LOGIC BEHIND THE THREE PATTERNS OF SAMPLE SIZE FOR COST-EFFECTIVENESS ANALYSIS

Henry A. Glick

This note provides the logic behind the patterns of sample size that are depicted in slides 23-29 of the Sample Size lecture, "samplesizeworkshopslides.011921.pptx"

Slides 23-25 demonstrate that sample size can be decreasing as willingness to pay increases (slide 23, the most common assumption); it can be increasing as willingness to pay increases (slide 24, often a less intuitive assumption); and it can be decreasing, reach a minimum, and then can be increasing as willingness to pay increases (slide 25, typically a counterintuitive assumption). It is also possible to define an alternative version of experiment 3 where it is increasing, reaches a maximum, and then is decreasing as willingness to pay increases.

The material below (hopefully) explains these different patterns of results.

1. To estimate sample size and power, we hypothesize the expected differences in costs and effects, the standard DEVIATIONS for costs and effects, and the correlation between the difference in costs and effects that will be observed in an experiment. In essence, we have declared the results we expect to observe at the end of the trial (difference in costs, difference in effects, standard ERRORSs, correlation), and thus we have also declared the sampling uncertainty for the cost-effectiveness ratio that we believe we will observe.

2. Once we have made this declaration, there is a direct link between the values of willingness to pay that define narrower and wider confidence limits for the cost-effectiveness ratio and the sample size required to be confident that the experiment's point estimate for the cost-effectiveness ratio represents good or bad value. Values of willingness to pay that define the experiment's narrower confidence limits will require a larger number of participants if there is to be strong evidence of value, whereas values of willingness to pay that define its wider confidence limits will require a smaller number of participants to provide evidence of value.

3. Thus if increasing values of willingness to pay define the limits of increasingly wider confidence intervals, the required sample size will decrease as our willingness to pay increases. If, on the other hand, decreasing values of willingness to pay define the limits of increasingly wider confidence limits, the required sample size will increase as willingness to pay increases. Finally, if increasing (decreasing) values of willingness to pay initially define the limits of increasingly wider confidence interval, but later increasing (decreasing) values of willingness to pay define the limits of increasingly narrower confidence intervals, we will see a nonmonotonic pattern of sample size (power).

4. Experiment 1 (slide 26), in which sample size decreases as willingness to pay increases is an example where increasing values of willingness to pay define the limits of increasingly larger confidence intervals for the cost-effectiveness ratio. As can be seen in the figures, we require the largest sample size and have the lowest power if willingness to pay equals the point

estimate, and the required sample size decreases / power increases for increasing values of willingness to pay of \$24,978, \$49,740, \$89,325, and \$∞.

5. Experiment 2 (slide 27), in which the sample size increases as willingness to pay increases is an example where increasing values of willingness of pay define the limits of increasingly smaller confidence intervals for the cost-effectiveness ratio. As can be seen in the figures, the 36.264817% confidence interval is the narrowest one that has a positive confidence limit (∞). Increasingly wider intervals have limits whose lower limits are decreasing in magnitude: the 99% interval has a lower limit of 102,868; the 99.9999% interval has a lower limit of 37,367, and the 100% interval has a lower limit of \$0.

6. Finally, in experiment 3 (slide 29), we see the nonmonotonic pattern of power. In this experiment, the 70.61% interval is the narrowest one that has a positive confidence limit (0). The 99.131% confidence interval is the narrowest one for which both limits are positive: the lower limit equals ∞, whereas the upper limit equals 21,000. Given that ∞ and 21,000 represent the limits of the same confidence interval, an identical sample size is required to demonstrate good value for either willingness to pay. Thereafter, as the sizes of the intervals increase (e.g., 99.35% and 99.52875% confidence intervals), the lower limits decrease (from ∞ to 185,243 for the 99.35% interval to 50,000 for the 99.5287544% interval) and the upper limits increase (from 21,000 to 26,120 for the 99.35% interval to 50,000 for the 99.5287544% interval).

Elsewhere (e.g., in my sampling uncertainty lectures), I have defined the widest possible confidence interval. The magnitude of this interval is defined by the ellipse for which there is only one line that passes through the origin of the cost-effectiveness plane AND that is tangent to one of the confidence ellipses. In experiment 3, the widest possible interval is the 99.5287544% interval. Both the lower and upper limits are 50,000.

The sign of the widest possible confidence interval partially defines which of the three patterns will be observed for an experiment. As in experiment 3, when the widest definable limit is positive there will always a nonmonotonic pattern. That is, there will always be some values of willingness to pay for which increasingly larger values of willingness to pay require increasingly smaller sample sizes and other values for which increasingly larger values of willingness to pay require increasingly larger sample sizes. Given that the parameter values that yield a positively valued widest possible confidence interval are unexceptional, the nonmonotonic pattern is probably more common that may be assumed.

When, on the other hand, the widest possible confidence interval is negative, EITHER as in experiment 1, increasing values of willingness to pay require increasingly smaller sample sizes, OR as in experiment 2, increasing values of willingness to pay require increasingly larger sample sizes. If the interval for which one of the limits equals 0 (for experiment 1, the 0% interval) is smaller than the interval for which one of the limits equals ∞ (for experiment 1, the 99.5% interval), then increasing values of willingness to pay define the limits of increasingly larger confidence intervals for the cost-effectiveness ratio. Hence, required sample size decreases as willingness to pay increases.

If the interval for which one of the limits equals ∞ (for experiment 2, the 36.264817% interval) is smaller than the interval for which one of the limits equals 0 (for experiment 2, the ~100% interval), then increasing values of willingness to pay define the limits of increasingly smaller confidence intervals for the cost-effectiveness ratio. Hence, required sample size increases as willingness to pay is decreased.