Reviewer's report

Title: High mortality during tuberculosis treatment does not indicate long diagnostic delays in Vietnam: a cohort study

Version: 1 Date: 16 May 2007

Reviewer: Hans L Rieder

Reviewer's report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

This is an important study as it shows an expected finding.

General comments:

This study does not find that a delay in diagnosis is associated with death during treatment. The finding is obviously counter-intuitive, and the authors search for explanations for the finding, but cannot come up with a satisfying answer. It seems to be true for virtually any disease that the later the diagnosis the poorer the prognosis, and tuberculosis has not been that much different. There might be two major reasons why this is not found in this study.

The first is that patients at the highest risk of death are those with the most fulminant presentations who would tend to have a short history, and if immunosuppressed may also do not have the capability to form cavities and thus present with low grade sputum smear counts. HIV is not a major among these patients, but other factors (some known, some not) are possibly present that were not amenable to identification. The authors discuss this at least in part.

A second possible explanation is that the delay was so short in all patients (given the high quality of the program) that it really did not matter whether there was a week less or more delay as chemotherapy is sufficiently powerful to overcome this. Of course, there is always the uncertainty about the precision of obtaining a history of delay.

While this reviewer is in full concordance with the authors that the data should speak first, such a counter-intuitive finding is worth more in-depth reflection not on what was found, but why what is expected could not be found.

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

Minor comments:

The authors state "Case fatality, i.e. death during the course of tuberculosis treatment...". The definition of "Case fatality rate" is the proportion of deaths from the disease (numerator), who have the disease (numerator) within a specified period of time. "Case fatality" would then perhaps be this proportion without defining the time (e.g., during treatment). In contrast, "mortality" uses the same numerator, but the denominator is the population from which the cases arose. The authors introduce "early mortality" which is in fact an "early fatality". It seems that there is somewhat of a mix-up of the terms.

The authors write "Blinded to the original forms, information on 10% of randomly selected patients was double collected and checked for inconsistencies (1.7% of items)" and a couple of paragraphs later "Data were entered using Epi Info 2002 and a 10% randomly selected sample of forms were re-entered in blinded fashion, resulting in inconsistencies in 0.22% of items." It is unclear how these two sentences relate so that they result in different numbers.

The authors state "As diagnostic delay as a continuous variable was not normally distributed, it was transformed by taking its natural logarithm (Ln)." Why is a log transformation needed if there is a normal
distribution? I was under the impression that such transformation was used to account for a) skewed
distributions, b) outliers, or c) unequal variation, none of which is the case if there is a "normal distribution".

The line legend in figure 4 does not match the actual lines in the figure.

Discretionary Revisions (which the author can choose to ignore)

**What next?:** Accept after minor essential revisions

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests