



* A two-stage IPDMA approach was used ('deft', i.e. interaction estimate solely based on within-trial interactions): First, a binomial regression was fitted in each trial separately, adjusted for age and the covariate, whilst including the treatment and the treatment-covariate interaction, using restricted maximum likelihood estimation (with Firth's penalisation correction in case of sparse data), to produce a treatment-covariate interaction estimate and its variance. Second, the interaction estimates are combined across trials in a random-effect model ("the true interactions are assumed random across trials"), using restricted maximum likelihood estimation and the confidence interval for the summary interaction derived using the Hartung-Knapp Sidik-Jonkman approach. Sizing of all squares are in proportion to the inverse of the variance of the estimates.