TICOSPA Supplementary file 4: economic evaluation

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Unit costs

Resource type	Unit cost (2019)*	Source
GP, visit	€34.72	Dutch guideline for economic evaluations in healthcare [1]
Rheumatologist, visit	€95.74	Dutch guideline for economic evaluations in healthcare [1]
Other specialists, visit	€95.74	Dutch guideline for economic evaluations in healthcare [1]
Emergency department, visit	€272.49	Dutch guideline for economic evaluations in healthcare [1]
Nurse specialist, visit	€34.72	Dutch guideline for economic evaluations in healthcare [1]
Physical therapist, visit	€34.72	Dutch guideline for economic evaluations in healthcare [1]
Rehabilitation, visit	€160.97	Dutch guideline for economic evaluations in healthcare [1]
Hospital stay, per day	€483.97	Dutch guideline for economic evaluations in healthcare [1]
bDMARD use, per day	€23.01	Assumption, based on annual bDMARD cost of €8,400
Infusion	€177.80	Dutch guideline for economic evaluations in healthcare [1]
Sick leave, per missed day	€292.48	Dutch guideline for economic evaluations in healthcare [1]

†If applicable, unit costs were updated to 2019 prices using the consumer price index, and adjusted for patients from France and Belgium using purchasing power parities conversion factors.

References

1. Zorginstituut Nederland [National Health Care Institute of the Netherlands]. Richtlijn voor het uitvoeren van economische evaluaties in de gezondheidszorg [Guideline for economic evaluations in healthcare]. *Diemen: Zorginstituut Nederland* 2015.

Resources utilisation at baseline (past 12 weeks) and during the trial (48 weeks), by category and treatment arm*

	Baseline (past 12 weeks)		Follow-up (48 weeks)	
	TC/T2T	**UC**	**TC/T2T**	**UC**
	N = 80	**N = 80**	**N = 80**	**N = 80**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
	Median(IQR)	**Median(IQR)**	**Median(IQR)**	**Median(IQR)**
Visits/day care				
GP	1.6 (1.7)	2.1 (1.8)	4.0 (4.1)	4.9 (4.2)
	1 (0-2)	2 (1-3)	3.0 (1.8-5.3)	3.5 (1-8)
Rheumatologist	1.6 (1.2)	1.6 (1.1)	6.0 (3.7)	3.6 (2.3)
	1 (1-2)	1 (1-2)	5.5 (3-9)	4 (2-5)
Other specialists	0.5 (1.2)	0.7 (1.2)	1.6 (3.3)	2.1 (3.6)
	0 (0-1)	0 (0-1)	0 (0-2)	1 (0-2)
Emergency department	0.1 (0.3)	0.1 (0.4)	0.5 (0.8)	0.5 (1.7)
	0 (0-0)	0 (0-0)	0 (0-1)	0 (0-1)
Nurse specialist	0.3 (1.1)	0.5 (1.3)	2.7 (6.1)	2.8 (4.7)
	0 (0-0)	0 (0-0.3)	1 (0-3)	1 (0-3)
Physical therapist	2.6 (5.3)	4.0 (7.2)	11.3 (15.1)	19.2 (21.0)
	0 (0-2)	0 (0-6)	2.5 (0-18.3)	14.5 (0-26.8)
Rehabilitation	0.0 (0.2)	0.2 (0.6)	0.1 (0.6)[#]	2.3 (9.8)[#]
	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
Hospital	0.3 (1.0)	0.5 (3.4)	0.1 (0.8)	0.6 (2.4)
	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
Medication-related				
Infusion	0.0 (0.0)	0.0 (0.2)	0.2 (1.1)	0.2 (1.1)
	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
bDMARD use (days)	0.0 (0.0)	0.0 (0.0)	141.3 (132.9)	74.7 (121.4)
Work-related				
Sick leave (days)	6.4 (12.5)	8.7 (18.8)	16.4 (35.2)	24.2 (50.4)
	0 (0-6.8)	0 (0-3)	3 (0-14.3)	1 (0-17.1)

Data are expressed as mean (SD), unless stated otherwise.

* data are based on imputed resources.#: 3 patients in the TC/T2Tand 12 patients in the UC attended one or more rehabilitation sessions

Costs at baseline and during the trial (48 weeks), by category and treatment arm*

	TC/T2T (n=80)		UC (n=80)	
	Baseline†	**Follow-up (48 weeks)**	**Baseline†**	**Follow-up (48 weeks)**
Visits / day care				
GP	€56 (60)	€137 (143)	€74 (63)	€170 (146)
Rheumatologist	€153 (116)	€573 (353)	€148 (107)	€342 (216)
Other specialists	€50 (112)	€154 (314)	€67 (110)	€203 (341)
Emergency department	€23 (89)	€123 (225)	€37 (112)	€146.5 (453)
Nurse specialist	€10 (38)	€93 (210)	€18 (45)	€98 (163)
Physical therapist	€89 (185)	€392 (524)	€137 (251)	€667 (731)
Rehabilitation	€4 (25)	€14 (93)	€36 (89)	€366 (1577)
Hospital	€157 (460)	€85 (368)	€254 (1664)	€302.5 (1181)
Medication-related				
Infusion	€0 (0)	€38 (189)	€7 (34)	€42 (192)
bDMARD use	€0 (0)	€3252 (3058)	€0 (0)	€1719 (2793)
Work-related				
Sick leave	€1863 (3661)	€4809 (10291)	€2545 (5507)	€7082 (14744)
Healthcare costs, total	**€542 (554)**	**€4975.5 (3206)**	**€779 (1864)**	**€4175 (4020)**
Societal costs, total	**€2405 (3880)**	**€9785 (11172)**	**€3324 (6378)**	**€11257 (15819)**

Data are expressed as mean (SD), unless stated otherwise.

*The above data are based on imputed costs.

†Resource use during the 12 weeks pre-baseline was used to calculate baseline costs.

Part I. Base-case analyses

1. Unadjusted analysis

A. Societal perspective

Point estimates of model (non-bootstrapped)

	iCosts	iQALY	ICUR	iNMB*
Usual care	-	-	-	-
Tight control	-€1,472	0.069	Dominates UC	€2,860

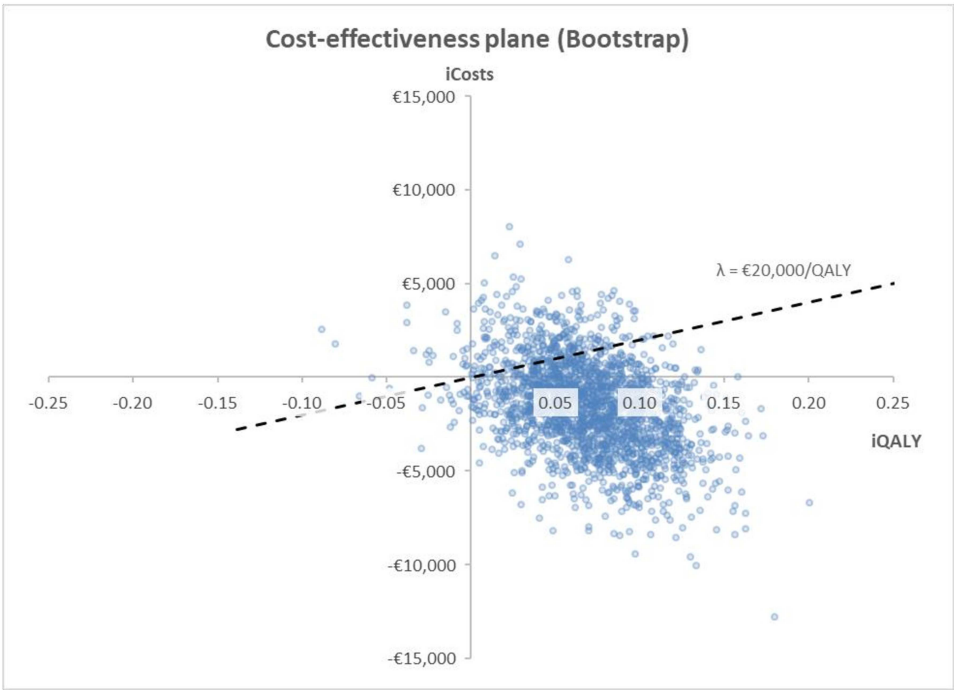
*For lambda = €20,000/QALY

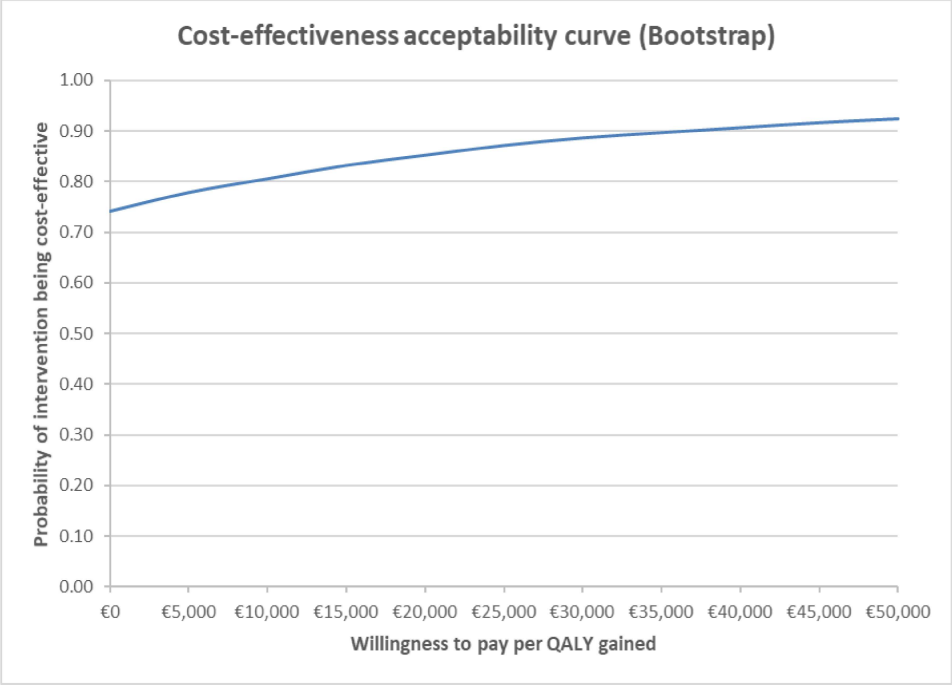
Bootstrapping results (two-stage bootstrap, n=5000):

