$z_{1-(\alpha/2)} = 1.96$ from Table 10.3, the formula reduces to:

$$z_{1-\beta} = \sqrt{\frac{50(0.5-0.3)^2}{(0.5(1-0.5)+0.3(1-0.3))}} - 1.96,$$

$$z_{1-\beta} = \sqrt{\frac{50(0.2)^2}{(0.5(0.5)+0.3(0.7))}} - 1.96,$$

$$z_{1-\beta} = \sqrt{\frac{2}{0.46}} - 1.96,$$

$$z_{1-\beta} = \sqrt{4.35} - 1.96,$$

$$z_{1-\beta} = 0.125$$

A standard computing program or a statistical table can be used to obtain the value of β corresponding to a critical value of 0.125, which may be rounded to 0.13. Using Table 10.3, we see that the critical value of 0.13 corresponds to $z_{1-\beta}$ where β is 0.45. Given that power is calculated as $1-\beta = 1-0.45 = 0.55$, we see that power is just over 50% for this study. With the probability of showing a successful result nearing that of a coin-flip, the Chief Medical Officer may decide to put the study on hold until sufficient time can be devoted to obtain a more reasonable number of subjects or she may choose to evaluate single-arm study options which may be reasonable in this indication.

XII. TIME TO EVENT VARIABLES: TESTING FOR DIFFERENCES BETWEEN TWO GROUPS USING THE LOGRANK TEST

In certain clinical studies, the primary endpoint is based on the length of time until an event occurs, such as death or progression, in an oncology study or until symptoms alleviate, as in a study of influenza. For these studies, subjects are followed for either a set study period or for varying lengths of time. There is the possibility that the subject may never experience the event, and the response would have to be censored in some way. The logrank test is commonly used to assess differences between two groups with a time to event endpoint. Here, there are two sample sizes that have to be established: the number of events to be observed and the number of subjects. Following the work of Schoenfeld (10), the total number of events required to be observed during the study is given by the formula:

$$n_{Events} = 4\frac{\left(z_{1-(\alpha/2)}+z_{1-\beta}\right)^2}{(\ln(h))^2}$$

and the number of subjects required in each treatment group to be able to see the required number of events is given by:

$$n = \left(\frac{4}{(p_1+p_2)}\right)\left(\frac{\left(z_{1-(\alpha/2)}+z_{1-\beta}\right)^2}{(\ln(h))^2}\right)$$

where p_1 is the proportion of subjects in group 1 who will experience the event at any time in the study, p_2 is the proportion of group 2 who will experience the event at any time in the study, h is the hazard ratio, which is defined as $\ln(1-p_1)/\ln(1-p_2)$, α is the type I error rate under evaluation, β is the type II error rate, $z_{1-(\alpha/2)}$ and $z_{1-\beta}$ are critical values from a standard normal distribution. As before, values for the quantity $(z_{1-(\alpha/2)}+z_{1-\beta})^2$ can be obtained from Table 10.2 for commonly chosen values of α and β. It should be noted that the formula for the number of events is for the total number of events between both treatment groups, whereas the formula for the number of subjects is for the number of subjects in each treatment group. To get the total number of subjects required, the number of subjects per group should be multiplied by two.

[10]Schoenfeld D. The asymptotic properties of nonparametric tests for comparing survival distributions. Biometrika 1981;68:316–9.