Bias in reporting of randomised controlled trials in breast cancer

A meta-analysis of randomised controlled trials in breast cancer reports that a third are biased in their reporting of treatment efficacy and two-thirds do not report toxicity appropriately.

Overview: Randomised controlled trials can be biased by several possible factors, which can reduce the credibility of trial results. Selection bias is when the groups of patients selected to take part in studies have different characteristics that could affect the treatment outcomes. Performance bias may result from differences in the care provided to each group. Detection bias may occur if outcomes are determined differently between groups. Attrition bias results from differences in how many people in each group withdraw from the study. Reporting bias is selective reporting of results.

Current advice: The Consolidated Standards of Reporting Trials (CONSORT) statement is an evidence-based set of recommendations for reporting of randomised controlled trials. It aims to help authors to report results completely and transparently. Many medical journals endorse the CONSORT statement and should, therefore, publish only randomised controlled trials that report their results in accordance with the standards.

New evidence: Vera-Badillo et al. (2013) conducted an analysis of 164 randomised controlled trials in breast cancer to assess bias and ‘spin’ in the reporting of efficacy and toxicity end points. Only phase III trials with 200 participants or more and a primary end point measuring time to the end point event were included. For recent trials, the reported primary end point was checked against that listed in the trials registry ClinicalTrials.gov. Bias was defined as inappropriate reporting of the primary end point and toxicity. The authors placed emphasis on the reporting in study abstracts, because they noted that busy clinicians often read only the abstracts of publications. Studies that specified multiple primary end points in which at least one end point was significant were not assessed for bias. Spin was defined as the reporting of trials’ secondary end points as evidence that a treatment is beneficial when the primary end point did not show a statistically significant result.

About half of included trials (49.4%) were of adjuvant treatments, and a similar proportion (50.6%) were in women with metastatic breast cancer. Most trials (83.5%) used disease-free or progression-free survival as the primary end point; the remainder (16.5%) used overall survival. Only 30 trials (18%) were registered on ClinicalTrials.gov, and of these, 7 (23.3%) reported a different primary end point than was registered. More than half of trials (56.1%) had a negative result, with no significant difference between groups in the primary end point.

Around a third of trials (32.9%) were reported in a positive manner on the basis of non-primary end points. Studies with a negative primary outcome were more likely to omit the primary end point from the abstract than were studies with a positive primary end point (odds ratio [OR]=5.15, 95% confidence interval [CI] 1.86 to 14.26, \( p=0.001 \)). Two-thirds of studies (67.1%) were rated as having
bias in reporting of adverse events. Industry funding was not associated with bias in the reporting of primary end points or toxicity.

Commentary: “Decision-making for women with breast cancer and their clinicians is difficult. Many practical and personal aspects need factoring in. Coping with treatment toxicities, their after effects, and everything that will impinge on living life well thereafter will depend on patients and doctors being confident about the quality, reliability and completeness of the information available to share in the consultation.

“This information may be gleaned from many sources, all of which will be dependent on data having been fully, promptly and accurately reported in trial reports and systematic reviews. The facts and findings communicated through the whole chain of reporting depend entirely on honest, objective, impartial and complete reporting by the initial investigators, as free as possible of spin and biases. Without trust in their proper accounting we are lost. Proper motivation is required of everyone involved.

“Researchers must remember always that the purpose of their joint endeavours is to faithfully reduce treatment uncertainties, which requires that they report all potential benefits and harms in full and balanced measure. The Equator Network provides meticulously devised checklists that can be used to meet every practical and ethical obligation of recording and reporting research information. Unbiased research reporting is an essential factor that helps clinicians and patients to make good treatment choices together.” - Hazel Thornton, Honorary Visiting Fellow, Department of Health Sciences, University of Leicester

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