HEALTH ECONOMIC EVALUATION ALONGSIDE RANDOMIZED CLINICAL TRIALS
STEP-BY-STEP METHODOLOGY

A tutorial by Alfredo Polo MD, PhD

June 2020


health
economics


TYOGA
5
4
3
2
1
© AFP/GETTY IMAGES

HEE ALONGSIDE RCT: STEP-BY-STEP METHODOLOGY

THE 9 STEPS TO CONDUCT A HEALTH ECONOMIC EVALUATION FROM A RCT DATA

1. Calculate point estimates for cost and outcomes from raw trial data
2. Manage uncertainties in raw data (re-sampling data)
3. Calculate ICER (incremental cost-effectiveness ratio) and NMB (net monetary benefit)
4. Plot the cost-effectiveness plane
5. Plot the iNMB (incremental net monetary benefit)
6. Calculate and plot the CEAC (cost-effectiveness acceptability curve)
7. Perform BIA (budget impact analysis)
8. Programme budgeting and marginal analysis (PBMA)
9. Overall interpretation

HEE ALONGSIDE RCT: STEP-BY-STEP METHODOLOGY

THE 9 STEPS TO CONDUCT A HEALTH ECONOMIC EVALUATION FROM A RCT DATA

1. Calculate point estimates for cost and outcomes from raw trial data
2. Manage uncertainties in raw data (re-sampling data)
3. Calculate ICER (incremental cost-effectiveness ratio) and NMB (net monetary benefit)
4. Plot the cost-effectiveness plane
5. Plot the iNMB (incremental net monetary benefit)
6. Calculate and plot the CEAC (cost-effectiveness acceptability curve)
7. Perform BIA (budget impact analysis)
8. Programme budgeting and marginal analysis (PBMA)
9. Overall interpretation

CALCULATE POINT ESTIMATES FOR COSTS AND OUTCOMES FROM RAW TRIAL DATA

Group (arm)	Patient ID	Cost A (component A of the treatment, e.g. drugs, hospital expenses…)	Cost B (component B of the treatment, e.g. RT related costs…)	Outcome (baseline)	Outcome 1 (e.g. 1 year)	Outcome 2 (e.g. 2 years)	QALY
Arm 1	#1						
Arm1	#2						
…	…						
Arm 2	#n-1						
Arm 2	#n						

CALCULATE POINT ESTIMATES FOR COSTS AND OUTCOMES FROM RAW TRIAL DATA

Group (arm)	Patient ID	Cost A (component A of the treatment, e.g. drugs, hospital expenses…)	Cost B (component B of the treatment, e.g. RT related costs…)	Outcome (baseline)	Outcome 1 (e.g. 1 year)	Outcome 2 (e.g. 2 years)	QALY
Arm 1	#1						
Arm1	#2						
…	…						
Arm 2	#n-1						
Arm 2	#n						
		Total costs A	Total costs B				Effect

Total costs for each arm

Total effect for each arm

C1 = Total cost (A+B) for arm 1

C2 = Total cost (A+B) for arm 2

E1 = Total effect for arm 1

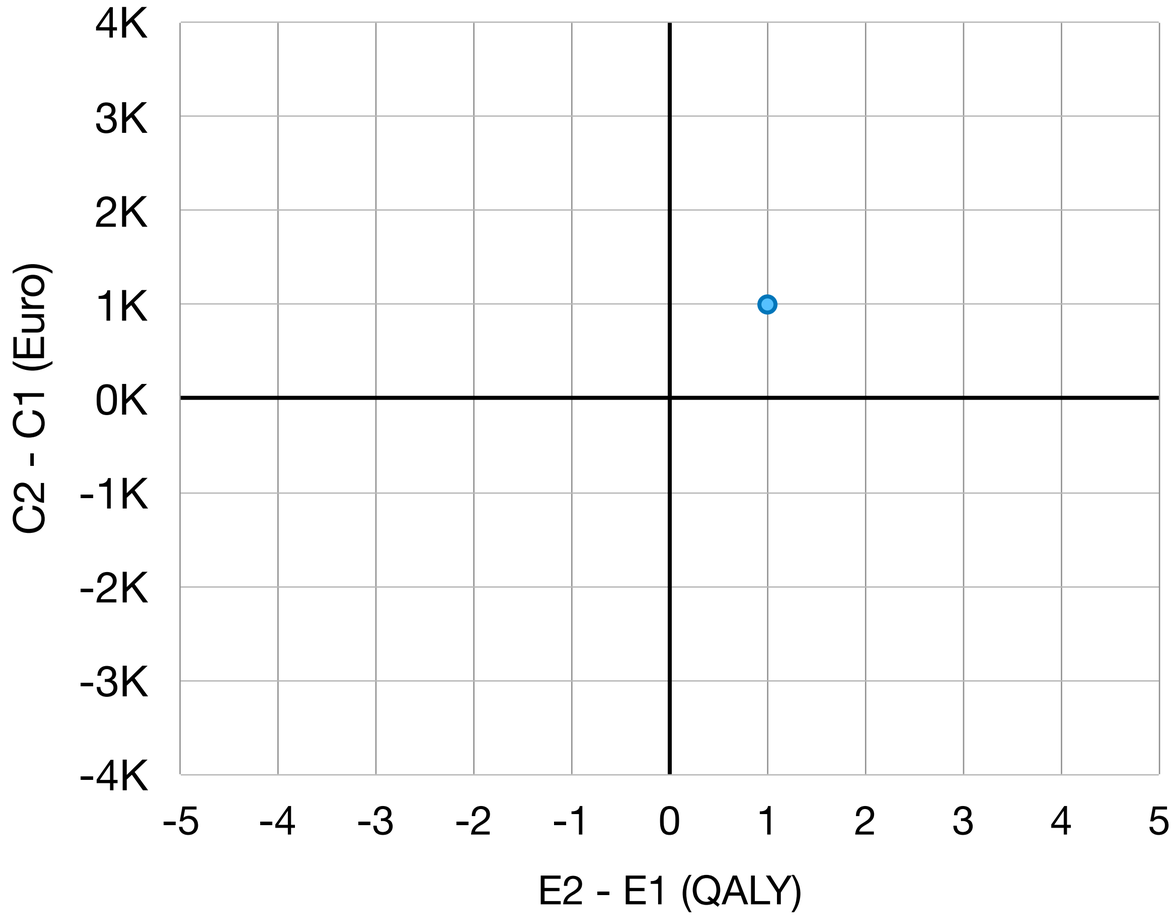
E2 = Total effect for arm 2

CALCULATE POINT ESTIMATES FOR COSTS AND OUTCOMES FROM RAW TRIAL DATA

$$ICER = \frac{C2 - C1}{E2 - E1}$$

$$ICER = \frac{20000 - 19000}{2 - 1}$$

ICER = 1000 EUR/QALY



CALCULATE POINT ESTIMATES FOR COSTS AND OUTCOMES FROM RAW TRIAL DATA

A PRACTICAL EXAMPLE

Standard arm (1)					
Patient	**Cost**	**EQ-5D_base**	**EQ-5D_12m**	**EQ-5D_24m**	**QALYs**
1	£1.364	0,778	0,843	0,873	1,669
2	£1.217	0,753	0,852	0,742	1,600
3	£1.636	0,762	0,643	0,761	1,404
4	£1.385	0,696	0,842	0,700	1,540
5	£1.385	0,763	0,806	0,698	1,537
6	£1.349	0,720	0,766	0,775	1,514
7	£1.706	0,746	0,758	0,773	1,518
8	£1.148	0,672	0,756	0,692	1,438
9	£1.239	0,626	0,710	0,758	1,402
10	£1.367	0,775	0,856	0,775	1,630
11	£1.914	0,778	0,775	0,631	1,480
12	£1.365	0,649	0,719	0,799	1,443
13	£2.109	0,688	0,705	0,738	1,418
14	£1.449	0,770	0,691	0,777	1,464
15	£1.745	0,902	0,774	0,781	1,616
16	£1.277	0,686	0,792	0,839	1,554
17	£1.738	0,812	0,656	0,730	1,427
18	£1.430	0,805	0,689	0,888	1,535
19	£1.681	0,898	0,698	0,667	1,481
20	£1.306	0,792	0,879	0,727	1,638
21	£1.737	0,777	0,713	0,767	1,485
22	£1.824	0,623	0,746	0,762	1,438
23	£1.142	0,634	0,792	0,755	1,487
24	£1.790	0,757	0,652	0,803	1,432
25	£1.240	0,692	0,826	0,756	1,550
26	£886	0,637	0,841	0,607	1,463
27	£1.278	0,746	0,704	0,803	1,478
28	£1.247	0,677	0,833	0,742	1,542
29	£1.632	0,649	0,769	0,886	1,537
30	£1.528	0,729	0,796	0,705	1,513
Mean	**£1.470**	**0,733**	**0,763**	**0,757**	**1,508**

