

## Main text

### 1. Intro paragraph

- (a) Describe E-value and why extend to regression
- (b) If you have raw data, could choose somewhere to dichotomize and use E-value for SMD or RR
- (c) We provide E-value for cases where only standard regression info is reported
- (d) Approach involves converting regression results to SMD with well-defined effect size (say why critical for E-value): show table with RR and lower and upper RR

### 2. $\beta$ -amyloid example

- (a) .

### 3. Caveats

- (a) What to do with preventative
- (b) Multiple regression
- (c) Be careful with interpretation: depends on  $\Delta$
- (d) Interpretation: E-value for a  $\Delta$ -unit increase in X and any dichotomization of Y

In general, we would recommend using  $\Delta = 1$  in order to assess the E-value for the effect size corresponding directly to the regression coefficient, which represents a 1-unit contrast in  $X$ . However, if the units of  $X$  are very fine-grained (e.g., if  $X$  is blood pressure in mmHg), then a 1-unit increase may not be considered clinically meaningful, and a different choice of  $\Delta$  may be used (e.g.,  $\Delta = 10$  to represent an increase in blood pressure of 10 mmHg), which is equivalent to rescaling the regression coefficient. It is imperative to report the choice of  $\Delta$  if it is not taken to be 1, since it directly impacts the size and interpretation of the E-value analog.

## $\beta$ -amyloid example

```
##           point      lower      upper
## RR       0.3783315 0.2887908 0.4956347
## E-values 4.7272287      NA 3.4504987

##           point      lower      upper
## RR       1.037101 0.7406488 1.452211
## E-values 1.233257 1.0000000      NA

##           point      lower      upper
## RR       0.505352 0.3366446 0.7586062
## E-values 3.370546      NA 1.9658663

##           point      lower      upper
## RR       0.6880847 0.4813375 0.9836354
## E-values 2.2649736      NA 1.1466895
```

## Appendix - NEW VERSION

Cover somewhere:

\*Assumptions inherited from Chinn's conversion from d to log-OR: distribution of Y within each outcome group is logistic, but according to Chinn, this is basically the same as normality

## Converting univariable regression results to Cohen's d

**Lemma 1.** As usual in OLS regression, suppose that  $Y = \beta_0 + \beta_1 X + \epsilon$  with  $X \perp \epsilon$  and  $E[\epsilon] = 0$ . Then  $\sigma_Y^2 =$

*Proof.*

$$\begin{aligned}
 \sigma_Y^2 &= E[\sigma_{Y|X}^2] + \text{Var}(E[Y|X]) \\
 &= \sigma_{Y|X}^2 + \text{Var}(\beta_0 + \beta_1 X) && \text{(homoskedasticity)} \\
 &= \sigma_{Y|X}^2 + \beta_1^2 \sigma_X^2 \\
 &= \sigma_{Y|X}^2 + r_{YX}^2 \sigma_Y^2 \\
 \sigma_{Y|X}^2 &= (1 - r_{YX}^2) \sigma_Y^2
 \end{aligned}$$

Thus, QED. □

Suppose we estimate the conditional mean of an outcome Y given a continuous exposure of interest, X, via ordinary least squares:

$$E[Y | X] = \beta_0 + \beta_X X$$

where  $\beta_0$  denotes the intercept and  $\beta_X$  denotes the estimated coefficient of X. Suppose that the effect size of interest is the increase in Y caused by a  $\Delta$ -unit increase in X.

Assume that (X, Y) are bivariate normal and consider the Cohen's d associated with an increase of  $\Delta$  units in X:

$$\begin{aligned}
 d &= \frac{E[Y | X = c + \Delta] - E[Y | X = c]}{\sigma_{Y|X}} \\
 &= \frac{\Delta \beta}{\sigma_Y \sqrt{1 - \rho_{XY}^2}} \\
 &= \frac{\Delta \beta}{\sigma_Y \sqrt{1 - \frac{\beta^2 \sigma_X^2}{\sigma_Y^2}}} \\
 &= \frac{\Delta \rho_{XY}}{\sigma_X \sqrt{1 - \rho_{XY}^2}}
 \end{aligned}$$

where the denominator comes from a well-known property of the bivariate normal distribution.

