A Phase III trial examined the effectiveness of a new treatment (T) versus active control (C) in patients with head lice. Randomization to treatment is to be carried out in a 1:1 manner. Patients are to be given the treatment for one day and are to be checked once to see if the head lice still exist (a yes/no dichotomous outcome) 21 days after treatment. The main objective of the trial is to show that T is not inferior to C with respect to the proportion of patients who still have head lice 21 days after treatment. Assume the true control group head lice rate after 21 days is 0.40 (40%).

Write the null and alternative hypothesis for this trial from a risk difference perspective, using a non-inferiority margin of 0.15.

H_0: $\pi_T - \pi_C \geq 0.15$ The new treatment is inferior to the control treatment.

H_A: $\pi_T - \pi_C < 0.15$ The new treatment is not inferior to the control treatment.

Determine the sample size needed to conduct this non-inferiority trial with 80% power using a one-sided 0.025 level of significance and a Farrington-Manning test. Please assume that the expected proportion of patients with head lice in each of the treatment groups (T and C) 21 days after treatment is 0.40. Use the non-inferiority margin of 0.15 (15%). Calculate sample size from a risk difference perspective only.

A sample size of 332, 166 per group, yields 80% power to detect a risk difference margin of 15% in proportion of head lice, using a 1:1 allocation ratio while assuming risk of 40% in the treatment and active control group.

Write an appropriate null and alternative hypothesis for this trial from a relative risk perspective. Determine the appropriate relative risk margin that is analogous to the risk difference information/margin in question a, assuming the true control group head lice rate after 21 days is 0.40.

$$\frac{\pi_T}{\pi_C} \geq \frac{\pi_T + \delta}{\pi_C}$$

$$\frac{\pi_T}{\pi_C} \geq \frac{0.4 + 0.15}{0.4}$$

$$\frac{\pi_T}{\pi_C} \geq 1.375$$

H_0: $\frac{\pi_T}{\pi_C} \geq 1.375$ The new treatment is inferior to the control treatment.

H_A: $\frac{\pi_T}{\pi_C} < 1.375$ The new treatment is not inferior to the control treatment.

Determine the sample size needed to conduct this non-inferiority trial from a relative risk perspective with 80% power, assuming a non-inferiority margin from part c and under the assumption that the proportion of patients still with head lice in each treatment group 21 days after treatment is 0.40 (40%). Use a one-sided 0.025 level of significance. How does the sample size compare to the previously calculated sample size?

A sample size of 472, 236 per group, yields 80% power to detect a relative risk margin of 15% in proportion of remaining head lice, using a 1:1 allocation ratio while assuming risk of 40% in the treatment and active control group. This required sample size using the RR method is larger than using the RD method, which is expected because the outcome of interest is negative.

Suppose that after the study is over, 131 of 227 patients in the new drug group still had head lice after 21 days as compared to 100 of 217 patients in the active group. Is non-inferiority of T versus C achieved at the one-sided 0.025 level of significance using a risk difference margin of 0.15 (or 15%)? Use the Farrington-Manning risk difference approach to test your hypotheses from earlier.

Rewrite your hypotheses from previously so that they match SAS (your margin should be negative). If they already do match SAS, please restate them. Present the 95% confidence interval of the risk difference and the p-value. Provide a concluding statement about whether you can reject the null hypothesis or not, explaining why based on the confidence interval as well as the p-value.

H_0: $\pi_C - \pi_T \leq -0.15$ The new treatment is inferior to the control treatment.
H_A: $\pi_C - \pi_T > -0.15$ The new treatment is not inferior to the control treatment.

$RD = -0.1163$ (95% confidence interval: -0.2086, -0.0240)

The p-value was 0.2360, which is greater than the α=0.025 significance level. The lower bound of the 95% confidence interval, -0.2086, is less than the non-inferiority margin, -0.15. The null hypothesis of the new treatment being inferior to the active control treatment cannot be rejected. There is insufficient evidence to support that the new treatment is not inferior or just as good as the active control.

Repeat the previous question but using the relative risk approach.

$$\frac{\pi_T}{\pi_C} \geq \frac{\pi_T + \delta}{\pi_C}$$
$$\frac{\pi_T}{\pi_C} \geq \frac{0.4 + 0.15}{0.4}$$
$$\frac{\pi_T}{\pi_C} \geq 1.375$$

$$\frac{\pi_C}{\pi_T} \geq \frac{0.4}{0.4 + 0.15}$$
$$\frac{\pi_C}{\pi_T} \geq 0.7273$$

H_0: $\frac{\pi_C}{\pi_T} \geq 0.7273$ T is inferior to C

H_A: $\frac{\pi_C}{\pi_T} < 0.7273$ T is not inferior to C

$RR = 0.7985$ (95% confidence interval: 0.6637, 0.9564)

The p-value was 0.1588, which is greater than the α=0.025 significance level. The lower bound of the 95% confidence interval, 0.6637, is less than the non-inferiority margin, 0.7273. The null hypothesis of the new treatment being inferior to the active control treatment cannot be rejected. There is insufficient evidence to support that the new treatment is not inferior or just as good as the active control.