Item 16. For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups

Examples—“The primary analysis was intention-to-treat and involved all patients who were randomly assigned.”

“One patient in the alendronate group was lost to follow up; thus data from 31 patients were available for the intention-to-treat analysis. Five patients were considered protocol violators … consequently 26 patients remained for the perprotocol analyses.”

Explanation—The number of participants in each group is an essential element of the analyses. Although the flow diagram (see item 13a) may indicate the numbers of participants analysed, these numbers often vary for different outcome measures. The number of participants per group should be given for all analyses. For binary outcomes, (such as risk ratio and risk difference) the denominators or event rates should also be reported. Expressing results as fractions also aids the reader in assessing whether some of the randomly assigned participants were excluded from the analysis. It follows that results should not be presented solely as summary measures, such as relative risks. Participants may sometimes not receive the full intervention, or some ineligible patients may have been randomly allocated in error. One widely recommended way to handle such issues is to analyse all participants according to their original group assignment, regardless of what subsequently occurred (see box 6). This “intention-to-treat” strategy is not always straightforward to implement. It is common for some patients not to complete a study they may drop out or be withdrawn from active treatment and thus are not assessed at the end. If the outcome is mortality, such patients may be included in the analysis based on register information, whereas imputation techniques may need to be used if other outcome data are missing. The term “intention-to-treat analysis” is often inappropriately used for example, when those who did not receive the first dose of a trial drug are excluded from the analyses. Conversely, analysis can be restricted to only participants who fulfil the protocol in terms of eligibility, interventions, and outcome assessment. This analysis is known as an “on-treatment” or “per protocol” analysis. Excluding participants from the analysis can lead to erroneous conclusions. For example, in a trial that compared medical with surgical therapy for carotid stenosis, analysis limited to participants who were available for follow-up showed that surgery reduced the risk for transient ischaemic attack, stroke, and death. However, intention-to-treat analysis based on all participants as originally assigned did not show a superior effect of surgery. Intention-to-treat analysis is generally favoured because it avoids bias associated with non-random loss of participants. Regardless of whether authors use the term “intention-to-treat,” they should make clear which and how many participants are included in each analysis (see item 13). Non-compliance with assigned therapy may mean that the intention-to-treat analysis underestimates the potential benefit of the treatment, and additional analyses, such as a per protocol analysis, may therefore be considered. It should be noted, however, that such analyses are often considerably flawed. In a review of 403 RCTs published in 10 leading medical journals in 2002, 249 (62%) reported the use of intention to-treat analysis for their primary analysis. This proportion was higher for journals adhering to the CONSORT statement (70% v 48%). Among articles that reported the use of intention-to-treat analysis, only 39% actually analysed all participants as randomised, with more than 60% of articles having missing data in their primary analysis. Other studies show similar findings. Trials with no reported exclusions are methodologically weaker in other respects than those that report on some excluded participants, strongly indicating that at least some researchers who have excluded participants do not report it. Another study found that reporting an intention-to-treat analysis was associated with other aspects of good study design and reporting, such as describing a sample size calculation.