

Table 1: Preference-based score descriptive statistics for observed cases at baseline across and within trial-arms

Parameter	Trial-arm	n ^a (N%)	Mean	Median	SD	Min	Max	P. floor	P. ceiling	N floor (%)	N ceiling (%)	UHSP ^b	UPBS ^c
EQ-5D-5L VSE	Both	355 (98.3)	0.730	0.783	0.163	-0.010	1	-0.285	1	0 (0.0)	3 (0.8)	111	100
	Int.	238 (98.8)	0.735	0.783	0.152	0.089	1	-0.285	1	0 (0.0)	2 (0.8)	83	75
	Cont.	117 (97.5)	0.722	0.783	0.182	-0.010	1	-0.285	1	0 (0.0)	1 (0.9)	57	54
EQ-5D-5L cross-walk	Both	355 (98.3)	0.652	0.721	0.202	0.076	1	-0.594	1	0 (0.0)	3 (0.8)	111	105
	Int.	238 (98.8)	0.656	0.718	0.193	0.119	1	-0.594	1	0 (0.0)	2 (0.8)	83	78
	Cont.	117 (97.5)	0.645	0.721	0.218	0.076	1	-0.594	1	0 (0.0)	1 (0.9)	57	56
ReQoL-UI	Both	353 (97.8)	0.778	0.807	0.141	0.115	0.995	-0.195	1	0 (0.0)	0 (0.0)	319	319
	Int.	237 (98.3)	0.788	0.806	0.123	0.242	0.979	-0.195	1	0 (0.0)	0 (0.0)	219	219
	Cont.	116 (96.7)	0.757	0.808	0.171	0.115	0.995	-0.195	1	0 (0.0)	0 (0.0)	114	114

Acronyms. Cont., Control; Int. Intervention; N, number of responders; O., observed; P., possible; ReQoL-UI, Recovering Quality of Life – Utility Index; SD, standard deviation; UHSP, unique health state profiles; UPBS, unique preference-based scores.

^a Number of participants at baseline was: Both trial-arms ('Both'), N = 361; Intervention-arm (Int.), N = 241; Control-arm (Cont.), N = 120.

^b Unique health state profiles (UHSP): the descriptive system element of the EQ-5D-5L and ReQoL-UI questionnaires produces a 5-digit or 7-digit health state profile, respectively, that represents the level of reported problems on each of the five or seven dimensions of health, e.g. 11223 for the EQ-5D-5L or 1112234 for the ReQoL-UI. Unique health state profiles (UHSP) refers to the number of unique health state profiles represented by the group of participants on that specific measure e.g. across both trial-arms (N= 361), 111 EQ-5D-5L health state profiles compared to 319 ReQoL-UI health state profiles are represented by the participant sample.

^c Unique preference-based scores (UPBS): UPBS refers to the number of unique preference-based scores represented by the group. For the ReQoL-UI, UHSP and UPBS is equal such that each health state is represented by a unique preference-based score. For the EQ-5D-5L VSE and cross-walk, the UPBS < UHSP as some health states are represented by the same preference-based score within the VSE or cross-walk e.g. on the VSE a preference-based score of 0.469 represents three health state profiles (22235, 13415, 11434), and for the cross-walk a preference-based score of 0.414 represents two health state profiles (12324, 11115) within our participant sample. NB our participant sample doesn't represent all possible UHSP and UPBS combinations; for example using the cross-walk algorithm, a preference-based score of 0.414 actually represents six health state profiles (11115, 12324, 14141, 24114, 31234, 41143) with the cross-walk producing 1079 UPBS relative to the 3125 UHSP the EQ-5D-5L purports to measure.

Table 2: Summary of costs, baseline and 8-week scores, unadjusted and BA QALYs by measure in the CC and MI analyses over the 8-week trial period

Measure	Metric	Intervention					Control				Dif. Trial-arm		
		Mean	SEM ^a	95% bCI ^b	Dif., t ₁ -t ₀ [BA] ^c		Mean	SEM ^a	95% bCI ^b	Dif. t ₁ -t ₀ [BA] ^c	Mean	Dif. t ₁ -t ₀ [BA] ^c	
CC - 8 weeks		N=194 (80%)					N=88 (73%)						
Costs	£, t ₁	£197.29	£18.22	£170.55	£247.34	-	£110.76	£35.54	£69.48	£245.72	-	£86.53	-
EQ-5D-5L	Score, t ₀	0.7362	0.0108	0.7150	0.7574	-	0.7278	0.0197	0.6893	0.7663	-	0.0084	-
VSE	Score, t ₁	0.7931	0.0106	0.7723	0.8138	0.0568	0.7571	0.0196	0.7188	0.7954	0.0293	0.0360	0.0275
	QALYs	0.1176	0.0015	0.1145	0.1203	-	0.1142	0.0028	0.1083	0.1193	-	0.0034	-
	BA QALYs	0.1173	0.0006	0.1129	0.1170	[-0.0003]	0.1150	0.0011	0.1160	0.1186	[0.0007]	0.0024	[-0.0011]
EQ-5D-5L cross-walk	Score, t ₀	0.6587	0.0136	0.6320	0.6853	-	0.6564	0.0224	0.6125	0.7004	-	0.0022	-
	Score, t ₁	0.7226	0.0132	0.6968	0.7485	0.0639	0.6767	0.0250	0.6278	0.7257	0.0203	0.0459	0.0436
	QALYs	0.1063	0.0018	0.1024	0.1095	-	0.1026	0.0033	0.0954	0.1086	-	0.0037	-
	BA QALYs	0.1062	0.0008	0.1045	0.1078	[-0.0001]	0.1027	0.0014	0.1000	0.1055	[0.0002]	0.0034	[-0.0003]
ReQoL-UI	Score, t ₀	0.7921	0.0086	0.7753	0.8090	-	0.7663	0.0192	0.7287	0.8039	-	0.0258	-
	Score, t ₁	0.8086	0.0101	0.7888	0.8284	0.0165	0.7915	0.0176	0.7569	0.8260	0.0251	0.0171	-0.0087
	QALYs	0.1231	0.0012	0.1204	0.1253	-	0.1198	0.0026	0.1140	0.1242	-	0.0033	-
	BA QALYs	0.1222	0.0007	0.1208	0.1235	[-0.0010]	0.1220	0.0009	0.1201	0.1239	[0.0022]	0.0001	[-0.0032]
MI - 8 weeks		N=236 (98%)					N=116 (97%)						
Costs	£, t ₁	£196.86	£18.06	£166.19	£235.92	-	£109.93	£35.04	£64.06	£193.79	-	£86.94	-
EQ-5D-5L	Score, t ₀	0.7352	0.0098	0.7159	0.7545	-	0.7225	0.0170	0.6892	0.7558	-	0.0127	-
VSE	Score, t ₁	0.7928	0.0097	0.7738	0.8119	0.0576	0.7560	0.0193	0.7181	0.7939	0.0335	0.0368	0.0241
	QALYs	0.1175	0.0013	0.1148	0.1202	-	0.1137	0.0025	0.1088	0.1184	-	0.0038	-
	BA QALYs	0.1170	0.0002	0.1167	0.1175	[-0.0005]	0.1147	0.0007	0.1137	0.1161	[0.0010]	0.0023	[-0.0015]
EQ-5D-5L cross-walk	Score, t ₀	0.6566	0.0125	0.6320	0.6812	-	0.6453	0.0204	0.6054	0.6852	-	0.0112	-
	Score, t ₁	0.7232	0.0122	0.6993	0.7471	0.0666	0.6769	0.0236	0.6306	0.7232	0.0315	0.0463	0.0351
	QALYs	0.1061	0.0017	0.1027	0.1094	-	0.1017	0.0029	0.0958	0.1075	-	0.0044	-
	BA QALYs	0.1057	0.0003	0.1053	0.1062	[-0.0004]	0.1026	0.0008	0.1012	0.1040	[0.0009]	0.0031	[-0.0013]
ReQoL-UI	Score, t ₀	0.7899	0.0077	0.7748	0.8051	-	0.7567	0.0159	0.7257	0.7878	-	0.0332	-
	Score, t ₁	0.8096	0.0093	0.7914	0.8278	0.0197	0.7914	0.0172	0.7577	0.8250	0.0346	0.0183	-0.0149
	QALYs	0.1230	0.0011	0.1208	0.1250	-	0.1191	0.0022	0.1146	0.1231	-	0.0040	-
	BA QALYs	0.1218	0.0002	0.1213	0.1220	[-0.0013]	0.1217	0.0006	0.1205	0.1228	[0.0026]	0.0001	[-0.0039]

Acronyms. BA: baseline adjusted; CC: complete cases analysis; CE: cost-effectiveness; bCI: bootstrapped confidence intervals; Dif. Mean: difference in mean values between trial arms; ICER: incremental cost-effectiveness ratio; MI: multiple imputation, using chained equations (MICE); QALY: quality adjusted life year; SEM: standard error of the mean.

