

Analysis of paired, screen-positive designs

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1 Model extension to Pepe and Alonzo (2001)

Pepe and Alonzo (2001) show how to fit regression models to paired, screen-positive designs. They use marginal models fitted to all of the data, including those with missing disease status. We propose a simple extension to their framework, where the model is fitted to those individuals with known disease status.

Following the notation used by Pepe and Alonzo (2001), we consider 0/1 tests Y_A and Y_B , with disease status D and covariates Z . Pepe and Alonzo define $\alpha Z = \log P(D = 1, Y_B = 1|Z)$ and $\alpha Z + \beta Z = \log P(D = 1, Y_A = 1|Z)$, and use $T = 1$ for test A and $T = 0$ for test B with Y for the test value.

Similar, we define an indicator $S = I(Y_A = 1 \text{ or } Y_B = 1)$ for whether one or either of the tests is positive, such that the disease status is known. Moreover, let $\alpha^* Z = \log P(D = 1, Y_B = 1|Z, S = 1)$ and $\alpha^* Z + \beta^* Z = \log P(D = 1, Y_A = 1|Z, S = 1)$, where we have conditioned on having one or more positive tests. Then, closely following the argument in Pepe and Alonzo (2001),

$$\begin{aligned}\beta^* Z &= \log \frac{P(D = 1, Y_A = 1|Z, S = 1)}{P(D = 1, Y_B = 1|Z, S = 1)} \\ &= \log \frac{P(Y = 1|D = 1, Z, T = 1, S = 1)P(D = 1|Z, T = 1, S = 1)}{P(Y = 1|D = 1, Z, T = 0, S = 1)P(D = 1|Z, T = 0, S = 1)} \\ &= \log \frac{P(Y_A = 1|D = 1, Z, S = 1)}{P(Y_B = 1|D = 1, Z, S = 1)}\end{aligned}$$

where $P(D = 1|Z, T = 1, S = 1) = P(D = 1|Z, T = 0, S = 1)$ for paired data. Noting that

$$\begin{aligned}P(Y = 1|D = 1, Z, T, S = 1) &= \frac{P(Y = 1|D = 1, Z, T) - P(Y = 1|D = 1, Z, T, S = 0)P(S = 0)}{P(S = 1)} \\ &= \frac{P(Y = 1|D = 1, Z, T)}{P(S = 1)}\end{aligned}$$

as $P(Y = 1|D = 1, Z, T, S = 0) = 0$, because no positive tests have $S = 0$, then

$$\begin{aligned}\beta^* Z &= \log \frac{P(Y_A = 1|D = 1, Z, S = 1)}{P(Y_B = 1|D = 1, Z, S = 1)} \\ &= \log \frac{P(Y_A = 1|D = 1, Z)}{P(Y_B = 1|D = 1, Z)} \\ &= \beta Z = \text{rTPF}(Z)\end{aligned}$$

In general, α^* does not equal α , as $P(D = 1, Y_B = 1|Z, S = 1)$ may be different to $P(D = 1, Y_B = 1|Z)$, and the intercept term also be shifted.

Care is further required in using a simplified model. Pepe and Alonzo (2001) fit a reduced PSA model by excluding the main effect due to race. However, [data-driven observation that requires a mathematical derivation], the estimated interaction effect for β^* is then a biased estimate of β .