Reviewer's report

Title: Screening for colorectal cancer with FOBT, Virtual colonoscopy and optical colonoscopy: protocol of a randomized clinical trial in the Florence district (SAVE study).

Version: 2 Date: 19 November 2012

Reviewer: Stuart SA Taylor

Reviewer's report:

This is a very important trial will clearly defined and important aims. When successfully completed, the results will be of major interest to the community

A few comments for clarifications

Major compulsory revisions-none

minor essential

Introduction

1. Please clarify “....procedural or biological risks” as not completely clear as to the meaning

2. .. this reason is affected by false negative and false positive results”. Can the authors give examples to illustrate this point

3. “Differently from FS,...”. please rephrase eg “unlike FS...”

4. . Please clarify “randomized per household and street” Are they randomised per house or per street? Bit unclear how it can be both

5. The internal validation of the information sheets is interesting. Can a bit more detail be provided?

6. Please briefly explain the ISPO , how it works and what information it collects

7. Please define “experienced” radiologist in terms of what they must achieve in the pre-read test dataset

8. How will less important extra-colonic findings be handled eg gallstones. Will patients need to be seen in the screening centre by the radiologist? If not, will the patient’s family practitioner be informed?

9. Will extra tests generated by CTC be actively recorded

10. It would be useful to give the definitions of the various polyp morphologies on CTC and colonoscopy, particularly for flat polyps which is important for subsequent comparison of detection rates

11. If patients request follow up CTC for polyps instead of colonoscopy-will this be allowed?

12. Cost effectiveness of the pathways is a stated aim. Can a little detail be added as to how this will be done eg handling of extra-colonic findings, cost
model assumptions etc?

Discretionary revisions

1. Can details be provided of the randomisation block and who will do this?
2. The information leaflets given to people will be key as they cover performance, risks etc. Can the journal print these as an appendix or on line supplement?
3. Perhaps list the contraindications to scopolamine as they can be controversial!
4. Is it possible or planned to offer the reduced bowel prep option to those refusing CTC with full bowel prep? This will help decipher if it is the bowel prep which is the problem or CTC screening itself
5. Will CTC colonic insufflation be done by a radiologist or technician
6. It seems CTC reading will be 2D based. Are there any stipulations as to the use of 3D endoluminal review? Will a 3D flythrough be permitted? Will 3D problem solving be available?
7. A first CAD read paradigm is very interesting and arguably how CTC would be read in a large volume screening setting given the lack of trained readers and need for efficiency. Is there any plan to compare this with the conventional second read CAD paradigm?
8. Presumably CTC read times will be measured
9. Which teleradiology system will be used? Will CTC data be anonymised for transfer?
10. How many CTC readers will take part in the study?
11. Will a proforma be provided for each recruited patient with regard to complications or will data collection rely on self reporting from recruitment sites?
12. Given the intention to treat analysis, patients with positive CTC refusing to undergo colonoscopy will presumably be classified as CTC pathway “negative” for advanced adenomas? Probably worth stating.
13. The assumption of 30% compliance with colonoscopy is arguably quite high. Have the trialists any local data to support this assumption
14. Also a stated aim is to test a teleradiology solution for CTC. Can the authors expand what aspects will actually be tested?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

In the past 5 years (but no longer) I was a reimbursed research consultant for
Medicsight plc, a company which has developed CAD software. The protocol of this study includes a CAD product from another manufacturer.