	iCosts	iQALY	ICUR*	iNMB†
Mean	-€1,506	0.068	-19,647	€2,874
Standard deviation	€2,415	0.034	61,557	€2,767
Median	-€1,501	0.068	-22,280	€2,854
2.5th percentile	-€6,271	0.002	-138,881	-€2,544
97.5th percentile	€3,323	0.133	124,042	€8,294
Minimum	-€12,771	-0.089	-29,508,796	-€7,547
Maximum	€8,005	0.200	3,512,726	€16,365

*ICURs outside the 99%CI excluded for calculation of mean/SD

†For lambda = €20,000/QALY


Cost-effectiveness plane (Bootstrap)
iCosts
€15,000
€10,000
€5,000
-€5,000
-€10,000
-€15,000
λ = €20,000/QALY
-0.25
-0.20
-0.15
-0.10
-0.05
0.05
0.10
0.15
0.20
0.25
iQALY


Cost-effectiveness acceptability curve (Bootstrap)
Probability of intervention being cost-effective
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
€0
€5,000
€10,000
€15,000
€20,000
€25,000
€30,000
€35,000
€40,000
€45,000
€50,000
Willingness to pay per QALY gained

B. Healthcare perspective

Point estimates of model (non-bootstrapped)

	iCosts	iQALY	ICUR	iNMB*
Usual care	-	-	-	-
Tight control	€801	0.069	€11,538/QALY (NE)	€587

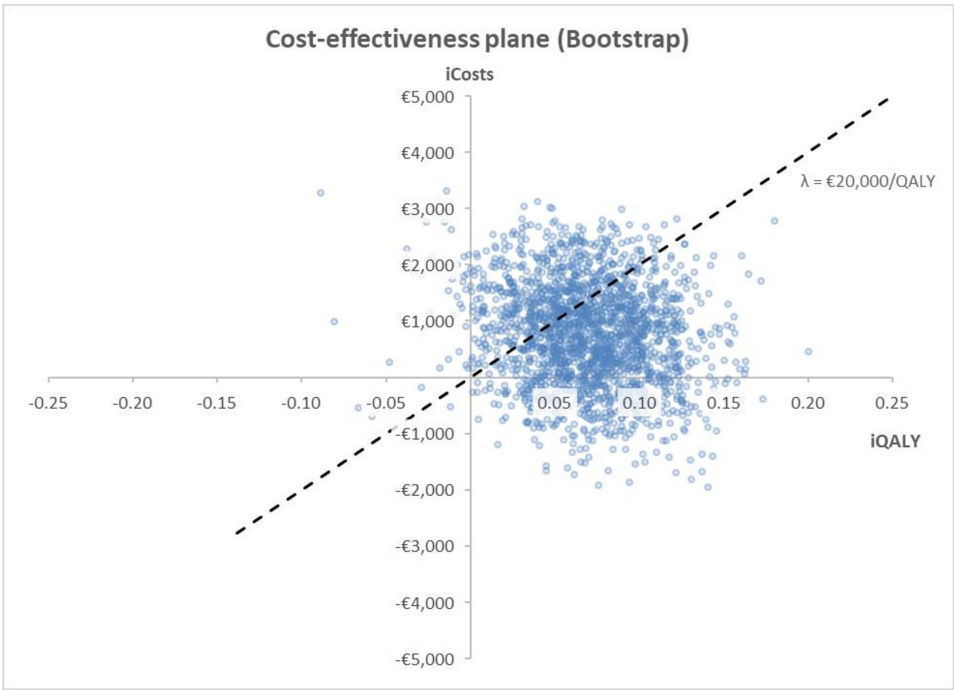
*For lambda = €20,000/QALY

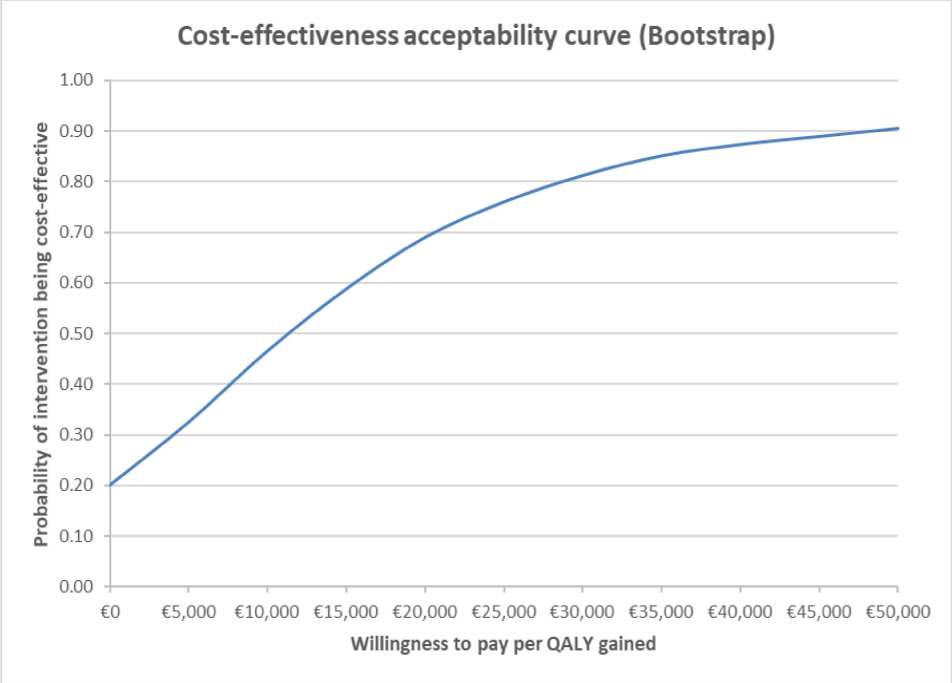
Bootstrapping results (two-stage bootstrap, n=5000):

	iCosts	iQALY	ICUR*	iNMB†
Mean	€779	0.068	15,472	€589
Standard deviation	€905	0.034	37,303	€1,210
Median	€785	0.068	10,704	€593
2.5th percentile	-€957	0.002	-27,918	-€1,840
97.5th percentile	€2,525	0.133	102,603	€2,973
Minimum	-€2,445	-0.089	-16,379,730	-€5,043
Maximum	€3,779	0.200	6,788,035	€4,754

*ICURs outside the 99%CI excluded for calculation of mean/SD

†For lambda = €20,000/QALY


Cost-effectiveness plane (Bootstrap)
iCosts
€5,000
€4,000
€3,000
€2,000
€1,000
-€1,000
-€2,000
-€3,000
-€4,000
-€5,000
λ = €20,000/QALY
-0.25
-0.20
-0.15
-0.10
-0.05
0.05
0.10
0.15
0.20
0.25
iQALY


Cost-effectiveness acceptability curve (Bootstrap)
Probability of intervention being cost-effective
1.00
0.90
0.80
0.70
0.60
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€10,000
€15,000
€20,000
€25,000
€30,000
€35,000
€40,000
€45,000
€50,000
Willingness to pay per QALY gained

2. Adjusted analysis

A. Societal perspective

Point estimates of model (non-bootstrapped)

	iCosts	iQALY	ICUR	iNMB*
Usual care	-	-	-	-
Tight control	-€472	0.041	Dominates UC	€1,295