Experimental arm (2)					
Patient	**Cost**	**EQ-5D_base**	**EQ-5D_12m**	**EQ-5D_24m**	**QALYs**
1	£3.650	0,926	1,000	1,000	1,963
2	£4.491	0,828	0,940	0,917	1,813
3	£4.991	0,712	0,809	0,789	1,559
4	£3.475	0,786	0,882	0,854	1,702
5	£3.337	0,735	0,816	0,873	1,620
6	£2.205	0,734	0,812	0,823	1,590
7	£3.165	0,692	0,805	0,758	1,530
8	£6.137	0,727	0,814	0,780	1,567
9	£2.411	0,625	0,720	0,716	1,390
10	£5.255	0,818	0,947	0,928	1,820
11	£3.689	0,720	0,836	0,784	1,588
12	£2.051	0,643	0,746	0,771	1,453
13	£2.282	0,745	0,852	0,788	1,619
14	£3.087	0,690	0,789	0,794	1,531
15	£3.472	0,773	0,868	0,878	1,694
16	£5.058	0,702	0,797	0,770	1,533
17	£3.700	0,700	0,820	0,803	1,571
18	£4.566	0,753	0,830	0,832	1,623
19	£1.279	0,754	0,831	0,835	1,626
20	£3.272	0,835	0,961	0,903	1,830
21	£3.147	0,608	0,714	0,747	1,391
22	£3.459	0,781	0,882	0,836	1,691
23	£2.327	0,641	0,750	0,700	1,421
24	£2.817	0,789	0,899	0,835	1,710
25	£4.389	0,682	0,799	0,762	1,520
26	£3.859	0,671	0,765	0,771	1,486
27	£5.305	0,828	0,924	0,905	1,791
28	£1.832	0,803	0,905	0,863	1,738
29	£2.448	0,695	0,795	0,772	1,529
30	£2.329	0,738	0,823	0,853	1,619
	£3.450	**0,738**	**0,838**	**0,821**	**1,617**

CALCULATE POINT ESTIMATES FOR COSTS AND OUTCOMES FROM RAW TRIAL DATA

A PRACTICAL EXAMPLE

Standard arm (1)					
Patient	**Cost**	**EQ-5D_base**	**EQ-5D_12m**	**EQ-5D_24m**	**QALYs**
1	£1.364	0,778	0,843	0,873	1,669
2	£1.217	0,753	0,852	0,742	1,600
3	£1.636	0,762	0,643	0,761	1,404
4	£1.385	0,696	0,842	0,700	1,540
5	£1.385	0,763	0,806	0,698	1,537
6	£1.349	0,720	0,766	0,775	1,514
7	£1.706	0,746			
8	£1.148	0,672			
9	£1.239	0,626			
10	£1.367	0,775			
11	£1.914	0,778			
12	£1.365	0,649			
13	£2.109	0,688			
14	£1.449	0,770			
15	£1.745	0,902			
16	£1.277	0,686			
17	£1.738	0,812			
18	£1.430	0,805			
19	£1.681	0,898			
20	£1.306	0,792			
21	£1.737	0,777			
22	£1.824	0,623			
23	£1.142	0,634			
24	£1.790	0,757			
25	£1.240	0,692	0,826	0,756	1,550
26	£886	0,637	0,841	0,607	1,463
27	£1.278	0,746	0,704	0,803	1,478
28	£1.247	0,677	0,833	0,742	1,542
29	£1.632	0,649	0,769	0,886	1,537
30	£1.528	0,729	0,796	0,705	1,513
Mean	**£1.470**	**0,733**	**0,763**	**0,757**	**1,508**

Experimental arm (2)					
Patient	**Cost**	**EQ-5D_base**	**EQ-5D_12m**	**EQ-5D_24m**	**QALYs**
1	£3.650	0,926	1,000	1,000	1,963
2	£4.491	0,828	0,940	0,917	1,813
3	£4.991	0,712	0,809	0,789	1,559
4	£3.475	0,786	0,882	0,854	1,702
5	£3.337	0,735	0,816	0,873	1,620
6	£2.295	0,734	0,812	0,823	1,590
		0,692	0,805	0,758	1,530
		0,727	0,814	0,780	1,567
		0,625	0,720	0,716	1,390
		0,818	0,947	0,928	1,820
		0,720	0,836	0,784	1,588
		0,643	0,746	0,771	1,453
		0,745	0,852	0,788	1,619
		0,690	0,789	0,794	1,531
		0,773	0,868	0,878	1,694
		0,702	0,797	0,770	1,533
		0,700	0,820	0,803	1,571
		0,753	0,830	0,832	1,623
		0,754	0,831	0,835	1,626
		0,835	0,961	0,903	1,830
		0,608	0,714	0,747	1,391
		0,781	0,882	0,836	1,691
		0,641	0,750	0,700	1,421
		0,789	0,899	0,835	1,710
25	£4.389	0,682	0,799	0,762	1,520
26	£3.859	0,671	0,765	0,771	1,486
27	£5.305	0,828	0,924	0,905	1,791
28	£1.832	0,803	0,905	0,863	1,738
29	£2.448	0,695	0,795	0,772	1,529
30	£2.329	0,738	0,823	0,853	1,619
	£3.450	**0,738**	**0,838**	**0,821**	**1,617**

$$ICER = \frac{C2 - C1}{E2 - E1}$$

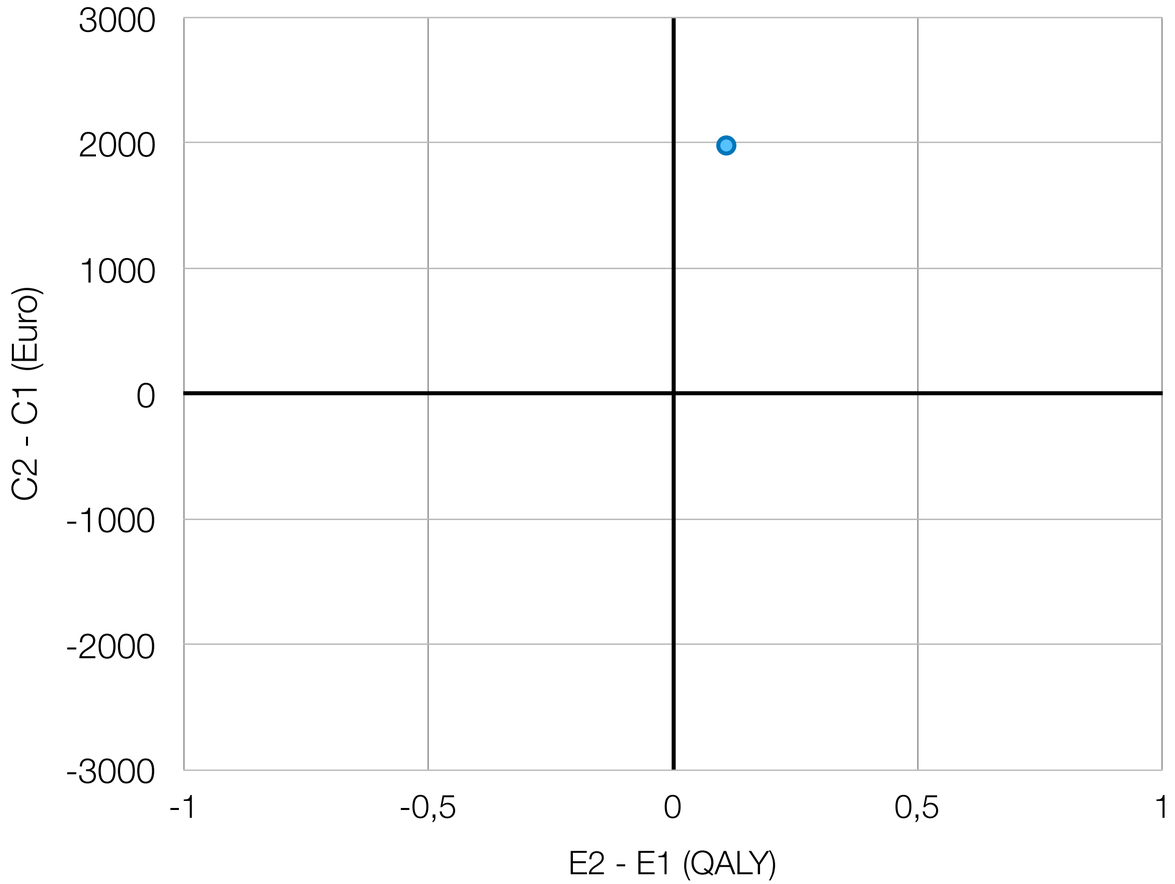
$$ICER = \frac{3450 - 1470}{1.617 - 1.508}$$

