

Correction methods for unmeasured confounding in non interventional studies

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Abstract

Confounding is a major source of bias which may arise mainly in the context of non-interventional clinical studies due to lack of randomization and to patient features being determinants of the exposure and, at the same time, of the outcome of interest.

The literature provides statistical techniques to detect and adjust bias when confounders are collected in the database (e.g. propensity score adjustments), but the situation becomes more complex when dealing with unmeasured confounding. Aim of the initial part of this work was to provide a general overview about state-of-the-art methods for unmeasured confounding: design-centered and analysis-centered techniques have been developed and different solutions can be undertaken according to the availability of external data about confounders. An a priori comparison of strengths and limits of the methods was performed together with the description of the tools.

Next, considering a subset of the above, the operating characteristics of the methods were assessed via Monte Carlo simulation in a variety of scenarios: the focus is on propensity score calibration and investigations will also consider instrumental variables.

An application to data from studies where unmeasured confounding was supposed to be present will complement the theoretical and simulation perspectives with further insights.

Finally, some practical recommendations and warnings might be issued for proper and effective use of these correction methods.