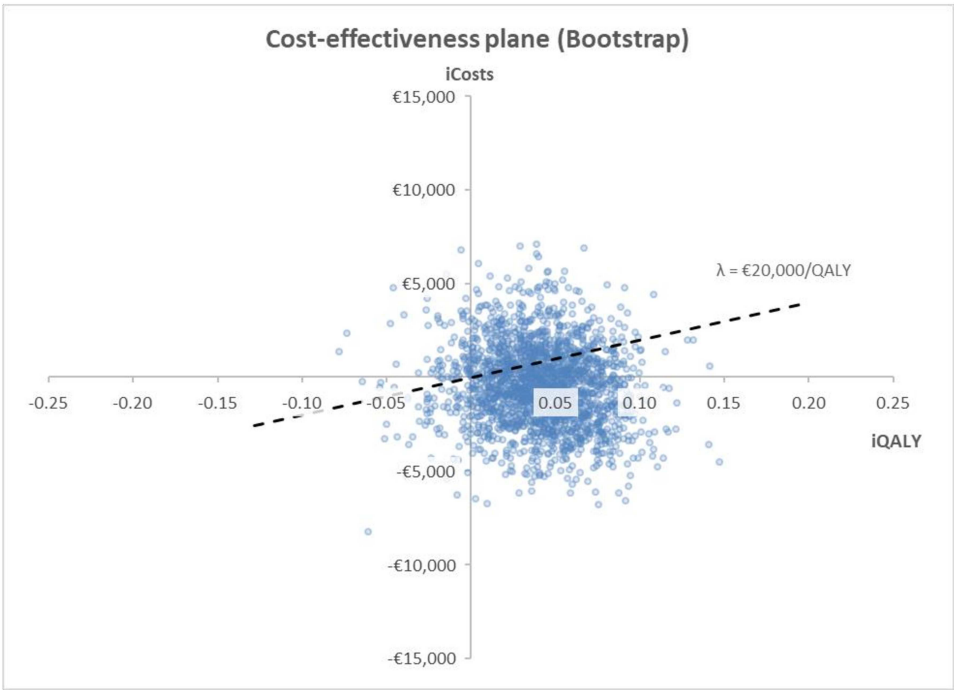
*For lambda = €20,000/QALY

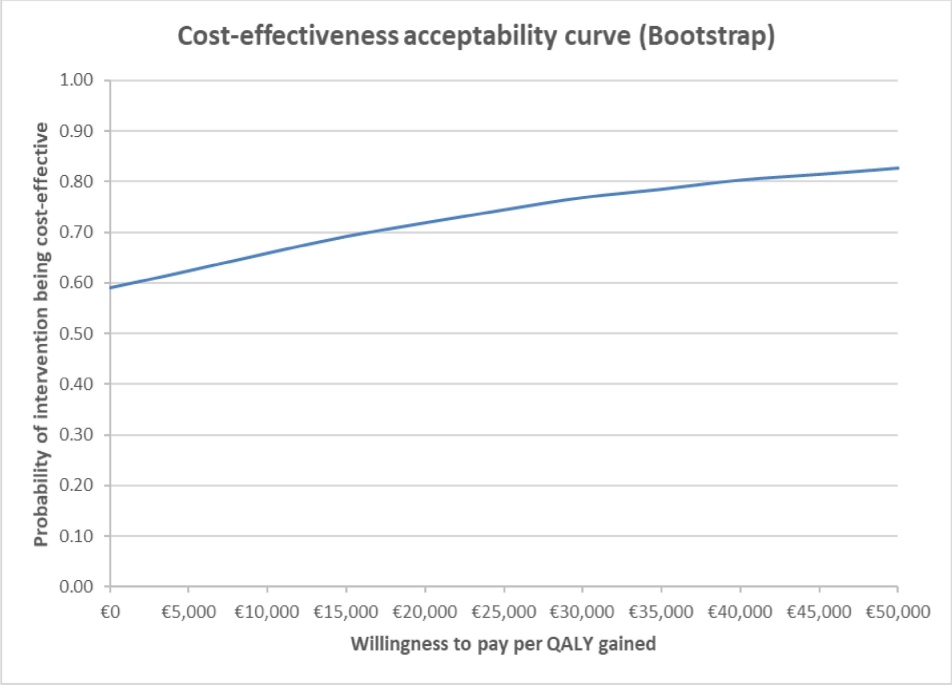
Bootstrapping results (two-stage bootstrap, n=5000):

	iCosts	iQALY	ICUR*	iNMB†
Mean	-€443	0.041	-8,930	€1,256
Standard deviation	€2,177	0.028	160,860	€2,307
Median	-€493	0.041	-10,723	€1,309
2.5th percentile	-€4,522	-0.016	-345,869	-€3,625
97.5th percentile	€4,019	0.093	332,447	€5,611
Minimum	-€8,559	-0.078	-100,166,342	-€8,073
Maximum	€8,218	0.147	111,414,588	€9,978

*ICURs outside the 99%CI excluded for calculation of mean/SD

†For lambda = €20,000/QALY


Cost-effectiveness plane (Bootstrap)
iCosts
€15,000
€10,000
€5,000
-€5,000
-€10,000
-€15,000
λ = €20,000/QALY
-0.25
-0.20
-0.15
-0.10
-0.05
0.05
0.10
0.15
0.20
0.25
iQALY


Cost-effectiveness acceptability curve (Bootstrap)
Probability of intervention being cost-effective
1.00
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0.70
0.60
0.50
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0.20
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€10,000
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€20,000
€25,000
€30,000
€35,000
€40,000
€45,000
€50,000
Willingness to pay per QALY gained

B. Healthcare perspective

Point estimates of model (non-bootstrapped)

	iCosts	iQALY	ICUR	iNMB*
Usual care	-	-	-	-
Tight control	€789	0.041	€19,430/QALY (NE)	€23

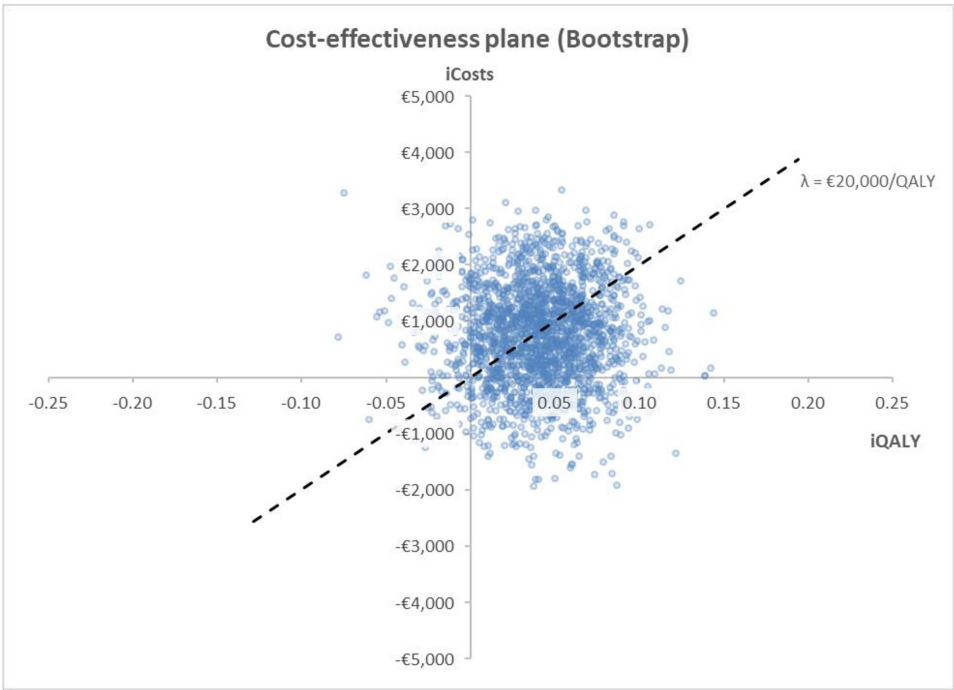
*For lambda = €20,000/QALY

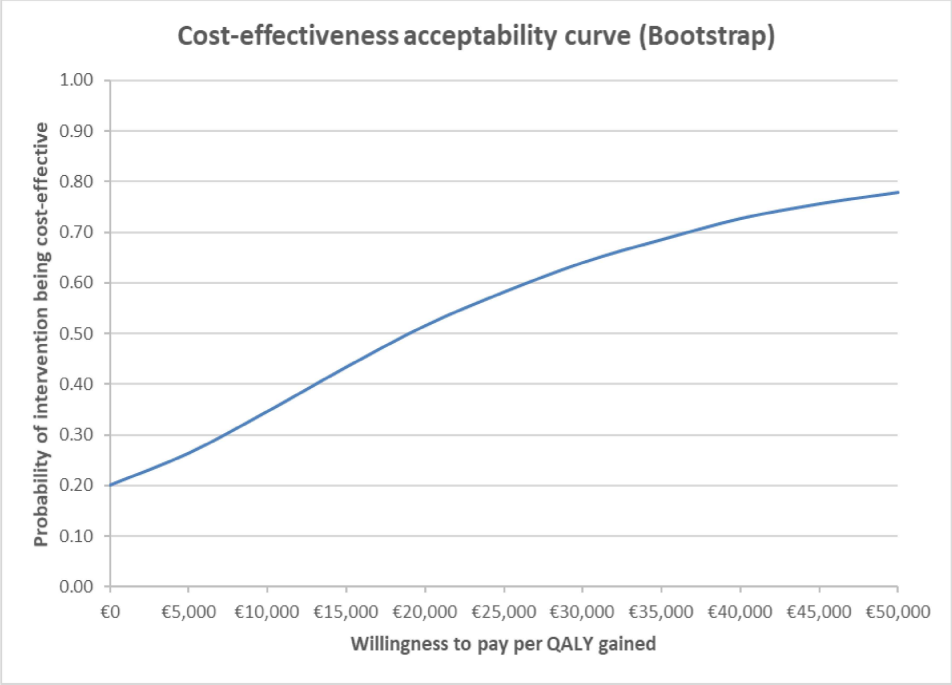
Bootstrapping results (two-stage bootstrap, n=5000):

	iCosts	iQALY	ICUR*	iNMB†
Mean	€763	0.040	22,401	€35
Standard deviation	€894	0.028	95,796	€1,036
Median	€768	0.040	16,144	€32
2.5th percentile	-€978	-0.016	-131,910	-€1,964
97.5th percentile	€2,491	0.092	224,560	€2,106
Minimum	-€2,446	-0.079	-33,520,131	-€4,776
Maximum	€3,737	0.144	14,513,331	€3,772