$$ICER = 18165 \text{ EUR/QALY}$$

CALCULATE POINT ESTIMATES FOR COSTS AND OUTCOMES FROM RAW TRIAL DATA

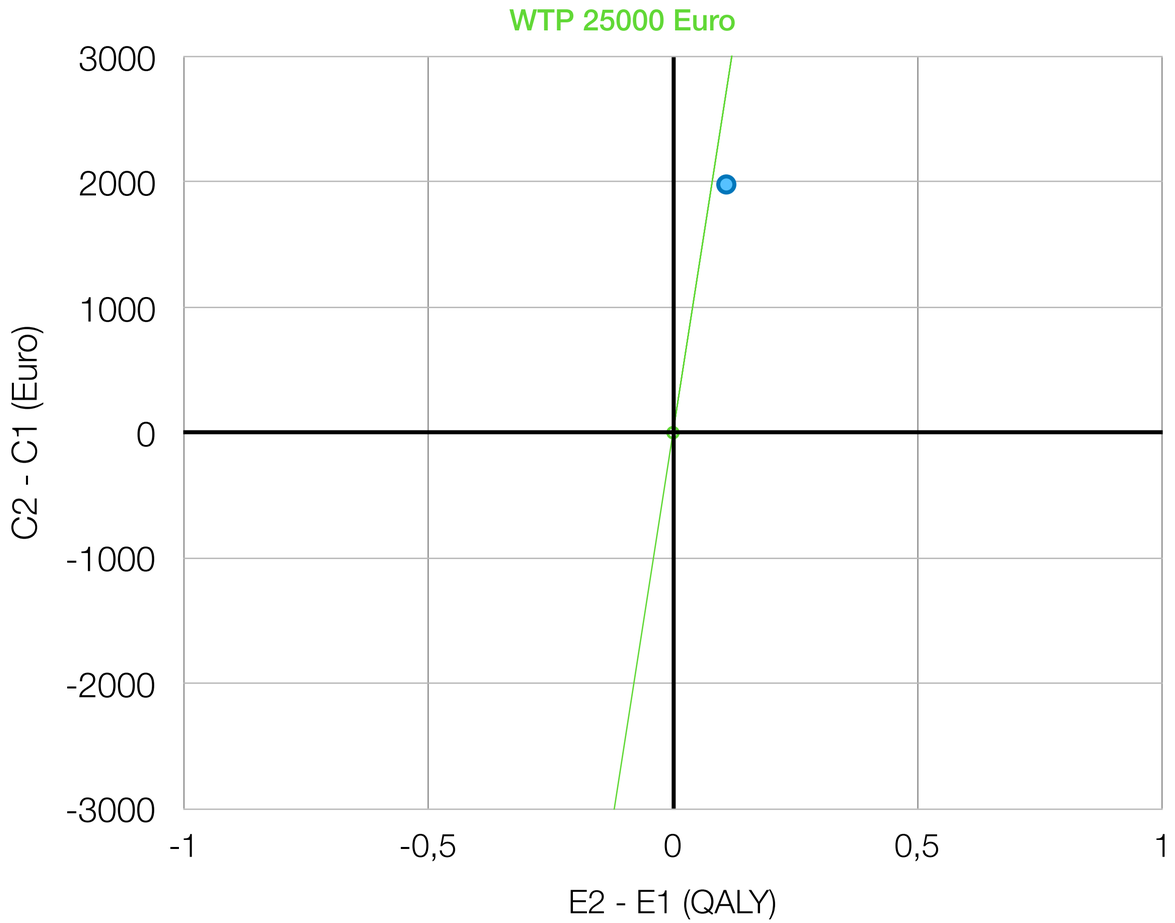
A PRACTICAL EXAMPLE

WHAT DOES AN ICER 18165 €/QALY MEAN?
IS THIS ICER COST-EFFECTIVE?
SHOULD WE DO ACCEPT THE NEW TREATMENT?



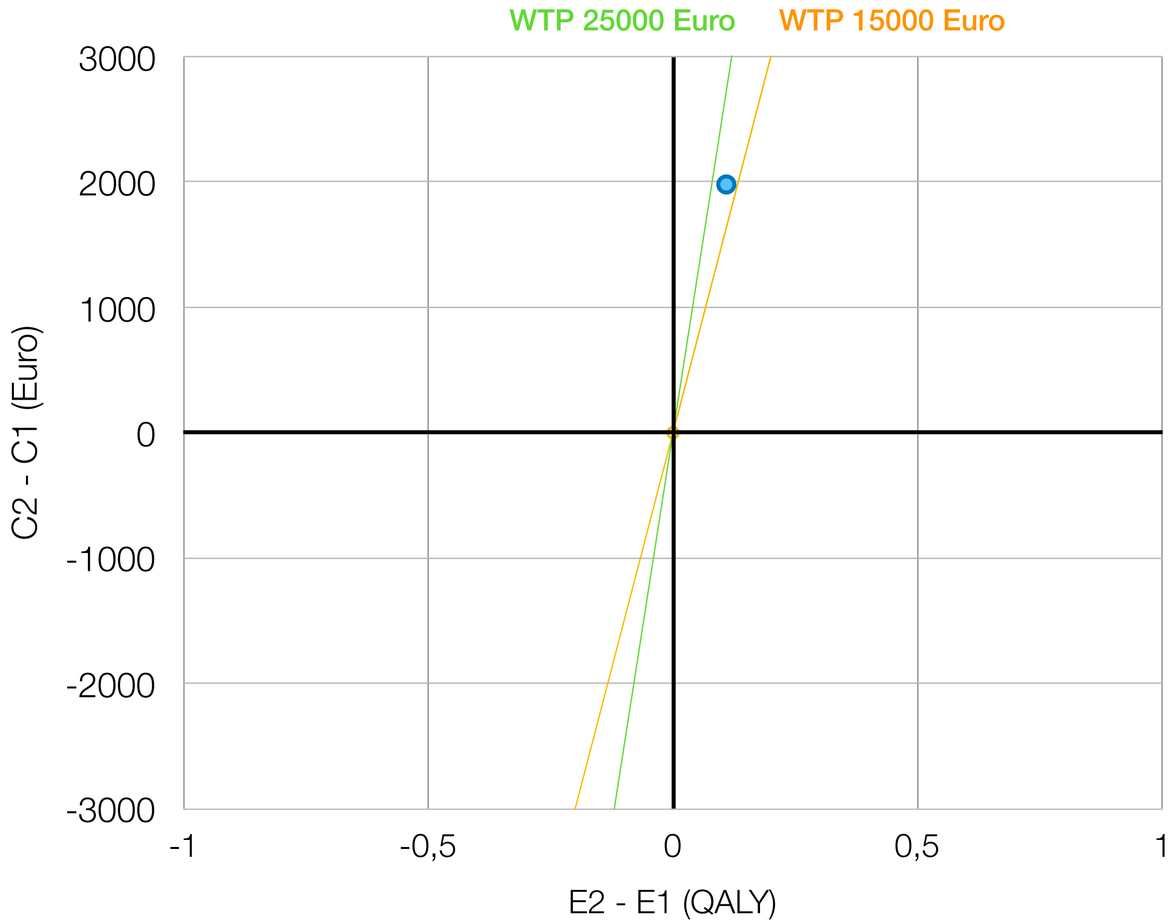
CALCULATE POINT ESTIMATES FOR COSTS AND OUTCOMES FROM RAW TRIAL DATA

A PRACTICAL EXAMPLE



CALCULATE POINT ESTIMATES FOR COSTS AND OUTCOMES FROM RAW TRIAL DATA

A PRACTICAL EXAMPLE



HEE ALONGSIDE RCT: STEP-BY-STEP METHODOLOGY

THE 9 STEPS TO CONDUCT A HEALTH ECONOMIC EVALUATION FROM A RCT DATA

1. Calculate point estimates for cost and outcomes from raw trial data
2. Manage uncertainties in raw data (re-sampling data)
3. Calculate ICER (incremental cost-effectiveness ratio) and NMB (net monetary benefit)
4. Plot the cost-effectiveness plane
5. Plot the iNMB (incremental net monetary benefit)
6. Calculate and plot the CEAC (cost-effectiveness acceptability curve)
7. Perform BIA (budget impact analysis)
8. Programme budgeting and marginal analysis (PBMA)
9. Overall interpretation

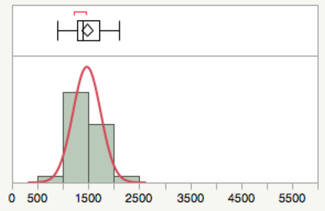
MANAGE UNCERTAINTIES IN RAW DATA (RE-SAMPLING DATA)

A PRACTICAL EXAMPLE USING BOOTSTRAPPING

Standard arm (1)

Patient	Cost	EQ-5D_base	EQ-5D_12m	EQ-5D_24m	QALYs
1	£1.364	0,778	0,843	0,873	1,669
2	£1.217	0,753	0,852	0,742	1,600
3	£1.636	0,762	0,643	0,761	1,404
4	£1.385	0,696	0,842	0,700	1,540
5	£1.385	0,763	0,806	0,698	1,537

Cost

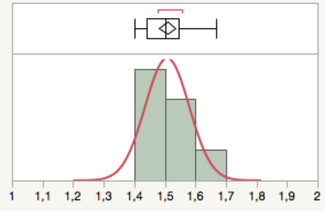


Normal(1470,49,272,103)

Quantiles		
100,0%	maximum	2109,03
99,5%		2109,03
97,5%		2109,03
90,0%		1821,04
75,0%	quartile	1713,89
50,0%	median	1385,00
25,0%	quartile	1269,14
10,0%		1155,22
2,5%		886,48
0,5%		886,48
0,0%	minimum	886,48

Summary Statistics	
Mean	1470,49
Std Dev	272,10
N	30,00
Minimum	886,48
Maximum	2109,03

QALYs



Normal(1,5079,0,07203)

Quantiles		
100,0%	maximum	1,67
99,5%		1,67
97,5%		1,67
90,0%		1,63
75,0%	quartile	1,54
50,0%	median	1,50
25,0%	quartile	1,44
10,0%		1,42
2,5%		1,40
0,5%		1,40
0,0%	minimum	1,40