CC sample size based on responders at baseline and 8-weeks: 198 (82%) intervention-arm and 91 (76%) control-arm; **MI sample size** across all time-points: 236 (98%) intervention-arm and 116 (97%) control-arm

^a Preference-based scores: SEMs are calculated using Rubin's rule for the MI analysis; (BA) QALYs: SEMs are bootstrapped.

^b In the CC analysis, bCIs are bias-corrected and accelerated (BCa); in the MI analysis, bCI are based on the Percentile method.

^c Score (Dif., t₁-t₀), the difference in mean score at 8-weeks (t₁) minus mean score at baseline (t₀); QALYs (Dif. [BA]), the difference in mean BA QALY minus mean (unadjusted) QALY.

Table 3: Incremental cost-effectiveness results by preference-based measure score in the CC and MI analyses over the 8-week trial period

Measure	Metric	Trial-arm differences					Mean ICER	ICERs by CE plane quadrant (%) ^b						Prob. CE < CE threshold (%)			
		Mean	bSEM	95% bCI ^a	Dif. BA			SE: >Q <£	SW: <Q <£	NE: >Q >£	NW: <Q >£	E: >Q	Dif. BA	<£20k	Dif. BA	<£30k	Dif. BA
CC – 8 weeks																	
Costs	£, t ₁	£86.53	£40.32	-£44.48	£140.39	-	-	-	-	-	-	-	-	-	-	-	-
EQ-5D-5L	QALY	0.0034	0.0031	-0.0020	0.0101	-	£25,348	2.1%	0.4%	84.7%	12.8%	86.8%	-	39.6%	-	55.1%	-
VSE	BA QALY	0.0024	0.0012	0.0000	0.0049	-0.0011	£36,803	2.5%	0.1%	94.9%	2.6%	97.4%	10.6%	19.5%	-20.1%	36.7%	-18.4%
EQ-5D-5L	QALY	0.0037	0.0038	-0.0030	0.0117	-	£23,385	1.9%	0.6%	82.4%	15.1%	84.4%	-	43.3%	-	57.7%	-
crosswalk	BA QALY	0.0034	0.0016	0.0004	0.0067	-0.0003	£25,287	2.5%	0.1%	95.9%	1.5%	98.4%	14.0%	33.6%	-9.7%	58.9%	1.2%
ReQoL-UI	QALY _s	0.0033	0.0028	-0.0017	0.0096	-	£26,192	2.2%	0.3%	85.9%	11.6%	88.1%	-	36.8%	-	54.0%	-
	BA QALY	<0.0001	0.0012	-0.0021	0.0025	-0.0032	£577,331	1.2%	1.3%	52.5%	44.9%	53.8%	-34.3%	4.0%	-32.9%	6.0%	-48.0%
MI – 8 weeks																	
Costs	£, t ₁	£86.94	£38.47	-£2.26	£150.32	-	-	-	-	-	-	-	-	-	-	-	-
EQ-5D-5L	QALY	0.0038	0.0027	-0.0015	0.0094	-	£22,828	2.7%	0.0%	88.4%	8.9%	91.0%	-	42.1%	-	58.6%	-
VSE	BA QALY	0.0023	0.0014	-0.0004	0.0051	-0.0015	£37,561	2.6%	0.1%	92.3%	5.0%	94.9%	3.9%	19.8%	-22.3%	36.3%	-22.3%
EQ-5D-5L	QALY	0.0044	0.0033	-0.0022	0.0112	-	£19,624	2.6%	0.1%	86.9%	10.4%	89.5%	-	49.2%	-	64.3%	-
crosswalk	BA QALY	0.0031	0.0018	-0.0003	0.0066	-0.0013	£27,684	2.6%	0.1%	93.7%	3.6%	96.3%	6.8%	31.7%	-17.5%	52.3%	-11.9%
ReQoL-UI	QALY	0.0040	0.0024	-0.0006	0.0089	-	£21,966	2.7%	0.0%	92.7%	4.6%	95.3%	-	42.9%	-	60.9%	-
	BA QALY	<0.0001	0.0012	-0.0023	0.0027	-0.0039	£1,252,542	1.7%	1.0%	48.3%	49.0%	50.1%	-45.3%	4.9%	-37.9%	7.4%	-53.5%