*ICURs outside the 99%CI excluded for calculation of mean/SD

†For lambda = €20,000/QALY


Cost-effectiveness plane (Bootstrap)
iCosts
€5,000
€4,000
€3,000
€2,000
€1,000
-€1,000
-€2,000
-€3,000
-€4,000
-€5,000
-0.25
-0.20
-0.15
-0.10
-0.05
0.05
0.10
0.15
0.20
0.25
iQALY
λ = €20,000/QALY


Cost-effectiveness acceptability curve (Bootstrap)
Probability of intervention being cost-effective
1.00
0.90
0.80
0.70
0.60
0.50
0.40
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€5,000
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€35,000
€40,000
€45,000
€50,000
Willingness to pay per QALY gained

Part II. Sensitivity analyses

1. Discounted bDMARD price (25%)

A. Societal perspective

Point estimates of model (non-bootstrapped)

	iCosts	iQALY	ICUR	iNMB*
Usual care	-	-	-	-
Tight control	-€856	0.041	Dominates UC	€1,678

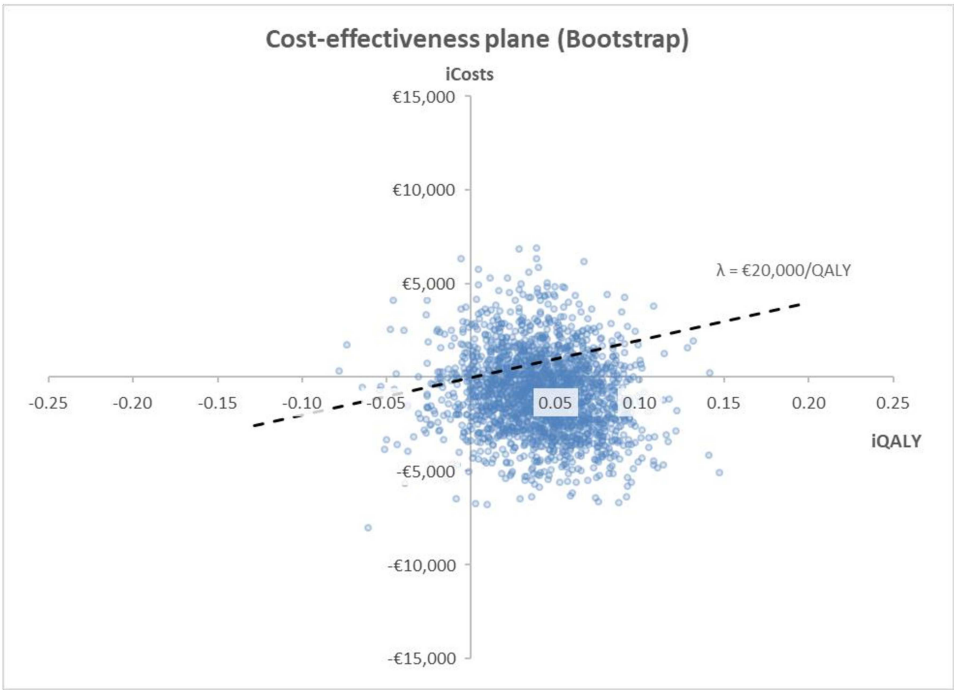
*For lambda = €20,000/QALY

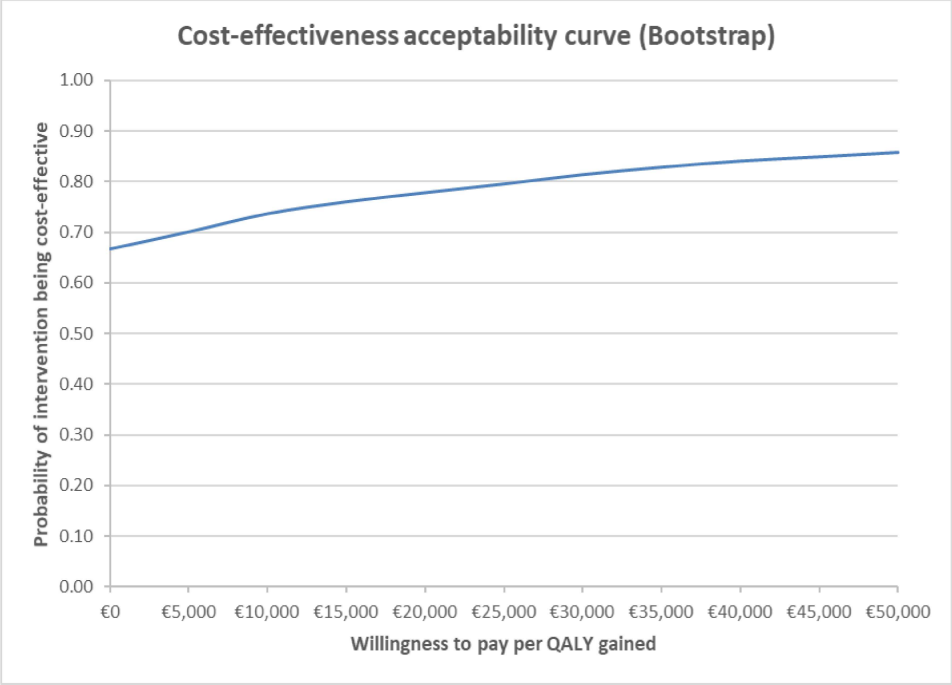
Bootstrapping results (two-stage bootstrap, n=5000):

	iCosts	iQALY	ICUR*	iNMB†
Mean	-€834	0.041	-18,864	€1,647
Standard deviation	€2,148	0.028	163,496	€2,283
Median	-€895	0.041	-19,003	€1,702
2.5th percentile	-€4,887	-0.016	-357,593	-€3,224
97.5th percentile	€3,673	0.093	312,114	€5,917
Minimum	-€8,467	-0.078	-26,216,158	-€7,449
Maximum	€7,630	0.147	38,792,311	€9,878

*ICURs outside the 99%CI excluded for calculation of mean/SD

†For lambda = €20,000/QALY


Cost-effectiveness plane (Bootstrap)
iCosts
€15,000
€10,000
€5,000
-€5,000
-€10,000
-€15,000
λ = €20,000/QALY
-0.25
-0.20
-0.15
-0.10
-0.05
0.05
0.10
0.15
0.20
0.25
iQALY


Cost-effectiveness acceptability curve (Bootstrap)
Probability of intervention being cost-effective
1.00
0.90
0.80
0.70
0.60
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€10,000
€15,000
€20,000
€25,000
€30,000
€35,000
€40,000
€45,000
€50,000
Willingness to pay per QALY gained

B. Healthcare perspective

Point estimates of model (non-bootstrapped)

	iCosts	iQALY	ICUR	iNMB*
Usual care	-	-	-	-
Tight control	€406	0.041	€9,888/QALY (NE)	€415

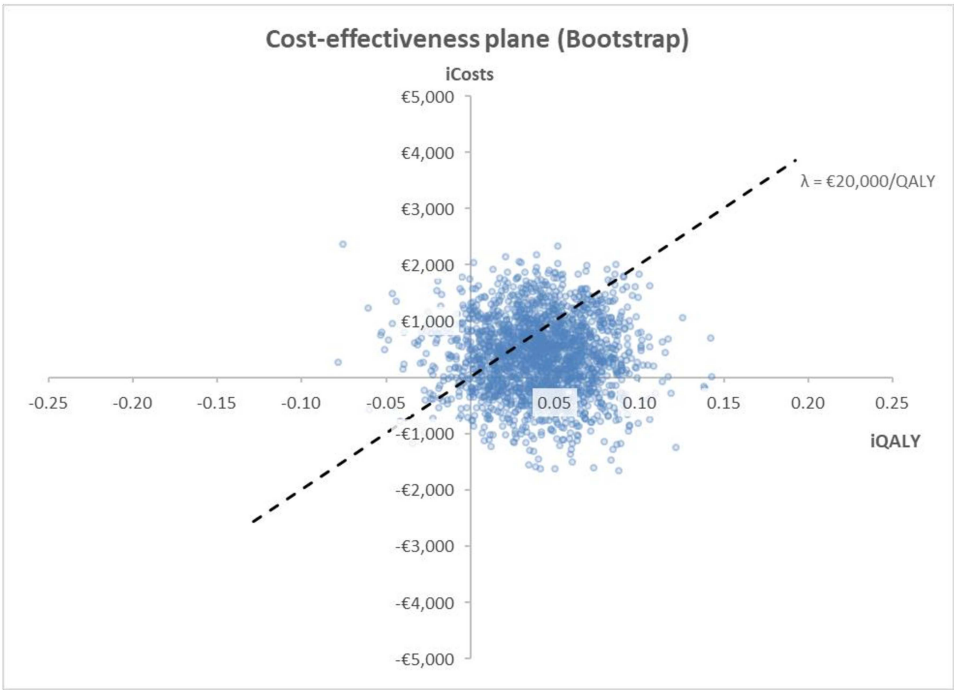
*For lambda = €20,000/QALY

Bootstrapping results (two-stage bootstrap, n=5000):

	iCosts	iQALY	ICUR*	iNMB†
Mean	€391	0.040	11,884	€415
Standard deviation	€676	0.028	65,048	€876
Median	€396	0.041	8,348	€408
2.5th percentile	-€950	-0.016	-88,617	-€1,278
97.5th percentile	€1,710	0.092	140,444	€2,143
Minimum	-€2,106	-0.079	-204,871,013	-€3,872
Maximum	€2,849	0.142	18,145,761	€3,675

