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:

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

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:

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

where the correction factor c is given as follows:

$$\begin{aligned} c &= V_{GM}/V_{AM}, \\ V_{GM} &= \text{the geometric mean for the variances of the outcomes across arms, and} \\ V_{AM} &= \text{the arithmetic mean for the variances of the outcomes across arms} \\ &= SD^2. \end{aligned}$$

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,

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

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

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

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

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.