Acronyms. BA: baseline adjusted; CC: complete cases analysis; CE: cost-effectiveness; bCI: bootstrapped confidence intervals; Dif. Mean: difference in mean values between trial arms; ICER: incremental cost-effectiveness ratio; MI: multiple imputation; Prob. CE: Probability of cost-effectiveness; QALY: quality-adjusted life year; bSEM: bootstrapped Standard Error of the mean.

Footnote. The CC analysis is based on 194 people (of 241; 80%) in the intervention-arm and 88 (of 120; 73%) in the control-arm; the MI analysis is based on 236 people (of 241; 98%) in the intervention-arm and 116 (of 120; 97%) in the control-arm.

^a In the CC analysis, bCIs are bias-corrected and accelerated (BCa); in the MI analysis, bCI are based on the Percentile method.

^b CE plane quadrants are South East (SE; less costly, more effective), South West (SW; less costly, less effective), North East (NE; more costly, more effective), North West (NW; more costly, less effective), and East (E; more effective).

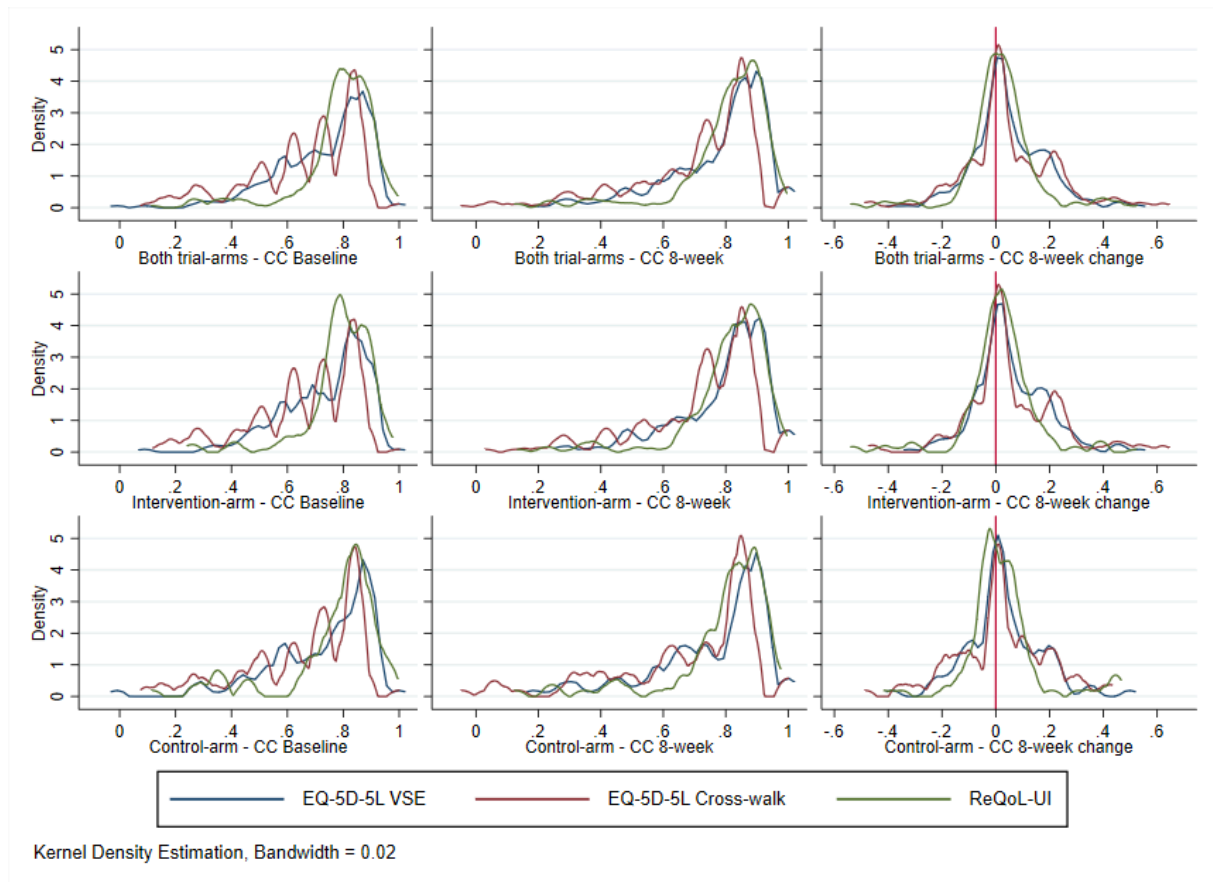


Figure 1: CC smoothed EQ-5D-5L VSE and cross-walk, and ReQoL-UI score distributions across and within trial-arms – baseline, 8-weeks, and 8-week change

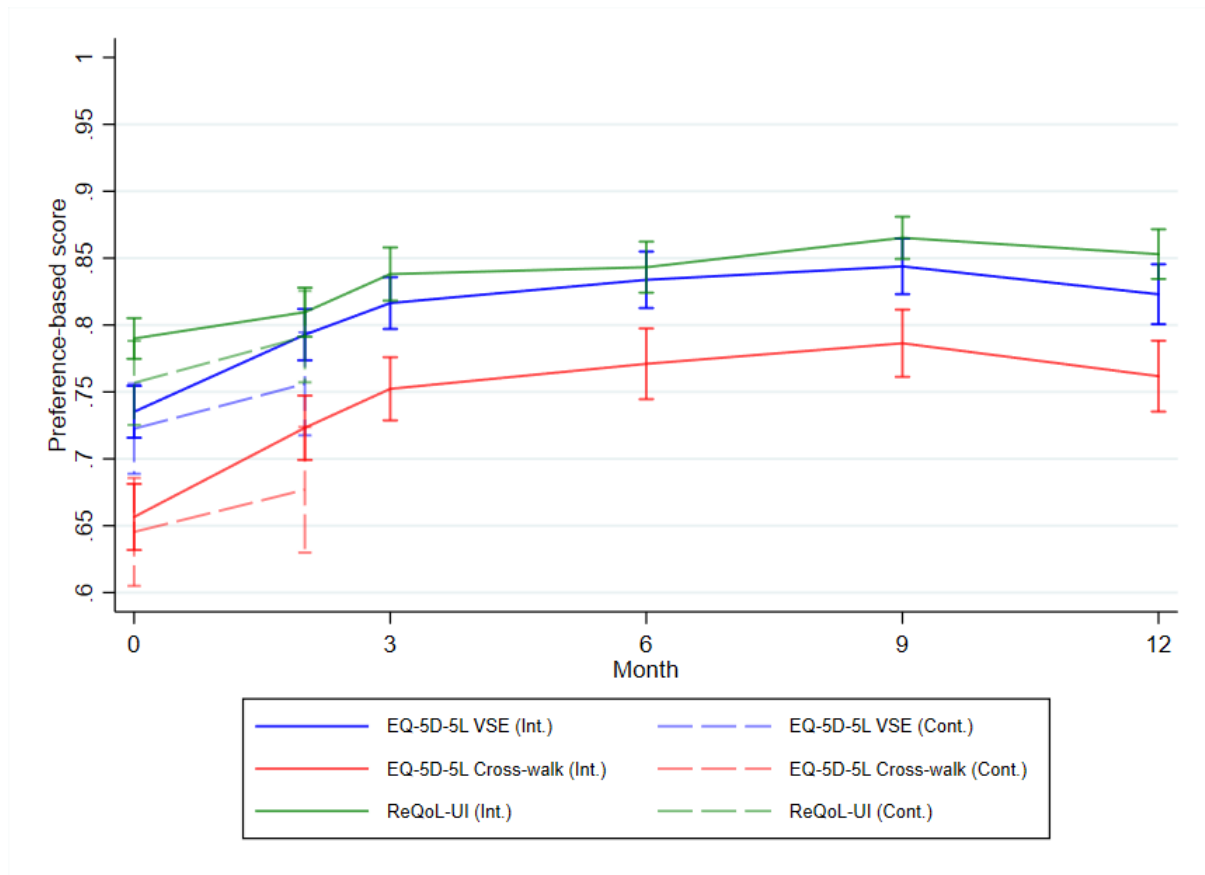


Figure 2: MI preference-based score means with 95% CIs at baseline and 8-week per trial-arm, and at 3-, 6-, 9-, 12-month in the intervention-arm

