Survival Analysis

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1 Sample Size

The $ln(HR)$ follows a normal distribution, we use this to calculate the sample size.

$$
\begin{aligned}
ln(\hat{\Delta}) &\sim N(ln(\Delta), \left(\frac{1}{d_1} + \frac{1}{d_2}\right)) \\
\left(\frac{1}{d_1} + \frac{1}{d_2})\right)^{-1} &= \left[\frac{(z_{\alpha/2} + z_\beta)^2}{(ln\Delta_0)^2}\right]
\end{aligned}
$$

If hazard ratio set at 2.1, then

$$
\begin{aligned}
\left(\frac{1}{d_1} + \frac{1}{d_2})\right)^{-1} &= \left[\frac{(1.96 + 0.58)^2}{(ln2.1)^2}\right] = 11.7 \\
\frac{1}{d_1} + \frac{1}{d_2} = \frac{1}{11.7} &= 0.085 \\
d_1 = d_2 &= 23.44
\end{aligned}
$$

Assume the overall event and censored rate is 20%, then the sample size is $48/0.2 = 240$. If overall event rate (including censoring) is 18%, then the sample size is $48/0.18 = 266$.

1.1 Hazard ratio assumption = 2.1

The assumption is that control group event rate 10% and treatment group event rate 20% at 6 months. Assume survival function is an exponential distribution:

$$
\begin{aligned}
S_t(t) = exp(-\lambda_1 t), &\qquad t = 0.5, S_t = 0.8, -\lambda_1 = ln(0.8)/0.5 \\
S_c(t) = exp(-\lambda_2 t), &\qquad t = 0.5, S_c = 0.9, -\lambda_2 = ln(0.9)/0.5 \\
HR = \frac{\lambda_1}{\lambda_2} & \\
= \frac{ln(0.8)}{ln(0.9)} = 2.117 &
\end{aligned}
$$

1.2 Hazard ratio actual = 0.55

The control group survival 76.8% and treatment group survival 86.2% at 6 months. Assume survival function is an exponential distribution:

$$S_t(t) = exp(-\lambda_1 t), \qquad t = 0.5, S_t = 0.862, -\lambda_1 = ln(0.862)/0.5$$
$$S_c(t) = exp(-\lambda_2 t), \qquad t = 0.5, S_c = 0.768, -\lambda_2 = ln(0.768)/0.5$$

$$HR = \frac{\lambda_1}{\lambda_2}$$
$$= \frac{ln(0.862)}{ln(0.768)} = 0.56$$