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Keeping track of colorectal cancer trials with the Dutch Colorectal Cancer Group mobile app

Joost Huiskens, Michael S. Gałek-Aldridge, Jean-Michel Bakker, Pim B. Olthof, Thomas M. van Gulik, Cornelis J.A Punt, Martijn G.H. van Oijen

Corresponding author:
J. Huiskens Department of Medical Oncology, Amsterdam University Medical Center Department of Medical Oncology Amsterdam

Handling editor:
Michal Heger
Department of Experimental Surgery, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands

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1st Editorial decision

Date: 24-Nov-2018

Ref.: Ms. No. JCTRes-D-18-00019
Keeping track of colorectal cancer trials with the Dutch Colorectal Cancer Group (DCCG) mobile app
Journal of Clinical and Translational Research

Dear author(s),

Reviewers have submitted their critical appraisal of your paper. The reviewers' comments are appended below. Based on their comments and evaluation by the editorial board, your work was FOUND SUITABLE FOR PUBLICATION AFTER MINOR REVISION.

If you decide to revise the work, please itemize the reviewers' comments and provide a point-by-point response to every comment. An exemplary rebuttal letter can be found on at http://www.jctres.com/en/author-guidelines/ under "Manuscript preparation." Also, please use the track changes function in the original document so that the reviewers can easily verify your responses.

Your revision is due by Dec 24, 2018.

To submit a revision, go to https://jctres.editorialmanager.com/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #2: To investigate the use and user satisfaction of a freely available mobile application featuring all ongoing clinical trials of the Dutch Colorectal Cancer Group (DCCG) over the first two years.

Clearly written and in my view an important issue to highlight among researchers.

Minor details;
Who did you send the survey; researchers, docters, physician assistents, nurse practinioners etc in what percentages and was there a difference in responses between the different groups? Were all trials started when the app was already available? I think you have to mention this in the discussion. Otherwise you could have an indication of the usefulness of the app.

Reviewer #3: Review Report - JCTRes D-18-00019

This special issue articles addresses the introduction of a mobile application to keep track of clinical trials within the field of colorectal cancer in the Netherlands. The authors used Google Analytics and an online survey to show that the application was used by medical doctors, nurses, and research staff to aid in clinical decision making with high user satisfaction. It is a concise but clinically relevant manuscript that addresses how to optimize trial (protocol) accessibility in daily medical practice, which has become increasingly busy and complex.

Introduction
- The introduction briefly mentions that study inclusion is an important reason for (early) study discontinuation. In the referenced papers, was it assessed whether this was somehow related to the complexity of the study protocol? And has the fraction of papers discontinued due to slow accrual indeed increased over the last decades, in parallel with growing protocol complexity? If so, this may be a more appropriate topic for a figure than the current Figure 1.

Materials and Methods
- Is patient information per trial directly available through the application? Or is mainly intended as a screening tool to assess patient eligibility, after which the trial coordinator or coordinating center needs to be contacted to set in motion actual patient enrollment in the trial of choice?
- In order to interpret the user statistics, I feel it may be relevant to also briefly outline how the application was rolled out, marketed, and advertised with the target audience.
- It is mentioned that the app is free to download, but is it also add-free? In other words, is there any financial incentive for the 'owners' of the application?
- Are the trials included in the DCCG all limited to the Netherlands, or are some of these trials also active in other countries? This information would help to interpret the data shown in Table 1. The finding that the bounce rate in countries other than the Netherlands is high makes sense, but why is the bounce rate in, for instance, Italy way lower than in the other

listed countries?
- In order to move forward with implementing trial applications in medical practice and increase trial participation, it would be useful to investigate factors associated with application use. In that respect, the survey seems to bee a bit brief. For instance, the age of participants was recorded (but not reported?), but the sex and medical subspecialty seem to be missing from the survey. In my view it would be interesting to see whether the application is mainly used by medical oncologists, surgeons, or radiation therapists, or that all specialties are equally represented in the application users. And that is only to give an example of what can be derived from a simple survey. Can the authors comment on this point? Or how are the authors planning to move forward with this application in general?