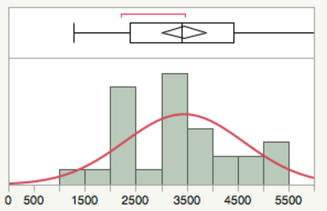
Summary Statistics	
Mean	1,51
Std Dev	0,07
N	30,00
Minimum	1,40
Maximum	1,67

Mean	**£1.470**	**0,733**	**0,763**	**0,757**	**1,508**

Experimental arm (2)

Patient	Cost	EQ-5D_base	EQ-5D_12m	EQ-5D_24m	QALYs
1	£3.650	0,926	1,000	1,000	1,963
2	£4.491	0,828	0,940	0,917	1,813
3	£4.991	0,712	0,809	0,789	1,559
4	£3.475	0,786	0,882	0,854	1,702
5	£3.337	0,735	0,816	0,873	1,620

Cost

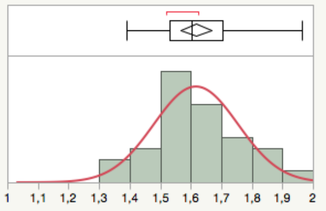


Normal(3449,58,1173,93)

Quantiles		
100,0%	maximum	6136,59
99,5%		6136,59
97,5%		6136,59
90,0%		5235,49
75,0%	quartile	4414,81
50,0%	median	3397,73
25,0%	quartile	2390,75
10,0%		2066,86
2,5%		1279,21
0,5%		1279,21
0,0%	minimum	1279,21

Summary Statistics	
Mean	3449,58
Std Dev	1173,93
N	30,00
Minimum	1279,21
Maximum	6136,59

QALYs



Normal(1,61723,0,13777)

Quantiles		
100,0%	maximum	1,96
99,5%		1,96
97,5%		1,96
90,0%		1,82
75,0%	quartile	1,70
50,0%	median	1,60
25,0%	quartile	1,53
10,0%		1,42
2,5%		1,39
0,5%		1,39
0,0%	minimum	1,39

Summary Statistics	
Mean	1,62
Std Dev	0,14
N	30,00
Minimum	1,39
Maximum	1,96

	£3.450	**0,738**	**0,838**	**0,821**	**1,617**

MANAGE UNCERTAINTIES IN RAW DATA (RE-SAMPLING DATA)

A PRACTICAL EXAMPLE USING BOOTSTRAPPING

Standard arm (1)					
Patient	**Cost**	**EQ-5D_base**	**EQ-5D_12m**	**EQ-5D_24m**	**QALYs**
1	£1.364	0,778	0,843	0,873	1,669
2	£1.217	0,753	0,852	0,742	1,600
3	£1.636	0,762	0,643	0,761	1,404
4	£1.385	0,696	0,842	0,700	1,540
5	£1.385	0,763	0,806	0,698	1,537
6	£1.349	0,720	0,766	0,775	1,514
7	£1.706	0,746	0,758	0,773	1,518
8	£1.148	0,672	0,756	0,692	1,438
9	£1.239	0,626	0,710	0,758	1,402
10	£1.367	0,775	0,856	0,775	1,630
11	£1.914	0,778	0,775	0,631	1,480
12	£1.365	0,649	0,719	0,799	1,443
13	£2.109	0,688	0,705	0,738	1,418
14	£1.449	0,770	0,691	0,777	1,464
15	£1.745	0,902	0,774	0,781	1,616
16	£1.277	0,686	0,792	0,839	1,554
17	£1.738	0,812	0,656	0,730	1,427
18	£1.430	0,805	0,689	0,888	1,535
19	£1.681	0,898	0,698	0,667	1,481
20	£1.306	0,792	0,879	0,727	1,638
21	£1.737	0,777	0,713	0,767	1,485
22	£1.824	0,623	0,746	0,762	1,438
23	£1.142	0,634	0,792	0,755	1,487
24	£1.790	0,757	0,652	0,803	1,432
25	£1.240	0,692	0,826	0,756	1,550
26	£886	0,637	0,841	0,607	1,463
27	£1.278	0,746	0,704	0,803	1,478
28	£1.247	0,677	0,833	0,742	1,542
29	£1.632	0,649	0,769	0,886	1,537
30	£1.528	0,729	0,796	0,705	1,513
Mean	**£1.470**	**0,733**	**0,763**	**0,757**	**1,508**

Experimental arm (2)					
Patient	**Cost**	**EQ-5D_base**	**EQ-5D_12m**	**EQ-5D_24m**	**QALYs**
1	£3.650	0,926	1,000	1,000	1,963
2	£4.491	0,828	0,940	0,917	1,813
3	£4.991	0,712	0,809	0,789	1,559
4	£3.475	0,786	0,882	0,854	1,702
5	£3.337	0,735	0,816	0,873	1,620
6	£2.205	0,734	0,812	0,823	1,590
7	£3.165	0,692	0,805	0,758	1,530
8	£6.137	0,727	0,814	0,780	1,567
9	£2.411	0,625	0,720	0,716	1,390
10	£5.255	0,818	0,947	0,928	1,820
11	£3.689	0,720	0,836	0,784	1,588
12	£2.051	0,643	0,746	0,771	1,453
13	£2.282	0,745	0,852	0,788	1,619
14	£3.087	0,690	0,789	0,794	1,531
15	£3.472	0,773	0,868	0,878	1,694
16	£5.058	0,702	0,797	0,770	1,533
17	£3.700	0,700	0,820	0,803	1,571
18	£4.566	0,753	0,830	0,832	1,623
19	£1.279	0,754	0,831	0,835	1,626
20	£3.272	0,835	0,961	0,903	1,830
21	£3.147	0,608	0,714	0,747	1,391
22	£3.459	0,781	0,882	0,836	1,691
23	£2.327	0,641	0,750	0,700	1,421
24	£2.817	0,789	0,899	0,835	1,710
25	£4.389	0,682	0,799	0,762	1,520
26	£3.859	0,671	0,765	0,771	1,486
27	£5.305	0,828	0,924	0,905	1,791
28	£1.832	0,803	0,905	0,863	1,738
29	£2.448	0,695	0,795	0,772	1,529
30	£2.329	0,738	0,823	0,853	1,619
	£3.450	**0,738**	**0,838**	**0,821**	**1,617**

MANAGE UNCERTAINTIES IN RAW DATA (RE-SAMPLING DATA)

A PRACTICAL EXAMPLE USING BOOTSTRAPPING

Standard arm (1)					
Patient	**Cost**	**EQ-5D_base**	**EQ-5D_12m**	**EQ-5D_24m**	**QALYs**
1	£1.364	0,778	0,843	0,873	1,669
2	£1.217	0,753	0,852	0,742	1,600
3	£1.636	0,762	0,643	0,761	1,404
4	£1.385	0,696	0,842	0,700	1,540
5	£1.385	0,763	0,806	0,698	1,537
6	£1.349	0,720	0,766	0,775	1,514
7	£1.706	0,746	0,758	0,773	1,518
8	£1.148	0,672	0,756	0,692	1,438
9	£1.239	0,626	0,710	0,758	1,402
10	£1.367	0,775	0,856	0,775	1,630
11	£1.914	0,778	0,775	0,631	1,480
12	£1.365	0,649	0,719	0,799	1,443
13	£2.109	0,688	0,705	0,738	1,418
14	£1.449	0,770	0,691	0,777	1,464
15	£1.745	0,902	0,774	0,781	1,616
16	£1.277	0,686	0,792	0,839	1,554
17	£1.738	0,812	0,656	0,730	1,427
18	£1.430	0,805	0,689	0,888	1,535
19	£1.681	0,898	0,698	0,667	1,481
20	£1.306	0,792	0,879	0,727	1,638
21	£1.737	0,777	0,713	0,767	1,485
22	£1.824	0,623	0,746	0,762	1,438
23	£1.142	0,634	0,792	0,755	1,487
24	£1.790	0,757	0,652	0,803	1,432
25	£1.240	0,692	0,826	0,756	1,550
26	£886	0,637	0,841	0,607	1,463
27	£1.278	0,746	0,704	0,803	1,478
28	£1.247	0,677	0,833	0,742	1,542
29	£1.632	0,649	0,769	0,886	1,537
30	£1.528	0,729	0,796	0,705	1,513
Mean	**£1.470**	**0,733**	**0,763**	**0,757**	**1,508**