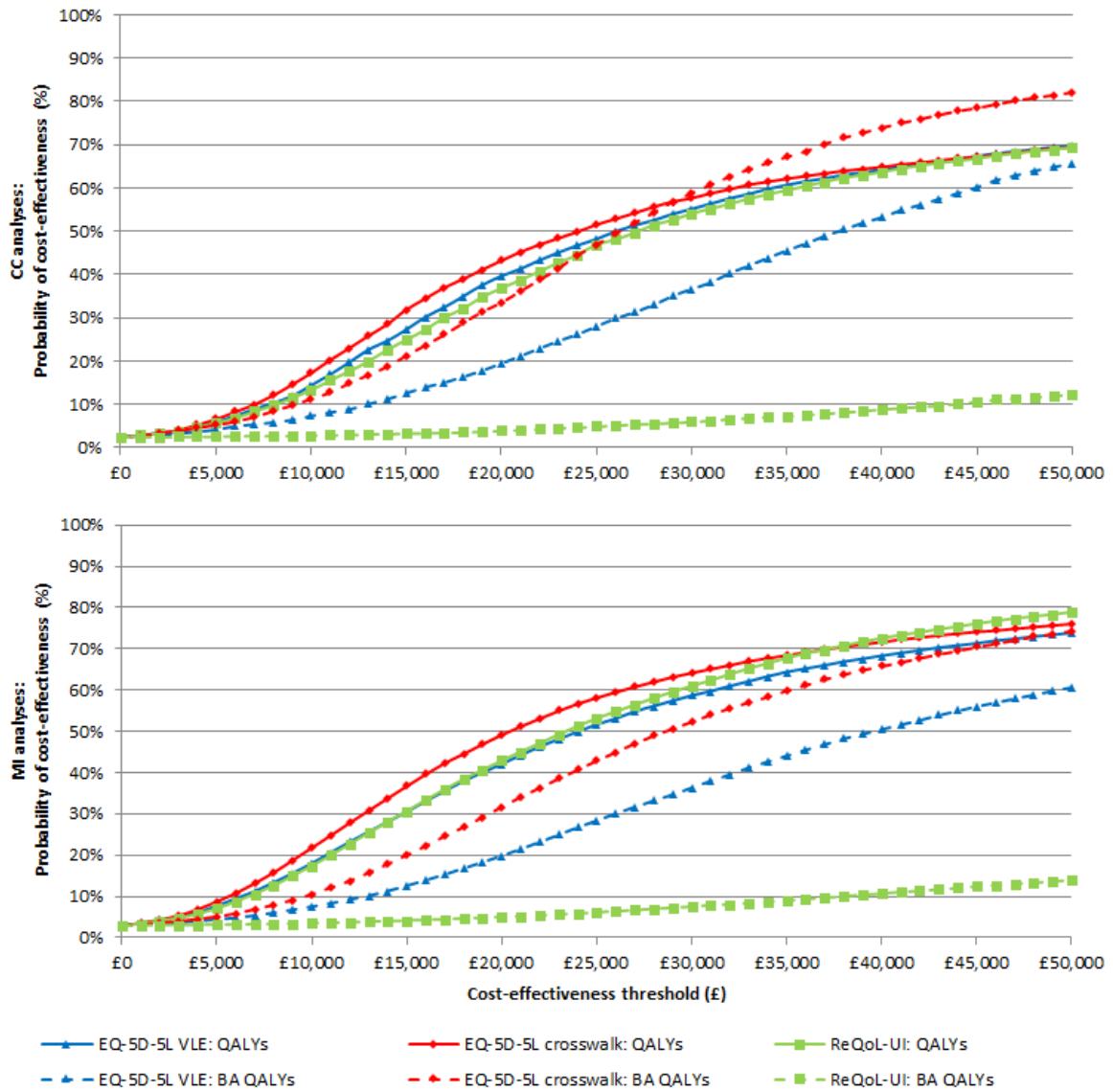


Figure 3: Cost-effectiveness acceptability curves (CEAC) for the CC (top) and MI (bottom) analyses dependent on baseline-adjusted and unadjusted QALYs