Author's response to reviews

Title: Evaluation of the use of decision-support software in Carcino-Embryonic Antigen (CEA)-based follow-up of patients with colorectal cancer

Authors:

Charlotte J Verberne (c.j.verberne@chir.umcg.nl)
Cornelis H Nijboer (chnijboer@hotmail.com)
Geertruida H de Bock (g.h.de.bock@umcg.nl)
Irene Grossmann (irene.grossmann@me.com)
Theo Wiggers (t.wiggers@umcg.nl)
Klaas Havenga (k.havenga@umcg.nl)

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Author's response to reviews: see over
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L.S.,

Hereby, we resubmit our paper on the evaluation the use of our software-supported follow-up in patients with colorectal cancer. We would like to thank the reviewers for the highly accurate review of our manuscript. We revised the whole manuscript; revisions are made visible using the “Remarks” tool. We are convinced that addressing the concerns and remarks of the reviewers has made the manuscript better and valuable for the readers of BMC Medical Informatics and Decision Making, and hope that the reviewers and editors will support publication of our manuscript. We think that the most important amelioration is the free accessible website to check and test our software; furthermore we have added a discussion section.

This letter gives a point-by-point response to the concerns of the reviewers.

Reviewer 1

The idea of a decision-support software to facilitate the follow-up of patients makes sense. And the evaluation of such software is necessary. However, in my opinion, it’s necessary to describe the software in great detail and, in order to evaluate it rigorously, the process needs to be improved. Some guidelines I consider should be followed are:

* The software should be described in great detail. At least, the manuscript should answer the following questions:
  - Is the software freely available for non-commercial use?; ¿Can it be downloaded for testing purposes?

We think that we have described the software in great detail, in the Software Manual. This manual was written by the developer of the Software, Hidde Nijboer, which is the second author of our manuscript. The Manual describes the rationale, the use and the technical issues of the software. The Software Manual is a separate attachment to this manuscript.

A demo version of the software is freely available for non-commercial use. This demo version is made specifically for the review and independent testing of the software, and is programmed by the same software developer, Hidde Nijboer. In an online version, it can be tested by going to http://ceawatch.x10.bz/ and simply follow the online instructions. If more detailed information is needed, the author can be contacted.

- ¿Could the software be used in other hospitals?; If the answer is "yes", ¿how the installation process should be achieved?

We would firmly encourage the use of our software in other hospitals, and are sure that this is possible. According to our analysis, all doctors working with the software are content with it, and it saves time and costs while the oncological follow-up is still safe. This is the reason why we think other hospitals could benefit as well from our software, and publication of our manuscript including links where the software can be downloaded could be useful in reaching this goal.

The installation process is different per hospital, since there are links between the hospital information system and the software. By using our manual, we think that the installation process can be achieved easily once these links are adjusted to the local situation.

- ¿What kind of data are stored into the CEAWatch database (what are the database fields)?

All database fields are given in the software manual on page 12, section “Database”

- When a patient goes to an external laboratory, ¿how can you be sure that the results of the analysis are introduced into the hospital information system?
We have contacted all laboratories in our region for this goal. Once a patient enters the study, he/she is labelled in our regional system to be a study participant. The blood drawn for CEA from study patients is sent to our own hospital laboratory for analysis to avoid interlaboratory differences. This fact is now made clearer in the Implementation Section, subheading “follow-up schedule”.

- What are the specific operations performed by the software? All operations performed by the software are described in the software manual. We would refer to the manual, especially pages 5-12; if this does not provide answers we would be happy to answer the question in more detail.

- In this work, the group of patients that is followed-up by means of the system follows a different protocol than the control group. So, it’s difficult to know if the time variation is due to the system or caused by the protocol. It is said that “patients in the study group were seen at the outpatient clinic once annually instead of four times a year and they had the possibility of having blood drawn at local laboratories instead of in the hospital”. Why is the number of visits reduced? Why the other group can’t have blood drawn at local laboratories? Why the group that is followed-up without the software can’t follow the same protocol?

This is a good and essential question. In this article, our software-supported system is compared to the follow-up care following the guidelines of the Dutch oncological guidelines. These guidelines are merely consensus based than evidence-based. The guidelines form the follow-up schedule for the control group, and this is the reason why they differ from the study group at more than one point. This point is further commented upon in the new Discussion section, 3rd paragraph, in which we recognize that the lack of a randomized controlled trial can lead to this type of selection bias.

Of course, it would be possible for the control group to have blood drawn at local laboratories too, but since these patients have to come to the outpatient ward anyhow it would not be useful for them.

*** Discretionary Revisions
I suggest avoiding writing conclusions from other works in the “Conclusions” section. It causes confusion.

We agree, and we have now summarized the conclusions from other works in the Discussion section. However, we have left the results of the study by our own group in the Conclusions section since we are convinced these conclusions are a worthy supplement to our own study.

Different names are used to refer to the group that is followed-up with the software (intensive follow-up group, study group,...) In my opinion, it is also confusing.

We agree, and we have now mentioned this group the study group everywhere in the manuscript.

*** Minor Essential Revisions
“Abstract”, first line, probably there are two blanks before “CEAwatch”.

“Authors Contributions”, 4th paragraph says “the idea of the idea for” when it should say either “the idea for” or “the idea of”.

“Efficacy of the software” there are a reference to Table 3. It should refer to Table 2.

We thank the reviewer for these punctual remarks; these minor essential revisions are now all addressed to.

