Reviewer’s report

Title: Disease specific mortality versus total mortality as outcome in trials of antifungal agents

Version: 1 Date: 16 February 2006

Reviewer: Geoffrey Playford

Reviewer’s report:

General
Thanks for the opportunity to review this manuscript. The research question is important, relevant and well defined. In the absence of objective and standardised diagnostic criteria, the method adopted, i.e. assessing whether the proportion of patients not dying from fungal infections but who died from another cause was different in the experimental and control arms of the trials, represents a reasonable approach to this question. However, the limitations of this approach have not been acknowledged in the manuscript. Misclassification of death from either a fungal infection or from another cause may occur in either direction and furthermore may be differential or nondifferential. Thus any misclassification may bias the results either towards or away from null. The potential problems of pooling trials where the direction of misclassification is unpredictable should be acknowledged. Further exploration of results could be acheived by sensitivity/subgroup analyses based on possible explanatory variables such as study methodological quality, particularly whether the trial was blinded and especially whether the outcome assessors were blinded to treatment allocation. Other subgroup analyses could include time of study or strictness of diagnostic criteria. The manuscript is succinct. The additional figures are important for the manuscript and should be included.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. Second paragraph of Methods "Provided the two groups are still comparable ..., the proportion of those who died from another cause than fungal infection would be expected to be the same in the two groups". I would have thought that the proportion in such a setting would just as likely be reduced (assuming that at least some of those who have been saved from a fungal death in the experimental arm do not die from another cause) as to stay the same.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)
1. Acknowledge the potential limitation of the methodology used to address the research questions.
2. Consider sensitivity/subgroup analyses

What next?: Accept after discretionary revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable
**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests