S1 Appendix

Sample size calculations. Considering a continuous outcome, the a priori hypothesis is a mean difference. Moreover, trialists need some assumption regarding the standard deviation of the outcome (often derived from previous studies) and set values for both the type I error (i.e., \(\alpha\)) and the nominal power of the trial (i.e., \(1-\beta\)). If we let \(\delta\) be the mean difference and \(\sigma\) the standard deviation of the outcome, the number of patients to be recruited in each group is \([1]\):

\[
 n = \frac{2(Z_\alpha + Z_\beta)^2}{\Delta^2}
\]

with the effect size

\[
 \Delta = \frac{\delta}{\sigma}
\]

and \(Z_q\) is the q-percentile of a standard normal distribution.

If the outcome is dichotomous (e.g., a success rate), the clinical hypothesis is a rate difference. Moreover, we have to specify the rate associated with the control group. If we define \(p_C\) and \(p_T\) as the success rate in the control and interventional groups, respectively, the number of patients to be recruited in each group could be calculated as \([2]\):

\[
 n = \frac{2(Z_\alpha + Z_\beta)^2}{\Delta^2}
\]

with

\[
 \Delta = \frac{p_T - p_C}{\sqrt{p_T(1-p_T)+p_C(1-p_C)}}
\]

Finally for time-to-event data, sample size is usually derived considering survival rates at some time point. Thus, assuming that the survival proportions is \(\pi_C\) in the control group and \(\pi_T\) in the treatment group, at some chosen time, the a priori hypothesis is the hazard ratio defined as \(HR = \frac{\log \pi_T}{\log \pi_C}\). The number of patients to be recruited in each group is then \([3]\):

\[
 n = \frac{(HR+1)^2(Z_\alpha + Z_\beta)^2}{2HR-1 - \pi_T - \pi_C}
\]

References

