

Appendix 2: The recommendations of each included paper. The text here reproduces the paper's own terminology for referring missing participant data terminology

Staquet et al. propose general reporting guidelines for clinical trials that report a quality of life measurement:[13]

- Clearly state the methods by which missing data were defined and analyzed;
- Report the number of patients with missing data separately in each arm of the trial;
- Document separately the types of missing data by cause, including: non-completion of the questionnaire due the death of the participant; non-completion of the questionnaire for reasons other than death; and non-response to items in the questionnaire;
- Compare and comment on the percentages of missing data by item in the questionnaire and by treatment group, with focus on the major endpoints as specified in the protocol.

Bernhard et al. discuss issues pertaining to missing quality of life data in cancer clinical trials.[12] They provide an estimation of the magnitude of the problem, and approaches to its prevention and solution. They state that trialists “have an obligation to provide enough information to allow the reader to assess the quality of the study”. They also suggest that good trial reports should allow the following three questions to be answered:

- How many missing data are there?
- Why were the data missing?

- How will the missing data affect the interpretation of the study results?

In addition, the authors recommend presenting separately the overall form submission rates for each scheduled assessment, with the aim of evaluating trends over time. They also recommend evaluating the quality of the completed questionnaire in terms of the item response rates.

Troxel et al. discuss statistical analysis of quality of life with missing data in cancer clinical trials. [20] They outline how missing data are often described as either 'dropout' or 'intermittent'.

The authors make the following suggestions on reporting missing data:

- Report detailed summaries of the completeness of study data with focus on the amount and reasons for missing data at each scheduled assessment, in order to allow for the evaluation of trends over time;
- Compare treatment group differences in quality of life compliance when applicable;
- Examine patient- and institution-related factors affecting missing data rates descriptively or by using logistic regression models;
- Present the data separately for patients with different reasons for dropout

Present the result of studies graphically, comparing scores for patients whose self-assessment was missing with those for whom it was not

Liu et al. review the International Conference on Harmonization (ICH) guidelines and the

Committee for Proprietary Medicinal Products (CPMP) provide guidance regarding reporting missing data in clinical trials [21]. The authors recommend reporting the extent, reasons, and patterns of missing data. They also recommend conducting and reporting the results from additional sensitivity analyses if the extent and pattern of missing data deviate substantially from those anticipated.

Amico et al. discuss attrition in research on antiretroviral therapy.[22] They also review recommendations on attrition pertaining to scientific rigor in longitudinal intervention trials, including the following:

- Clearly report the flow of participants
- Quantify and assess attrition for potential differential rates between the different treatment arms
- Categorize reasons for attrition
- Make transparent the assumptions for missing data and strategies to replace them

Sterne et al. review why missing data may lead to bias and information loss in clinical and epidemiological research.[23] They discuss the use of multiple imputations, its potential pitfalls, and guidance for conduct and reporting. They propose the following recommendations:

- Report the number of missing values for each variable of interest
- Provide reasons for missing values when possible

- Indicate the number of participants excluded because of missing data when reporting the flow of participants
- Describe reasons for missing data in terms of other variables
- Clarify whether there are important differences between individuals with complete and incomplete data
- Describe the types of analysis used to account for missing data and the assumptions made

The authors provide additional reporting guidelines for analyses based on multiple imputations (see box 2 in the original paper for further details).

Polit et al. discuss the definitions of intention to treat (ITT), and recommend strategies for implementing ITT in clinical trials [24]. They also discuss types of missing outcome data and offer the following reporting suggestions:

- Report any experimental-control group differences in attrition
- Description of characteristics distinguishing study completers from dropouts
- Discussion of the likely pattern of missingness (i.e., missing completely at random (MCAR) vs. missing at random (MAR) vs. missing not at random (MNAR))
- Report the results of any sensitivity analyses
- Discussion of the possible implications of missing values on estimates of intervention effects (e.g., high rates of missingness, or pattern of missingness that may not be at random or completely at random).

AlShurafa et al. conducted a systematic review of how authors of methodology articles define ITT when outcome data are not available for all participants and how they recommend handling missing outcome data when conducting an ITT analysis.[25] The authors provide “essential components to report in RCTs with respect to the analysis” that include items related to reporting the handling of missing outcome data:

- Whether there are individuals with missing outcome data;
- Whether those individuals are not considered in the analysis (complete/available case analysis);
- Whether the outcomes of those individuals were imputed; and in that case the imputation(s) used.

Gewandter et al conducted a systematic review to assess the frequency with which RCTs published in three pain journals reported strategies to prevent missing data, the number of completers, and statistical methods to handle missing data [26]. The authors made the following recommendations:

- Report methods used to prevent missing data in clinical trials
- Report the numbers of participants who were randomized, who completed the trial, and who were included in the analyses
- Explicitly state the number of participants who provided complete data in trials in which

the primary outcome variable is defined using data from multiple time points

- Describe the distribution of the percentage of data missing.

The CONSORT 2010 statement provides authors with a standardized approach for reporting trial findings. [3] The statement recommends reporting a flow diagram of the progress of participants through the phases of the trial by study group, including loss to follow-up with reasons, and the number of participants excluded from the analysis.

CONSORT-Patient Reported Outcomes (PRO) extension[6] provides the following additional recommendations:

- State the statistical approaches for dealing with missing data.
- Make the number of PRO outcome data at baseline and at subsequent time points transparent
- Include information on the reason for missing PRO forms (e.g., lack of questionnaire return, unavailable translations of the questionnaire, or other known reasons).
- Provide information regarding reasons for missing PRO forms in either a tabulated form (by treatment group), or in footnotes of the CONSORT flow diagram.
- Discuss the potential reasons for missing PRO data in relation to the clinical context and implications for interpretation of findings.
- Discuss the interpretation of any supportive (e.g., sensitivity) analyses undertaken.

The CONSORT harm extension provides guidance for authors of trials: includes a set of recommendations for the proper reporting of harms in RCTs [5]. The extension provided the following recommendations specific to reporting of MPD:

- Report participants who are non-adherent or lost to follow-up as this may reflect intolerance of the intervention.
- Report the denominator for each analysis (that is, which participants and what follow-up time count toward total exposure to the allocated treatment) in RCTs in which time-on-treatment differs from total follow-up.

The CONSORT extension for cluster trials recommends reporting for each group, losses and exclusions for both clusters and individual cluster members [4].