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Estimation for treatment policy strategies with missing data: Introducing retrieved dropout reference-base centred multiple imputation

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Introduction

A treatment policy strategy if often used to handle intercurrent events such as treatment withdrawal. However, missing data after treatment withdrawal complicates analysis. Retrieved dropout multiple imputation can be used to impute off-treatment data based on observed off-treatment data. But this may be impractical with limited observed data post-treatment withdrawal. Alternatively, reference-based multiple imputation assumes treatment withdrawals behave like those observed in a specified reference group. But this makes strong assumptions and disregards observed off-treatment outcomes. We introduce a novel approach that draws its influences from these two approaches, retrieved dropout reference-base centred multiple imputation.

Methods

An extended multiple imputation model is constructed, using (i) a core reference-based model and (ii) a retrieved dropout compliance model. The extended model is parametrised to have the structure of the core reference-based model plus some additional parameters, which represent the difference between the core model and the retrieved dropout model.

For imputation, the extended model is fitted using a Bayesian framework with mildly informative zero-centred priors for the additional parameters. We analytically explore expected bias and root mean square error (RMSE) and then apply this method to an anti-depression trial.

Results

Bias and RMSE depend on the trustworthiness of the core reference-based model, additional parameters prior’s variance and the amount of observed off-treatment data. The anti-depression trial demonstrates how increasing the prior’s variance for the additional parameters increases the estimated treatment effect's variance by a small amount.

Discussion

Reference-base centred multiple imputation provides a useful tool for estimation warranting further exploration.