Handling Missing Data in Within-Trial Cost-Effectiveness Analysis: A Review with Future Recommendations

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Introduction
Missing data are common in CEA, especially within a RCT framework, in both effect and cost variables. According to recent reviews (Noble et al., 2012; Diaz-Ordaz et al., 2014), the performance of each method depends on the plausibility of the missing data assumptions they rely on. Some of the most popular are:

- **Complete Case Analysis**: Partially observed cases are simply deleted. Efficiency loss and possible bias.
- **Single Imputation**: Imputation of missing data given observed data and a distribution φ to account for uncertainty. Estimates combine via Rubin’s rules (Rubin, 1987). Correct imputation model is essential.
- **Sensitivity Analysis**: Exploration of plausible departures from base-case missings uncommon assumptions to account for more uncertainty in assessing the robustness of the results. Typically requires explicit modeling of the missing data mechanism.

Missing Data Mechanisms

To conduct inferences with partially observed variables we rely on the joint consideration of two modules. The analysis model (MoA), the data generating process, and the missingness model (MoM), describing the data generating process, and the missingness model (MoM), describing the way the missingness probability is generated.

**Missing Completely At Random (MCAR)**
- Fully observed cases can be thought as a representative sample of the full data sample.
- Examples are loss in efficiency, possible biases in the parameter estimates and possible misleading conclusions of CEA.

**Missing At Random (MAR)**
- Partially observed cases are systematically different from fully observed cases with the difference being captured by $x_i$.

**Missing Not At Random (MNAR)**
- Fully observed cases with the difference being captured by a representative sample of the full data sample.

Quality Evaluation Scheme

We provide guidelines on missing data information reporting.

- Three ordered components: Description, Method and Limitations
- Grades assigned to articles based on the information provided on each component: Null, Partial, Full
- Articles matched to scores (0-12) and grouped into classes (E-A) based on grades

Conclusion
High missing data proportions in within-trial CEA may lead to imprecise economic evidences. This is an issue for bodies who need imprecise economic evidences. This is an issue for bodies who need to make evidence-based decisions. Therefore, it is important to improve the quality of missing data handling.

References


