

# Cost-Effectiveness Analysis for Clinical Trials with CEACT

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## 1 Overview

CEACT implements cost-effectiveness analyses for two-arm clinical trials: observed incremental summaries, non-parametric bootstrap uncertainty, cost-effectiveness planes, cost-effectiveness acceptability curves (CEACs), net monetary benefit, and deterministic sensitivity analysis.

The package follows standard practice in trial-based economic evaluation, where patient-level costs and effects are observed alongside treatment allocation (Glick et al. 2014; Drummond et al. 2015).

Let  $C_i$  denote cost,  $E_i$  denote effect, and  $A_i \in \{0, 1\}$  denote treatment assignment, with  $A_i = 0$  for the reference group and  $A_i = 1$  for treatment.

## 2 Core Quantities

Mean costs and effects by arm are

$$\bar{C}_a = \frac{1}{n_a} \sum_{i:A_i=a} C_i, \quad \bar{E}_a = \frac{1}{n_a} \sum_{i:A_i=a} E_i.$$

Incremental cost and incremental effect are

$$\Delta C = \bar{C}_1 - \bar{C}_0, \quad \Delta E = \bar{E}_1 - \bar{E}_0.$$

When  $\Delta E \neq 0$ , the incremental cost-effectiveness ratio is

$$ICER = \frac{\Delta C}{\Delta E}.$$

Because ratios can be unstable when  $\Delta E$  is near zero, CEACT also uses net monetary benefit at willingness-to-pay threshold  $k$  (Stinnett and Mullahy 1998):

$$INMB(k) = k\Delta E - \Delta C.$$

Treatment is cost-effective at threshold  $k$  when  $INMB(k) > 0$ . The CEAC is the probability of this event over an uncertainty distribution:

$$CEAC(k) = Pr\{k\Delta E - \Delta C > 0\}.$$

CEACT estimates this probability from non-parametric bootstrap replicates (Efron and Tibshirani 1993), preserving treatment-arm sample sizes by stratified resampling. CEACs and planes are widely used to communicate decision uncertainty in cost-effectiveness studies (Fenwick, Claxton, and Sculpher 2001; Briggs, O'Brien, and Blackhouse 2002).

### 3 Real Trial-Based CEA Example

The example below first uses the `trial_cea` dataset included with CEACT package. This patient-level dataset contains treatment assignment, total costs, and QALYs for 500 trial participants and is suitable for demonstrating the package workflow.

```
data("trial_cea")
trial <- trial_cea

head(trial)
#>   id treat cost    qaly dissev race    blcost    blqaly male    group
#> 1  1     1 2439 0.76059 0.335    1 2113.3491 0.9943529    0 treatment
#> 2  2     0 2598 0.70727 0.302    1  508.5120 0.8351629    1 control
#> 3  3     0 6315 0.68618 0.405    0 2271.8215 0.7526733    0 control
#> 4  4     0 1332 0.44657 0.199    1  653.7864 0.8441091    1 control
#> 5  5     1 2972 0.66752 0.302    0 1438.7561 0.8653243    1 treatment
#> 6  6     0 3699 0.59028 0.447    0 1773.7224 1.0000000    0 control

observed <- cea(cost + qaly ~ group, data = trial, ref = "control")
summary(observed)
#> Cost-Effectiveness Summary
#> Formula: cost + qaly ~ group
#> Reference group: control
#> Treatment group: treatment
#> Incremental cost: 25
#> Incremental effect: 0.042
#> ICER: 588.802
#>
#> Outcome Reference Treatment Difference
#> delta_cost Cost 3015 (SD 1582.802) 3040 (SD 1168.737) 25.000
#> delta_effect Effect 0.573 (SD 0.217) 0.615 (SD 0.205) 0.042
#> CI p.value
#> delta_cost [-219.54; 269.54] 0.8409
#> delta_effect [0.005; 0.08] 0.0251
```

The observed treatment arm produces more QALYs with a small increase in mean cost. The ICER is the additional cost per additional QALY.

## 4 Bootstrap Uncertainty

```
set.seed(42)
boot_res <- boot_icer(cost + qaly ~ group, data = trial, ref = "control",
                     R = 1000, ci.type = "perc")
summary(boot_res)
#>               Metric Observed BootstrapMean StdError   Bias
#> DeltaCost      Delta Cost    25.000      22.690  122.813  -2.310
#> DeltaEffect    Delta Effect     0.042     0.044    0.018   0.002
#> ICER           ICER    588.802     729.717 10682.651 140.915
#>               CI
#> DeltaCost      [-221.62; 259.395]
#> DeltaEffect    [0.007; 0.079]
#> ICER           [-7579.75; 11119.446]
```

The bootstrap distribution summarizes sampling uncertainty in  $\Delta C$ ,  $\Delta E$ , and the ICER. For publication-quality analyses, the number of replications should generally be increased beyond this vignette if computation time allows (Willan and Briggs 2006).

```
plot_ceplane(boot_res, k = 20000)
```

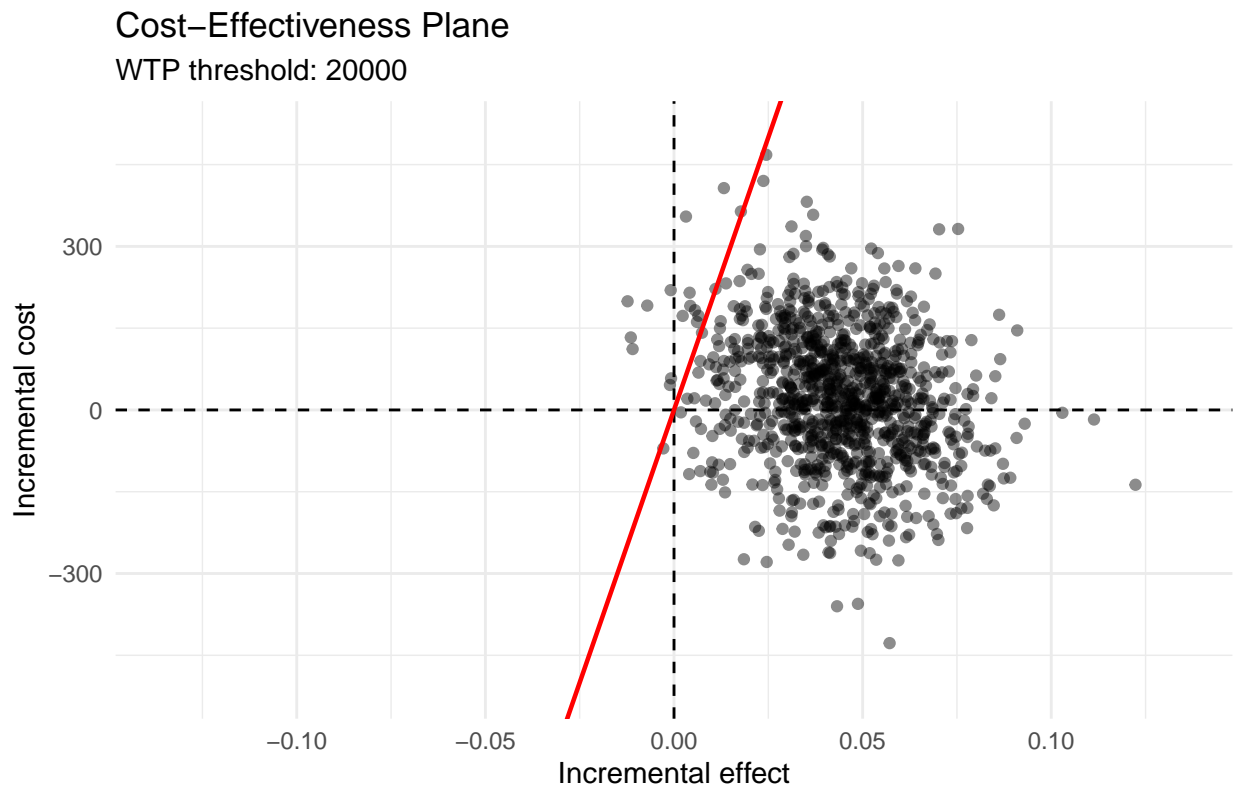


Figure 1: Cost-effectiveness plane from stratified non-parametric bootstrap replicates. The red line is the willingness-to-pay threshold.

Most simulated replicates lie in the north-east quadrant, indicating higher cost and higher effect for treatment.

Replicates below the threshold line are cost-effective at that threshold.

