

A Case-Only Approach to Estimating the RR in the CR-TND

Suzanne Dufault

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1 Set Up

Existing methods for estimating the RR from CR-TND data require the use of test-positive (case) and test-negative (control) counts from each cluster. Because the treatment is randomized, it is possible to estimate the intervention RR using only the test-positive counts. This approach is explored here.

Suppose there are $2m$ clusters in the study with m assigned to the intervention and the remaining m to control. Let $j \in I$ specify a cluster j in the intervention arm and $j \in C$ be a cluster j in the control arm. In each cluster, the number of test-positive individuals n_{D_j} is recorded. A proposed test-statistic is then:

$$T = \sum_{j \in I} n_{D_j} - \sum_{j \in C} n_{D_j} \quad (1)$$

$$= n_{D_I} - n_{D_C} \quad (2)$$

2 At the Null

2.1 Total

At the null, we expect half of all cases (n_D) to fall in each arm:

$$E[n_{D_I}] = E[n_{D_C}] = \frac{n_D}{2} \quad (3)$$

Hence, at the null, $T = 0$

$$E[T] = E[n_{D_I}] - E[n_{D_C}] \quad (4)$$

$$= E[n_{D_I}] - (n_D - E[n_{D_I}]) \quad (5)$$

$$= 2E[n_{D_I}] - n_D \quad (6)$$

$$= 2 \frac{n_D}{2} - n_D \quad (7)$$

$$= 0 \quad (8)$$

2.2 Variance

The variance of T is estimated as follows:

$$Var(T) = Var(2 \times [n_{D_I}] - n_D) \quad (9)$$

$$= 2^2 Var(n_{D_I}) \quad (10)$$

$$= 2^2 \frac{(2m)^2}{m} \frac{m}{2m-1} \frac{\sigma^2}{m} \quad (11)$$

$$= \frac{16m}{2m-1} \sigma^2 \quad (12)$$

where σ^2 is the population variance of the $2m$ test-positive counts.

2.3 Standardized Statistic

Hence, the standardized test statistic is $\frac{T}{\sqrt{\frac{16m}{2m-1} \sigma^2}} \sim N(0, 1)$.

3 Recovering the Intervention RR

When an intervention is applied to reduce the number of cases in the intervention arm, we would like to estimate the intervention effect through the RR (λ). In the test-positive setting, this can be accomplished through a simple ratio of the sums in the two arms:

$$\lambda = \frac{n_{D_I}}{n_{D_C}} \quad (13)$$

$$= \frac{n_{D_I}}{n_D - n_{D_I}} \quad (14)$$

3.1 Variance of the Intervention RR

In order to estimate the variance of the intervention RR λ , we can use the delta method. We know the properties of n_{D_I} , and λ is a simple transformation of n_{D_I} .

Hence if $x = n_{D_I}$:

$$g(x) = \frac{x}{n_D - x} \quad (15)$$

$$g'(x) = \frac{n_D}{(n_D - x)^2} \quad (16)$$

Implying:

$$\hat{\lambda} \approx N \left(\lambda, \left[\left(\frac{n_D}{(n_D - x)^2} \right)^2 Var(x) \right] \right) \quad (17)$$

$$= N \left(\lambda, \left[\left(\frac{n_D}{(n_D - n_{D_I})^2} \right)^2 Var(n_{D_I}) \right] \right) \quad (18)$$

$$= N \left(\lambda, \left[\left(\frac{n_D}{(n_D - n_{D_I})^2} \right)^2 \frac{4m^2}{m} \frac{m}{2m-1} \frac{\sigma^2}{m} \right] \right) \quad (19)$$

$$= N \left(\lambda, \left[\left(\frac{n_D}{(n_D - n_{D_I})^2} \right)^2 \frac{4m}{2m-1} \sigma^2 \right] \right) \quad (20)$$

We know $Var(T)$, but in order to estimate it, we need to replace the population variance σ^2 with an estimate.

$$\hat{Var}(T) = 2^2 \hat{Var}(n_{D_I}) \quad (21)$$

$$= 4(2m)^2 \frac{1}{2} \frac{s^2}{m} \quad (22)$$

$$= 8ms^2 \quad (23)$$

where $s^2 = \frac{1}{m-1} \sum_{j \in I, j=1}^m (n_{D_j} - \bar{n}_{D_J})^2$. Hence, we can compare $T/\sqrt{8ms^2}$ to a T distribution with $2(m-1)$ degrees of freedom.

The same is true for estimating $Var(\lambda)$.

$$Var(\lambda) = \left(\frac{n_D}{(n_D - n_{D_I})^2} \right)^2 Var(n_{D_I}) \quad (24)$$

$$\hat{Var}(\lambda) = \left(\frac{n_D}{(n_D - n_{D_I})^2} \right)^2 \hat{Var}(n_{D_I}) \quad (25)$$

$$= \left(\frac{n_D}{(n_D - n_{D_I})^2} \right)^2 4m^2 \frac{1}{2} \frac{s^2}{m} \quad (26)$$

$$= \left(\frac{n_D}{(n_D - n_{D_I})^2} \right)^2 2ms^2 \quad (27)$$