Conditional Power Assessment Details

The sample size, test statistic and Information fraction formulae used in the calculator are tabled below:

	Sample Size	Test Statistic (Z-score)	Information Fraction
Binomial	Planned sample sizes $N_2 = (N_1/r)*(1-r)$ and $N_1 =$ $r*\left[p_1(1-p_1)r^{-1} + p_2(1-p_2)(1-r)^{-1}\right]*\left[\frac{z_{\alpha/2}+z_\beta}{\delta}\right]^2$ Where r is the proportion randomized to the first arm, p_1 and p_2 are the anticipated proportions of outcomes/events in the two arms under the alternate hypotheses, $z_{\alpha/2}$ and the z_β are the $\alpha/2$th and βth right tail quantile of the standard normal distribution and $\delta = p_1 - p_2$.	$\frac{\hat{p}_1 - \hat{p}_2}{\sqrt{\hat{p}_1(1-\hat{p}_1)/n_1 + \hat{p}_2(1-\hat{p}_2)/n_2}}$ Where $\hat{p}_1$ and $\hat{p}_2$ are the observed proportions of the desired outcome in the two arms at the interim analysis and n_1 and n_2 are interim sample sizes.	$\frac{(\hat{p}_1(1-\hat{p}_1)/n_1 + \hat{p}_2(1-\hat{p}_2)/n_2)^{-1}}{(p_1(1-p_1)/N_1 + p_2(1-p_2)/N_2)^{-1}}$ Where the symbols are as defined in the first two columns.
Survival	# of Survival Events $N = r^{-1}(1-r)^{-1}\left[\frac{z_{\alpha/2}+z_\beta}{\ln(\theta)}\right]^2$ Where r is the proportion randomized to the first group, $z_{\alpha/2}$ and the z_β are as defined above, and θ is the hazard ratio (note that for the calculator please choose the groups in the denominator and numerator to give a hazard as a ratio >1) under the alternate hypothesis.	$\ln(\hat{\theta}) * \sqrt{nr(1-r)}$ Where n is the total number of events at the interim and $\hat{\theta}$ is the estimated interim hazard ratio. This is approximate. The calculator can take the Z-score equal to the logrank U statistic divided by it's standard error.	n/N
Normal	$N_1 = \left[\sigma^2(1-r)^{-1}\right]*\left[\frac{z_{\alpha/2}+z_\beta}{\delta}\right]^2$ and $N_2 = \left[\sigma^2 r^{-1}\right]*\left[\frac{z_{\alpha/2}+z_\beta}{\delta}\right]^2$ Where σ is the common standard deviation and δ is the difference between means $\mu_1 - \mu_2$.	$\frac{\hat{\mu}_1 - \hat{\mu}_2}{\sqrt{\hat{\sigma}^2\left(\frac{1}{n_1}+\frac{1}{n_2}\right)}}$ Where $\hat{\mu}_1$ and $\hat{\mu}_2$ are the interim sample means and $\hat{\sigma}$ is the pooled sample standard deviation.	$\frac{\left[\hat{\sigma}^2\left(\frac{1}{n_1}+\frac{1}{n_2}\right)\right]^{-1}}{\left[\sigma^2\left(\frac{1}{N_1}+\frac{1}{N_2}\right)\right]^{-1}}$

The B-value and Conditional Power

Proschan, Lan and Wittes (2006) define a discounted variable called a B-value which is given by $b = \sqrt{t}\, z_t$ (where z_t is the Z-score at information time t) which drifts about a expected value, linear in t, which goes from 0 at t=0 to the unknown expected Z-statistic at the end of the study (t=1). Given a value b at an interim analysis Proschan, Lan and Wittes compute a projected value of the test statistic at the end of the study using the null effect, the empirical effect and the alternate effect. These are given by b, b/t and $b+(1-t)*(z_{\alpha/2} + z_{\beta})$ and denoted by $E\{B(1)|B(t)=b\}$ with projected variance = 1-t. This results in the following expression for the conditional power $CP(t)$ given $B(t) = b$.

$$CP(t) = 1 - \Phi\left(\frac{z_{\alpha/2} - E\{B(1) \mid B(t) = b)\}}{\sqrt{1-t}} \right)$$

Here $\Phi(.)$ cumulative distribution function of the standard normal.

Proschan, Lan and Wittes also provide the expression for the Bayesian predictive power as follows

$$PP(t) = \Phi\left[\frac{(b - z_{\alpha/2})(1 + t\sigma_0^2) + (1-t)(\eta_0 + b\sigma_0^2)}{\sqrt{(1-t)(1+\sigma_0^2)(1+t\sigma_0^2)}} \right]$$

They recommend a prior distribution with mean $\eta_0 = z_{\alpha/2} + z_{\beta}$, which represents a prior consistent with the alternate hypothesis, and a variance σ_0^2 obtained from the weight w on this prior defined as $\sigma_0^2 = (1-w)/w$. The calculator uses these expressions for the mean and the variance of the prior.

References:

1) Proschan, Michael A., Lan, Gordon K.K., Wittes, Janet, Turk (2006). Statistical Monitoring of Clinical Trials- A Unified Approach. Springer Science+Business Media, LLC, New York, NY.
2) Cytel EAST 5 User Manual (2010).

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