## 5 Net Monetary Benefit and CEAC

```
ceac_tbl <- compute_nmb_ceac(  
  boot_res,  
  wtp_range = seq(0, 50000, 5000)  
)
```

```
ceac_tbl  
#>      WTP      ENMB Prob_CE  
#> 1      0    -25.0000  0.419  
#> 2    5000   187.2954  0.882  
#> 3   10000   399.5908  0.964  
#> 4   15000   611.8862  0.979  
#> 5   20000   824.1816  0.983  
#> 6   25000  1036.4770  0.984  
#> 7   30000  1248.7724  0.986  
#> 8   35000  1461.0678  0.988  
#> 9   40000  1673.3632  0.988  
#> 10  45000  1885.6586  0.989  
#> 11  50000  2097.9540  0.989
```

```
plot_ceac(ceac_tbl)
```

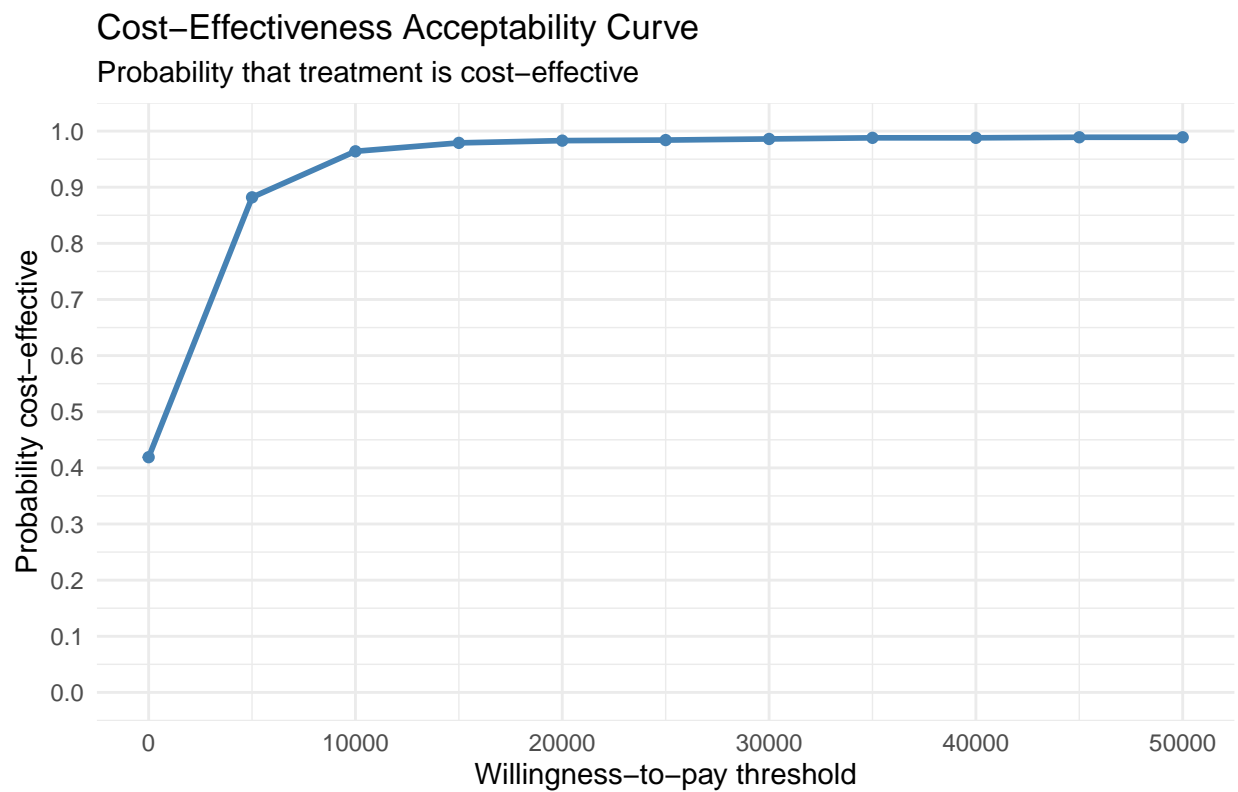


Figure 2: Cost-effectiveness acceptability curve. The curve gives the bootstrap probability that treatment is cost-effective at each willingness-to-pay threshold.

The CEAC rises as the willingness-to-pay threshold increases because the treatment's positive incremental effect receives more decision value. The curve should be interpreted as decision uncertainty, not as the expected size of the health benefit.

