World Academy of Science, Engineering and Technology
International Journal of Mathematical and Computational Sciences
Vol:16, No:12, 2022

A Comparison of Methods for Estimating Dichotomous Treatment Effects: A Simulation Study

Authors : Jacqueline Y. Thompson, Sam Watson, Lee Middleton, Karla Hemming

Abstract : Introduction: The odds ratio (estimated via logistic regression) is a well-established and common approach for estimating covariate-adjusted binary treatment effects when comparing a treatment and control group with dichotomous outcomes. Its popularity is primarily because of its stability and robustness to model misspecification. However, the situation is different for the relative risk and risk difference, which are arguably easier to interpret and better suited to specific designs such as non-inferiority studies. So far, there is no equivalent, widely acceptable approach to estimate an adjusted relative risk and risk difference when conducting clinical trials. This is partly due to the lack of a comprehensive evaluation of available candidate methods. Methods/Approach: A simulation study is designed to evaluate the performance of relevant candidate methods to estimate relative risks to represent conditional and marginal estimation approaches. We consider the log-binomial, generalised linear models (GLM) with iteratively weighted least-squares (IWLS) and model-based standard errors (SE); log-binomial GLM with convex optimisation and model-based SEs; log-binomial GLM with convex optimisation and permutation tests; modified-Poisson GLM IWLS and robust SEs; log-binomial generalised estimation equations (GEE) and robust SEs; marginal standardisation and delta method SEs; and marginal standardisation and permutation test SEs. Independent and identically distributed datasets are simulated from a randomised controlled trial to evaluate these candidate methods. Simulations are replicated 10000 times for each scenario across all possible combinations of sample sizes (200, 1000, and 5000), outcomes (10%, 50%, and 80%), and covariates (ranging from -0.05 to 0.7) representing weak, moderate or strong relationships. Treatment effects (ranging from 0, -0.5, 1; on the log-scale) will consider null (H0) and alternative (H1) hypotheses to evaluate coverage and power in realistic scenarios. Performance measures (bias, mean square error (MSE), relative efficiency, and convergence rates) are evaluated across scenarios covering a range of sample sizes, event rates, covariate prognostic strength, and model misspecifications. Potential Results, Relevance & Impact: There are several methods for estimating unadjusted and adjusted relative risks. However, it is unclear which method(s) is the most efficient, preserves type-I error rate, is robust to model misspecification, or is the most powerful when adjusting for non-prognostic and prognostic covariates. GEE estimations may be biased when the outcome distributions are not from marginal binary data. Also, it seems that marginal standardisation and convex optimisation may perform better than GLM IWLS log-binomial.

Keywords : binary outcomes, statistical methods, clinical trials, simulation study
Conference Title : ICSP 2022 : International Conference on Statistics and Probability
Conference Location : Sydney, Australia
Conference Dates : December 02-03, 2022