Experimental arm (2)					
Patient	**Cost**	**EQ-5D_base**	**EQ-5D_12m**	**EQ-5D_24m**	**QALYs**
1	£3.650	0,926	1,000	1,000	1,963
2	£4.491	0,828	0,940	0,917	1,813
3	£4.991	0,712	0,809	0,789	1,559
4	£3.475	0,786	0,882	0,854	1,702
5	£3.337	0,735	0,816	0,873	1,620
6	£2.205	0,734	0,812	0,823	1,590
7	£3.165	0,692	0,805	0,758	1,530
8	£6.137	0,727	0,814	0,780	1,567
9	£2.411	0,625	0,720	0,716	1,390
10	£5.255	0,818	0,947	0,928	1,820
11	£3.689	0,720	0,836	0,784	1,588
12	£2.051	0,643	0,746	0,771	1,453
13	£2.282	0,745	0,852	0,788	1,619
14	£3.087	0,690	0,789	0,794	1,531
15	£3.472	0,773	0,868	0,878	1,694
16	£5.058	0,702	0,797	0,770	1,533
17	£3.700	0,700	0,820	0,803	1,571
18	£4.566	0,753	0,830	0,832	1,623
19	£1.279	0,754	0,831	0,835	1,626
20	£3.272	0,835	0,961	0,903	1,830
21	£3.147	0,608	0,714	0,747	1,391
22	£3.459	0,781	0,882	0,836	1,691
23	£2.327	0,641	0,750	0,700	1,421
24	£2.817	0,789	0,899	0,835	1,710
25	£4.389	0,682	0,799	0,762	1,520
26	£3.859	0,671	0,765	0,771	1,486
27	£5.305	0,828	0,924	0,905	1,791
28	£1.832	0,803	0,905	0,863	1,738
29	£2.448	0,695	0,795	0,772	1,529
30	£2.329	0,738	0,823	0,853	1,619
	£3.450	**0,738**	**0,838**	**0,821**	**1,617**

MANAGE UNCERTAINTIES IN RAW DATA (RE-SAMPLING DATA)

A PRACTICAL EXAMPLE USING BOOTSTRAPPING

Standard arm (1)					
Patient	**Cost**	**EQ-5D_base**	**EQ-5D_12m**	**EQ-5D_24m**	**QALYs**
1	£1.364	0,778	0,843	0,873	1,669
2	£1.217	0,753	0,852	0,742	1,600
3	£1.636	0,762	0,643	0,761	1,404
4	£1.385	0,696	0,842	0,700	1,540
5	£1.385	0,763	0,806	0,698	1,537
6	£1.349	0,720	0,766	0,775	1,514
7	£1.706	0,746	0,758	0,773	1,518
8	£1.148	0,672	0,756	0,692	1,438
9	£1.239	0,626	0,710	0,758	1,402
10	£1.367	0,775	0,856	0,775	1,630
11	£1.914	0,778	0,775	0,631	1,480
12	£1.365	0,649	0,719	0,799	1,443
13	£2.109	0,688	0,705	0,738	1,418
14	£1.449	0,770	0,691	0,777	1,464
15	£1.745	0,902	0,774	0,781	1,616
16	£1.277	0,686	0,792	0,839	1,554
17	£1.738	0,812	0,656	0,730	1,427
18	£1.430	0,805	0,689	0,888	1,535
19	£1.681	0,898	0,698	0,667	1,481
20	£1.306	0,792	0,879	0,727	1,638
21	£1.737	0,777	0,713	0,767	1,485
22	£1.824	0,623	0,746	0,762	1,438
23	£1.142	0,634	0,792	0,755	1,487
24	£1.790	0,757	0,652	0,803	1,432
25	£1.240	0,692	0,826	0,756	1,550
26	£886	0,637	0,841	0,607	1,463
27	£1.278	0,746	0,704	0,803	1,478
28	£1.247	0,677	0,833	0,742	1,542
29	£1.632	0,649	0,769	0,886	1,537
30	£1.528	0,729	0,796	0,705	1,513
Mean	**£1.470**	**0,733**	**0,763**	**0,757**	**1,508**

Experimental arm (2)					
Patient	**Cost**	**EQ-5D_base**	**EQ-5D_12m**	**EQ-5D_24m**	**QALYs**
1	£3.650	0,926	1,000	1,000	1,963
2	£4.491	0,828	0,940	0,917	1,813
3	£4.991	0,712	0,809	0,789	1,559
4	£3.475	0,786	0,882	0,854	1,702
5	£3.337	0,735	0,816	0,873	1,620
6	£2.205	0,734	0,812	0,823	1,590
7	£3.165	0,692	0,805	0,758	1,530
8	£6.137	0,727	0,814	0,780	1,567
9	£2.411	0,625	0,720	0,716	1,390
10	£5.255	0,818	0,947	0,928	1,820
11	£3.689	0,720	0,836	0,784	1,588
12	£2.051	0,643	0,746	0,771	1,453
13	£2.282	0,745	0,852	0,788	1,619
14	£3.087	0,690	0,789	0,794	1,531
15	£3.472	0,773	0,868	0,878	1,694
16	£5.058	0,702	0,797	0,770	1,533
17	£3.700	0,700	0,820	0,803	1,571
18	£4.566	0,753	0,830	0,832	1,623
19	£1.279	0,754	0,831	0,835	1,626
20	£3.272	0,835	0,961	0,903	1,830
21	£3.147	0,608	0,714	0,747	1,391
22	£3.459	0,781	0,882	0,836	1,691
23	£2.327	0,641	0,750	0,700	1,421
24	£2.817	0,789	0,899	0,835	1,710
25	£4.389	0,682	0,799	0,762	1,520
26	£3.859	0,671	0,765	0,771	1,486
27	£5.305	0,828	0,924	0,905	1,791
28	£1.832	0,803	0,905	0,863	1,738
29	£2.448	0,695	0,795	0,772	1,529
30	£2.329	0,738	0,823	0,853	1,619
	£3.450	**0,738**	**0,838**	**0,821**	**1,617**

MANAGE UNCERTAINTIES IN RAW DATA (RE-SAMPLING DATA)

A PRACTICAL EXAMPLE USING BOOTSTRAPPING

Standard arm (1)					
Patient	Cost	EQ-5D_base	EQ-5D_12m	EQ-5D_24m	QALYs
1	£1.364	0,778	0,843	0,873	1,669
2	£1.217	0,753	0,852	0,742	1,600
3	£1.636	0,762	0,643	0,761	1,404
4	£1.385	0,696	0,842	0,700	1,540
5	£1.385	0,763	0,806	0,698	1,537
6	£1.349	0,720			
7	£1.706	0,746			
8	£1.148	0,672			
9	£1.239	0,626			
10	£1.367	0,775			
11	£1.914	0,778			
12	£1.365	0,649			
13	£2.109	0,688			
14	£1.449	0,770			
15	£1.745	0,902			
16	£1.277	0,686			
17	£1.738	0,812			
18	£1.430	0,805			
19	£1.681	0,898			
20	£1.306	0,792			
21	£1.737	0,777			
22	£1.824	0,623			
23	£1.142	0,634			
24	£1.790	0,757			
25	£1.240	0,692			
26	£886	0,637	0,841	0,607	1,463
27	£1.278	0,746	0,704	0,803	1,478
28	£1.247	0,677	0,833	0,742	1,542
29	£1.632	0,649	0,769	0,886	1,537
30	£1.528	0,729	0,796	0,705	1,513
Mean	**£1.470**	**0,733**	**0,763**	**0,757**	**1,508**

REPEAT 1000 TIMES…

Experimental arm (2)					
Patient	Cost	EQ-5D_base	EQ-5D_12m	EQ-5D_24m	QALYs
1	£3.650	0,926	1,000	1,000	1,963
2	£4.491	0,828	0,940	0,917	1,813
3	£4.991	0,712	0,809	0,789	1,559
4	£3.475	0,786	0,882	0,854	1,702
5	£3.337	0,735	0,816	0,873	1,620
6		0,734	0,812	0,823	1,590
		0,692	0,805	0,758	1,530
		0,727	0,814	0,780	1,567
		0,625	0,720	0,716	1,390
		0,818	0,947	0,928	1,820
		0,720	0,836	0,784	1,588
		0,643	0,746	0,771	1,453
		0,745	0,852	0,788	1,619
		0,690	0,789	0,794	1,531
		0,773	0,868	0,878	1,694
		0,702	0,797	0,770	1,533
		0,700	0,820	0,803	1,571
		0,753	0,830	0,832	1,623
		0,754	0,831	0,835	1,626
		0,835	0,961	0,903	1,830
		0,608	0,714	0,747	1,391
		0,781	0,882	0,836	1,691
		0,641	0,750	0,700	1,421
		0,789	0,899	0,835	1,710
				0,682	0,799	0,762	1,520
26	£3.859	0,671	0,765	0,771	1,486
27	£5.305	0,828	0,924	0,905	1,791
28	£1.832	0,803	0,905	0,863	1,738
29	£2.448	0,695	0,795	0,772	1,529
30	£2.329	0,738	0,823	0,853	1,619
	£3.450	**0,738**	**0,838**	**0,821**	**1,617**

HEE ALONGSIDE RCT: STEP-BY-STEP METHODOLOGY

THE 9 STEPS TO CONDUCT A HEALTH ECONOMIC EVALUATION FROM A RCT DATA

1. Calculate point estimates for cost and outcomes from raw trial data
2. Manage uncertainties in raw data (re-sampling data)
3. Calculate ICER (incremental cost-effectiveness ratio) and NMB (net monetary benefit)
4. Plot the cost-effectiveness plane
5. Plot the iNMB (incremental net monetary benefit)
6. Calculate and plot the CEAC (cost-effectiveness acceptability curve)
7. Perform BIA (budget impact analysis)
8. Programme budgeting and marginal analysis (PBMA)
9. Overall interpretation

MANAGE UNCERTAINTIES IN RAW DATA (RE-SAMPLING DATA)

