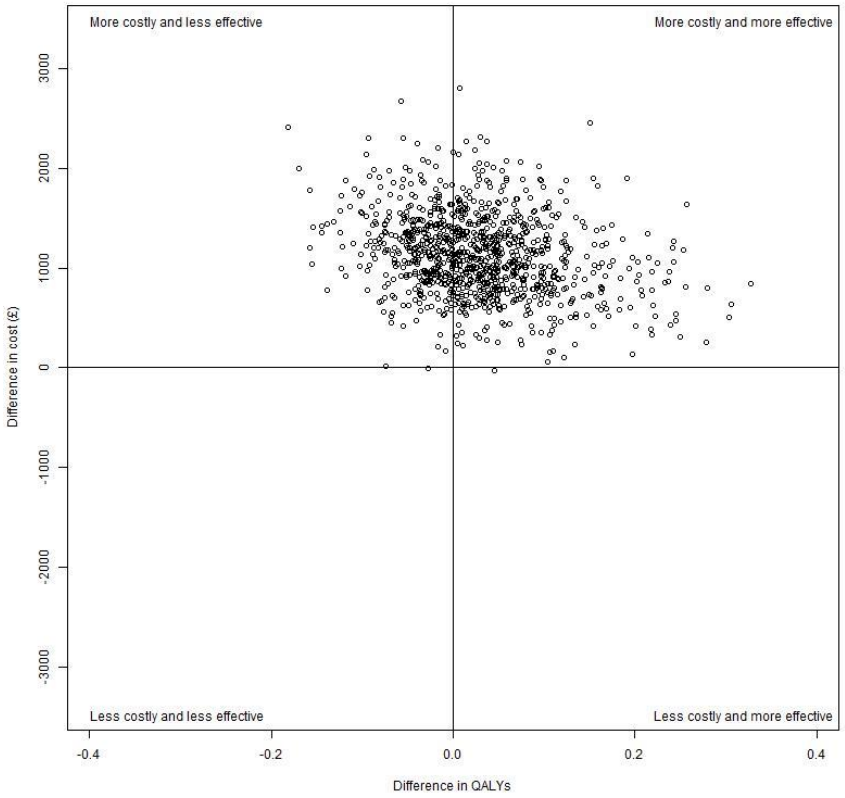
a) Warfarin, 50 years old, males



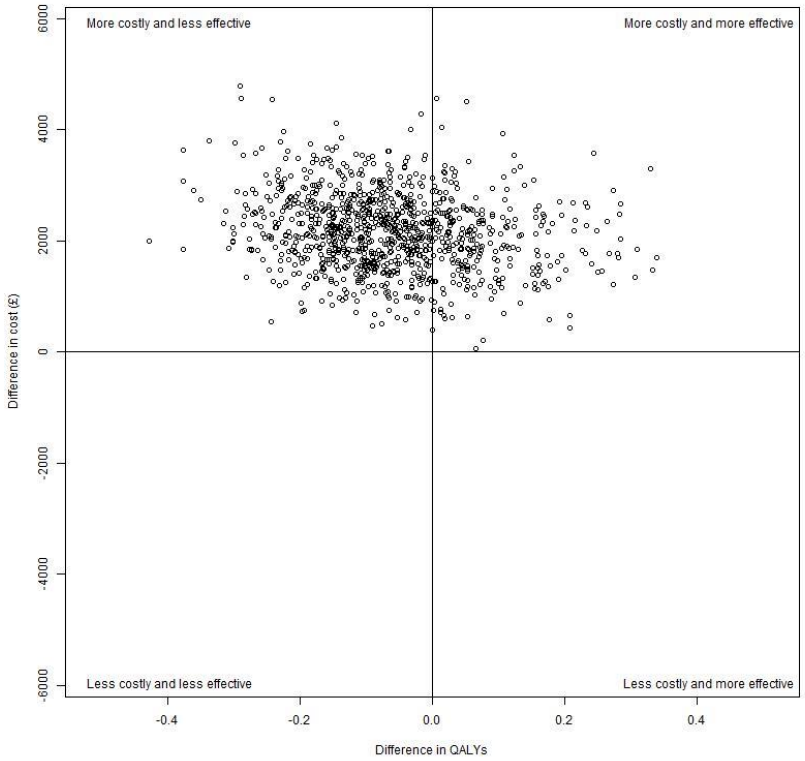
b) Warfarin, 50 years old, females



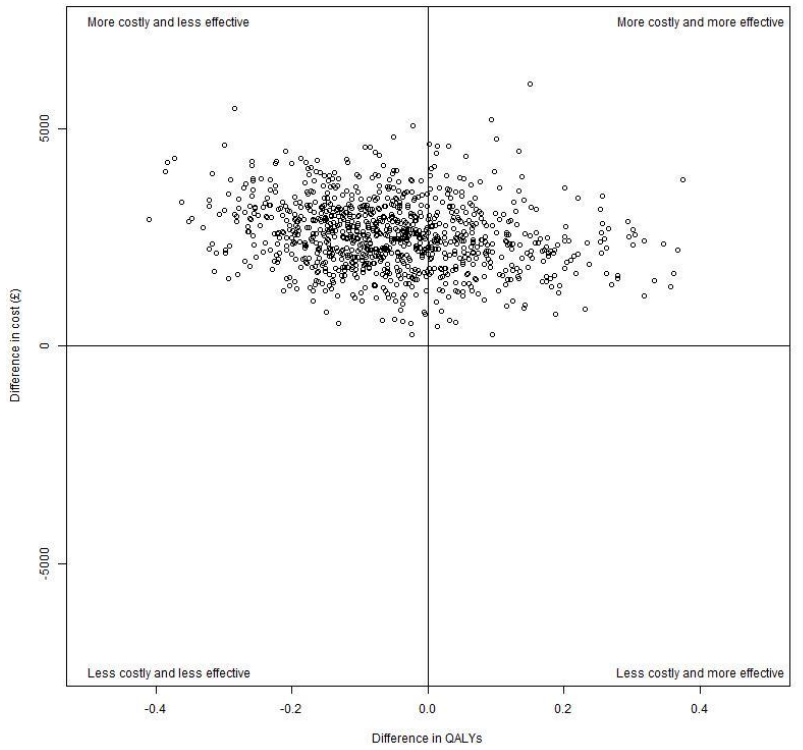
c) Warfarin, 65 years old, males



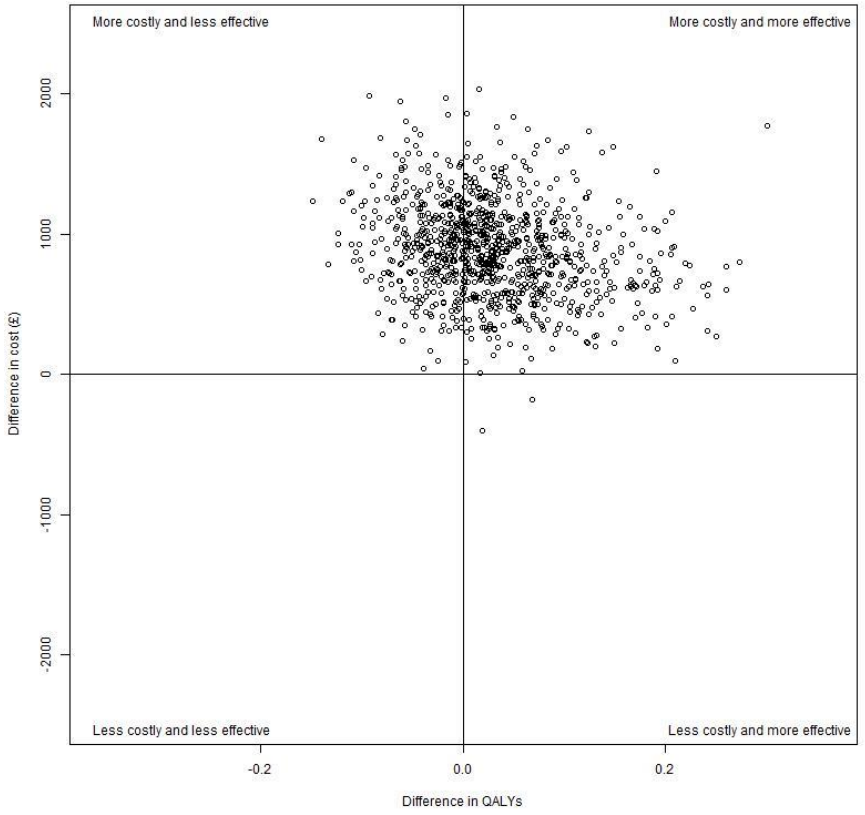
d) Warfarin, 65 years old, females



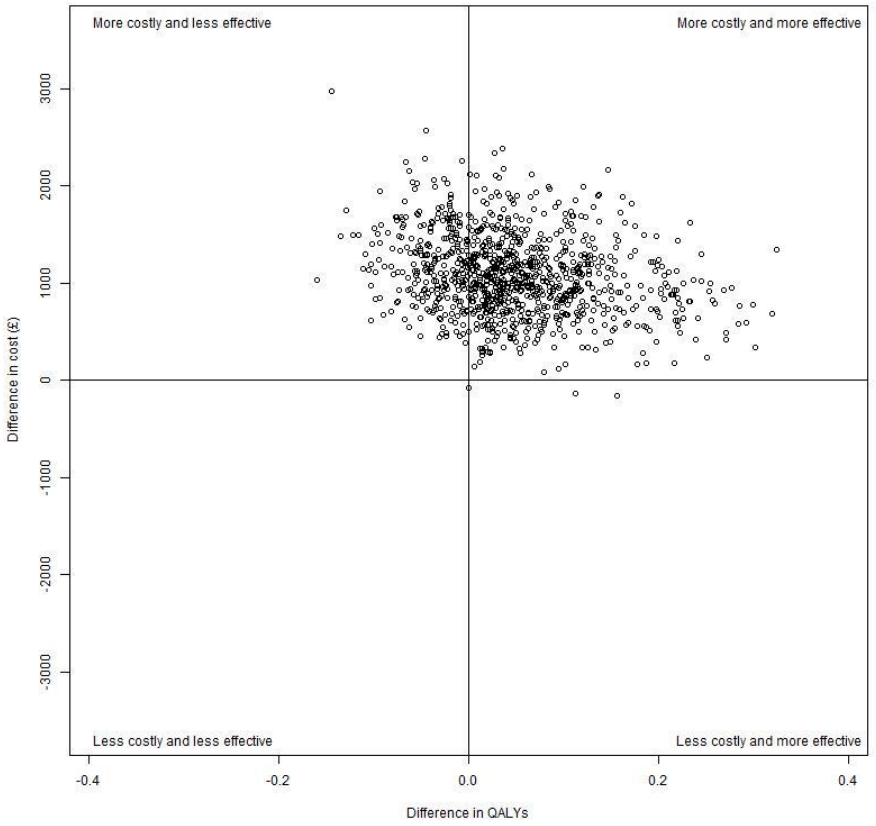
e) Rivaroxaban, 50 years old, males



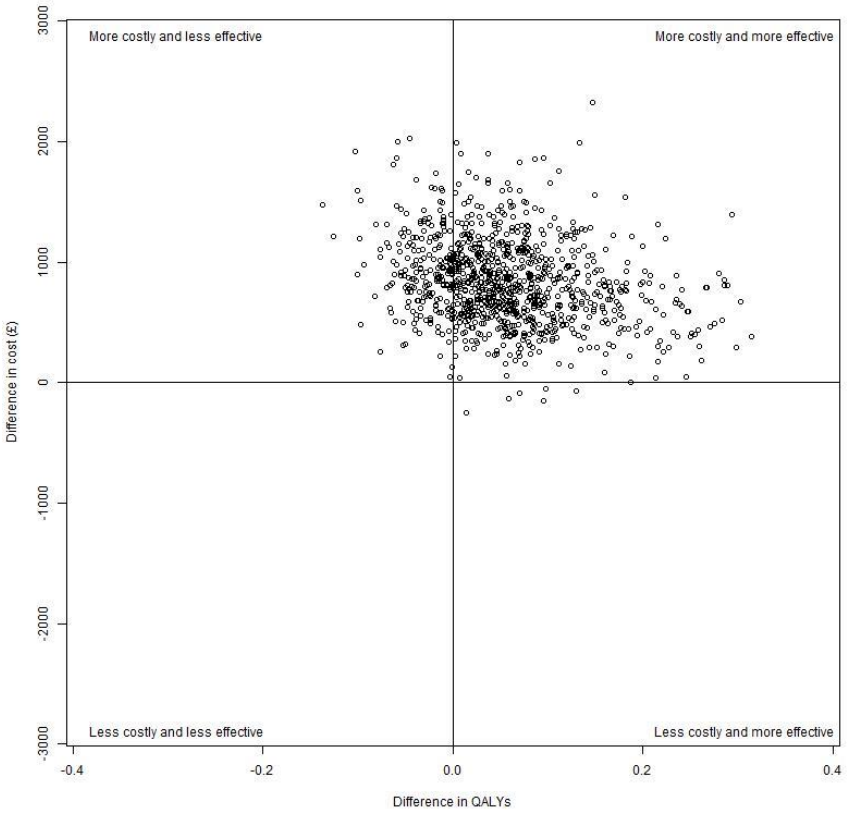
f) Rivaroxaban, 50 years old, females



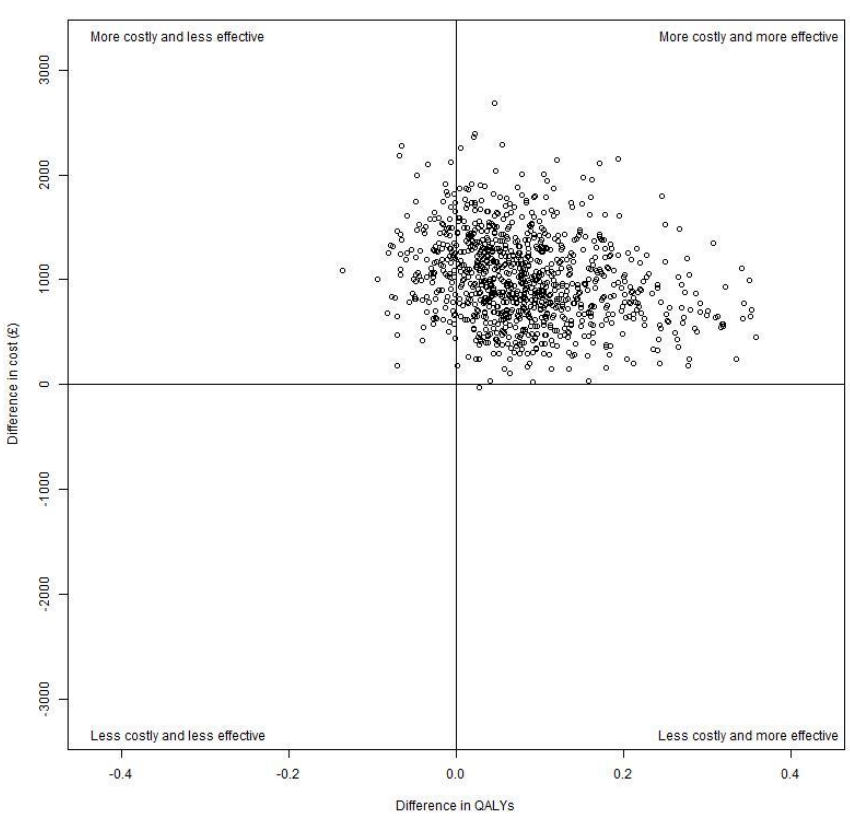
g) Rivaroxaban, 65 years old, males



h) Rivaroxaban, 65 years old, females



i) Dabigatran 65 years old, males



j) Dabigatran, 65 years old, females

Table 5 Scatterplots of estimated differences in health outcomes (in QALYs) and cost between the TTE and no TTE strategy for the ten populations simulated. QALY: Quality-adjusted life years. TTE: transthoracic echocardiography

Appendix E: Summary of cost-effectiveness results of TTE compared with no TTE strategies for the 10 patient populations under consideration

