Trastuzumab publication bias

We thank Drs Perez and Suman (August 23) for their response[1] about the non-publication of sequential arm (Arm B) data for the NCCTG-N9831 trial of adjuvant trastuzumab.[2] Their explanation hinges on observing statistical best practice as defined by the NCI and the FDA.

If anything it was the concurrent vs. control arm comparison data that were immature. These gained their effect from just 137 combined events (published). This compares with 220 events for the sequential vs. control arms (but unpublished); the concurrent comparison results were therefore based on 83 fewer events than the sequential results (38% less).

Intriguingly, the NCI and the FDA seem happy for the trial to have it both ways – to preferentially publish positive results and cardiotoxicity results[2], but withhold negative results[3] pending an event count. These practices make publication bias very likely indeed.

Regardless of whether N9831 can yet be analysed on its own terms, the data from all three arms should be made available for meta-analysis[4], not just Arms A (concurrent) and C (standard treatment)[5]. This is a completely separate matter from the study's internal validity in terms of maturity of the data.

We urge the N9831 data monitoring committee, the NCI and the FDA to review their policies on meta-analysis of data from N9831's sequential arm. They should ensure the interests of women are as well served as is statistical dogma.

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Conflicts: We co-wrote the original May 2008 commentary in The Lancet, to which Drs Perez and Suman have responded. All conflicts are described in the original commentary, along with the contributions of others originally.

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References

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