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

Reviewer 2. I would like to congratulate the authors for such a timely and interesting study. This is a relatively novel study with a high practical significance. The authors have developed simple software
to assist in the high volume and cumbersome follow-up of patients with colorectal cancer. Although the study design was not optimal, some findings of this study may help with the design of a randomised controlled trial. Furthermore, most of the important limitations of this study are well addressed by the authors in the “conclusions” section. I would support the publication of this study as long as the following issues are addressed in the manuscript:

Major:

1) The authors should indicate whether this software was integrated in the hospital EPR system or not. If not, this should be included in the limitations section of this paper.

   The software is fully integrated in the electronic patient record system, and this is mentioned in the Conclusions section. The EPR user needs a log-in name and password to enter the CEAwatch software. Once a patient is included in the study group, all necessary patients’ personal data including his CEA values and operation data are withdrawn from the EPR to the software database. On the other hand, patient’s letters generated by CEAwatch are automatically put in the EPR from the patient, to guarantee that all EPR users (also the ones without access to CEAwatch) can see what happens with the patients. This point is further commented upon in the Conclusions section, third paragraph.

2) This paper lacks of a discussion section. The discussion and conclusions of the manuscript are not well balanced and not adequately supported by the data. Within this section, there should be a separate paragraph indicating all the limitations of this study. Within the discussion section, the authors should provide more information of similar software available in the literature (such as follow-up software).

   According to the journal’s style for Software articles, we have now added a Discussion section within the results section. We give both an overview of the limitations of our study in this section and provide more information of similar literature.

3) The authors should provide a demo version of the software without real patient data available in the internet. They should also state that the software is freely available for non-commercial use (note that this is a condition of publication) and if the availability of the software and any restrictions on its use exist.

   We have now provided a demo version without real patient’s data on the internet. The software is freely available and we encourage other hospitals to use it. This demo version is made specifically for the review and independent testing of the software, and is programmed by the same software developer, Hidde Nijboer. In an online version, it can be tested by going http://ceawatch.x10.bz/ and simply follow the online instructions. If more detailed information is needed, the author can be contacted.

4) The title is misleading: The title reads “Evaluation of decision-support software…” However the authors did not formally evaluate the software. The word “evaluation” should be removed from the title and the title must be rephrased.

   Technically, we agree to the reviewer that there was no formal evaluation of the software, but evaluation of the use of the software, and therefore we changed title of the manuscript into “Evaluation of the use of decision-support software in Carcino-Embryonic Antigen (CEA)-based follow-up of patients with colorectal cancer”

5) Already partially presented data available in the internet: The authors should declare in the “cover page” that this study was partially presented at a conference. Please see: http://www.slideshare.net/ESOSLIDES/150211-1430-havenga

   The reviewer is right and we apologize for the fact that we did not mention this yet. It is now declared in the cover page.

6) The authors should include the following issues in the “limitations section” of the paper:
a) Selection bias: not a randomised control trial. (The fact that it is not an RCT is mentioned in the conclusions section, however the implication of the selection bias of the patient recruitment is not clearly mentioned. This should allow the readers to interpret the findings with caution).
b) Lack of a proper software evaluation: The evaluation of the software was not scientifically sound. The authors simply performed some unstructured interviews of surgeons. The patients, outpatient clinic nurses, etc were not involved. This should also be mentioned in the limitations section. The authors are also stating the their evaluation had “face validity” but such information is not reported in the paper. How was face validity assessed?
c) Lack of user friendliness data.
d) Lack on data regarding the software implementations and potential difficulties.
e) Lack of patient survival data: The authors did not report whether there were differences in the 3 or 5 year patient survival between the two groups. If the data are not available, this should be mentioned in the limitations section. The reason for this is that if the survival is worse in the CEAwatch group, this should be an alarming finding when it comes to automated software driven patient follow up.

We thank the reviewer for this remarks and added information about the limitations and shortcomings in the discussion section. Point b regarding the evaluation of the software by patients was addressed to in the Conclusions section, since this work was done by our own group.

Minor:
• The authors should acknowledge the IT specialists that helped with the development of this software
  The second author, Hidde Nijboer, is the only medical student and IT specialist which developed the software and integrated it into our EPR system.

• The authors are referring to patient with colorectal cancer as: “Colorectal cancer patients” This is degrading to the patients and should be changed to “Patients with colorectal cancer”.
  We agree and have now changed this phrase.

• Colonoscopy findings: This software did not include follow-up colonoscopy data. Where the patients followed up with for example a 3-year follow-up colonoscopy? These data may change the frequency of CEA measurements.
  According to the Dutch national guideline, all patients underwent colonoscopy 3 years after resection, this is not in the scope of our software evaluation but we have now mentioned it in the Implementation section.

• Some patients may have a CEA negative colorectal cancer recurrence. These patients would be missed by the software follow-up. This should be mentioned in the discussion section.
  Of course, the reviewer is right, and this is the reason to perform a CT scan once annually in every patient. This is independent on the frequency that CEA is tested. The control group also underwent only one CT scan yearly for radiologic follow-up, which is why we think that radiologic imagings in follow-up are beyond the scope of our presented research. We have now mentioned this in the Implementation section, in the subheading “Follow-up schedule”.

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: I declare that I have no competing interests
We hope we have made everything clear and that our changes and additions to the manuscript encourage the editor and the reviewers to support publication.

Sincerely,

On behalf of all authors,

Charlotte Verberne, first author
PS. My email address is now changed into c.j.verberne@umcg.nl