CORRELATIONS IN MULTIVARIATE META-ANALYSES: WHAT ASSOCIATIONS ARE BEING MEASURED?

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In multivariate meta-analysis, multiple outcomes are analyzed jointly to derive summary treatment effect estimates from a single model, which also yields an estimate of the correlation between effects. This can be used to infer about the dependence between responses to treatment for the various outcomes. We carried out a simulation study to examine if the measured correlation reflects this relationship or is distorted by other factors. We simulated studies of the effect of a treatment on two dichotomous endpoints from a conceptual model that allowed dependence between treatment effects, biological relationships between endpoints and correlated random-effects to represent the shared impact of study-level factors. We derived log-odds-ratios (LORs) for endpoints in a set of studies in scenarios where we varied the presence and magnitude of the different sources of correlation, the strength of treatment and commonness of endpoints. The correlation between LORs was calculated empirically to determine if the observed values accurately reflect the dependence between treatment effects. Correlations measured between LORs were potentially strongly affected by biological associations between endpoints and, more so by correlated random-effects. High correlations (>0.5) were observed between LORs for the two outcomes even when effects were independent. Conversely, when only the treatment effects were dependent, very low correlations (<0.25) were observed regardless of the assumed strength of the dependence. There was considerable overlap in correlations across scenarios when we allowed associations from all sources. Thus, with just study-level data, the dependence between treatment effects could not be assessed reliably.