A PRACTICAL EXAMPLE USING BOOTSTRAPPING

RESAMPLED DATA					
Repetition	**C2-C1**	**E2-E1**	**ICER (Euro/QALY)**	**iNMB (Euro) for WTP = 15000**	**INMB (Euro) for WTP = 25000**
1	-554	0,214	-2588	3764	5904
2	686	0,275	2494	3439	6189
3	1539	0,345	4460	3636	7086
4	1950	0,103	18932	-405	625
5	3200	0,120	26666	-1400	-200
6	…	…	…	…	…
7	…	…	…	…	…
8	…	…	…	…	…
9	…	…	…	…	…
10	…	…	…	…	…
…	…	…	…	…	…
…	…	…	…	…	…
…	…	…	…	…	…
…	…	…	…	…	…
…	…	…	…	…	…
…	…	…	…	…	…
…	…	…	…	…	…
…	…	…	…	…	…
…	…	…	…	…	…
990	…	…	…	…	…
991	…	…	…	…	…
992	…	…	…	…	…
993	…	…	…	…	…
994	…	…	…	…	…
995	…	…	…	…	…
996	…	…	…	…	…
997	…	…	…	…	…
998	…	…	…	…	…
999	…	…	…	…	…
1000	2286	0,106	21566	-696	364

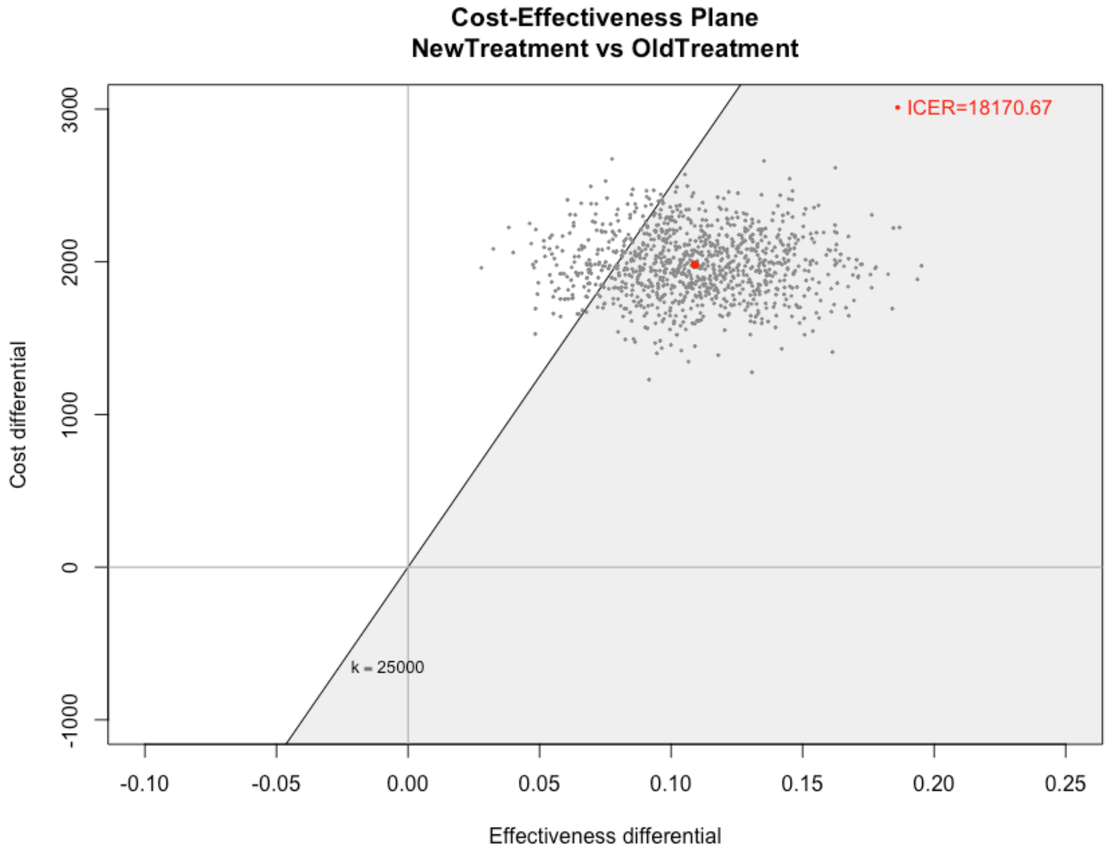
HEE ALONGSIDE RCT: STEP-BY-STEP METHODOLOGY

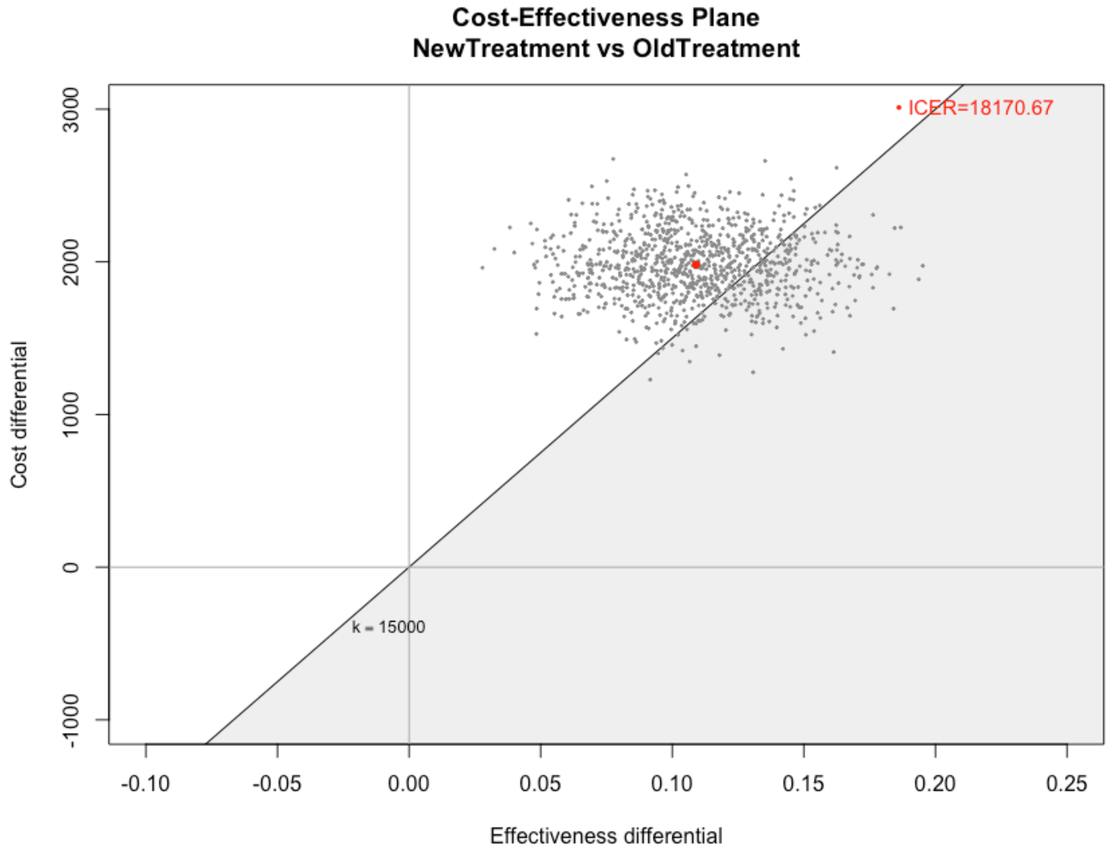
THE 9 STEPS TO CONDUCT A HEALTH ECONOMIC EVALUATION FROM A RCT DATA

1. Calculate point estimates for cost and outcomes from raw trial data
2. Manage uncertainties in raw data (re-sampling data)
3. Calculate ICER (incremental cost-effectiveness ratio) and NMB (net monetary benefit)
4. Plot the cost-effectiveness plane
5. Plot the iNMB (incremental net monetary benefit)
6. Calculate and plot the CEAC (cost-effectiveness acceptability curve)
7. Perform BIA (budget impact analysis)
8. Programme budgeting and marginal analysis (PBMA)
9. Overall interpretation