*ICURs outside the 99%CI excluded for calculation of mean/SD

†For lambda = €20,000/QALY


Cost-effectiveness plane (Bootstrap)
iCosts
€5,000
€4,000
€3,000
€2,000
€1,000
-€1,000
-€2,000
-€3,000
-€4,000
-€5,000
λ = €20,000/QALY
-0.25
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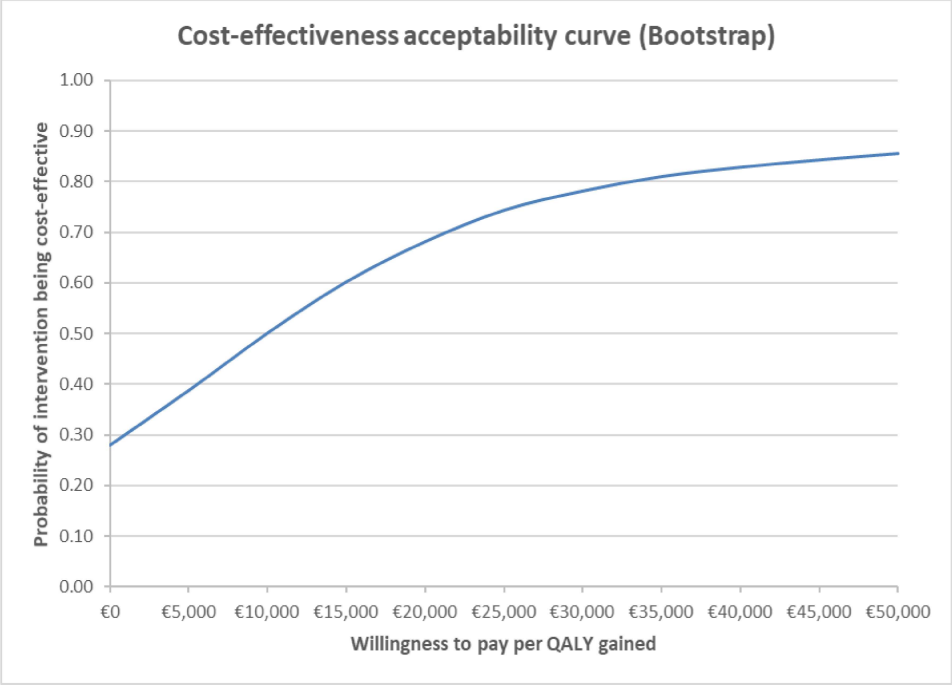
-0.15
-0.10
-0.05
0.05
0.10
0.15
0.20
0.25
iQALY


Cost-effectiveness acceptability curve (Bootstrap)
Probability of intervention being cost-effective
1.00
0.90
0.80
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€25,000
€30,000
€35,000
€40,000
€45,000
€50,000
Willingness to pay per QALY gained

2. Discounted bDMARD price (50%)

A. Societal perspective

Point estimates of model (non-bootstrapped)

	iCosts	iQALY	ICUR	iNMB*
Usual care	-	-	-	-
Tight control	-€1,239	0.041	Dominates UC	€2,060

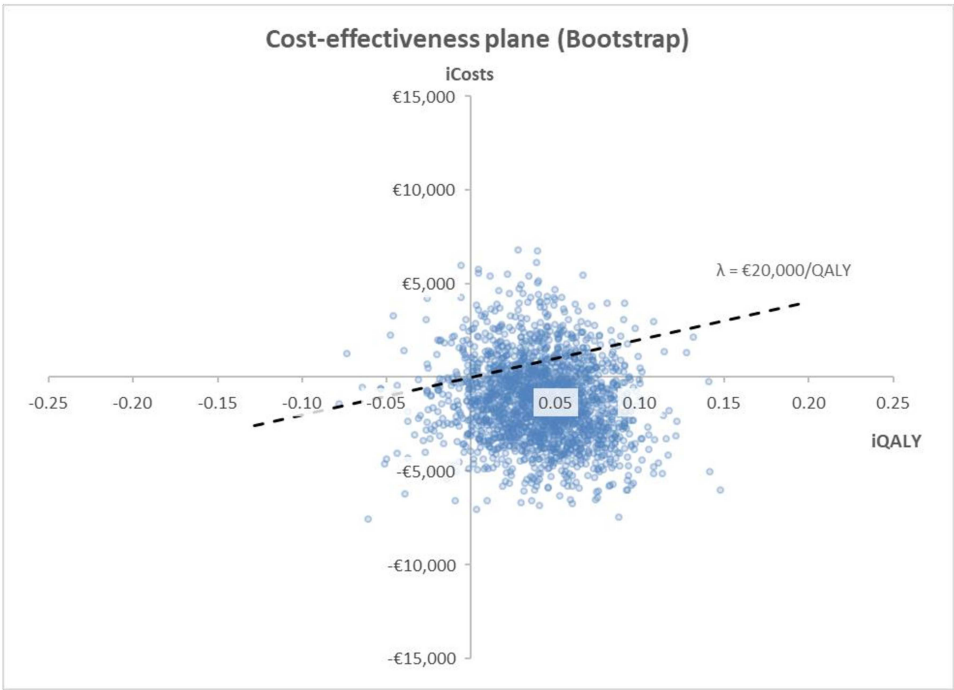
*For lambda = €20,000/QALY

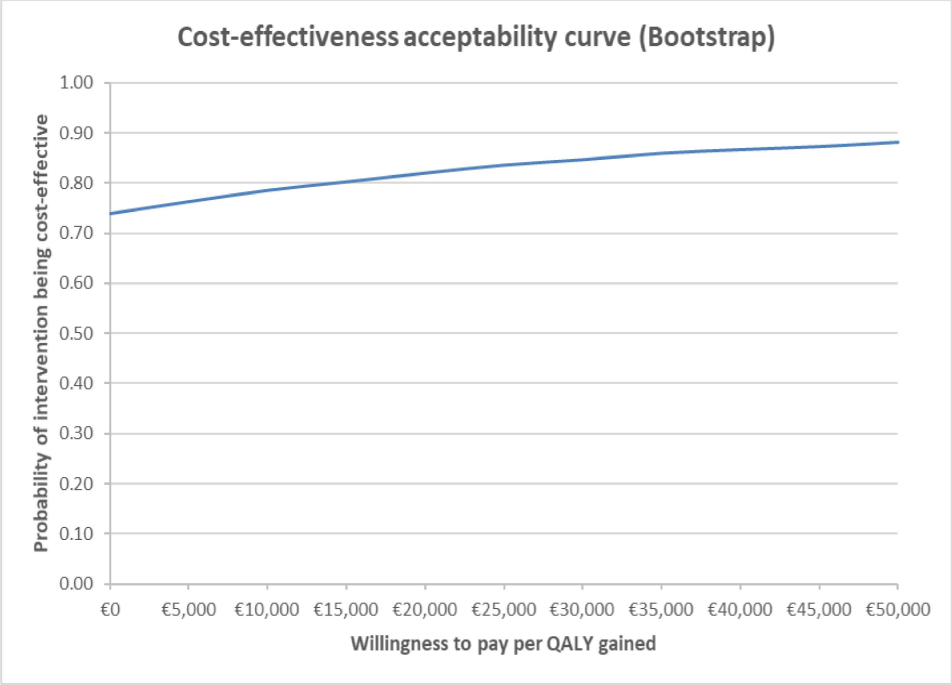
Bootstrapping results (two-stage bootstrap, n=5000):

	iCosts	iQALY	ICUR*	iNMB†
Mean	-€1,246	0.041	-31,433	€2,057
Standard deviation	€2,195	0.028	177,447	€2,328
Median	-€1,303	0.041	-28,371	€2,127
2.5th percentile	-€5,249	-0.016	-408,725	-€2,894
97.5th percentile	€3,415	0.093	316,855	€6,332
Minimum	-€8,189	-0.078	-18,949,232	-€6,928
Maximum	€7,141	0.148	82,317,237	€9,582

*ICURs outside the 99%CI excluded for calculation of mean/SD

†For lambda = €20,000/QALY


Cost-effectiveness plane (Bootstrap)
iCosts
€15,000
€10,000
€5,000
-€5,000
-€10,000
-€15,000
λ = €20,000/QALY
-0.25
-0.20
-0.15
-0.10
-0.05
0.05
0.10
0.15
0.20
0.25
iQALY


Cost-effectiveness acceptability curve (Bootstrap)
Probability of intervention being cost-effective
1.00
0.90
0.80
0.70
0.60
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€0
€5,000
€10,000
€15,000
€20,000
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€35,000
€40,000
€45,000
€50,000
Willingness to pay per QALY gained

B. Healthcare perspective

Point estimates of model (non-bootstrapped)

	iCosts	iQALY	ICUR	iNMB*
Usual care	-	-	-	-
Tight control	€23	0.042	€553/QALY (NE)	€809