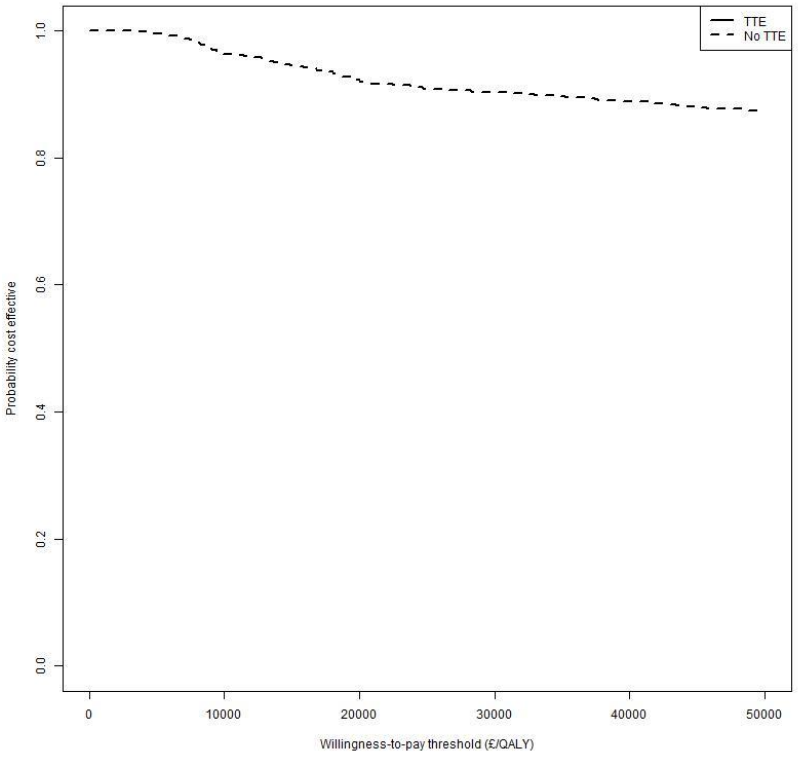
OAC	Patient Population	Strategy	Mean Cost (£)	Mean QALY	ICER (95% CrI), £/QALY	TTE dominated?
Warfarin	Male, Aged 50	No TTE	2459	13.60	-26 489 (-26 552 to -26 408)	Yes
		TTE	4712	13.51		
	Female, Aged 50	No TTE	2815	14.27	-34 078 (-34 175 to -33 952)	Yes
		TTE	5405	14.19		
	Male, Aged 65	No TTE	1527	9.12	66 793 (66 217 to 67 599)	No
		TTE	2467	9.13		
	Female, Aged 65	No TTE	1974	9.94	39 485 (39 291 to 39 754)	No
		TTE	3106	9.97		
Rivaroxaban	Male, Aged 50	No TTE	2449	13.61	-34 060 (-34 170 to -33 910)	Yes
		TTE	4614	13.54		
	Female, Aged 50	No TTE	2779	14.27	-47 535 (-47 773 to -47 271)	Yes
		TTE	5315	14.22		
	Male, Aged 65	No TTE	1510	9.12	30 310 (30 179 to 30 487)	No
		TTE	2393	9.15		
	Female, Aged 65	No TTE	1955	9.95	22 751 (22 681 to 22 844)	No
		TTE	3039	9.99		
Dabigatran	Male, Aged 65	No TTE	1487	9.13	14 728 (14 693 to 14 782)	No
		TTE	2321	9.18		
	Female, Aged 65	No TTE	1942	9.95	12 314 (12 290 to 12 348)	No
		TTE	2946	10.01		

Table 6 Summary of cost effectivness results. ICER: Incremental cost effectivness ratio. TTE: transthoracic echocardiography; QALY: Quality-adjusted life year. Dominated: the strategy is both more expensive and less effective than the strategy to which it is compared

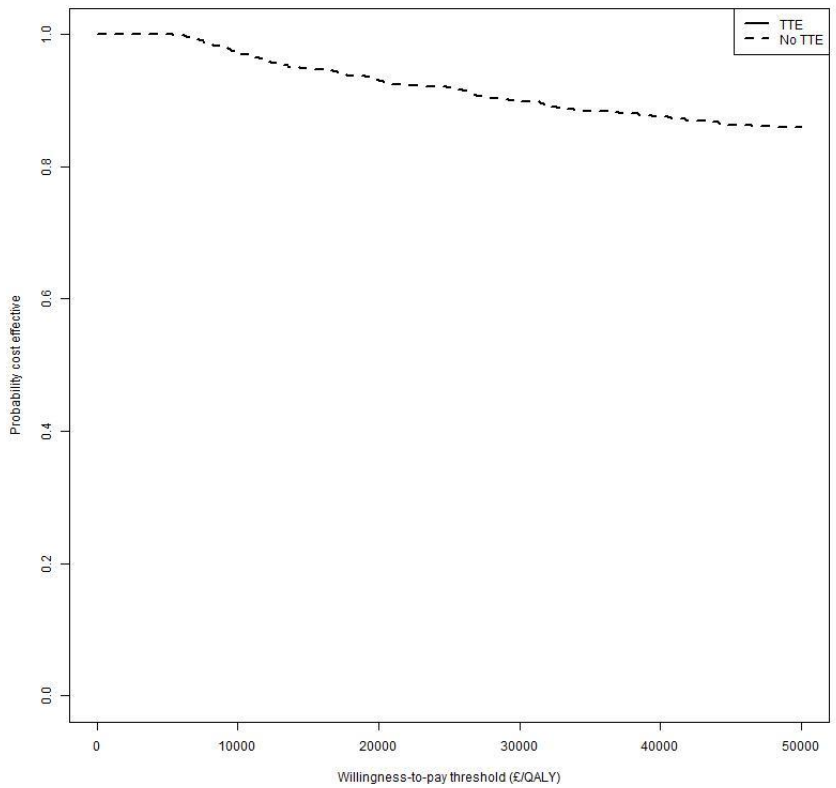
Appendix F: Cost effectiveness acceptability frontiers

Introduction

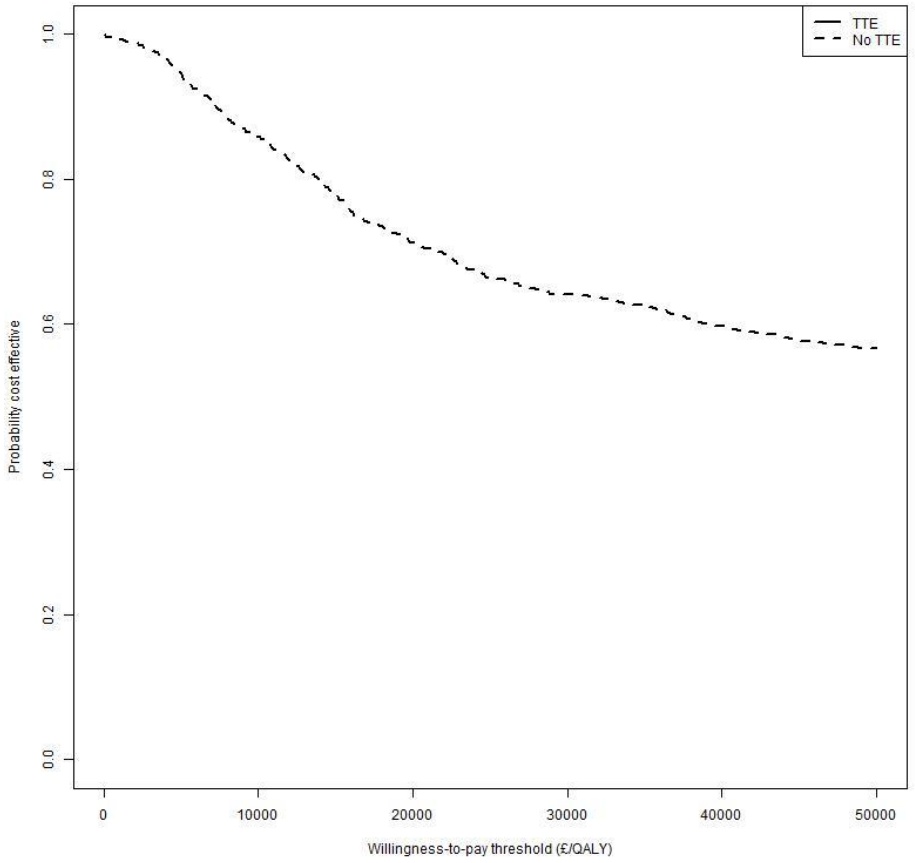
This section presents cost-effectiveness acceptability frontiers (CEAFs) of the with- and without-TTE strategies for each of the scenarios presented in appendix D and elsewhere. CEAFs differ from cost-effectiveness acceptability curves (CEACs) as they plot, for each willingness-to-pay threshold, only the option with the highest expected net benefit. They therefore show uncertainty in the adoption decision. As there are only two options (the With TTE Strategy and the Without TTE Strategy) there is no loss of information, as the cost effectiveness of each option is simply the complement of (i.e. one minus) the other option.