PLOT THE COST-EFFECTIVENESS PLANE

A PRACTICAL EXAMPLE

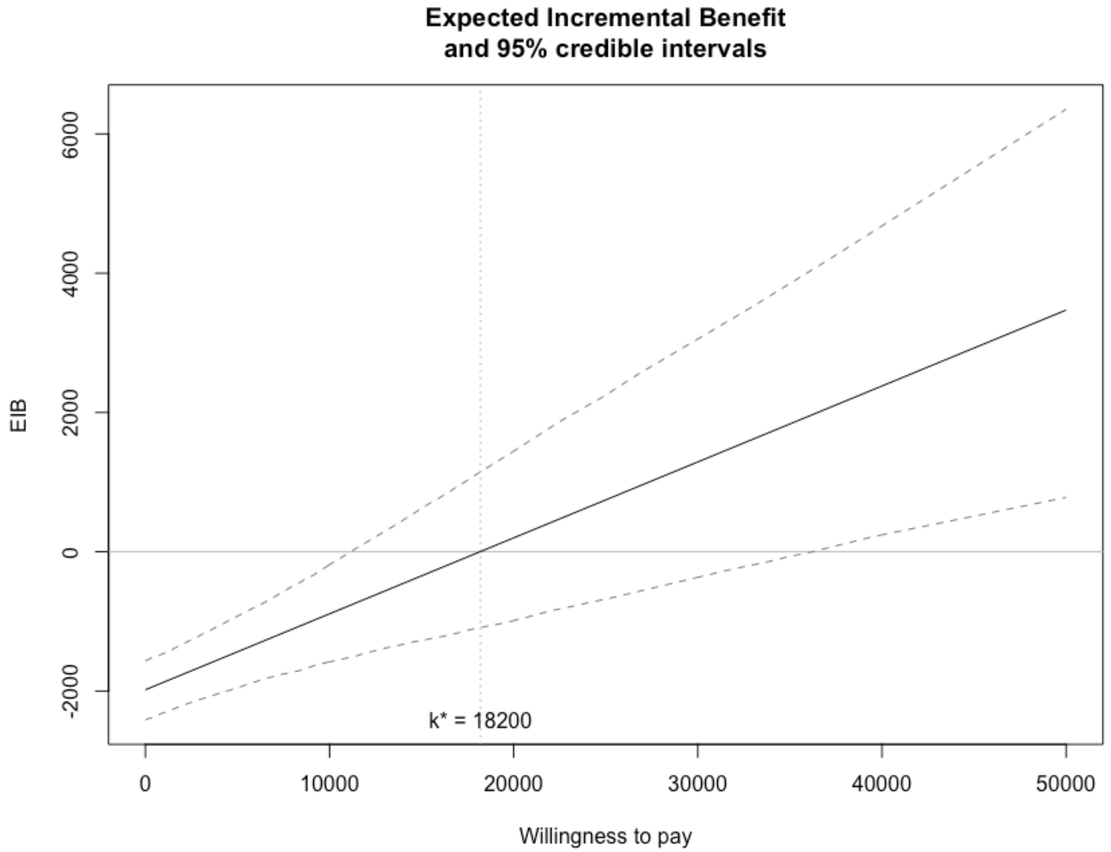




HEE ALONGSIDE RCT: STEP-BY-STEP METHODOLOGY

THE 9 STEPS TO CONDUCT A HEALTH ECONOMIC EVALUATION FROM A RCT DATA

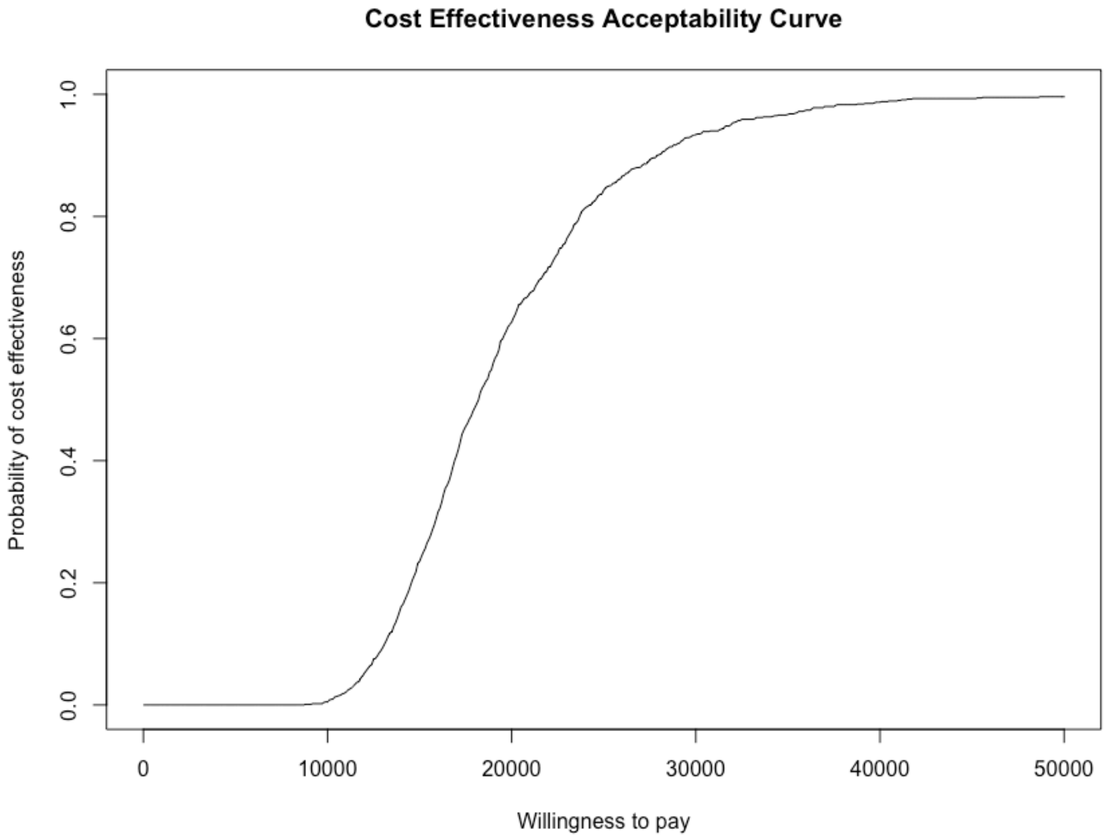
1. Calculate point estimates for cost and outcomes from raw trial data
2. Manage uncertainties in raw data (re-sampling data)
3. Calculate ICER (incremental cost-effectiveness ratio) and NMB (net monetary benefit)
4. Plot the cost-effectiveness plane
5. Plot the iNMB (incremental net monetary benefit)
6. Calculate and plot the CEAC (cost-effectiveness acceptability curve)
7. Perform BIA (budget impact analysis)
8. Programme budgeting and marginal analysis (PBMA)
9. Overall interpretation


Expected Incremental Benefit
and 95% credible intervals
EIB
6000
4000
2000
0
-2000
k* = 18200
0
10000
20000
30000
40000
50000
Willingness to pay

HEE ALONGSIDE RCT: STEP-BY-STEP METHODOLOGY

THE 9 STEPS TO CONDUCT A HEALTH ECONOMIC EVALUATION FROM A RCT DATA

1. Calculate point estimates for cost and outcomes from raw trial data
2. Manage uncertainties in raw data (re-sampling data)
3. Calculate ICER (incremental cost-effectiveness ratio) and NMB (net monetary benefit)
4. Plot the cost-effectiveness plane
5. Plot the iNMB (incremental net monetary benefit)
6. Calculate and plot the CEAC (cost-effectiveness acceptability curve)
7. Perform BIA (budget impact analysis)
8. Programme budgeting and marginal analysis (PBMA)
9. Overall interpretation


Cost Effectiveness Acceptability Curve
Probability of cost effectiveness
0.0
0.2
0.4
0.6
0.8
1.0
0
10000
20000
30000
40000
50000
Willingness to pay

HEE ALONGSIDE RCT: STEP-BY-STEP METHODOLOGY

THE 9 STEPS TO CONDUCT A HEALTH ECONOMIC EVALUATION FROM A RCT DATA

1. Calculate point estimates for cost and outcomes from raw trial data
2. Manage uncertainties in raw data (re-sampling data)
3. Calculate ICER (incremental cost-effectiveness ratio) and NMB (net monetary benefit)
4. Plot the cost-effectiveness plane
5. Plot the iNMB (incremental net monetary benefit)
6. Calculate and plot the CEAC (cost-effectiveness acceptability curve)
7. Perform BIA (budget impact analysis)
8. Programme budgeting and marginal analysis (PBMA)
9. Overall interpretation

PERFORM A BUDGET IMAPCT ANALYSIS (BIA)

THE 6 STEPS TO CONDUCT BUDGET IMPACT ANALYSIS

1. Estimating the target population
2. Selecting a time horizon
3. Identifying the current and projected case-mix
4. Estimating current and future treatment costs
5. Estimate changes in disease-related costs
6. Estimating and presenting changes in annual budget and health outcomes