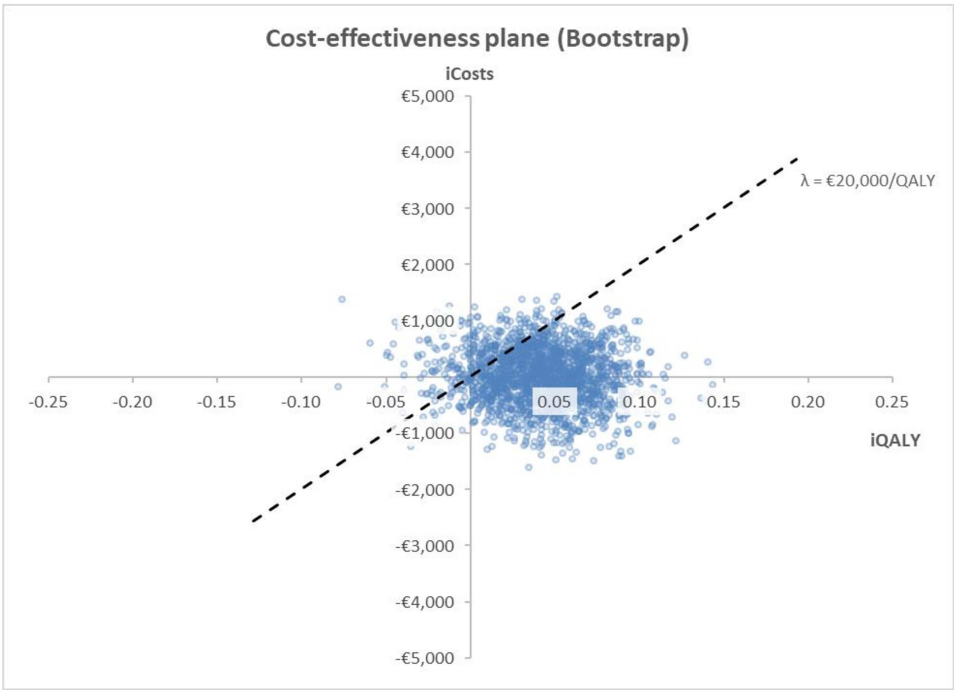
*For lambda = €20,000/QALY

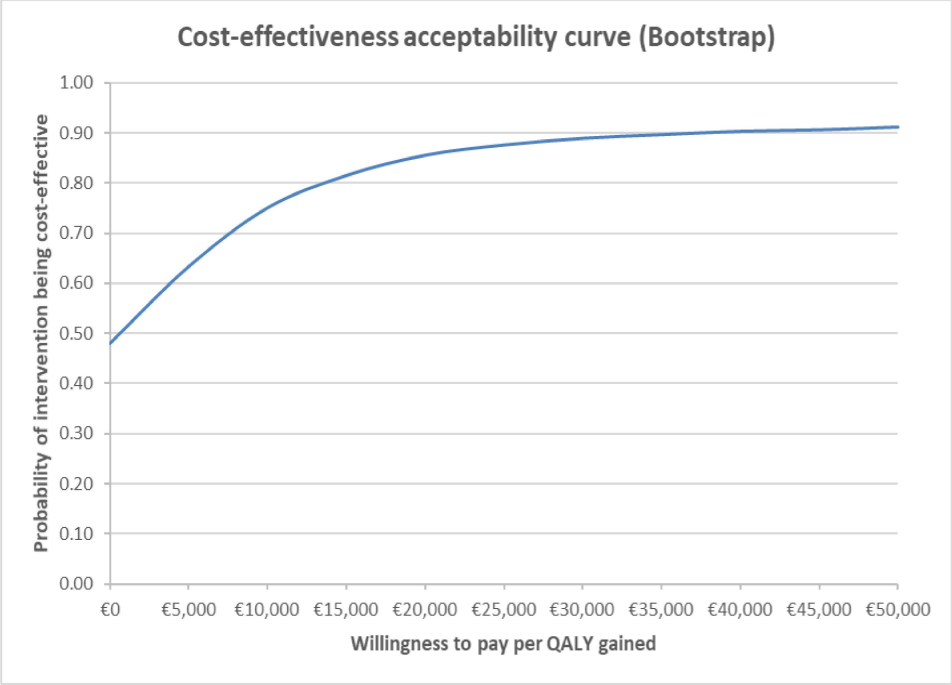
Bootstrapping results (two-stage bootstrap, n=5000):

	iCosts	iQALY	ICUR*	iNMB†
Mean	€18	0.041	179	€798
Standard deviation	€495	0.028	42,376	€769
Median	€24	0.041	336	€798
2.5th percentile	-€960	-0.015	-66,836	-€689
97.5th percentile	€979	0.092	77,786	€2,300
Minimum	-€2,083	-0.078	-33,769,027	-€2,900
Maximum	€1,914	0.143	5,800,150	€3,579

*ICURs outside the 99%CI excluded for calculation of mean/SD

†For lambda = €20,000/QALY


Cost-effectiveness plane (Bootstrap)
iCosts
€5,000
€4,000
€3,000
€2,000
€1,000
-€1,000
-€2,000
-€3,000
-€4,000
-€5,000
λ = €20,000/QALY
-0.25
-0.20
-0.15
-0.10
-0.05
0.05
0.10
0.15
0.20
0.25
iQALY


Cost-effectiveness acceptability curve (Bootstrap)
Probability of intervention being cost-effective
1.00
0.90
0.80
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€5,000
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€35,000
€40,000
€45,000
€50,000
Willingness to pay per QALY gained

3. ASAS-HI utility

A. Societal perspective

Point estimates of model (non-bootstrapped)

	iCosts	iQALY	ICUR	iNMB*
Usual care	-	-	-	-
Tight control	-€466	0.018	Dominates UC	€817

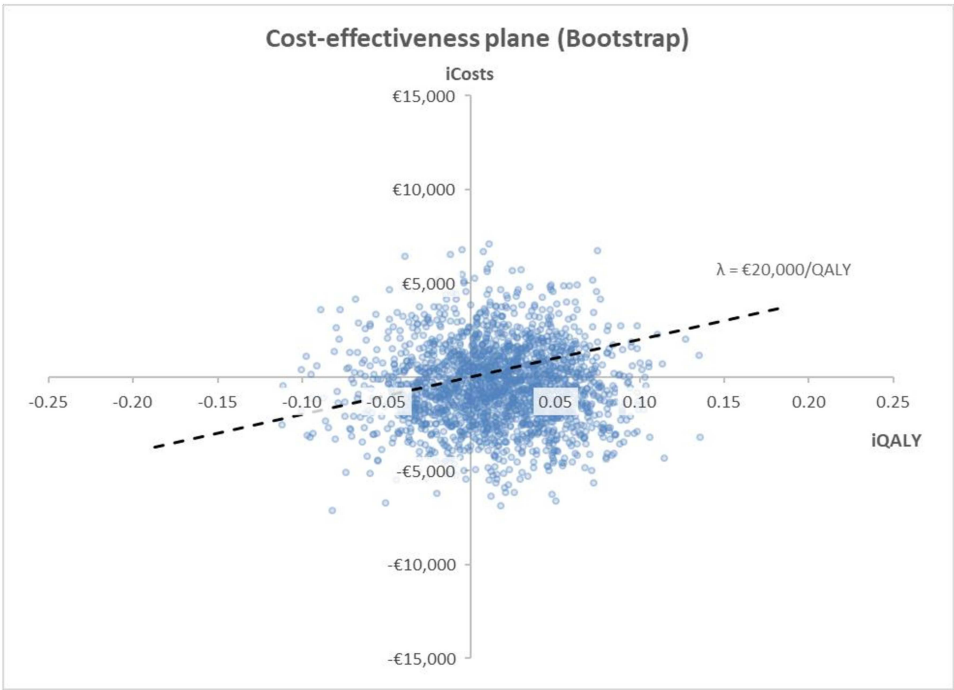
*For lambda = €20,000/QALY

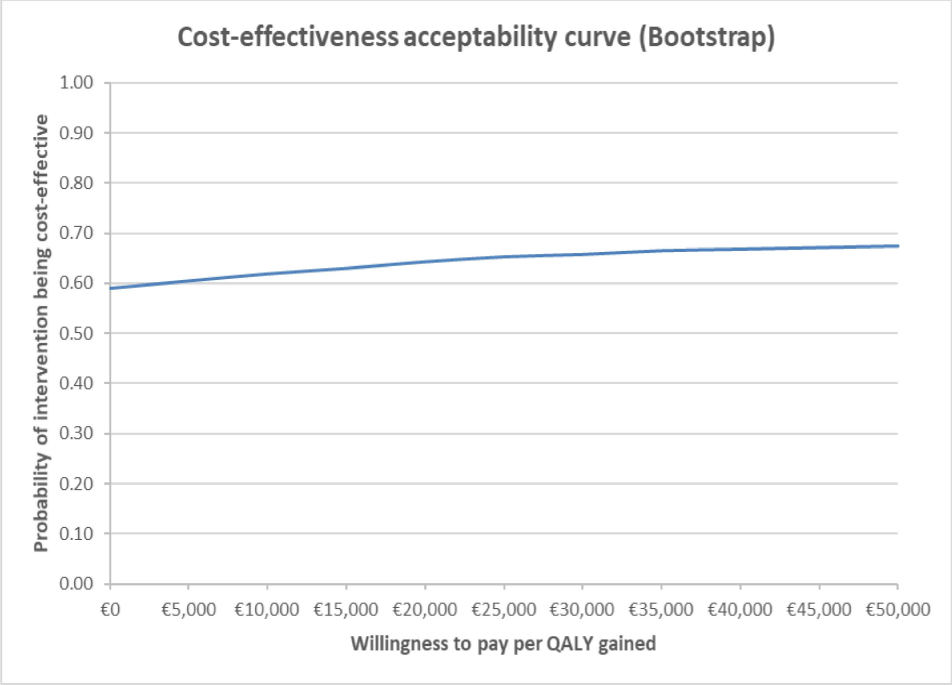
Bootstrapping results (two-stage bootstrap, n=5000):

	iCosts	iQALY	ICUR*	iNMB†
Mean	-€441	0.015	-908	€736
Standard deviation	€2,157	0.037	298,989	€2,270
Median	-€480	0.015	-3,841	€788
2.5th percentile	-€4,521	-0.062	-561,242	-€4,001
97.5th percentile	€3,957	0.084	682,412	€4,974
Minimum	-€7,994	-0.137	-379,636,432	-€8,585
Maximum	€8,253	0.138	79,493,574	€8,285