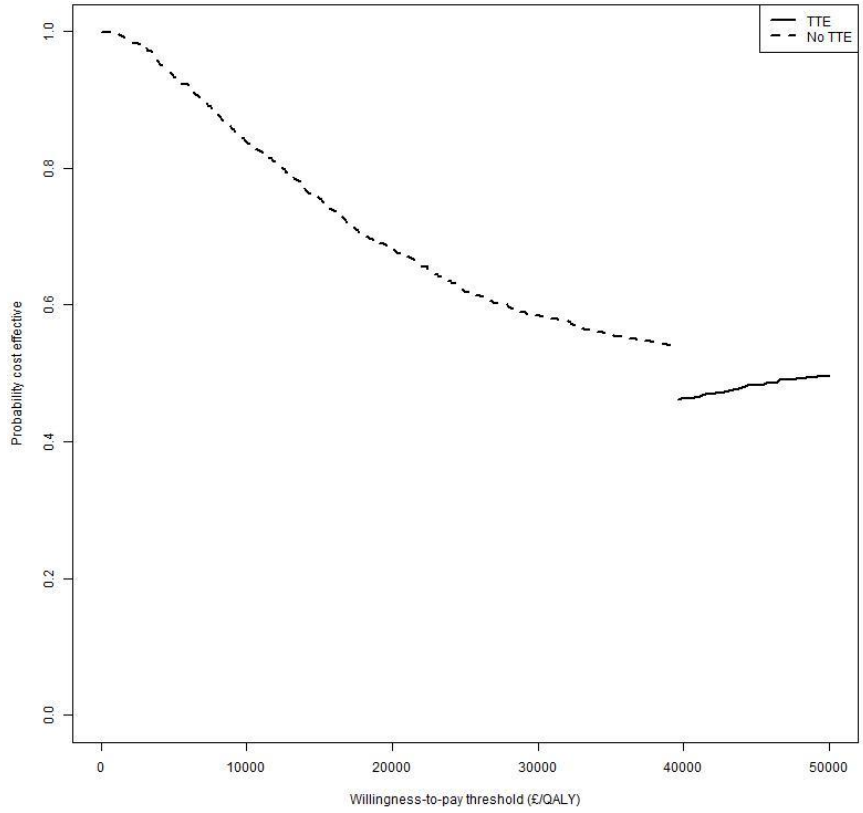
a) Warfarin, 50 years old, males



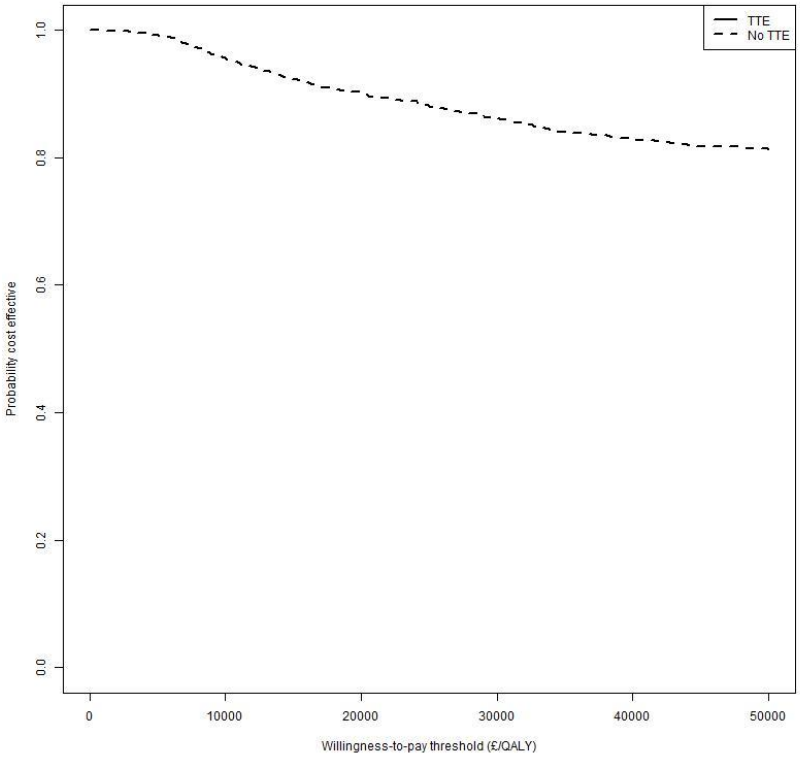
b) Warfarin, 50 years old, females



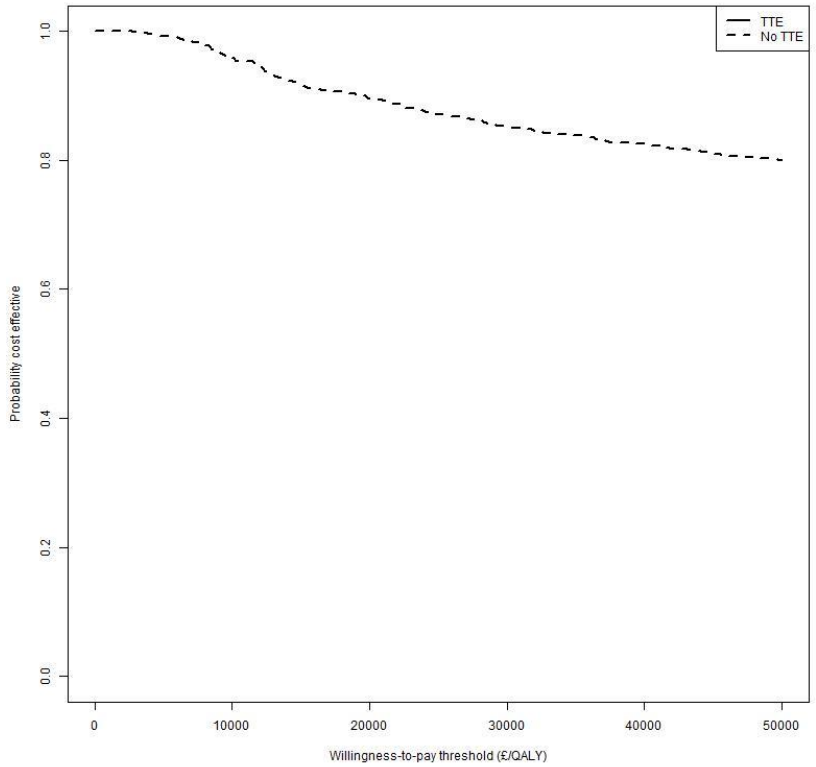
c) Warfarin, 65 years old, males



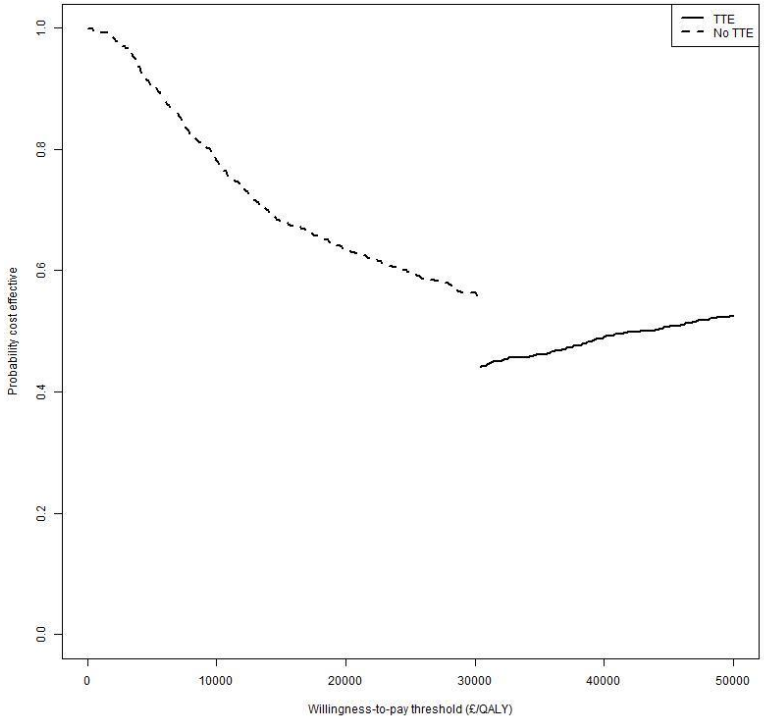
d) Warfarin, 65 years old, females



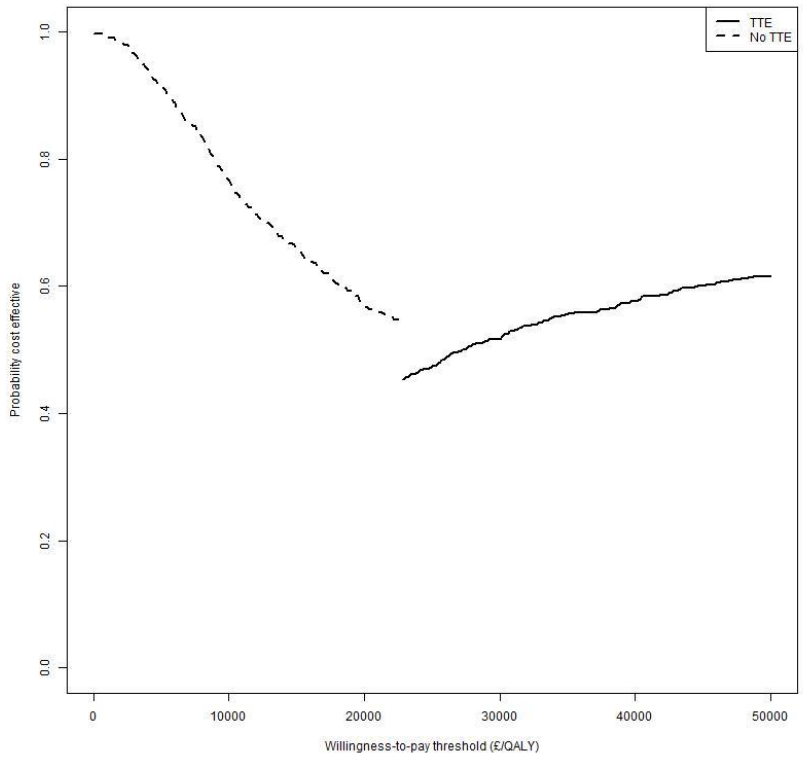
e) Rivaroxaban, 50 years old, males



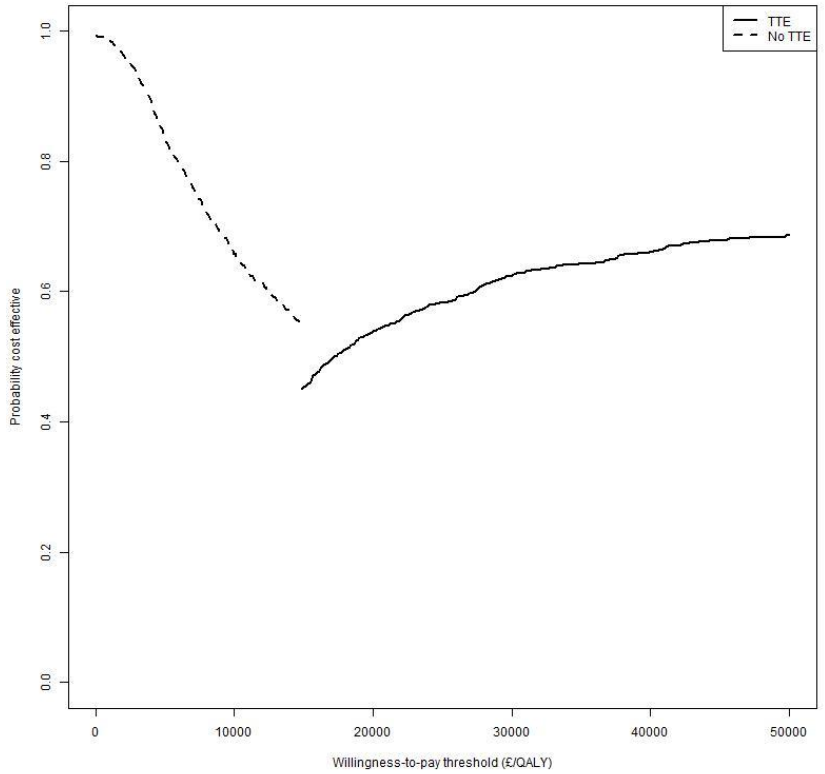
f) Rivaroxaban, 50 years old, females



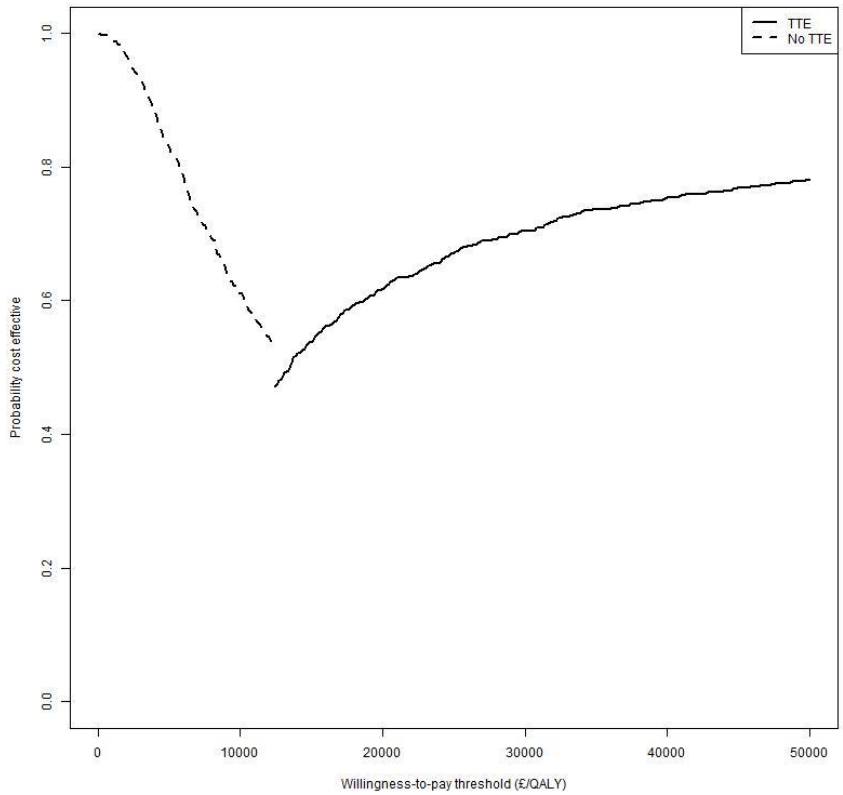
g) Rivaroxaban, 65 years old, males



h) Rivaroxaban, 65 years old, females



i) Dabigatran 65 years old, males



j) Dabigatran, 65 years old, females

Table 7 Scatterplots of estimated differences in health outcomes (in QALYs) and cost between the TTE and no TTE strategy for the ten populations simulated. QALY: Quality-adjusted life years. TTE: transthoracic echocardiography

Appendix G: Full Incremental Analyses

Introduction

This appendix presents full incremental analyses, including efficiency frontiers, for the following four patient groups:

- Males, aged 50 years at diagnosis
- Females, aged 50 years at diagnosis
- Males, aged 65 years at diagnosis
- Females, aged 65 years at diagnosis

Males, aged 50 years at diagnosis

The cost-effectiveness plane for this patient group is shown in Figure 1. Of the four strategies evaluated, the No TTE strategy, using Rivaroxaban as the OAC of choice, is estimated to dominate all the other three options.

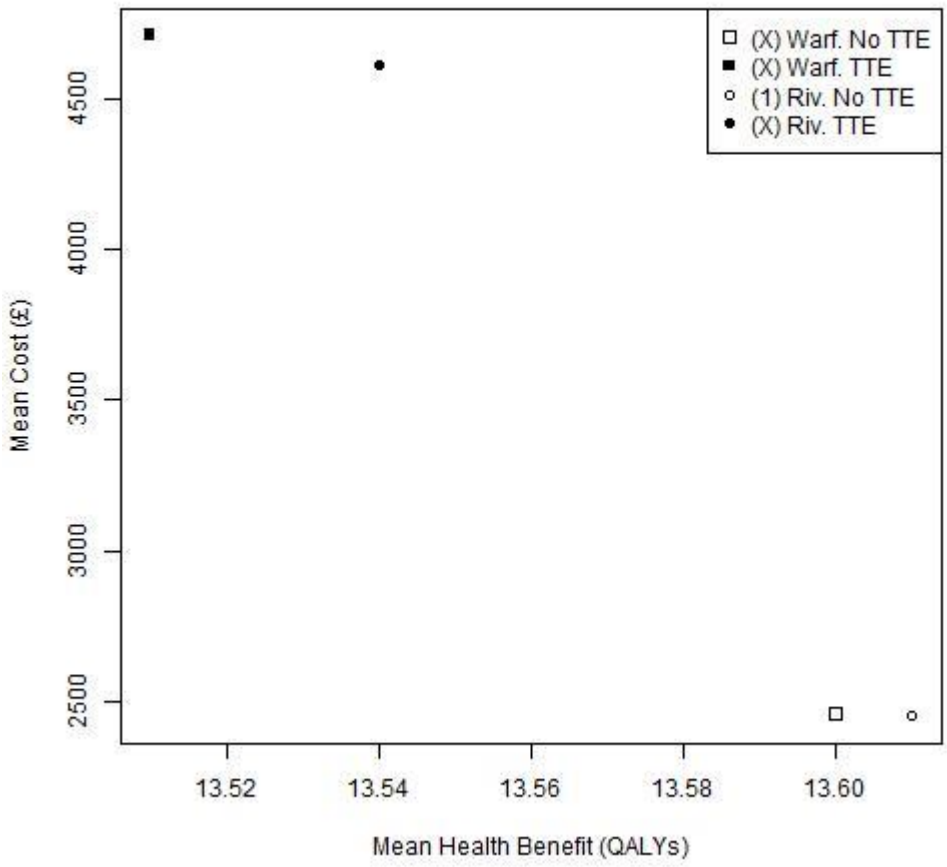


Figure 1 Cost-effectiveness plane of mean costs and mean QALYs for males aged 50 years at diagnosis. Warf: Warfarin; Riv: Rivaroxaban; TTE: Transthoracic Echocardiography

Females, aged 50 years at diagnosis

The cost-effectiveness plane for this patient group is shown in Figure 2. As for males of the same age, of the four strategies evaluated, the No TTE strategy, using Rivaroxaban as the OAC of choice, is estimated to dominate all the other three options. However, the differences in estimated cost and QALY benefit between this option and the No TTE strategy using Warfarin as the OAC of choice are extremely small.

