

Erratum

Kravitz, Duan, and Braslow (2004) defined heterogeneity of treatment effects (HTE) as the standard deviation for the individual treatment effects (ITEs) across a target population, and provided the following formula for the HTE:

$$(1) \quad \text{HTE} = \sqrt{2} \text{SD} \sqrt{1 - \rho},$$

where SD denotes the pooled standard deviation of the outcome across treatment arms, A and B, and ρ denotes the correlation between the outcome for individuals under treatment A compared with treatment B.

Formula (1) is actually missing a term, and should be modified as follows:

$$(2) \quad \text{HTE} = \sqrt{2} \text{SD} \sqrt{1 - c\rho},$$

where the correction factor c is given as follows:

$$c = V_{\text{GM}}/V_{\text{AM}},$$

V_{GM} = the geometric mean for the variances of the outcomes across arms, and

V_{AM} = the arithmetic mean for the variances of the outcomes across arms
= SD^2 .

More specifically, let Y_{Ai} (Y_{Bi}) denote the outcome for the i -th patient under treatment A (B), and V_A (V_B) denote the variance for the outcome across patients in the target population under treatment A (B). Then,

$$V_{\text{GM}} = \sqrt{V_A \times V_B}, \quad \text{and}$$

$$V_{\text{AM}} = (V_A + V_B)/2.$$

When the variance is the same under the two treatment conditions, i.e., when $V_A = V_B$, the factor c is one, the correct formula (2) simplifies to the wrong formula (1). When the variance differs between the two conditions, the factor c is smaller than one. Unless the two variances differ

enormously, the factor c is usually pretty close to one. For example, if the two variances differ by fourfold, say, $V_A = 1$ and $V_B = 4$, we have $V_{GM} = 2$, $V_{AM} = 2.5$, thus $c = V_{GM}/V_{AM} = 2/2.5 = 0.8$. Therefore, even when the two variances differ as substantial as fourfold, the factor c is still pretty close to one, i.e., the wrong formula (1) is a reasonable approximation to the correct formula (2).

We have provided below the derivation for formula (2). The individual treatment effect for the i -th individual, ITE_i , is given by

$$ITE_i = Y_{Ai} - Y_{Bi}.$$

By our definition, HTE is the standard deviation for ITE across individuals, therefore

$$\begin{aligned} HTE^2 &= \text{Var}(ITE) = \text{Var}(Y_A - Y_B) \\ &= \text{Var}(Y_A) - 2 \times \text{Cov}(Y_A, Y_B) + \text{Var}(Y_B) \\ &= \text{Var}(Y_A) - 2 \times \rho \times \sqrt{\text{Var}(Y_A) \times \text{Var}(Y_B)} + \text{Var}(Y_B) \\ &= (V_A + V_B) - 2 \times \rho \times \sqrt{V_A \times V_B} \\ &= 2 \times V_{AM} - 2 \times \rho \times V_{GM} \\ &= 2 \times V_{AM} \times (1 - \rho \times (V_{GM}/V_{AM})) \\ &= 2 \times V_{AM} \times (1 - \rho \times c) \\ &= 2 \times SD^2 \times (1 - c\rho). \end{aligned}$$

Formula (2) follows by taking the square root on the two sides of the above equation.

Reference

Kravitz, R.L., N. Duan, and J. Braslow. 2004. Evidence-Based Medicine, Heterogeneity of Treatment Effects, and the Trouble with Averages. *The Milbank Quarterly* 82(4):661–87.