Results
- Did you record an increase in application use in the second year after introduction? This would yield credence to the high user satisfaction.
- Is there any meaningful data available on whether the introduction of the application had an impact on the rate of patient inclusion in DCCG trials? Was there a change noticed in the number of trials that had to be prematurely terminated due to patient accrual problems?
- I would stick with either the 24 h or the AM/PM system, not a combination of both. So 17-18 pm should be 5-6 PM, or just 17:00-18:00.
- Are data available on whether the physicians in teaching hospitals who used the application worked in hospitals that participate in the DCCG trials? Or does this group mainly comprise physicians who work in teaching hospitals and are willing to refer patients to other centers to allow for study enrollment?

Discussion
- I think the discussion lacks one important aspect: what is the future of trial applications? Is it supposed to be limited to providing concise trial information such as inclusion and exclusion criteria and the contact information of the study coordinator? Or can these applications also become a means to actually enroll patients in a trial? Are data available on digital patient information packages or digital consent forms with digital signatures? In other words, will it be possible to conduct fully digital trials in the future, without the need for the massive amounts of paperwork currently linked to RCTs?
- Is any literature available on comparable trial applications? If so, please briefly discuss how these compare to the presented application.

Figures
- In general, the Figure legends seem to be missing from the submission PDF.
- Figure 1: please specify what the color/number in the in-figure legend mean exactly.

Authors' rebuttal

Rebuttal letter

Manuscript ID: JCTRes-D-18-00019

Manuscript title: Keeping track of colorectal cancer trials with the Dutch Colorectal Cancer Group (DCCG) mobile app

We would like to thank the reviewers for their comments. We feel their concerns have improved to quality of the manuscript. Below is out point-by-point response.

Reviewer #2: To investigate the use and user satisfaction of a freely available mobile application featuring all ongoing clinical trials of the Dutch Colorectal Cancer Group (DCCG) over the first two years.

Clearly written and in my view an important issue to highlight among researchers.

Minor details;

Who did you send the survey; researchers, docters, physician assistents, nurse practinioners etc in what percentages and was there a difference in responses between the different groups?

The survey was sent to members of the DCCG newsletter and mailing-list, and well as through the DCCG app itself. Due to this method we do not know how many persons received the survey invitation and consequently we have no accurate response rate. Doctors, (specialized) nurses, datamanagers, and researchers are included in the mailinglist.

There were no differences in APP satisfaction between groups.

Were all trials started when the app was already available? I think you have to mention this in the discussion. Otherwise you could have an indication of the usefulness of the app.

Not all trials were open at the launch of the application. The system allows easy introduction of new trials and direct adaptation of existing trials. This was specified in the discussion.

Reviewer #3: Review Report - JCTRes D-18-00019

This special issue articles addresses the introduction of a mobile application to keep track of clinical trials within the field of colorectal cancer in the Netherlands. The authors used Google Analytics and an online survey to show that the application was used by medical doctors, nurses, and research staff to aid in clinical decision making with high user satisfaction. It is a concise but clinically relevant manuscript that addresses how to optimize trial (protocol) accessibility in daily medical practice, which has become increasingly busy and complex.

Introduction

- The introduction briefly mentions that study inclusion is an important reason for (early) study discontinuation. In the referenced papers, was it assessed whether this was somehow related to the complexity of the study protocol? And has the fraction of papers discontinued due to slow accrual indeed increased over the last decades, in parallel with growing protocol complexity? If so, this may be a more appropriate topic for a figure than the current Figure 1.

We did not find references that show the trial complexity is directly related to slow accrual or trial discontinuation. This is very difficult to objectify, how to define and quantify trial complexity. Also, protocol adaptations and sample size adjustments confound these potential analyses. However, this would be a good subject for a systematic review.

Materials and Methods

- Is patient information per trial directly available through the application? Or is mainly intended as a screening tool to assess patient eligibility, after which the trial coordinator or coordinating center needs to be contacted to set in motion actual patient enrollment in the trial of choice?

The app is intended as a screening tool, and the trial coordinator need to be contacted for patient enrollment. We discussed implementation of a direct enrollment tool, but due to privacy and ethical regulations, this will not be possible in the near future.

- In order to interpret the user statistics, I feel it may be relevant to also briefly outline how the application was rolled out, marketed, and advertised with the target audience.