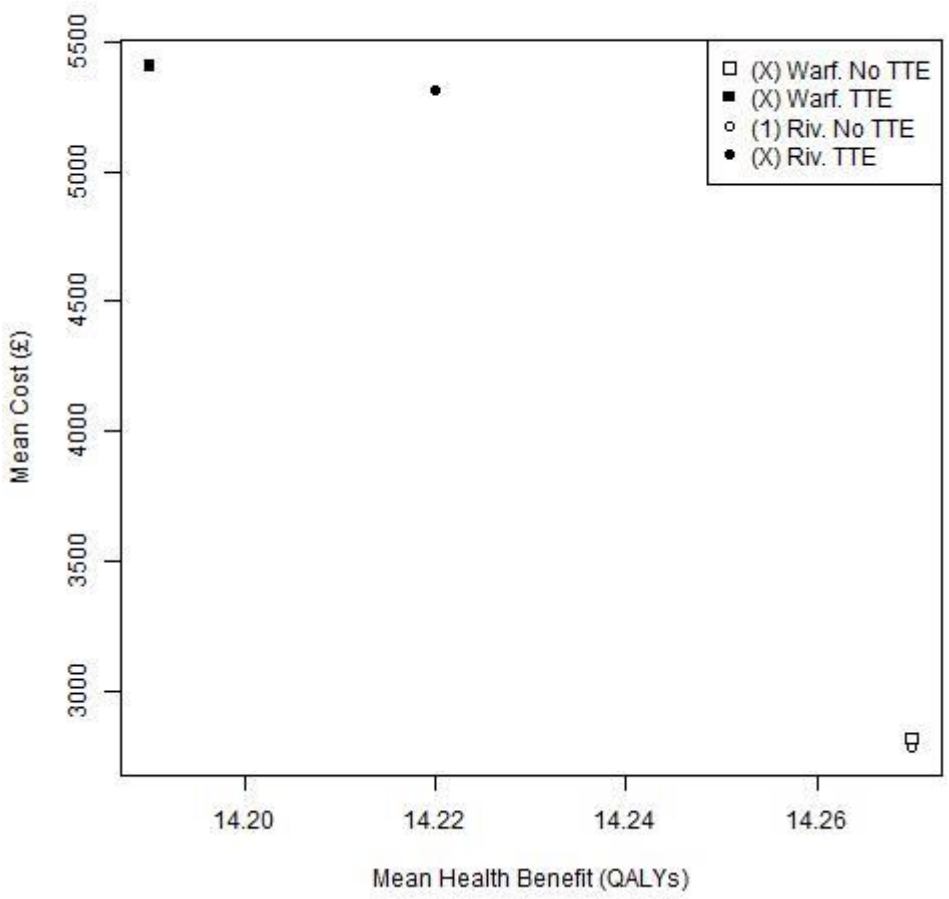


Figure 2 Cost-effectiveness plane of mean costs and mean QALYs for females aged 50 years at diagnosis. Warf: Warfarin; Riv: Rivaroxaban; TTE: Transthoracic Echocardiography

Males, aged 65 years at diagnosis

The cost-effectiveness plane for this patient group is shown in Figure 3. Of the six strategies evaluated, the No TTE strategy using dabigatran as the OAC of choice (Dab, No TTE) is estimated to be the lowest cost option, and so forms the start of the efficiency frontier. The equivalent TTE strategy (Dab, TTE) forms the next and final part of the efficiency frontier, with an ICER, compared

with Dab, No TTE, of £14 728 / QALY, as shown in Appendix E. All other options are ruled out by simple or extended dominance.

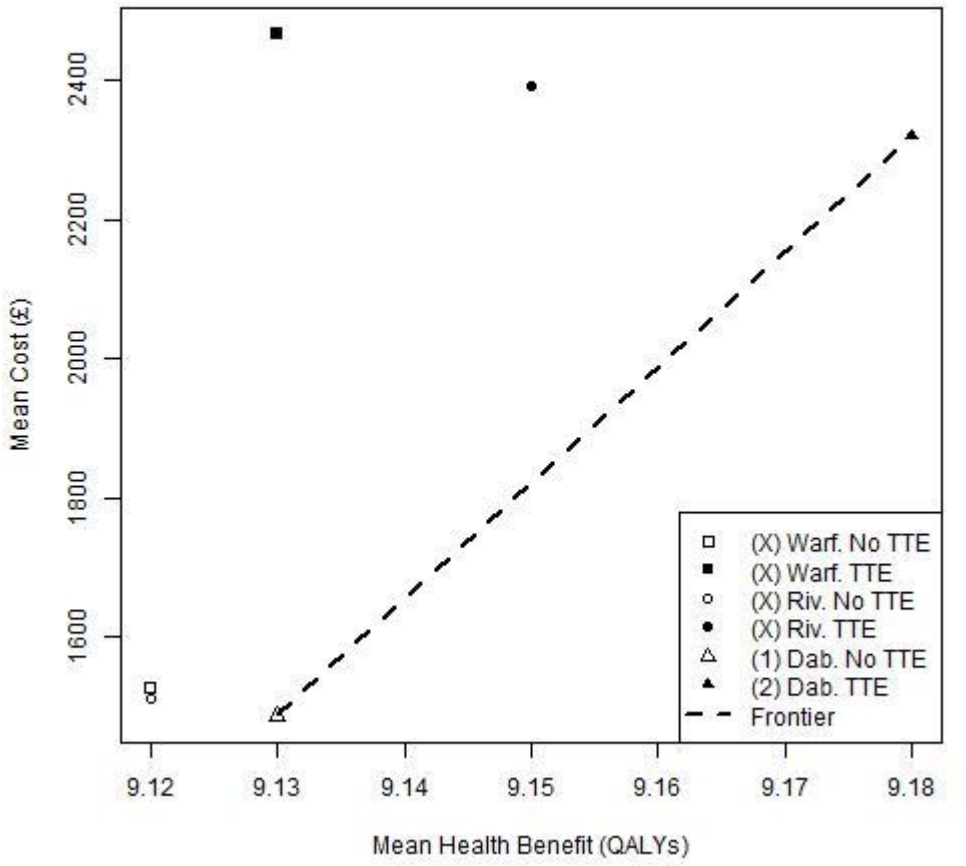


Figure 3 Cost-effectiveness plane of mean costs and mean QALYs for males aged 65 years at diagnosis. Warf: Warfarin; Riv: Rivaroxaban; Dab: Dabigatran; TTE: Transthoracic Echocardiography

Females, aged 65 years at diagnosis

The cost-effectiveness plane for this patient group is shown in Figure 4. As for males of the same age, of the six strategies evaluated, the strategy Dab, No TTE is estimated to be the cheapest, and so forms the start of the efficiency frontier. The next and final option in the frontier is the strategy Dab, TTE, with an ICER of £12 314 / QALY, as shown in Appendix E. All other options are estimated to be ruled out by simple or extended dominance. However, the absolute differences in costs and QALYs between the Riv. No TTE and Dab. No TTE options are extremely small.

