Reviewer's report

Title: Predicting Smear Negative Pulmonary Tuberculosis with Classification Trees and Logistic Regression: a cross-sectional study

Version: 1 Date: 28 October 2005

Reviewer: Juan Wisnivesky

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General
The manuscript describes the development and validation of a clinical prediction rule to diagnose smear negative pulmonary tuberculosis. This is a potentially useful tool, particularly for physicians practicing in low resources areas.

Mayor Revisions
1) Several details regarding the assembly of the study cohort should be provided. The authors report that patients with 2 negative AFB smears were included in the study (page 4). How many of these patients then underwent sputum induction and/or bronchoscopy? How many additional sputum samples were obtained per patient and for how long were these cultures kept to assess MTB growth? If the goal standard for some patients was based on MTB culture from bronchoscopy samples this may not be adequate as the sensitivity of BAL samples is less than for spontaneous or induced sputum. The authors should provide data regarding the number of patients undergoing these procedures.

2) Additional details should be provided regarding the review of chest radiographs. Who reviewed the films (radiologists vs investigators) and was the reviewer blinded to the results of TB cultures and clinical predictors?

3) TB cases were defined as patients with positive TB cultures or with clinical improvement after 3 months of anti-TB therapy. Was the decision to start treatment standardized? If not, this definition may be weaker. The authors should perform a sensitivity analysis to assess how their conclusions change by using the more stringent case definition based only on the results of the TB cultures.

4) Statistical analysis (Page 6), consider not reporting positive and negative predictive values as these depend on the prevalence of disease, which was considerably high in this cohort (almost 50%).

5) It's not clear why the investigators decided to use a significant level of 10% to include predictors into the final logistic model. Additionally, the authors used backward elimination; however automatic model selection may exclude important variables. A manual process may be preferable.

6) The authors used logistic regression and CART to build the predictive models. Although both methods are adequate and valid it is unclear why the authors used two different techniques. Part of the problem arises from the fact that the authors developed 3 predictive models that include different variables. Which model should clinicians use? What happens if one model indicates that the patient is likely to have TB whereas the other model doesn't?

7) Results (page 7). The authors should give more detailed definition for the clinical predictors to allow reproducibility of their findings. The percentage of HIV positive patients should be also reported. Additional information regarding other clinical predictors (such as fever, self-reported PPD, TB risk factors, history of shortness of breath) that have been reported as important predictors of TB in other similar studies should be provided.

8) The authors used a cutoff for the models that gives a sensitivity of approximately 70% and a specificity of 60%. This cutoff is not very helpful as it would not considerably change the pretest probability of TB. I would suggest that the authors report the sensitivity/specificity and/or LR of
different cutoffs or alternatively use a cutoff that either maximizes sensitivity or specificity.
9) The authors should consider discussing in further detail the potential problem of spectrum bias as almost 50% of the patients had TB.

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

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Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No

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