Details on the Sample Size Calculator for Single Sample Survival

This sample size calculator is for an early phase single sample trial where we want to compare the survival for a new therapy to a historical norm under the assumptions of an exponential distribution. We want to the test the null hypothesis H0: $\lambda_1 = \lambda_0$, that the new therapy has a hazard rate λ_1 equal to the historical hazard rate λ_0 versus the alternate H1: $\lambda_1 \neq \lambda_0$,

The asymptotic distribution, provided in Lachin (2000, pg 409-11), of the log hazard rate $LN(\hat{\lambda})$ under the null hypothesis is normal with $LN(\lambda_0)$ and variance $E(D/\lambda_0)^{-1}$ where $E(D/\lambda_0)$ is the expected total number of events under the null. This is given by

$$E(D/\lambda_0) = NE(\delta/\lambda_0, \eta) = \frac{N\lambda_0}{\lambda_0+\eta}\left[1 - \frac{e^{-(\lambda_0+\eta)(T_S-T_R)} - e^{-(\lambda_0+\eta)T_S}}{(\lambda_0+\eta)T_R}\right],$$

where N is the sample size,
$E(\delta/\lambda_0,\eta)$is the probability the event will be observed,
η is exponential dropout rate,
T_S is the maximum total length of the study and
T_R is the enrollment period.

The sample size is then given by

$$N = \frac{\left(Z_\beta + Z_{\varepsilon/2}\right)^2}{\left(LN(\lambda_1) - LN(\lambda_0)\right)^2 E(\delta/\lambda_0)},$$

where β is the false negative rate = (1-power),
α is the false negative rate or significance level,
$LN()$ is the natural logarithm of it's argument and
Z_β and $Z_{\alpha/2}$ are the quantiles of the standard normal distribution with probabilities β and $\alpha/2$ in the tails.

For sample sizes which are large enough, one would test the null by comparing the test statistic T below against the $\alpha/2$ quantile of the standard normal.

$$T = \left(LN(\hat{\lambda}) - LN(\lambda_0)\right)\sqrt{NE(\delta/\lambda_0)}$$

Here $\hat{\lambda}$ can be estimated as the number of events divided by the sum of the event times and the censored times. $E(\delta/\lambda_0)$ now has η =0 as N on completion factors in the drop-outs.

Lachin, John M (2000). *Biostatistical Methods: The assessment of Relative Risks*. John Wiley & Sons, New York, NY.

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