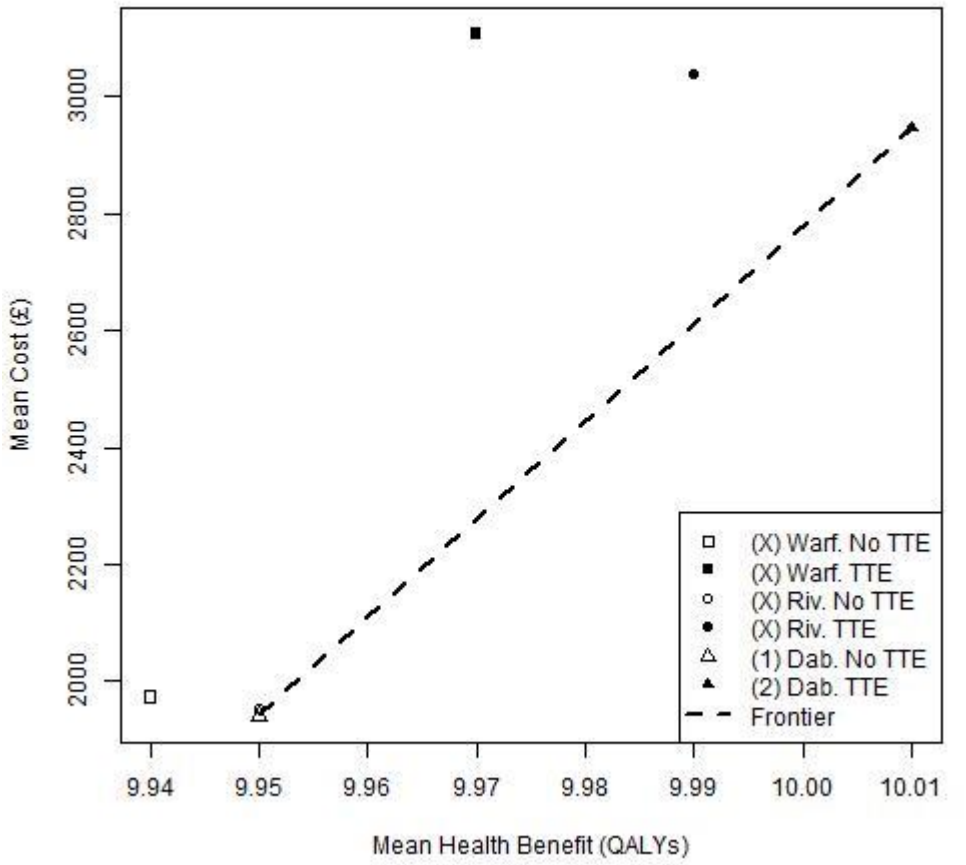


Figure 4 Cost-effectiveness plane of mean costs and mean QALYs for females aged 65 years at diagnosis. Warf: Warfarin; Riv: Rivaroxaban; Dab: Dabigatran; TTE: Transthoracic Echocardiography

Appendix H: Additional Exploratory Analysis – the relationship between true prevalence of LAABN and mean ICER

Introduction

This appendix illustrates how the ICER of the TTE with the No TTE strategies change, for each of the four patient groups, and each of the OACs, as a function of the estimated proportion of the patients with LA ABN, here defined as true proportion high risk (TPHR). In this sensitivity analysis, TPHR is varied between 0 and 20%.

As before, it is assumed that the OACs to be considered are warfarin and rivaroxaban for persons aged 50 years at diagnosis; and warfarin, rivaroxaban and dabigatran for person aged 65 years at diagnosis.

It is seen in all analyses (Figure 5 to Figure 8) that higher estimates of TPHR lead to lower ICERs and so greater cost-effectiveness of using TTE for the OAC decision at any given willingness to pay threshold. It is also seen that the rank order of the cost-effectiveness of each OAC is preserved; i.e. that at any TPHR, rivaroxaban has a lower ICER than warfarin in persons aged 50 at diagnosis, and dabigatran is estimated to have the lowest ICER in persons aged 65 at diagnosis.

Persons aged 50 years at diagnosis

Figure 5 shows how the mean ICER varies for males aged 50 years at diagnosis; Figure 6 presents the equivalent estimates for females. Gender has a smaller influence on the relationship between TPHR and ICER than the OAC assumed to be prescribed if the feature were identified. Where warfarin is assumed to be the OAC of choice, using TTE in this way is not estimated to be cost-effective at a high willingness-to-pay threshold of £30,000/QALY. By contrast, the ICER of TTE is estimated to be below £30,000/QALY when rivaroxaban is assumed to be the OAC prescribed following a positive identification

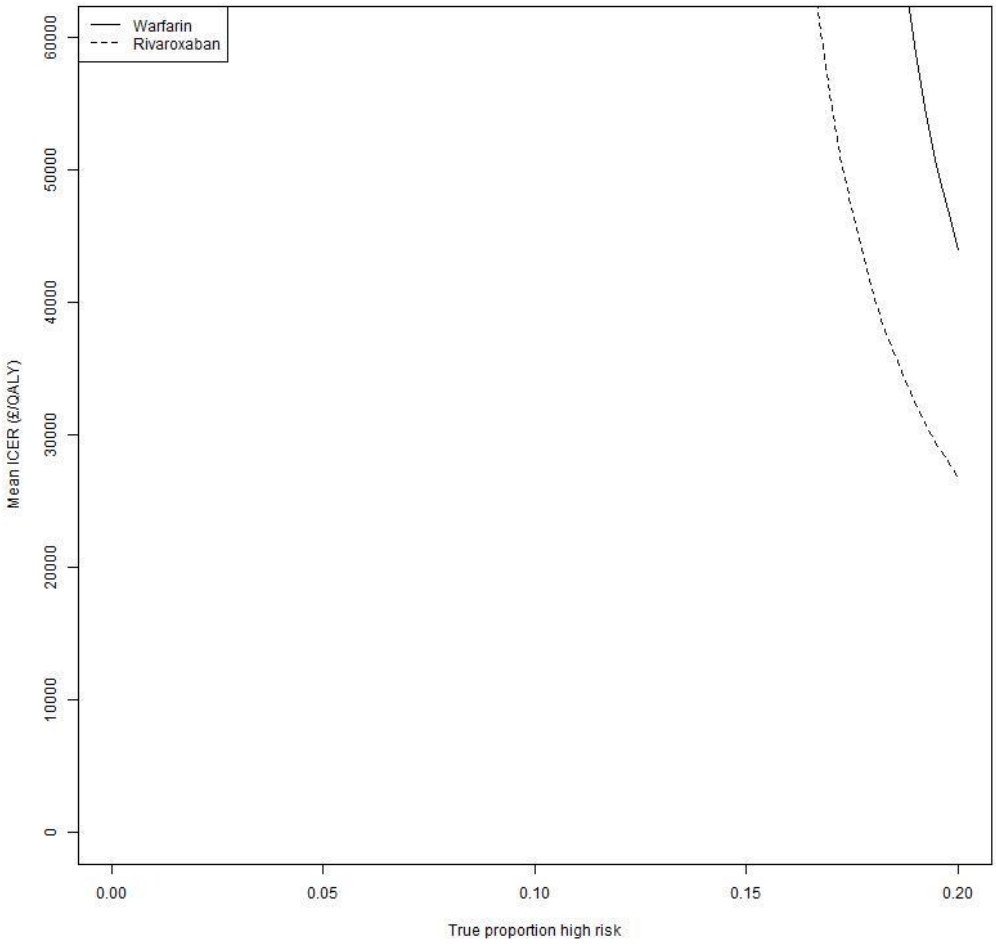


Figure 5 Relationship between mean ICER and True Proportion High Risk (TPHR) for males aged 50 years at diagnosis, if either warfarin or rivaroxaban was the OAC of choice

