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| **A**im | Evaluate the performance of commonly used multiple imputation methods in in RWD-based cost-effectiveness analysis under different confounding scenarios. |
| **D**ata Generating Mechanism | * Parametric simulation * Missing data mechanism: MAR * 1 time point; variables based on distributions taken from routinely collected data provided by GGZinGeest. * **Levels of confounding:** none, low (<10%), intermediate (10-20%), high (>20%) * low level of confounding = if the confounder changes (adjusted vrs not adjusted estimates) the difference in costs and effects below 10% * intermediate level of confounding= if the confounder change the difference in costs and effects between 10-20% * high level of confounding = if the confounder change the difference in costs and effects above 10% * **Percentage of missing data:** 10%, 25%, 50% * **Sample size:** pending to decide * **Number of simulated dataset (n sim):** pending Monte Carlo calculation, don’t forget to justify it in the text! 2000 (put as ref Morris et al. paper)   **Scenarios (to be discussed):**   1. **Missings in costs and outcome (Y)** (108 scenarios in total \* 2000 datasets)   1a. Missingness model: missingness predictors are the same as the confounders (i.e., age, rom, depression) (36 scenarios in total \* 2000 datasets, only taking into account imputation model, not the cost-effectiveness model).  1b. Missingness model: including only 1 confounder as a predictor of missingness + treatment  1c. Missingness model: missingness predictor does not include all confounders (TBD)   1. **Missings in cost, outcome (Y) and confounders (TBD)**   2a. Missingness model: missingness predictors are the same as the confounders (i.e., age, rom, depression).  2b. Missingness model: including only 1 confounder as a predictor of missingness + treatment  2c. Missingness model: missingness predictor does not include all confounders (TBD) |
| **E**stimand(s) | * Treatment effect * Treatment costs |
| **M**ethod(s) | 1. Benchmark method    1. CCA 2. Multiple imputation methods:    * 1. Multiple imputation by chained equations (MICE)🡪 To deal with non-normally distributed data:         1. MICE-standard         2. MICE-PMM         3. MICE-log (?)         4. MICE-CART         5. MVNI (?)/ Joint modelling |
| **P**erformance measures | * Empirical bias 🡪 is estimator biased? * Root mean square error (RMSE) 🡪 is estimator efficient? * Coverage 🡪 is standard error adequate? |