We added a section on the launch of the application in the methods section

- It is mentioned that the app is free to download, but is it also add-free? In other words, is there any financial incentive for the 'owners' of the application?

There is no financial incentive. The app is add-free.

- Are the trials included in the DCCG all limited to the Netherlands, or are some of these trials also active in other countries? This information would help to interpret the data shown in Table 1. The finding that the bounce rate in countries other than the Netherlands is high makes sense, but why is the bounce rate in, for instance, Italy way lower than in the other listed countries?

Some trials are international multicenter trials, such as the RAPIDO trial, however no Italian centers participate. We do not have a clear explanation for the lower bounce rate in Italy. It could be European countries are more interested in Dutch RCTs since they are usually considered high quality and clinical practice in European centers is similar as opposed to the United States or Asia. This is however just speculation.

- In order to move forward with implementing trial applications in medical practice and increase trial participation, it would be useful to investigate factors associated with application use. In that respect, the survey seems to bee a bit brief. For instance, the age of participants was recorded (but not reported?), but the sex and medical subspecialty seem to be missing from the survey. In my view it would be interesting to see whether the application is mainly used by medical oncologists, surgeons, or radiation therapists, or that all specialties are equally represented in the application users. And that is only to give an example of what can be derived from a simple survey. Can the authors comment on this point? Or how are the authors planning to move forward with this application in general?

We agree the survey is brief. Since surveys are increasingly common we shortened the survey in order to ensure more respondents would fill it out. We agree in depth analyses would be of interest, but for this first analysis we chose quantity of the quality of in-depth analyses.

The way forward is a new application that contains all registered clinical trials in which scientific collaborations such as the DCCG, healthcare departments or individuals can make their own lists of 'trials of interest' and personalize their app.

Results

- Did you record an increase in application use in the second year after introduction? This would yield credence to the high user satisfaction.

From February 1th 2015 until January 31th 2016 the application amassed a total of 8,818 sessions and 44.006 pageviews. From February 1th 2016 until February 1th 2017 the application amassed a total of 7,247 sessions and 45,705 pageviews. This is added to the results.

- Is there any meaningful data available on whether the introduction of the application had an impact on the rate of patient inclusion in DCCG trials? Was there a change noticed in the number of trials that had to be prematurely terminated due to patient accrual problems?

The factors influencing patient accrual is too complicated to mention any impact of the application. Since the DCCG has a limited number of trials, 13 in the app, data on terminated trials is not available.

- I would stick with either the 24 h or the AM/PM system, not a combination of both. So 17-18 pm should be 5-6 PM, or just 17:00-18:00.

We agree and changed it throughout the manuscript.

- Are data available on whether the physicians in teaching hospitals who used the application worked in hospitals that participate in the DCCG trials? Or does this group mainly comprise physicians who work in teaching hospitals and are willing to refer patients to other centers to allow for study enrollment?

For the sake of privacy we did not record the hospital of the survey respondents.

Discussion

- I think the discussion lacks one important aspect: what is the future of trial applications? Is it supposed to be limited to providing concise trial information such as inclusion and exclusion criteria and the contact information of the study coordinator? Or can these applications also become a means to actually enroll patients in a trial? Are data available on digital patient information packages or digital consent forms with digital signatures? In other words, will it be possible to conduct fully digital trials in the future, without the need for the massive amounts of paperwork currently linked to RCTs?

We added a section to the discussion. We do believe completely digital RCTs are the future, however, a digital paper trail need to be developed together with governmental bodies that regulate clinical trial oversight.

- Is any literature available on comparable trial applications? If so, please briefly discuss how these compare to the presented application.

We did not find any similar studies.

Figures

- In general, the Figure legends seem to be missing from the submission PDF.

The figure legends are brief and were included in the submission manuscript. This will be corrected.

- Figure 1: please specify what the color/number in the in-figure legend mean exactly.

Corrected

2nd Editorial reponse

Date: 03-Dec-2018

Ref.: Ms. No. JCTRes-D-18-00019R1
Keeping track of colorectal cancer trials with the Dutch Colorectal Cancer Group (DCCG) mobile app
Journal of Clinical and Translational Research

Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers: