**Reliability of the Incremental Costs Effectiveness Ratio**

In a randomized clinical trial on locally advanced lymphoma two treatments were compared with respect to (i) 3-year mortality and (ii) costs of the treatment and other health-care costs incurred by the patients. The data are provided in the file “costefficacydata.csv”.

In total 409 patients were included in the trial, 206 in group 1 and 203 in group 2. It was expected that treatment 1 had lower mortality than treatment 2 but also that it was more costly mainly due to additional health care needs to treat side-effects. The main question of the trial was to quantify the ***cost-effectiveness ratio*.**

The csv-file contains four columns:

patnr = patient number

trt = number of the treatment (1 or 2)

event = patient is alive (1) or not (0) after 3 years of follow-up

costs = all health care costs incurred by the patient

The assignment for this week is to calculate the incremental cost-efficacy ratio and have an indication of how reliable it is. The idea is to use bootstrapping and to compare the bootstrap distribution with a simulated sampling distribution.

1. Calculate the event-proportions (p1 and p2) and the mean costs (m1 and m2) in both treatment groups.
2. Calculate the ICER as (m1-m2)/(p1-p2).
3. Use a bootstrap procedure to obtain a 95% confidence interval of the ICER. Check if the interval is biased and, if so, use a bias-correction method.
4. Also plot the bootstrap-estimates of (m1-m2) versus (p1-p2) and count how many points are in the first, second, third and fourth quadrants.
5. Fit parametric distributions to the costs-data in the 2 treatment groups; consider at least the normal, logistic, weibull, gamma and lognormal distributions. Check their fit by visually inspecting qqplots.
6. Finally simulate 1000 times sampling 206 and 203 patients: i.e. (i) draw cost-data from the estimated distributions at step 5, (ii) draw events from binomial distributions with p1 and p2, and (iii) calculate ICERs for each simulation. Compare this sampling distribution with the bootstrap distribution of step 3.
7. To earn extra credit, you may derive an asymptotic confidence interval of the ICER by applying the delta-method.This also requires (repeated) application of the rules of variances and covariances of sums of stochasts.

Make a small (powerpoint) presentation presenting the observed ICER together with some indication of its reliability.

Upload your results into the canvas-site before Monday 4 November 2024, 09.00, or email it to [a.h.zwinderman@amsterdamUMC.nl](mailto:a.h.zwinderman@amsterdamUMC.nl). Don’t forget to write your names in/on the presentation.

Success and some fun, kind regards Koos Zwinderman