Reporting of missing data and methods used to accommodate them in recent analgesic clinical trials: ACTTION systematic review and recommendations

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ARTICLE INFO

ABSTRACT

Missing data in clinical trials can bias estimates of treatment effects. Statisticians and government agencies recommend making every effort to minimize missing data. Although statistical methods are available to accommodate missing data, their validity depends on often untestable assumptions about why the data are missing. The objective of this study was to assess the frequency with which randomized clinical trials published in 3 major pain journals (ie, *European Journal of Pain*, *Journal of Pain*, and *Pain*) reported strategies to prevent missing data, the number of participants who completed the study (ie, completers), and statistical methods to accommodate missing data. A total of 161 randomized clinical trials investigating treatments for pain, published between 2006 and 2012, were included. Approximately two-thirds of the trials reported at least 1 method that could potentially minimize missing data, the most common being allowance of concomitant medications. Only 61% of the articles explicitly reported the number of patients who were randomized and completed the trial. Although only 14 articles reported that all randomized participants completed the study, fewer than 50% of the articles reported a statistical method to accommodate missing data. Last observation carried forward imputation was used most commonly (42%). Thirteen articles reported more than 1 method to accommodate missing data; however, the majority of methods, including last observation carried forward, were not methods currently recommended by statisticians. Authors, reviewers, and editors should prioritize proper reporting of missing data and appropriate use of methods to accommodate them so as to improve the deficiencies identified in this systematic review.

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1. Introduction

The analysis and interpretation of clinical trial data are complicated by missing data. Experts generally recommend making every effort to minimize missing data in clinical trials [16,17,24,33]. When missing data inevitably occur, however, the choice of statistical method to properly accommodate them is less clear. Because every missing data situation is unique, it is impossible to provide precise guidelines on when to use specific methods. Statisticians have emphasized using models that make realistic assumptions about the missing data mechanism (ie, models for the probability that a set of values is missing, given the actual observed and unobserved values). These models are commonly associated with 1 of 3 assumptions outlined in Table 1 [18].

Because it is usually impossible to determine the missing data mechanism, it is likewise impossible to determine whether the assumptions implicit in statistical methods used for the analysis are correct. Inferences about treatment effects may thus be compromised. Statisticians [8,16–18,22], the US Institute of Medicine

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