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

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

Incremental cost and incremental effect are

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

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

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

Because ratios can be unstable when ΔE 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 <- booticer(cost + qaly ~ group, data = trial, ref = "control",
                     R = 1000, ci.type = "perc")
summary(boot_res)
#> Bootstrap replicates span several quadrants of the cost-effectiveness plane; an ICER interval is not
#> # basetable: 3 x 6
#>         Metric Observed BootstrapMean StdError   Bias                  CI
#> 1   Delta Cost   25.000        22.690  122.813 -2.310 [-221.62; 259.395]
#> 2 Delta Effect    0.042         0.044    0.018  0.002     [0.007; 0.079]
#> 3         ICER  588.802            NA       NA     NA                <NA>
```

The bootstrap distribution summarizes sampling uncertainty in ΔC, ΔE, 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).

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

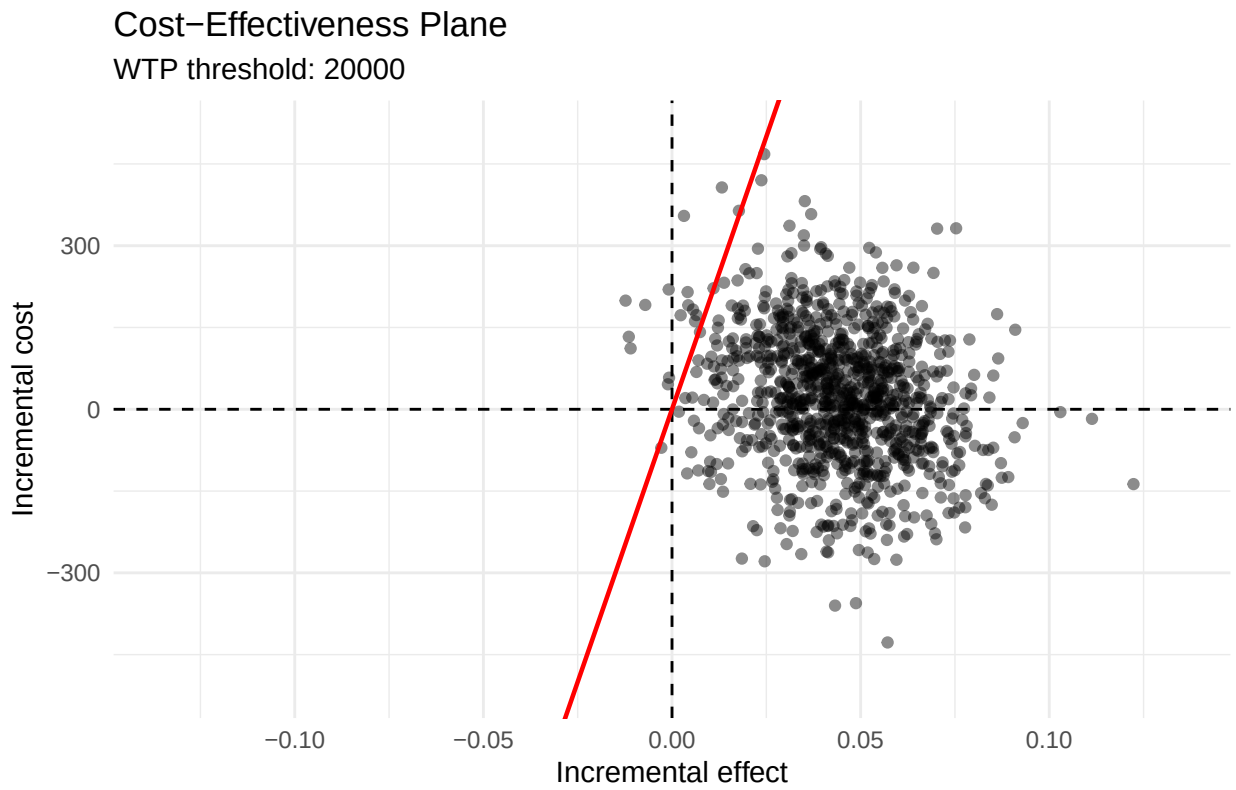


Figure 1: Cost-effectiveness plane from stratified non-parametric bootstrap replicates. The red line is the willingness-to-pay threshold.

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 <- computenmbceac(
  boot_res,
  wtp_range = seq(0, 50000, 5000)
)

ceac_tbl
#> # basetable: 11 x 3
#>      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
#> # 1 more rows
```

```
plotceac(ceac_tbl)
```

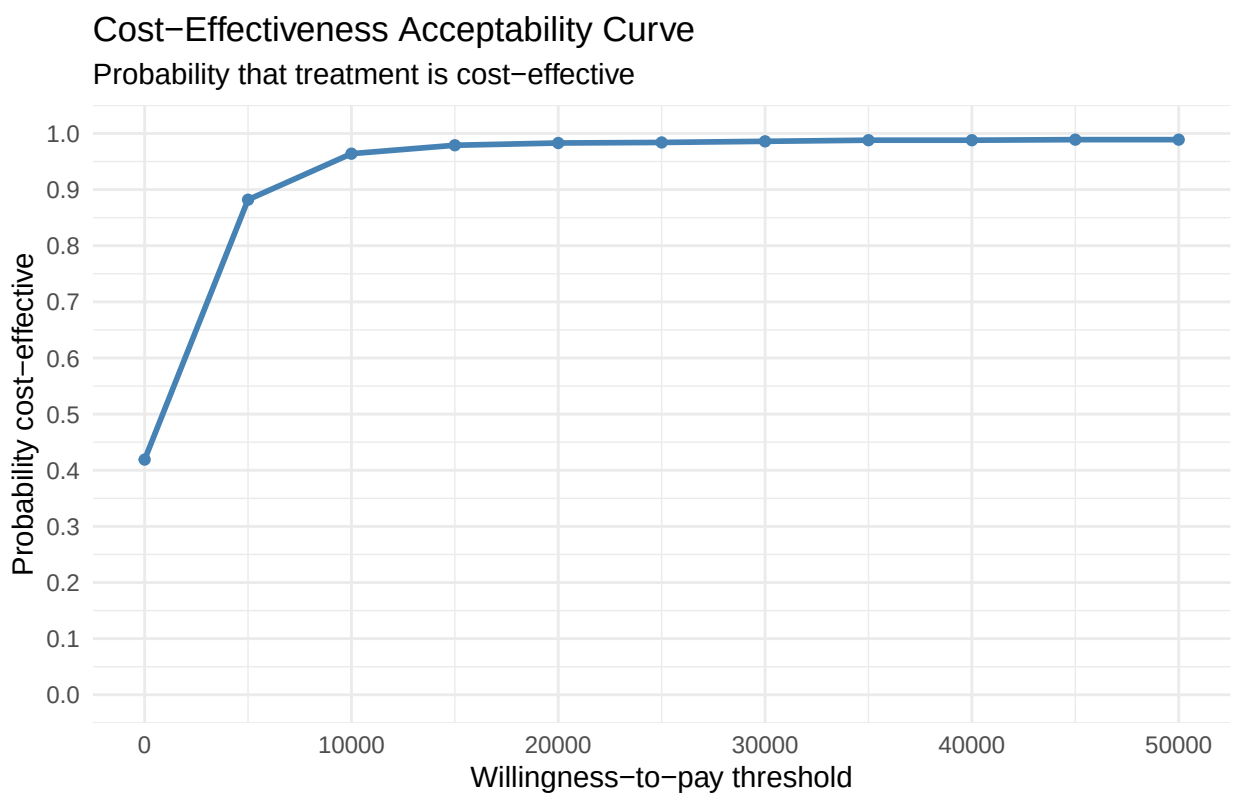


Figure 2: Cost-effectiveness acceptability curve. The curve gives the bootstrap probability that treatment is cost-effective at each willingness-to-pay threshold.

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

dsa_effect
#> # basetable: 9 x 2
#>   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
```

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

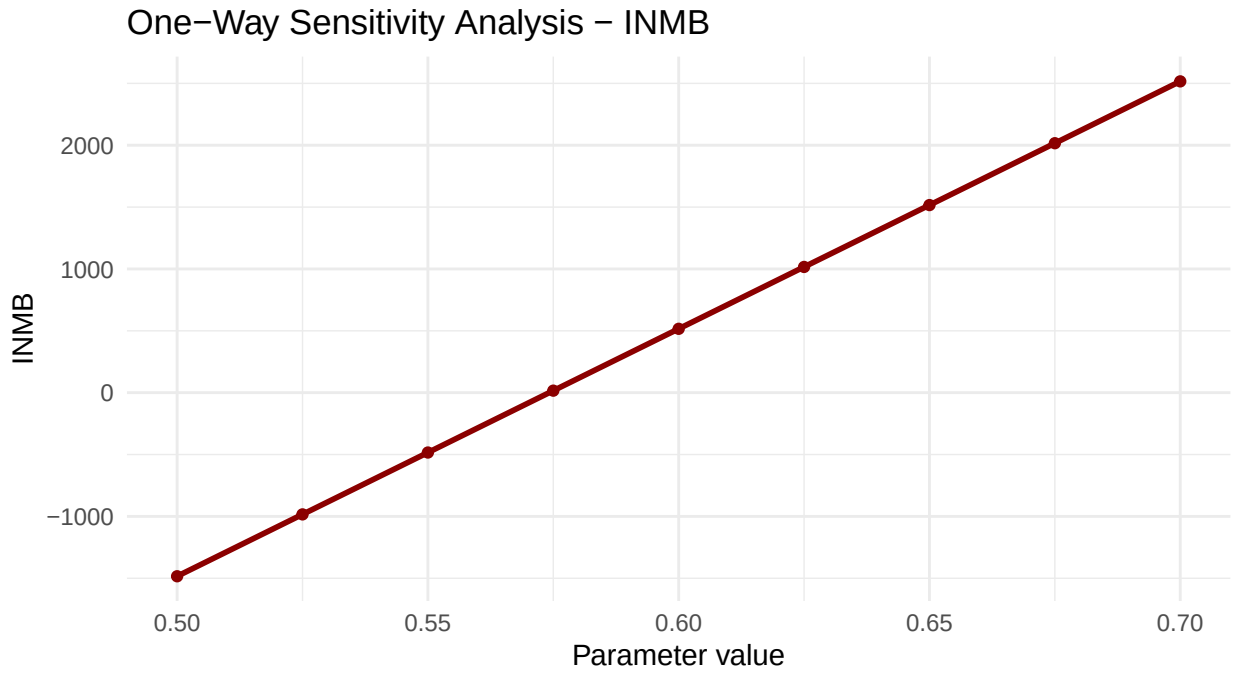


Figure 3: One-way deterministic sensitivity analysis varying treatment-arm effect.

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 ΔC, ΔE, 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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