Author's response to reviews

**Title:** A Systematic Review of the Diagnostic Accuracy of Physical Examination for the Detection of Cirrhosis

**Authors:**

Guy de Bruyn (gdebruyn@fhcrc.org)
Edward A. Graviss (egraviss@bcm.tmc.edu)

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PDF covering letter
Reply to reviewers

We thank the reviewers for their thoughtful comments, and the close attention they gave to our paper. As far as possible, we have addressed each of points raised. Below, we list the amendments to our paper, along with the response to the reviewer. The valuable suggestions made by the reviewers have helped to strengthen the paper considerably.

The paper is more extensively referenced, particularly with articles of methodological relevance. We have also included the reference mentioned by Dr Sackett in the relevant portion of the methods section.

We would also like to point out changes made to the legend of figure 3. In the original submission, the numbers referred to incorrect authors names. This was an editing error made during the creation of the legend. The actual analyses were originally done using the studies listed in the revised manuscript, and so consequently, the results are unchanged.

Reviewer: Dr Sackett

A. Major questions

A.1. Should there be a more detailed description and discussion (beyond the brief items on pages 4, 5 and 10) of the potential effects of a tarnished gold standard on the results of the study?

We have added further discussion (page 11) on the influence of an imperfect reference standard on diagnostic test assessment. Additionally, we have created tables in two new appendices that demonstrate these effects using sample calculations.

A.2. Would it be important to state whether the definition of the reference standard in this study was the same as that of the former studies?

We have made this explicit on page 5, paragraph 4.

A.3. Should there be more discussion of the bias when a reference standard is not applied?

This point is discussed on page 12, paragraph 2

A.4. Should there be a discussion of the effect of the site on the results?

All of paragraph 3 on page 12 are devoted to this issue.

A.5. Do the clinical implications of the study results deserve more attention?

We have made the role of high specificity in clinical decision making more explicit (page 13, paragraph 2), and amended the conclusions accordingly.

A.6. Is the conclusion on line 4… justified?

This point has been amended.

A.7. Would it be useful to discuss the potential usefulness of combinations of physical findings?

We have added a point to this effect on page 13, bottom paragraph.

A.8. Should there be more discussion of the implications of the absence of any items from the medical history on the results of this study?
This is a difficult issue to address within the constraints imposed by the data. It seems reasonable to assert that clinicians who took a history before eliciting physical signs had different ideas of the presence of disease, which may have influenced how the exam was performed. This is raised on page 12, last paragraph.

B. Minor points
B.1. Would it be more informative to use the word METHODS...?
This change was made.

B.2. Would it be useful to provide the actual values for the sensitivity and specificity of ultrasound?
Data from primary studies, cited in article 19 to support this conclusion, have been added.

B.3. Would it aid understanding to include specific AND/OR terminology.
The Boolean terms used are more clearly described on page 4, bottom paragraph.

B.4. Are the study selection criteria accurate?
The selection criteria are accurate. As noted, this study should properly be described as a case-control study. We have altered the text to make this clear. The implications of such a design are also discussed further in the discussion, page 11, bottom paragraph.

B.5. Would it be useful to define TPR and FPR in unambiguous terms?
We have replaced these acronyms with sensitivity and specificity throughout.

B.6. Is the term "screened" the best one to use...?
This term has been changed.

B.7. Would it be helpful to remind the reader what the covariates are?
The covariates examined were: study size, independence of application of examination and reference test, etiology of cirrhosis, study design. This has been restated in the relevant section.

B.8. Would it be helpful to clarify this statement?
The sentence in question has been rephrased to clarify the intended meaning.

B.9. Is the reference incorrect?
Sharp eyes! The citation was corrected.

Reviewer: Dr Straus
1. Appraisal
The study appraisal was carried out by one reviewer (GdB), as was the data extraction (GdB). This is made explicit in the methods section, page 3, paragraph 3.

2. Study validity
We have discussed the relevant impact of aspects of study design on the outcome of studies of diagnostic tests in the discussion, beginning on page 11, bottom paragraph. In addition, we have added sensitivity
analyses that examine the impact on our particular results of including studies for which particular types of bias were likely.

3. Description of the patient population

Also see B.6. above. The specific inclusion criteria for each study are highlighted in Table 1. We have changed the heading of column three to improve the presentation of this information.

4. Description of the reference standard.

See points A.1., A.2., and A.3. above. A fuller description of relevant information retrieved from the primary studies has been added to the paper, beginning on page 8, paragraph 2.

5. Description of the clinical exam maneuvers

This item was generally deficient in the primary studies. A discussion of this point is included on page 8, bottom paragraph, and page 13, second paragraph.

6. Reliability of the clinical examination

Data regarding reliability of the examination findings between examiners was only presented in one study. This information is now included on page 8, bottom paragraph.

7. Examination of the test characteristics across the referral spectrum.

See point A.4. above.

Respectfully,

Guy de Bruyn
Edward A. Graviss