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

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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. The total number of test-positive individuals is denoted n_D. The sum of test-positives from the intervention arm are denoted A_+ and those from the control arm, G_+.

$$T = A_+ - G_+ \tag{1}$$

2 At the Null

2.1 Total

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

$$E[A_+] = E[G_+] = \frac{n_D}{2} \tag{2}$$

Hence, at the null, $T = 0$

$$\begin{aligned}
E[T] &= E[A_+] - E[G_+] && (3)\\
&= E[A_+] - (n_D - E[G_+]) && (4)\\
&= 2E[A_+] - n_D && (5)\\
&= 2\frac{n_D}{2} - n_D && (6)\\
&= 0 && (7)
\end{aligned}$$

2.2 Variance of Sample Counts

First, let's define $Var(A_+)$ as it will come up often:

The variance of a sample sum can be estimated as follows in the setting of sampling without replacement:

$$Var(A_+) = n\sigma^2 \frac{N-n}{N-1} \tag{8}$$

$$= m\sigma^2 \frac{m}{2m-1} \tag{9}$$

We can estimate the population variance (σ^2) by using the sample variance of counts in either the treatment or control arm or both. Let V_D represent the pooled (averaged) sample variances (estimated with $n-1$ in the denominators) from the treatment and control arm. Then,

$$Var(A_+) = mV_D \frac{m}{2m} \tag{10}$$

$$= \frac{m}{2} V_D \tag{11}$$

The variance of T is then estimated as follows:

$$Var(T) = Var(A_+ - G_+) \tag{12}$$

$$= Var(A_+ - (n_D - A_+)) \tag{13}$$

$$= 2^2 Var(A_+) \tag{14}$$

$$= 4 \times \frac{m}{2} V_D \tag{15}$$

$$= 2mV_D \tag{16}$$

2.3 Standardized Statistic

Hence, the standardized test statistic is $\frac{T}{\sqrt{2mV_D}} \sim N(0, 1)$.

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:

$$\lambda = \frac{A_+}{G_+} \tag{17}$$

$$= \frac{A_+}{n_D - A_+} \tag{18}$$

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 A_+, and λ is a simple transformation of A_+.

Hence if $x = A_+$:

$$g(x) = \frac{x}{n_D - x} \tag{19}$$

$$g'(x) = \frac{n_D}{x(n_D - x)} \tag{20}$$

where n_D is fixed and x is the random variable.

$$\begin{aligned}
Var(\log\lambda) &= Var(\log\frac{x}{n_D - x}) && (21)\\
&\approx f'(x)^2 Var(x) \qquad \text{via delta method} && (22)\\
&= \frac{n_D^2}{x^2(n_D - x)^2} Var(x) && (23)\\
&= \frac{n_D^2}{\left(\frac{n_D}{2}\right)^2\left(\frac{n_D}{2}\right)^2} Var(x) \qquad \text{at the null } \frac{n_D}{2} = x = n_D - x && (24)\\
&= \frac{16}{n_D^2} Var(x) && (25)\\
&= \frac{16}{n_D^2}\frac{m}{2} V_D && (26)
\end{aligned}$$