*ICURs outside the 99%CI excluded for calculation of mean/SD

†For lambda = €20,000/QALY


Cost-effectiveness plane (Bootstrap)
iCosts
€15,000
€10,000
€5,000
-€5,000
-€10,000
-€15,000
λ = €20,000/QALY
-0.25
-0.20
-0.15
-0.10
-0.05
0.05
0.10
0.15
0.20
0.25
iQALY


Cost-effectiveness acceptability curve (Bootstrap)
Probability of intervention being cost-effective
1.00
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0.80
0.70
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€5,000
€10,000
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€20,000
€25,000
€30,000
€35,000
€40,000
€45,000
€50,000
Willingness to pay per QALY gained

B. Healthcare perspective

Point estimates of model (non-bootstrapped)

	iCosts	iQALY	ICUR	iNMB*
Usual care	-	-	-	-
Tight control	€793	0.015	€51,938/QALY (NE)	-€487

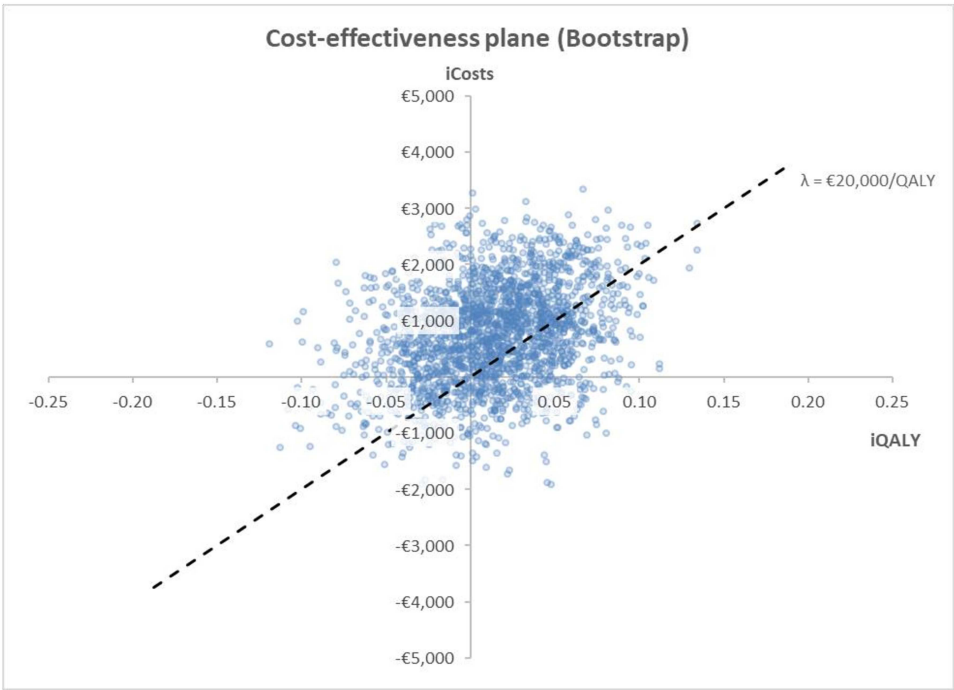
*For lambda = €20,000/QALY

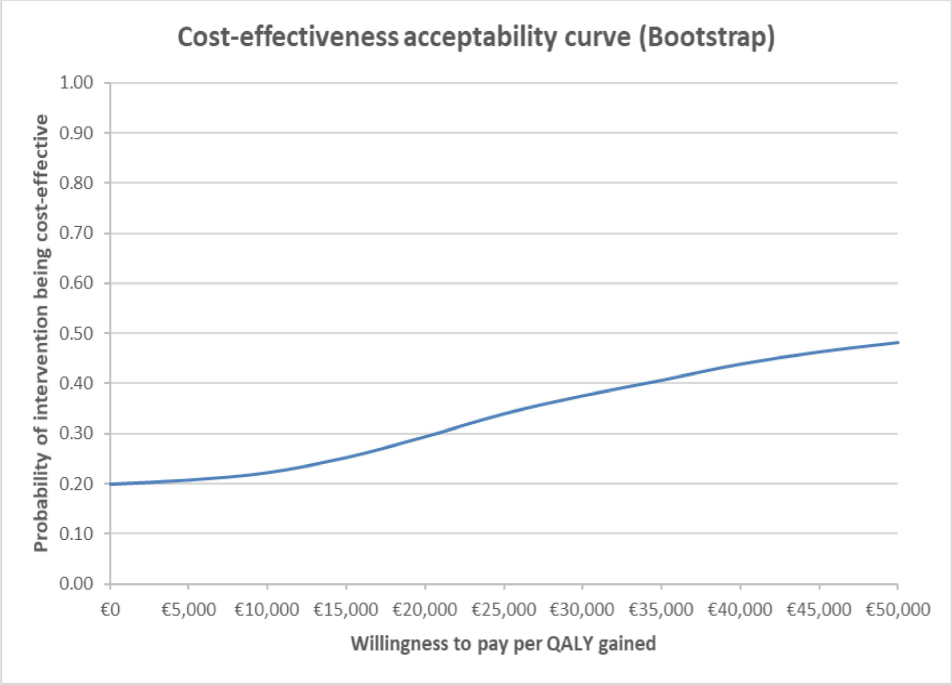
Bootstrapping results (two-stage bootstrap, n=5000):

	iCosts	iQALY	ICUR*	iNMB†
Mean	€761	0.013	20,432	-€495
Standard deviation	€894	0.037	170,353	€960
Median	€766	0.014	15,928	-€495
2.5th percentile	-€982	-0.063	-331,508	-€2,413
97.5th percentile	€2,489	0.083	389,335	€1,438
Minimum	-€2,443	-0.138	-22,849,461	-€4,150
Maximum	€3,726	0.138	8,741,179,760	€2,871

*ICURs outside the 99%CI excluded for calculation of mean/SD

†For lambda = €20,000/QALY


Cost-effectiveness plane (Bootstrap)
iCosts
€5,000
€4,000
€3,000
€2,000
€1,000
-€1,000
-€2,000
-€3,000
-€4,000
-€5,000
-0.25
-0.20
-0.15
-0.10
-0.05
0.05
0.10
0.15
0.20
0.25
iQALY
λ = €20,000/QALY


Cost-effectiveness acceptability curve (Bootstrap)
Probability of intervention being cost-effective
1.00
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0.70
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€25,000
€30,000
€35,000
€40,000
€45,000
€50,000
Willingness to pay per QALY gained

4. Friction cost approach (societal perspective only)

A. Societal perspective

Point estimates of model (non-bootstrapped)

	iCosts	iQALY	ICUR	iNMB*
Usual care	-	-	-	-
Tight control	€183	0.042	€4,400/QALY (NE)	€648