An approximate standard error can be derived using the delta method. Let  $z_{fis} = XXX$  be the Fisher-transformed correlation, which is approximately normal with variance  $\frac{1}{N-3}$ . Define the transformation:

$$\begin{aligned}
 g(z_{fis}) = d &= \frac{\Delta \tanh(z_{fis})}{\sigma_X \sqrt{1 - \tanh^2(z_{fis})}} \\
 SE_d &\approx \sqrt{\text{Var}(z_{fis}) (g'(z_{fis}))} \\
 &= \frac{1}{\sqrt{N-3}} \times \frac{\Delta}{\sigma_X \sqrt{\text{sech}^2(z_{fis})}} \\
 &= \frac{\Delta}{\sigma_X \sqrt{(N-3)(1 - \rho_{XY}^2)}} \\
 &= \frac{\Delta}{\sigma_X \sqrt{(N-3) \left(1 - \beta^2 \frac{\sigma_X^2}{\sigma_Y^2}\right)}}
 \end{aligned}$$

### E-value for a univariable regression

$$RR \approx \exp \left( 0.91 \times \frac{\Delta \rho_{XY}}{\sigma_X \sqrt{1 - \rho_{XY}^2}} \right)$$

CI:

$$\begin{aligned}
 RR_{lb} &\approx \exp \left( 0.91 \times \frac{\Delta \rho_{XY}}{\sigma_X \sqrt{1 - \rho_{XY}^2}} - 1.78 \times SE_d \right) \\
 &= RR_{ub} \approx \exp \left( 0.91 \times \frac{\Delta \rho_{XY}}{\sigma_X \sqrt{1 - \rho_{XY}^2}} + 1.78 \times SE_d \right)
 \end{aligned}$$

### Converting multivariable regression results to Cohen's $d$

Extend the regression model in (EQUATION) to include arbitrary measured covariates  $\mathbf{Z}$ :

$$\hat{E}[Y | X, \mathbf{Z}] = \hat{\beta}_0 + \hat{\beta}_X X + \hat{\beta}'_{\mathbf{Z}} \mathbf{Z}$$

where  $\hat{\beta}_{\mathbf{Z}}$  denotes a vector of estimated coefficients for  $\mathbf{Z}$ .

$$\begin{aligned}
 R_{Y \sim X | Z}^2 &= 1 - \frac{SSE_{full}}{SSE_{red}} \\
 &= 1 - \frac{\sigma_{Y|X, \mathbf{Z}}^2}{\sigma_{Y|\mathbf{Z}}^2} \\
 \sigma_{Y|X, \mathbf{Z}}^2 &= \sigma_{Y|\mathbf{Z}}^2 (1 - R_{Y \sim X | Z}^2)
 \end{aligned}$$

DOES THIS USE MVN ASSUMPTION? FLESH OUT THIS STEP. SEEMS LIKE WE ONLY NEED NORMAL ERRORS.

$$\begin{aligned}
 d &= \frac{E[Y \mid X = c + \Delta, \mathbf{Z}] - E[Y \mid X = c, \mathbf{Z}]}{\sigma_{Y|X, \mathbf{Z}}} \\
 &= \frac{\Delta\beta}{\sigma_{Y|\mathbf{Z}} \sqrt{1 - R_{Y \sim X|Z}^2}} \\
 &\geq \frac{\Delta\beta}{\sigma_Y \sqrt{1 - R_{Y \sim X|Z}^2}}
 \end{aligned}$$

Unlike in the univariable case, a simple relationship between  $\beta$  and  $R_{Y \sim X|Z}^2$  is not available with additional distributional assumptions, so both quantities are needed to approximate  $d$ .

Note that you can use partial correlation or partial  $R^2$  from regression table.

Standard error: Going to be hard because inference for  $R_{Y \sim X|Z}^2$  won't be available. For an approximation, can use  $Var(z_{YX|Z}^f) \approx Var(z_{YX}^f) = \frac{1}{N-3}$

- describe what to do for preventive: just set delta to be negative?
- say that, for univariable case, if SD of X isn't available, can set Delta = SD of X

## References