Reviewer's report

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

Authors:

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Reviewer: Dr David Sackett

Level of interest: A paper of considerable general medical or scientific interest

Advice on publication: Unable to decide on acceptance or rejection until I see revised version

A systematic review of the diagnostic accuracy of physical examination for the detection of cirrhosis; de Bruyn G, Graviss EA. 20 pages plus 5 tables and 3 figures
Reviewed by DL Sackett

MAJOR QUESTIONS:

NOTE: I believe it is vital to have the analyses carried out in this paper reviewed by Les Irwig or Stephen Walter (whose important papers on the systematic review of diagnostic tests are included in the references [24, 28, 60]) AND Jon Deeks (whose more recent important paper [BMJ 2001;323:157-62] on this same topic is not).

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? Given the sensitivity of biopsy for cirrhosis of only 76%, should the reader be educated a bit more (with sample calculations) about the effects of this on the sensitivity and specificity of the signs under study?

2. Page 5, 3rd paragraph: In a similar vein, 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 (in which its sensitivity was 76%)?

3. Page 8, top paragraph: Similarly, should there be more discussion of the bias introduced when the reference standard is not applied [study 41] or generates an indeterminate result?

4. Discussion: Should there be a brief discussion of the effect of the site (primary care vs. referral centre) on the results of such investigations? Because patients with positive histories and physical exams are more likely to be referred onward, these findings' specificities may fall sharply along the way. Alternatively, the over-reading of findings in primary care (to avoid missing any cases) may inflate specificities along the way.

5. Page 9, middle paragraph: Do the clinical implications of the study results deserve more attention?
Given the high sensitivity of many of these findings, should clinical readers use them to "rule-in" cirrhosis in patients with moderate to high pre-test probabilities? Or is this unwise?

6. Page 11: Similarly, is the conclusion on line 4 ("physical signs are unhelpful") justified by the data showing their high specificity? To be sure, they appear unhelpful in ruling-out cirrhosis, but aren't they helpful in ruling it in?

7. Page 11: Would it be useful to discuss the potential usefulness of combinations of physical findings? Is it clinically sensible to hypothesize that the combination of gynaecomastia, testicular atrophy, white nails and parotidomegaly might rule in the diagnosis, and does this deserve mention?

8. Page 11: Should there be some discussion of the implications of the absence of any items from the medical history on the results of this study? Do you think it could have made a difference?

MINOR QUESTIONS:

1. Page 2 Abstract: Would it be more informative to use the word METHODS rather than STUDY SELECTION, given that the paragraph also describes extraction and analysis?

2. Page 3, 4th line from the bottom: Given the imperfect sensitivity for biopsy and the modest sensitivity for the physical findings described in the study, would it be useful to provide the actual values for the sensitivity and specificity of ultrasound reported from other studies?

3. Page 4, bottom paragraph: Would it aid understanding (and replications of this study for other conditions) to include the specific AND/OR terminology in describing the search, especially when describing the combination of "medical history taking" and "physical examination"? (When I carry out such searches, I use ORs, which yield up to 94 times as many hits.)

4. Page 5, top: Are the "study selection criteria" accurate? Weren't Zoli's controls "normals" rather than "known or suspected liver disease or cirrhosis?"

5. Page 5, bottom: Would it be useful to define TPR and FPR in unambiguous terms (given the way that they are misused in some reports)? If they are meant to describe Sensitivity and (1-Specificity) wouldn't it be useful to say so (and thus prepare readers for the SROC curves that follow)?

6. Page 7, lower paragraph (and tables): Is the term "screened" the best one to use in describing the eligibility criteria applied to potential study patients? Might it be confused with the more conventional use of the term "screening" to describe the testing of symptomless patients for unrelated disease?

7. Page 8, bottom: Would it be helpful to remind the reader what the covariates are?

8. Page 10, line 2: Would it be helpful to clarify this statement? Previous attempts of what sort, and on what literature? For example, aren't these methods pretty routine in systematic reviews of therapy?


NOTE: As I believe that there is no place for anonymity in science, I routinely send copies of my referee's reports to the authors with the request that they contact me if they think I've been unfair of have simply missed the boat.
Potential Competing Interests for David L. Sackett

Dave Sackett has been wined, dined, supported, transported, and paid to speak by countless pharmaceutical firms for over 40 years, beginning with two research fellowships and interest-free loans that allowed him to stay to finish medical school. Dozens of his randomised trials have been supported in part (but never in whole) by pharmaceutical firms, who never received or analysed primary data and never had veto power over any reports, presentations, or publications of the results. He has twice worked as a paid consultant to advise pharmaceutical firms whether their products caused lethal side-effects; on both occasions he told them "yes." He has testified as an unpaid expert witness for a stroke victim who successfully sued a manufacturer of oral contraceptives, and as a paid expert in preparing a class-action suit against a manufacturer of prosthetic heart valves. He was paid by a pharmaceutical firm to develop "levels of evidence" for determining the causation of adverse drug reactions. His wife inherited and sold stock in a pharmaceutical company. While head of a division of medicine he enforced the banning of drug-detail personnel from clinical teaching units (despite the threat of withdrawal of drug industry funding for resident research projects). He received the Pharmaceutical Manufacturers' Association of Canada Medal of Honour (and cash) for "Contributions to Medical Science in Canada" for the decade 1984-94. His most recent award (the 2001 Senior Investigator Award of the Canadian Society of Internal Medicine) was sponsored by Merck Frosst Canada.

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