WHAT IS THE APPROPRIATE SAMPLE SIZE FOR ECONOMIC QUESTIONS?

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- Prior to the development of the literature that described confidence intervals for cost-effectiveness ratios, a common approach for estimating sample size was to base it on the larger of the sample sizes needed for estimating pre-specified cost and effect differences - i.e., what sample size was required to identify a $1000 difference in costs, and what was required to identify a 10% reduction in mortality

- Current sample size methods base their calculations on the number of study subjects needed to rule out unacceptably high upper confidence limits for the cost-effectiveness ratio (equivalently, to rule out that the net monetary benefits of the intervention are less than 0)

SAMPLE SIZE FORMULA

- Sample size for NMB uses the following formula *

\[
n = \frac{(\alpha + \beta)^2 \cdot (2 \text{ sd}_c^2) + (2 \text{ rc} \cdot \text{ sd}_c^2) - (2 \text{ rc} \cdot \rho \cdot (2 \text{ sd}_c^2)^{0.5} \cdot (2 \text{ sd}_e^2)^{0.5})}{\Delta \text{NMB}^2}
\]

where n equals n/group; sd = the standard deviation for costs (q); rc equals the ceiling ratio one wishes to be able to rule out; and \( \rho \) equals the correlation of the difference in cost and effect

http://www.uphs.upenn.edu/dgimhsr/stat%20samps.htm

- Basic data for such calculations include the magnitude of the incremental costs and outcomes (in the formula, they appear in the NMB term); the standard deviations for costs and outcomes; and **the correlation between costs and outcomes**

* See attached STATA-based sample size / power programs

CORRELATION BETWEEN COSTS AND EFFECTS

- Win/Lose (positive) correlation: As the effectiveness (cost) increases, the cost (effectiveness) increases

- Win/Win (negative) correlation: As the effectiveness (cost) increases, the cost (effectiveness) decreases

- Correlation between costs and effects can have dramatic effects on the confidence interval for the cost effectiveness ratio/NMB and thus on the sample size required to demonstrate value for the cost
WHERE TO OBTAIN THE NECESSARY DATA?

- If both therapies are already in use, expected differences in outcomes and standard deviations can be derived from feasibility studies or from records of patients like those who will be enrolled in the trial
  - Potential sources
    * Medical charts of administrative data sets
    * Patient logs of their health care resource use
    * Asking patients and experts about the kinds of care received by those with the condition under study
  - In addition, at least one study has suggested that the simple correlation between costs and effects observed in these data may be an adequate proxy for the measure of correlation used for estimating sample size

WHERE TO OBTAIN THE NECESSARY DATA? (II)

- For novel therapies, information about the magnitude of the incremental costs and outcomes may not be available
  - May need to be generated by assumption
  - Data on the standard deviations for those who receive usual care/placebo may be obtained from feasibility studies or patient records
    * One may assume that the standard deviation will apply equally to both treatment groups, or one may make alternative assumptions about their relative magnitudes
  - The correlation also would be obtained from such data

RELATIVE SAMPLE SIZE FOR CLINICAL AND ECONOMIC QUESTIONS

- Generally accepted that economic results have less power than do clinical results
- Exceptions exist:
  - Results from the fact that the joint outcome can be more powerful than the individual outcomes
  - Would you accept such a finding?