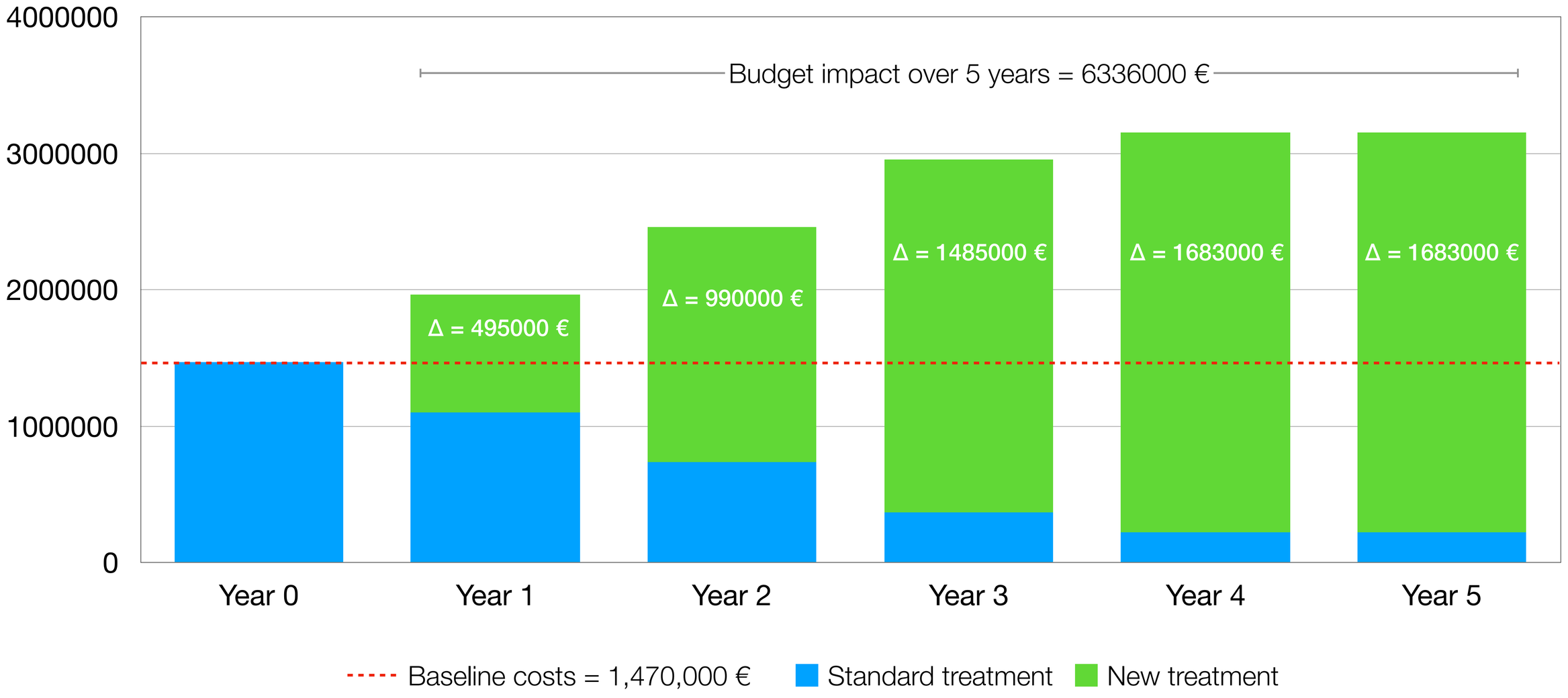
BUDGET IMPACT ANALYSIS

Year	Number of indications	Adoption of new treatment	Case mix (standard/ new)	Cost standard treatment	Cost new treatment	Total cost	Budget impact	Health outcomes	Health outcome impact
1	1000	25 %	750/250	1102500	862500	1965000	495000	1535	27
2	1000	50 %	500/500	735000	1725000	2460000	990000	1562	54
3	1000	75 %	250/750	367500	2587500	2955000	1485000	1589	81
4	1000	85 %	150/850	220500	2932500	3153000	1683000	1600	92
5	1000	85 %	150/850	220500	2932500	3153000	1683000	1600	92
Total	5000	-	1800/3200	2646000	11040000	13686000	6336000 (*)	7888	348

Baseline (costs): 1000 patients per year treated with the standard treatment (1,470 €) during 5 years = 7,350,000 €
Baseline (effects): 1000 patients per year treated with the standard treatment (1.508 QALYs) during 5 years = 7540 QALYs
(*) Difference between baseline cost and actual cost = 13,686,000 - 7,350,000

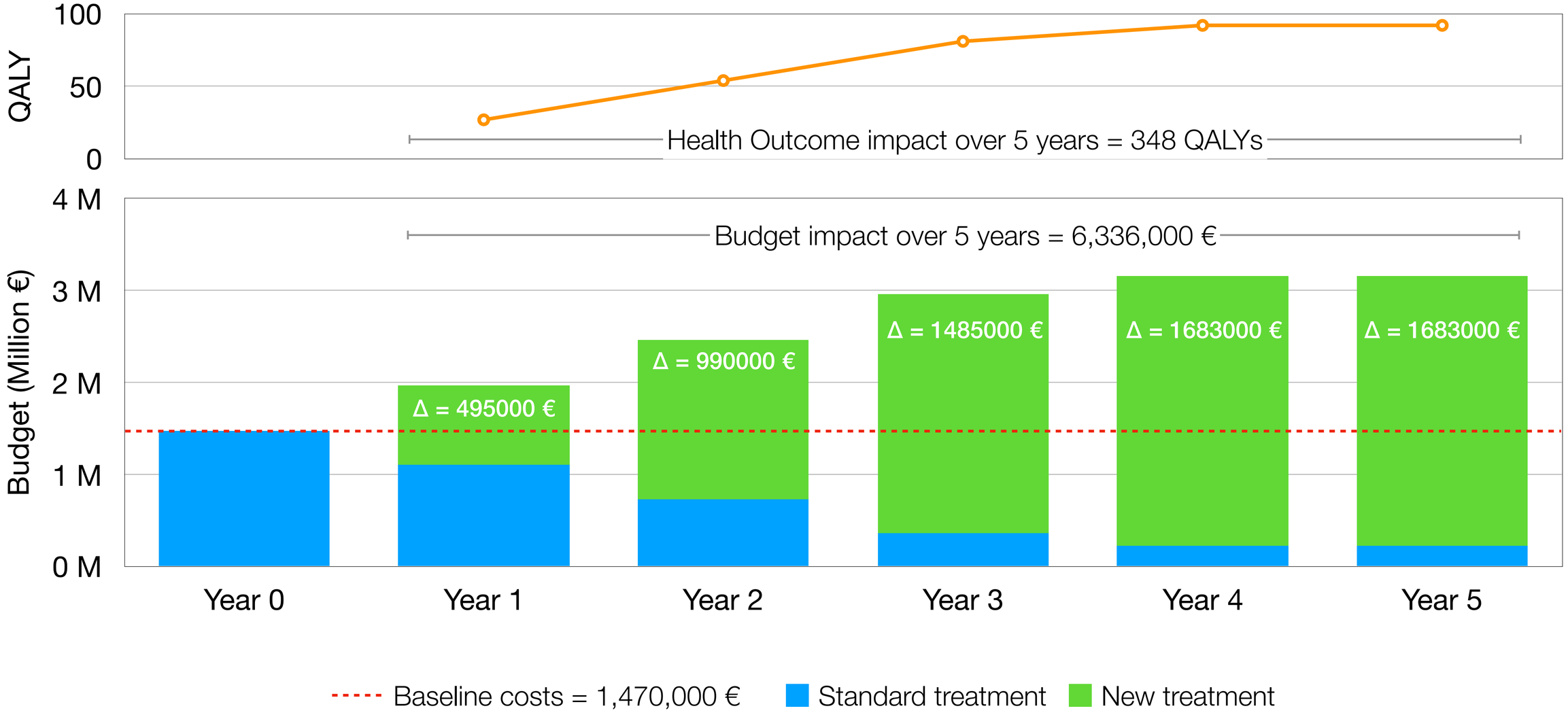
BUDGET IMPACT ANALYSIS

A PRACTICAL EXAMPLE



BUDGET IMPACT ANALYSIS

A PRACTICAL EXAMPLE



HEE ALONGSIDE RCT: STEP-BY-STEP METHODOLOGY

THE 9 STEPS TO CONDUCT A HEALTH ECONOMIC EVALUATION FROM A RCT DATA

1. Calculate point estimates for cost and outcomes from raw trial data
2. Manage uncertainties in raw data (re-sampling data)
3. Calculate ICER (incremental cost-effectiveness ratio) and NMB (net monetary benefit)
4. Plot the cost-effectiveness plane
5. Plot the iNMB (incremental net monetary benefit)
6. Calculate and plot the CEAC (cost-effectiveness acceptability curve)
7. Perform BIA (budget impact analysis)
8. Programme budgeting and marginal analysis (PBMA)
9. Overall interpretation

PROGRAMME BUDGETING AND MARGINAL ANALYSIS (PBMA)

HOW TO MAXIMIZE HEALTH BENEFITS FOR THE ENTIRE POPULATION

PBMA is a tool to aid decision-making in setting priorities in the provision of health services. PBMA is based on the notion of allocative efficiency. Allocative efficiency is achieved when health related benefits from a service or a set of services are maximised for a group of individuals.

1. Defining programme areas to be examined (and create the programme budget)
2. Identify services which may be potential options for expansion or contraction
3. Rank these services in terms of CE and costs of delivery
4. Re-allocate resources

HEE ALONGSIDE RCT: STEP-BY-STEP METHODOLOGY

THE 9 STEPS TO CONDUCT A HEALTH ECONOMIC EVALUATION FROM A RCT DATA

1. Calculate point estimates for cost and outcomes from raw trial data
2. Manage uncertainties in raw data (re-sampling data)
3. Calculate ICER (incremental cost-effectiveness ratio) and NMB (net monetary benefit)
4. Plot the cost-effectiveness plane
5. Plot the iNMB (incremental net monetary benefit)
6. Calculate and plot the CEAC (cost-effectiveness acceptability curve)
7. Perform BIA (budget impact analysis)
8. Programme budgeting and marginal analysis (PBMA)
9. Overall interpretation

OVERALL INTERPRETATION

COST-EFFECTIVENESS ANALYSIS SUMMARY

Optimal decision:

- k < 18200: choose OldTreatment
- k ≥18200: choose NewTreatment

Analysis for willingness to pay parameter k = 25000

- ICER: 18171 €/QALY
- CEAC: 84%
- NMB: 744 €
- Optimal intervention: NewTreatment

BUDGET IMPACT ANALYSIS (BIA)

- 5000 patients over 5 years
- Progressive adoption of new treatment (25% to 85%)
- Budget impact 6.3 Million €