Reviewer's report

Title: Exploring the Uncertainties of Early Detection Results: Model-Based Interpretation of Mayo Lung Project

Version: 1 Date: 12 July 2010

Reviewer: Oscar M Rueda

Reviewer's report:

Shi et al. present a simulation model to explore the results of the Mayo Lung Project for lung cancer screening. The manuscript tries to explain why the results of that famous trial did not show a reduction in lung cancer mortality when a screening strategy was applied to a randomized group.

There are several theories about this that the authors try to address with the aid of MISCAN, a microsimulation model of early detection of chronic diseases adapted to lung cancer.

Major Compulsory revisions:
1.- I would like the authors to summarize a little more MISCAN's assumptions. Figure I is not very clear and has no explanation. What is being represented in vertical and horizontal axes? Time? Evolution of the disease?

There is some information scattered through additional file number 4 and a reader guide referenced, but the manuscript would be much improved if a good summary of the model would be provided, because the assumptions (how do they model the times and probabilities of going through the different stages, etc.) can be relevant to the results.

2.-Related to that, I would like the authors to comment on the limitations of their model to detect pitfalls in the trial.

Minor essential revisions:
3.- I would include some of the results of the table into the manuscript, especially the information relevant to the fit of the different models.

My overall impression is that manuscript is interesting, because shows how simulation can help in the interpretation of complex biological processes and in this case, the results of clinical trials. But it the paper must state very clearly how good the simulated model reflects the biological process and if it takes any assumption that might benefit any of the explanations that are being tested.

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

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