



# Transparent reporting of missing outcome data in clinical trials: applying the general principles of CONSORT 2010

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In clinical trials, missing outcome data can be problematic, potentially introducing bias and affecting internal and external study validity.<sup>1-7</sup> These concerns are not new. Multiple guidelines for investigators emphasise the importance of first minimising the causes of missing data, such as loss to follow-up, and then using appropriate statistical strategies to account for missing values.<sup>5 8-11</sup>

In spite of the increased focus on addressing missing outcome data in the design and analysis phases of clinical trials, there continues to be significant variability in how the missing data—and the related statistical analyses—are reported in the medical literature.<sup>2 12</sup> Systematic reviews of published studies have found that few clinical trial reports provide a complete description of the investigators' strategy for addressing missing outcome data,<sup>2 12</sup> which can significantly impact the interpretation of study findings.<sup>1 3 4 6 7</sup> As the recommended statistical approaches to missing data grow increasingly complex,<sup>8 13-15</sup> there is more need than ever to ensure that clinical trials are reported clearly and include sufficient detail to allow readers to critically assess the underlying assumptions made by investigators.

The CONSORT (Consolidated Standards of Reporting) statement,<sup>16</sup> which was developed to improve the reporting of clinical trials, is widely used as the standard for the format and content of clinical trial reports. While the guidelines in the updated CONSORT 2010 statement only explicitly call for investigators to address missing outcome data in the results section,<sup>17</sup> additional general CONSORT principles can be used to guide the systematic reporting of key details related to missing data in the abstract, methods and discussion sections, with the goal of increasing the clarity and transparency of the report. The relevant CONSORT guidelines for each manuscript section, and the way in which they can inform the inclusion of key information related to missing data, are reviewed here.

**Abstract:** CONSORT generally recommends that the abstract consist of a concise and accurate summary of the study methods and findings. The specific CONSORT guidelines for the structured abstract already recommend presenting the number of participants randomised and the number analysed (CONSORT Item 1b).<sup>17</sup> When outcome data are missing, however, but statistical strategies are used to include such participants in the analysis, these numbers may be misleading. While the space constraints of the abstract preclude a lengthy discussion of statistical strategies used to address missing data, a brief description as general as 'missing data were addressed using multiple imputation' can help the reader contextualise the study findings and serve as a reminder that important additional details can be found in the full text of the report.

**Methods:** The statistical methods used to address missing outcome data should be described in detail in the methods section, where CONSORT calls for investigators to describe 'statistical methods used to compare groups for primary and secondary outcomes' (Item 12a).<sup>17</sup> In this section, the statistical approach to missing data should be relayed in sufficient detail to allow for replication and should also include information related to assumptions made by the investigators regarding the missing values, such as whether the missing values are felt to be missing completely at random, missing at random or missing not at random. Investigators should indicate whether their approach to the missing data was established prospectively, as recommended in the current guidelines for clinical trial protocols.<sup>18</sup>

While there is no universally recommended statistical approach to address missing outcome data, there is general consensus that more simplistic methods commonly used in the past are insufficient for most studies.<sup>8 13-15</sup> These approaches include 'complete analysis', which excludes participants with missing outcome data from the analysis, and simple imputation, such as 'last outcome carried forward', where a single baseline or interim measure is used in place of a missing outcome measure. A specific type of simple imputation, whereby missing outcomes are coded as intervention failures, has commonly been used in smoking cessation and other addiction trials.<sup>19 20</sup>

While these approaches are easy to describe and carry out, they are likely to introduce significant bias and can distort the study conclusions. The CONSORT guidelines, which generally refrain from making recommendations about study conduct and analysis, warn investigators of the limitations of these methods. They rely on strong assumptions, such as that the data are missing completely at random, and typically underestimate the SE and CI width by not accounting for the uncertainty of the missing values. Even the 'missing = failure' approach, touted as a conservative estimate of the intervention impact, can have the opposite effect, especially when the missing data are not distributed equally between the randomised study groups.<sup>19 20</sup> In the clinical trial report, investigators who elect to use a complete analysis or simple imputation approach need to justify their selection given the known limitations.

Multiple imputation, an approach whereby regression techniques are used to predict the missing outcome values, is generally preferred over complete analysis or simple imputation but requires that investigators make assumptions about the missing data that should be made explicit in the report.<sup>13 14</sup> Both multiple imputation and the recommended accompanying sensitivity analyses require more sophisticated statistical modelling than other approaches to missing data. To reconcile the usual limitations of overall manuscript length with the



need for clear and complete reporting, a detailed description of the approach could conceivably be included in an 'online only' supplement, depending on where the report is published.

**Results:** Here, the CONSORT 2010 guidelines are specific with regard to missing data and include recommendations that were added during the most recent revision.<sup>17</sup> The guidelines review the impact of missing data on a true 'intention-to-treat' analysis and recommend a robust description of which participants were analysed, in which groups, and why. Along with providing a diagram of participant flow, investigators should explicitly describe 'for each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome' (Item 13a), as well as 'losses and exclusions after randomisation, together with reasons' (Item 13b), and the 'number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups' (Item 16).<sup>17</sup> In addition, investigators should present the results of multiple imputation or other analyses for missing data, as well as the associated sensitivity analyses, when reporting the 'results of any other analyses performed' (Item 18).<sup>17</sup>

**Discussion:** When discussing limitations (Item 20),<sup>17</sup> investigators should explicitly address the overall potential impact of the missing outcome data on the study findings. The section should also include a description of the strengths and weaknesses of the statistical approaches that were used to account for the missing values, as well as the plausibility of the assumptions that were made regarding the missing data.

While the presentation of information regarding missing outcome data in these sections—with the exception of the results—is not explicitly required by the CONSORT checklist, the application of the general CONSORT guidelines can promote a clear and transparent presentation of the issues related to missing values. The routine inclusion of more detailed information, particularly with respect to the imputation and sensitivity analyses, may require utilisation of online only supplements but should provide readers with data that will enable them to more accurately analyse and interpret study findings when outcome data are missing.

**Competing interests** None.

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