After rearranging the terms, we have:

$$\frac{n_1}{n_2} = \frac{\theta_2^2}{\theta_1^2} = \left(\frac{\theta_2}{\theta_1}\right)^2$$

Here, we see that the size difference is inversely related to the squared ratio of the effect size. This indicates that if the effect size of scenario 1 is larger than the effect size of scenario 2, the sample size corresponding to scenario 1 is less than the sample size of scenario 2 and vice versa. Power curves corresponding to various effect sizes are presented in Fig. 10.2. Here, it is very clear that increases to effect size yield lower sample sizes and decreasing values of effect size require larger sample sizes. From a practical viewpoint, this is quite reasonable given that smaller differences should be more difficult to uncover and, hence, require a larger sample size to show evidence of a positive result.

XI. BINARY VARIABLES: TESTING THE DIFFERENCE BETWEEN TWO PROPORTIONS

Qualitative endpoints are often utilized in clinical trials. When these endpoints are dichotomous in nature, they are referred to as binary endpoints. Binary endpoints are used where the subject's outcome can be classified as a "success" or "failure." Examples include having undetectable HIV-1 RNA at 48 weeks in studies of HIV-infected subjects or being free of bacteria at the test of cure visit in trials of antibiotics. The sample size formula for testing the difference of two proportions is derived from that used for difference in two means due to the fact that for large samples, the binomial distribution is approximated by the normal distribution through the use of the central limit theorem. Here, we find that:

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

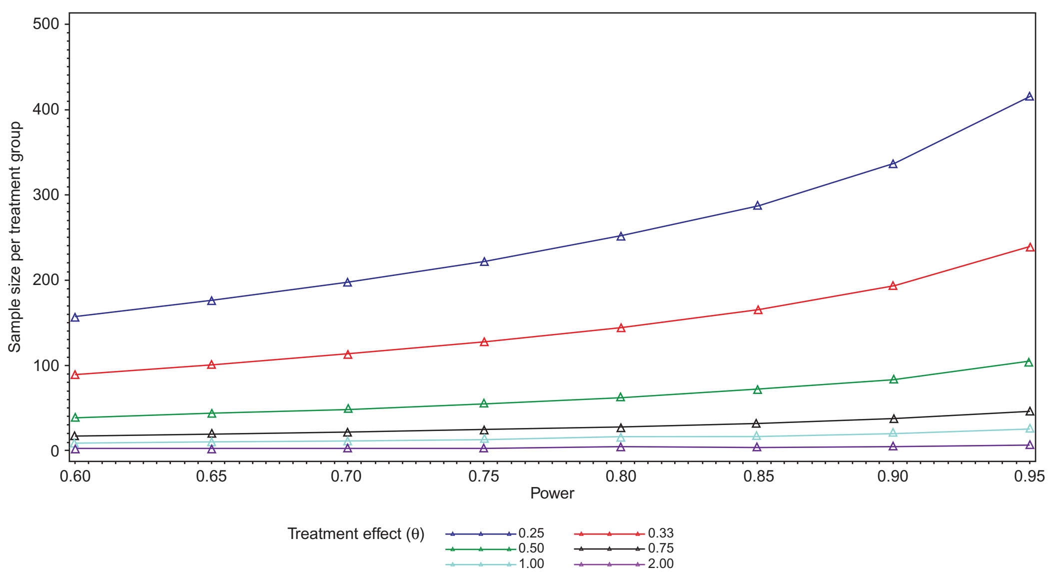

FIGURE 10.2 Power curves corresponding to various effect sizes, θ (theta), when $\alpha = 0.05$.