The interaction:effect ratio (IER_{AB}) equals the interaction term ($I_{AB} = \mu_0 - \mu_a - \mu_b + \mu_{ab}$) divided by the simple effect of A (δ_A):

$$IER_{AB} = I_{AB} / \delta_A = (\mu_0 - \mu_a - \mu_b + \mu_{ab}) / (\mu_a - \mu_0) \quad (1)$$

Simple effects comprise the difference in means between the group receiving one treatment and the group not receiving that treatment ($\delta_A = \mu_a - \mu_0$). When all treatments have the same direction of effect (e.g. when A and B both increase cost, or both decrease cost), the factor defined as A is the one for which the simple effects has the smaller absolute magnitude (where $|\mu_a - \mu_0| < |\mu_b - \mu_0|$). For mixed interactions, factor A should be the factor for which δ_A has the opposite sign to I_{AB}. These rules ensures that qualitative interactions (those changing the ranking of treatments) have interaction:effect ratios <-1. In all cases, interaction:effect ratios <-1 indicate qualitative interactions, ratios between -1 and 0 indicate sub-additive or mixed interactions, ratios equal to 0 indicate additive effects, while interaction:effect ratios >0 indicate super-additive interactions.

[1] The interaction:effect ratio differs from the “interaction ratio” used by McAlister et al [10]. McAlister’s interaction ratio is simply the relative effect (e.g. odds ratio) of A vs. not-A for patients also receiving B, divided by the relative effect of A vs. not-A for patients not receiving B (interaction ratio = $(odds_{ab} / odds_b) \div (odds_a / odds_0)$) and therefore equals the interaction on a logarithmic scale (interaction on log-scale = $\exp[(\ln[odds_{ab}] - \ln[odds_b]) - (\ln[odds_a] - \ln[odds_0])]$). Unlike our interaction:effect ratio, McAlister’s interaction ratio is appropriate only for data interpreted on a multiplicative scale and does not distinguish between qualitative and non-qualitative interactions. At least one previous paper has used the interaction divided by simple

effect to describe the ranges of interaction magnitude in which different analytical approaches performed best [3]. However, this study did not include any adjustment for mixed interactions, did not link the ranges of ratio values with different types of interaction and did not propose this ratio as a method for describing interactions in general.