Ambiguity of study population analysis and reporting in asthma clinical trials

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Abstract

Background: Extensive recommendations, including the CONSORT statement, provide guidance on the analysis and reporting of populations in clinical trials to minimize bias. Objectives: This study investigated the clarity of reporting the populations analyzed in clinical trials of asthma interventions. Methods: Randomized controlled trials of the clinical effectiveness and safety of inhaled corticosteroids and long-acting beta2-gonists for chronic asthma were identified in a systematic review. Data on populations and analyses were systematically extracted by one reviewer and checked independently by another. Results: Peer-reviewed papers reporting 84 relevant trials published from 1985 to 2006 were included. Analyses were difficult to interpret for many of the studies because the populations used in statistical analyses were not defined (n = 23 studies), sample sizes were not reported for clinical effectiveness outcomes (n = 36), or sample sizes for outcomes were inconsistent with those reported for the analysis populations (n = 9). Intention-to-treat (ITT) analyses were mentioned in 50 studies and defined in 39, with eight different definitions of ITT discernible. The total number of asthma trials per year and the number that reported ITT analyses have both increased; however, the proportion that defined the ITT population as all subjects randomized to their original allocated treatment has declined (1/9 in 2006). Most (8/9) studies that conducted statistical equivalence tests of asthma interventions used ITT populations without explanation, despite criticism that this approach might lead to erroneous conclusions of equivalence. Seventy studies reported withdrawals (which accounted for > 30% of study participants in some studies; Figure 1), but it is unclear in the majority (n = 44) whether, or how, missing data were included in the analyses. This situation has not improved, with ambiguous handling of missing data affecting most (8/11) of the studies published in 2006 (Figure 1). Conclusions: Despite extensive recommendations and guidance, substantial uncertainties exist in the populations that are actually analyzed in asthma clinical trials. Our findings, together with those from other disciplines, question the effectiveness of CONSORT and related guidance at improving standards of reporting in clinical trials. Reasons for the persistence of poor reporting standards warrant investigation.