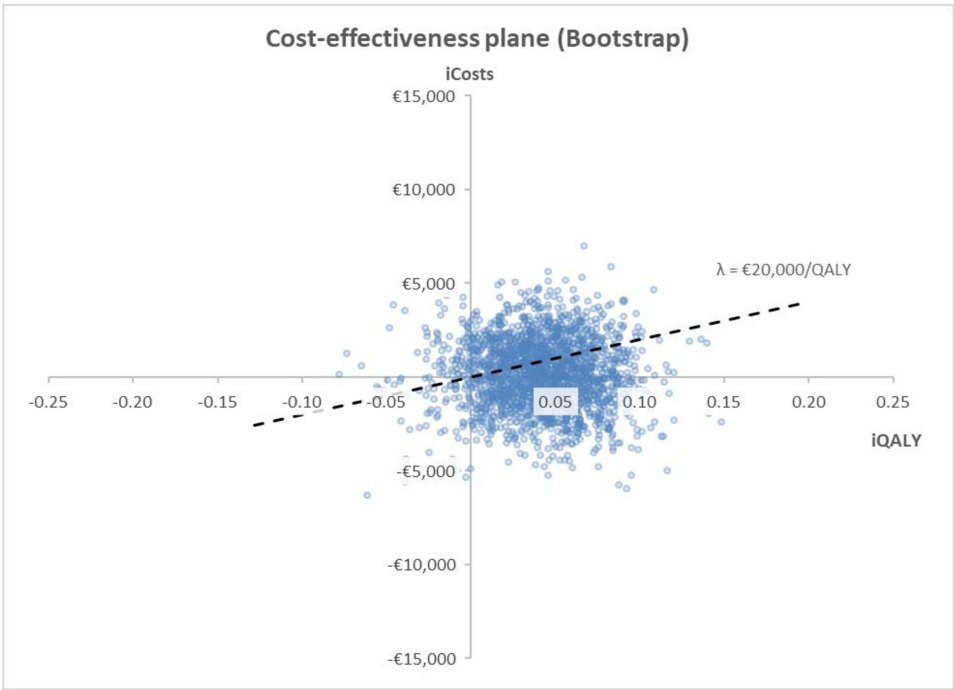
*For lambda = €20,000/QALY

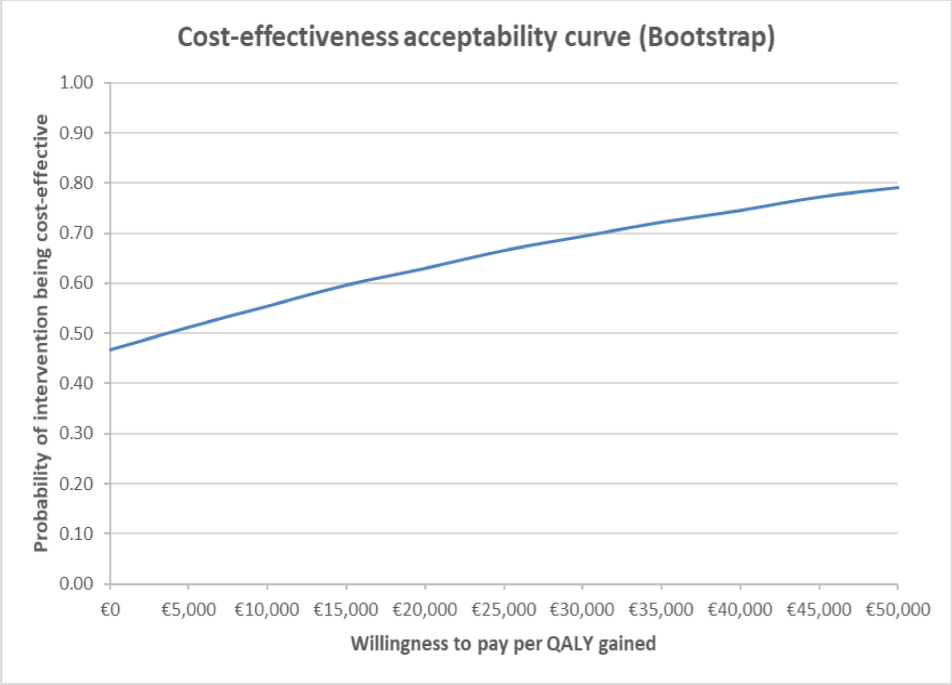
Bootstrapping results (two-stage bootstrap, n=5000):

	iCosts	iQALY	ICUR*	iNMB†
Mean	€163	0.041	5,307	€656
Standard deviation	€1,859	0.028	153,584	€1,954
Median	€151	0.041	3,022	€691
2.5th percentile	-€3,487	-0.016	-250,732	-€3,216
97.5th percentile	€3,863	0.093	313,244	€4,596
Minimum	-€8,223	-0.078	-11,440,354	-€6,441
Maximum	€7,613	0.148	96,398,295	€9,836

*ICURs outside the 99%CI excluded for calculation of mean/SD

†For lambda = €20,000/QALY


Cost-effectiveness plane (Bootstrap)
iCosts
€15,000
€10,000
€5,000
-€5,000
-€10,000
-€15,000
λ = €20,000/QALY
-0.25
-0.20
-0.15
-0.10
-0.05
0.05
0.10
0.15
0.20
0.25
iQALY


Cost-effectiveness acceptability curve (Bootstrap)
Probability of intervention being cost-effective
1.00
0.90
0.80
0.70
0.60
0.50
0.40
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0.20
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€0
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€10,000
€15,000
€20,000
€25,000
€30,000
€35,000
€40,000
€45,000
€50,000
Willingness to pay per QALY gained

5. Costs of presenteeism included (societal perspective only)

A. Societal perspective

Point estimates of model (non-bootstrapped)

	iCosts	iQALY	ICUR	iNMB*
Usual care	-	-	-	-
Tight control	-€876	0.040	Dominates UC	€1,679

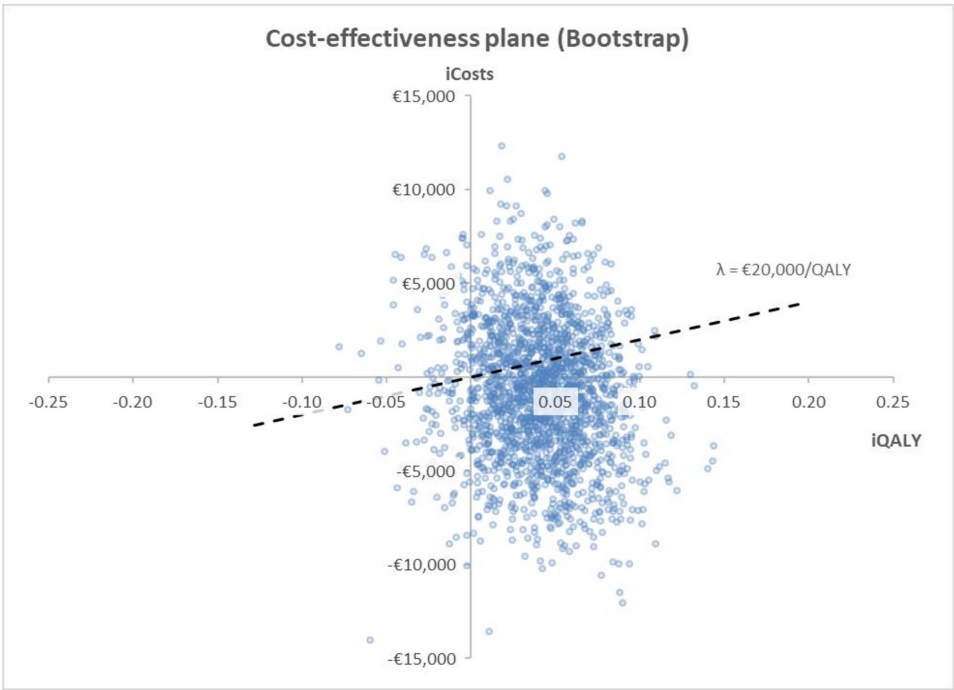
*For lambda = €20,000/QALY

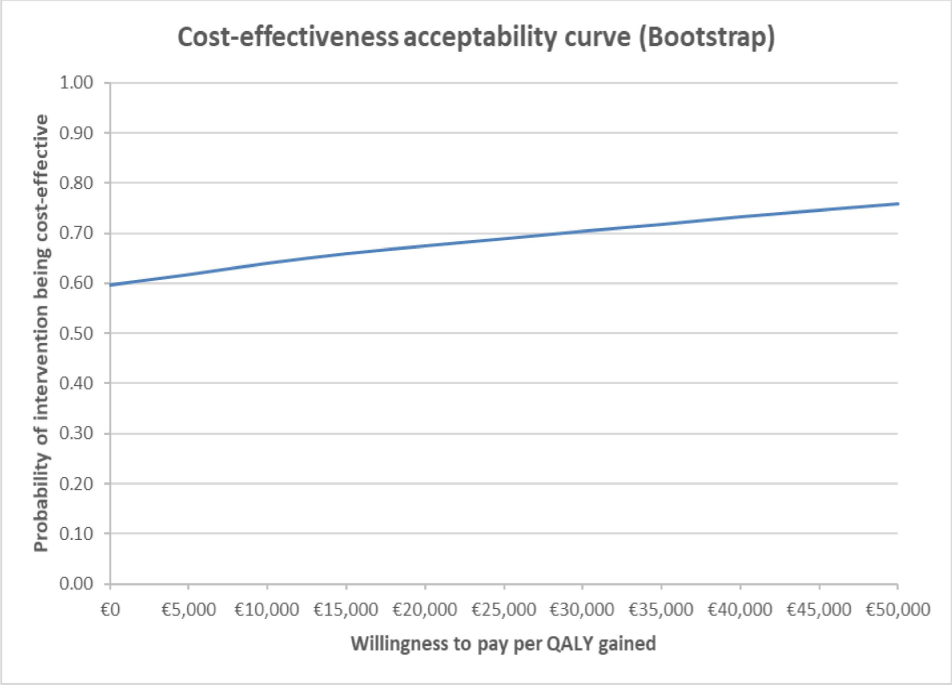
Bootstrapping results (two-stage bootstrap, n=5000):

	iCosts	iQALY	ICUR*	iNMB†
Mean	-€829	0.040	-21,044	€1,631
Standard deviation	€3,724	0.028	332,888	€3,843
Median	-€813	0.041	-18,641	€1,658
2.5th percentile	-€8,006	-0.017	-688,183	-€6,020
97.5th percentile	€6,616	0.092	586,797	€8,961
Minimum	-€14,019	-0.078	-21,954,314	-€13,626
Maximum	€14,282	0.144	48,325,857	€14,629

*ICURs outside the 99%CI excluded for calculation of mean/SD

†For lambda = €20,000/QALY


Cost-effectiveness plane (Bootstrap)
iCosts
€15,000
€10,000
€5,000
-€5,000
-€10,000
-€15,000
λ = €20,000/QALY
-0.25
-0.20
-0.15
-0.10
-0.05
0.05
0.10
0.15
0.20
0.25
iQALY


Cost-effectiveness acceptability curve (Bootstrap)
Probability of intervention being cost-effective
1.00
0.90
0.80
0.70
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€45,000
€50,000
Willingness to pay per QALY gained