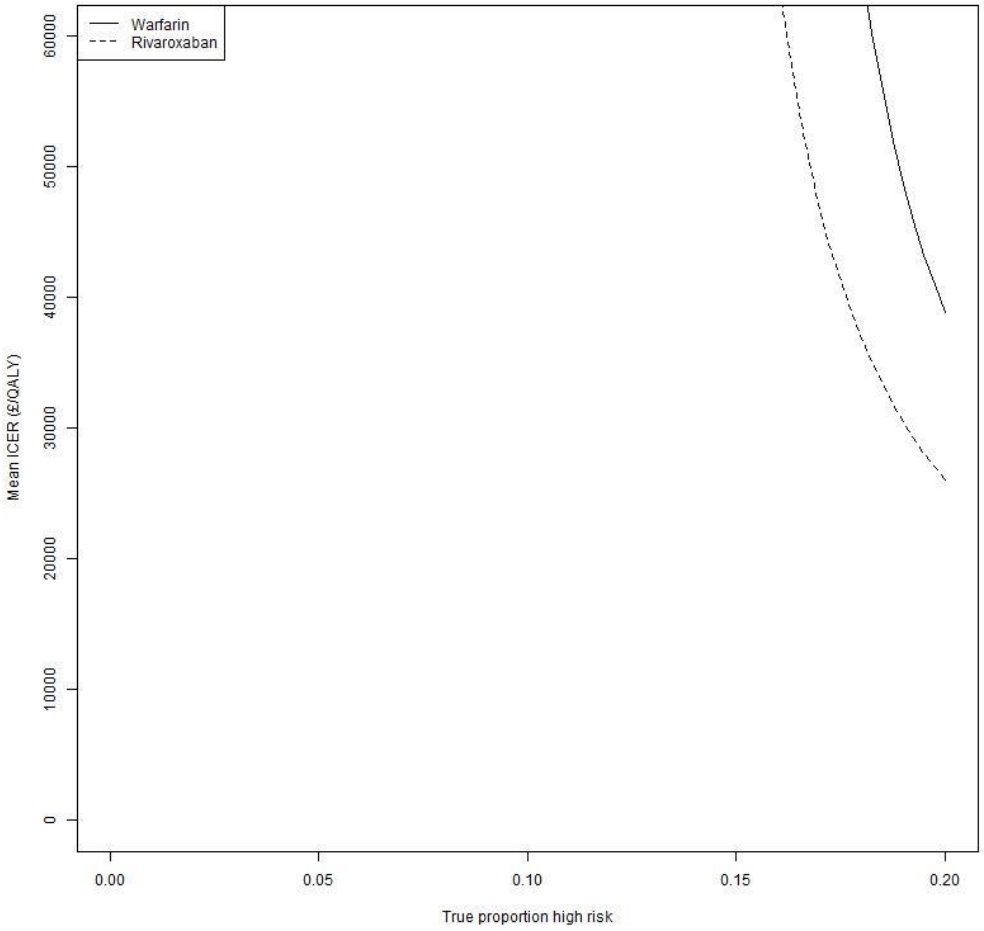


Figure 6 Relationship between mean ICER and True Proportion High Risk (TPHR) for females aged 50 years at diagnosis, if either warfarin or rivaroxaban was the OAC of choice

Persons aged 65 years at diagnosis

Figure 7 shows how the mean ICER varies for males aged 65 years at diagnosis; Figure 8 presents the equivalent estimates for females. Dabigatran is now assumed to be an option for these patient groups, and uses of TTE involving dabigatran are estimated to have lower ICERs regardless of the TPHR level assumed. At higher TPHR estimates, the differences in ICERs in TTE strategies involving different OAC options decreases, and is substantially below £20,000/QALY regardless of OAC assumed. As with the scenarios involving persons diagnosed at the aged of 50 years, the OAC assumed appears to have much greater effect on estimated cost effectiveness than gender.

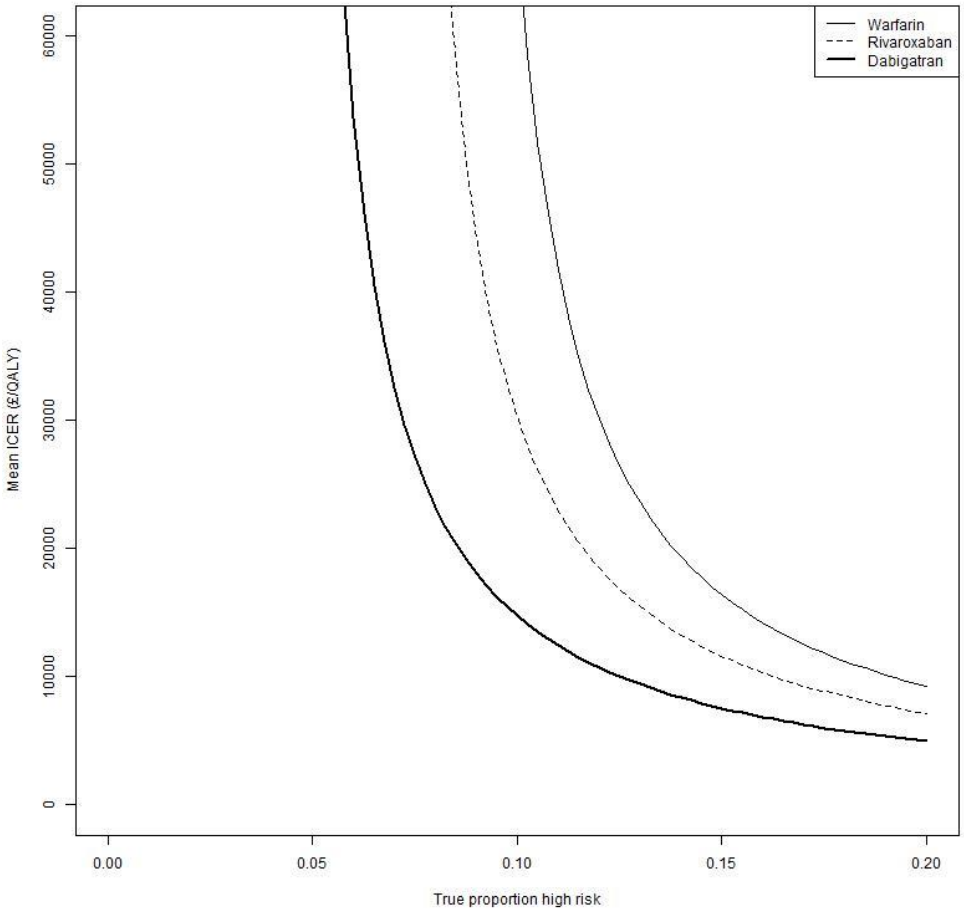


Figure 7 Relationship between mean ICER and true proportion high risk (TPHR) for males aged 50 years at diagnosis, if either warfarin, dabigatran or rivaroxaban was the OAC of choice

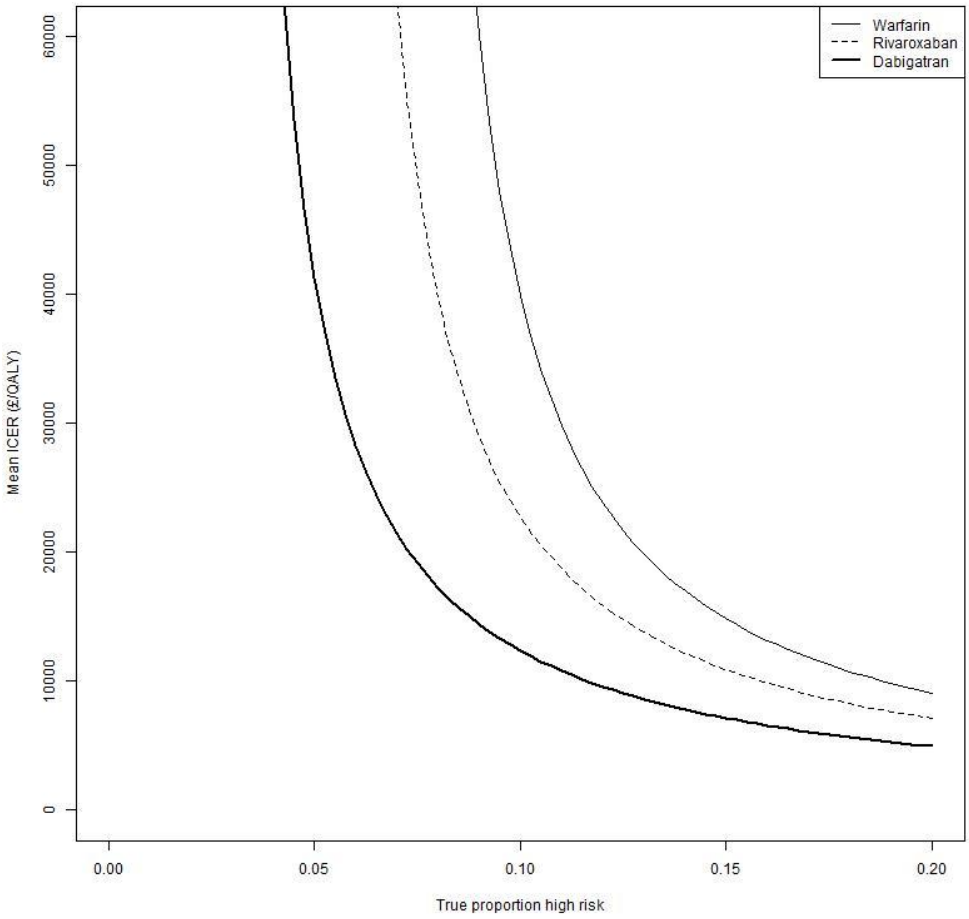


Figure 8 Relationship between mean ICER and True Proportion High Risk (TPHR) for females aged 65 years at diagnosis, if either warfarin, dabigatran or rivaroxaban was the OAC of choice