Reviewer’s report

Title: Value of signs, symptoms and plasma heart-type fatty acid-binding protein (H-FABP) in evaluating patients presenting with symptoms possibly matching acute coronary syndrome: background and methods of a diagnostic study in primary care

Version: 2 Date: 23 September 2014

Reviewer: Susan Smith

Reviewer’s report:

Review Protocol H-FABP in ACS

Thank you for asking me to review this protocol for an interesting study that may have clinical importance. The authors have presented many of the issues clearly, particularly in relation to outcome definition. Potential risks of bias for this type of study have been addressed though some remain and need to be addressed as outlined in my comments below. It may be worth explicitly grouping risks of bias and how they are addressed using the McGinn criteria outlined in the reference below and used in the development of a CPR register (see Keogh et al, Ann Fam Med July/August 2014 vol. 12 no. 4 359-366). This would improve the reporting of the paper overall.

I have the following major comments:

1. The authors describe this study as a “delayed type cross-sectional study”. I don’t understand what this means really. It seems to me that the study is what would be called a derivation study for a clinical prediction rule or algorithm and there is a substantial literature developing in this area. This study is essentially seeking to develop a CPR that combines discriminating signs and symptoms with the 4ng/ml cut-point PoC H-FABP test (see McGinn et al for one of the definitive papers on this topic - McGinn TG, Guyatt GH, et al ;Evidence-Based Medicine Working Group. Users’ guides to the medical literature: XXII: how to use articles about clinical decision rules. JAMA.2000;284(1):79–84)

2. The overall presentation of the study protocol is a little unclear, partly due to the lack of fluency in English but also because of the lack of clarity in design.

3. Abstract need to report the comparison group

4. There are multiple instances throughout the text where wording is used that is not standard eg 'beneficial' causes of chest pain as opposed to benign causes.

5. I think it would be interesting if the authors commented on the wide range in prevalence of 1.5% to 22% of cases in primary care. Does this vary at practice level as if so need to consider some kind of practice level analysis as well

6. How will you monitor fidelity to the protocol, particularly in relation to reading the test before or during the decision making process which may take longer than
5 minutes. Why not ask an independent person to read the test if it is not meant to play a part in the process. This may be important as GPs are expected to change their mind and then refer the patient if the test turns out to be positive, which might be difficult to do in front of a patient and in the specified time frame.

7. Analysis: Can you comment on why you are not presenting a C Statistic to determine model discrimination.

8. Sample size: A rough guide for derivation studies is that there should be at least 10 outcome events for every variable in the final prediction rule—this seems likely to be the case but the previous published work will give you an idea of how many predictors remained in the model (see McGinn et al).

9. Why are you presuming you will have 100% uptake in the 60 GPs identified—is there a larger pool from which they are being selected?

10. How will you monitor selection bias in terms of inclusion of the ten consecutive cases?

Minor issues

1. Protocols are usually written in the future tense. The authors use a mixture of present and future tense.

2. Wording as above—specialist setting would be more accurate than hospital setting as some hospitals don’t manage ACS.

3. Please clarify if practices re offered any incentive to participate.

4. If the ECG is one of the potential predictors—will it be a problem if they don’t all have one done.

5. What is meant by ‘coded data’ in the data management section?

6. Public disclosure means open access to the actual data not just published papers—is there a plan to make data accessible?

7. Are there any conflicts of interest based on the fact that the device being tested is likely to have economic value if found to be useful?

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

**Quality of written English:** Needs some language corrections before being published.

**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.