## 6 Deterministic Sensitivity Analysis

```
dsa_effect <- dsa_icer(
  cost + qaly ~ group,
  data = trial,
  param = "qaly",
  range = seq(0.50, 0.70, 0.025),
  ref = "control",
  metric = "INMB",
  k = 20000
)
```

```
dsa_effect
#>   Parameter      INMB
#> 1    0.500 -1483.71762
#> 2    0.525  -983.71762
#> 3    0.550  -483.71762
#> 4    0.575   16.28238
#> 5    0.600   516.28238
#> 6    0.625  1016.28238
#> 7    0.650  1516.28238
#> 8    0.675  2016.28238
#> 9    0.700  2516.28238
```

```
plot_dsa(dsa_effect, metric = "INMB")
```

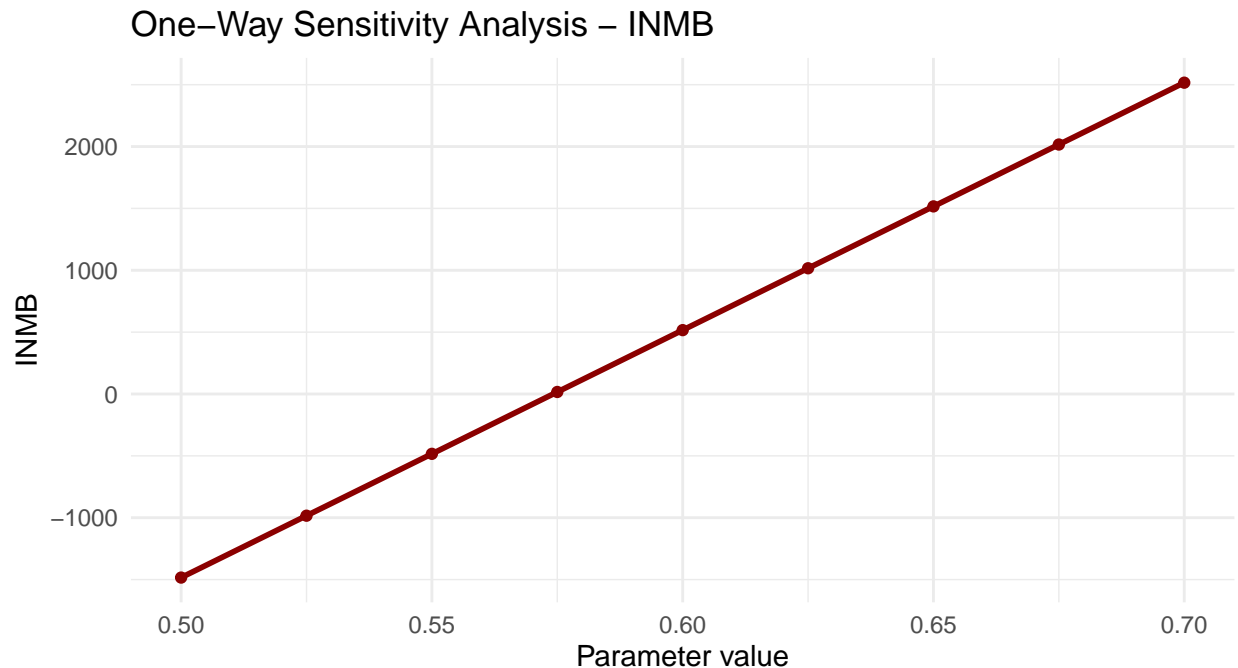


Figure 3: One-way deterministic sensitivity analysis varying treatment-arm effect.

This one-way analysis shows how the incremental net monetary benefit changes as the assumed treatment-arm effect changes. Such analyses are useful for checking which assumptions drive conclusions, but they do not replace probabilistic uncertainty analysis.

## 7 Reproducibility Checklist

- Define the reference and treatment arms before analysis.
- Report  $\Delta C$ ,  $\Delta E$ , ICER, and INMB at relevant thresholds.
- Use bootstrap or model-based uncertainty methods for CEACs.
- Interpret ICERs alongside the cost-effectiveness plane and net benefit.
- Report the willingness-to-pay thresholds used for decision interpretation.

## References

- Briggs, Andrew H., Bernie J. O'Brien, and Gordon Blackhouse. 2002. "Thinking Outside the Box: Recent Advances in the Analysis and Presentation of Uncertainty in Cost-Effectiveness Studies." *Annual Review of Public Health* 23: 377–401.
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