COMPARISON OF COSTS AND EFFECTS

- Cost-effectiveness ratios
  \[ \frac{\Delta C}{\Delta Q} \]
- Net monetary benefit
  \[ R_c \Delta Q - \Delta C \]
  where \( R_c \) equals willingness to pay

WERE COSTS AND EFFECTS COMPARED?

COST-EFFECTIVENESS RATIOS OR NMB?

- C/YOLS or C/QALY: 25%
- C/Other: 67%
- NMB: 8%

SAMPLING UNCERTAINTY

- The point estimates of cost and effect differences observed in a study are the result of a single sample drawn from a population
- Had one drawn a different sample, one would have obtained different point estimates
- One uses data from the current sample to provide a measure of the precision of the its estimates in the light of sampling uncertainty
METHODS FOR QUANTIFYING SAMPLING UNCERTAINTY FOR COST-EFFECTIVENESS ANALYSIS

- Confidence interval for cost-effectiveness ratio
- Confidence interval for NMB
- Acceptability curve

CONFIDENCE INTERVALS FOR COST-EFFECTIVENESS RATIOS

- Sampling uncertainty expressed as a confidence interval for the cost-effectiveness ratio is most easily interpreted on the cost-effectiveness plane
- Confidence limits for cost-effectiveness ratios are defined by lines through the origin that each exclude \( \alpha/2 \) of the distribution of the difference in costs and effects (e.g., \( \alpha/2 \) of the distribution falls to the right and below the dashed and solid lower limit line)

POLICY INFERENCES FOR EXPERIMENT 1, CER

1) Confident B cost-effective compared to A

2) Not confident A differs from B

3) Confident A cost-effective compared to B

CONCEPTUALIZING A CONFIDENCE INTERVAL FOR NMB
Confidence Intervals for NMB

- What conclusions would you draw about one's maximum willingness to pay and one's confidence in adopting or rejecting drugs A and B?

Policy Inferences for Experiment #1, NMB

- One must calculate separate CI for each policy-relevant willingness to pay
- CI -- and resulting policy inference -- derived for a single willingness to pay (e.g., 50,000) may have little in common with CI -- and resulting policy inference -- derived for other willingnesses to pay (e.g., 10,000 or 250,000)
Plotting the proportion of the distribution of the difference in costs and effects that falls on the acceptable surface of the cost-effectiveness plane as a function of willingness to pay results in what is referred to as the cost-effectiveness acceptability curve.

What conclusions would you draw about one’s maximum willingness to pay and one’s confidence in adopting or rejecting drugs A and B?
ARE WE PAYING ATTENTION?

- In a recent study, authors reported that the difference in costs equalled 449 Euros; and the difference in YOLS equalled 0.04; and the cost per YOLS ratio equalled 11,225 Euros
- They also reported the following acceptability curve:
- Finally, they concluded as follows:

"The predicted cost-effectiveness ratios were well below the threshold values generally considered cost-effective. Adding clopidogrel to aspirin appeared to be cost-effective in this model analysis of patients with unstable CAD undergoing PCI in Sweden."
- Do you agree with their conclusion?
ACCEPTABILITY CURVE IGNORED

- The authors’ conclusion is based solely on their point estimates of the ratio of the cost-per-year-of-life-saved.
- The acceptability curve indicates that it is unlikely that one can be more than 40% to 60% confident that the therapies differ from one another.
  - The acceptability curve intersects the Y axis at the 1-tailed p-value for the difference in costs. Thus, the observed cost difference has a $p \approx 0.2$ (two-tailed).
  - As the willingness to pay approaches infinity, the height of the curve represents the 1 minus the one-tailed p-value for the difference in effects. Thus, assuming the curve is approaching 0.8, the observed YOLS difference has a $p \approx 0.4$.
  - If the 95% CI are defined, the two limits are both negative and the resulting interval ranges from the lower right quadrant, through all of the upper right quadrant, and conclude in the upper left quadrant.
    * i.e., all policy relevant willingnesses to pay are included in all confidence intervals >80%.

RECONSTRUCTING THE RESULTS

- If $\Delta C = 449$ and the 1-tailed p-value = 0.1
  - t-statistic = 1.28
  - because $\Delta C / SE = t$: $SE \approx 350$
- If $\Delta Q = 0.04$ and the 1-tailed p-value = 0.2
  - t-statistic = 0.843
  - because $\Delta Q / SE = t$: $SE \approx 0.0475$

- Information required to plot parametric acceptability curve:
  $\Delta C$, $SE_c$, $\Delta Q$, $SEQ$, $\rho$, DOF
  - vary $\rho$ from -0.75 to 0.5; assume DOF = 1000
  http://www.uphs.upenn.edu/dgimhsr/stat%20cicer.htm

SIMULATED ACCEPTABILITY CURVE

Correlations vary between -0.75 and 0.5
MORE COMPLETE SIMULATED ACCEPTABILITY CURVE

SIMULATE DISTRIBUTION OF THE DIFFERENCE IN COSTS AND EFFECTS

CONCLUSIONS (I)

- The number of clinical trial-based economic evaluations reported in the literature has increased considerably over the last decade.
- During this same period, the methodologies for analysis and reporting of cost data collected alongside clinical trials has improved.
- The comparison of our key findings with those of Barber and Thompson’s (1997) review suggests improvement over time:
  - Studies performing a statistical test for the difference in cost increased from 53% in 1995 to 82% in 2003.
  - Proportion of studies performing non-parametric bootstrapping increased from 0% to 20%.
- Studies reporting an incremental cost-effectiveness ratio increased 3-fold (10% to 30%).
  - Over half of these studies also reported stochastic uncertainty around this estimate compared with none in 1995.

CONCLUSIONS (II)

- However, in terms of absolute numbers, our review reveals that concerns remain about the quality of the statistical methods in recent clinical-trial based economic studies.
- Furthermore, we only evaluated specific statistical methods used for the analysis and reporting of cost data; other design and analysis issues may pose additional threats.
- The ISPOR RCT-CEA Task force guidance document represents one of the many efforts that will be required to improve the quality and consistency of future studies.
REFERENCES