Controlled multiple imputation: an accessible flexible tool for sensitivity analysis of clinical trials with different types of missing data

Suzie Cro

Abstract

In clinical trials, loss to follow-up is almost inevitable and may occur for various reasons. Consequently, we often cannot measure what we intended for all individuals and a missing data problem arises. Since the true values of missing data are never known, it is necessary to assess the impact of untestable assumptions about any unobserved data in sensitivity analysis. One approach which enables contextually relevant sensitivity of clinical trials is Controlled Multiple Imputation (MI). Controlled MI procedures include $\delta$-based and reference-based procedures. In $\delta$-based MI an offset term, $\delta$, is added to missing values imputed under MAR to assess the impact of unobserved individuals having a worse or better response than those observed with similar characteristics. Reference-based MI draws imputed values with some reference to observed data in other groups of the trial, typically in other treatment arms. This enables one to assess the impact of the unobserved behaving like members of a specified reference group. I will illustrate the flexibility of controlled MI approaches, using data from a headache trial comparing acupuncture against standard of care, and show how different assumptions for unobserved data can be readily made for different groups of individuals in the same trial analysis.