Author's response to reviews

Title: Characteristics of clinical trial websites: information distribution between ClinicalTrials.gov and 13 primary registries in the WHO registry network

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Author's response to reviews: see over
MEMORANDUM DETAILING THE CHANGES TO THE MANUSCRIPT, MS: 7686139551174047

Title: Characteristics of clinical trial websites: information distribution between ClinicalTrials.gov and 13 primary registries in the WHO registry network
Authors: Daisuke Ogino, Kunihiko Takahashi, Hajime Sato

Editorial requests:
#1: Please restructure the Abstract. The Abstract should be composed of the following four sections: Background, Method, Results and Conclusion and should be no longer than 350 words.

Our response:
We have revised the abstract, which is now structured according to the four sections Background, Method, Results, and Conclusion; this section is within 350 words.

Reviewer 1
Reviewer's report:
Major Compulsory Revisions
Background
#1: “Several problems with the website have been pointed out by the clinical research/trial activation committee” – is it possible to provide a reference if the problems were documented?

Our response:
We have now provided the following references, which are written in Japanese. I have now provided an extra reference [6] which, together with reference [5], addresses this issue.

#2: To further motivate the study, please describe the benefits of improving clinical trial websites

Our response:
We have added the following sentences to the Background section:
“The benefits would include sharing the challenges of providing information, resulting in a portal site with three data providers and the government in JPRN. It would be possible to carry out improvement activities, such as system maintenance, data formatting, and quality control of the registration data. It could improve the system, including the website, while solving the problem and maintaining coordination with the network of primary register. The modification of the present Japanese clinical research/trial information search portal site would be more convenient for all users (patients, their families, medical professionals, pharmaceutical companies, researchers, and others), and address users’ requests for a more useable website. In addition, the promotion of participation in clinical research/trials, and greater understanding of clinical research would be beneficial to the public. Furthermore, an improvement in the quality of clinical research/trials, such as those investigating innovative new drugs, would be likely.”

**Methods**

#3: Please clarify if the checklist was completed by one or more reviewers.

**Our response:**

We have added the following sentences to the Methods section:

“The checklist was completed by all authors, and 14 websites were assessed by one author, who was the web designer and developer.”

#4: Was the checklist created based on problems identified by the clinical research/trial activation committee, and if important components from previous studies have been included (e.g. the suggested lay summary in Ref #10 or unique identifiers). Do you think that website feature for downloading crucial information in a standardized format is also helpful?

**Our response:**

We have added the following sentences to the Methods section:

“The authors created the checklist following a review of the literature. We focused on problems identified by the clinical research/trial activation committee [6] and the Website Usability Test Report: National Cancer Institute (NCI). International Clinical Trials Portal Website Usability Test, Report of Findings and Recommendations [9].”

**Results**

#5: “Five websites facilitated easy access to clinical trial information”. Please elaborate how ‘easy access’ was determined. Are there any features that are crucial to easy
access?

Our response:
We have added the following sentences to the Results section:
“The definition of “easy access” followed NCI recommendation 7 in the Website Usability Test Report [9]. This recommendation was “Redesign the home page to reduce the amount of text and make links to important topics on third-level pages visible.” We assessed each website in terms of what was displayed on the part of the banner area on the home page, and the global navigation system by which users can move around the site.”

We have provided the following reference:

#6: Tables 2-4: please clarify the difference between “No” and “-“.

Our response:
We have added the following sentences to the Methods section:
“In the tables, the assessment that was defined as “No” encompasses “not provided,” “no description,” and “no distinction”; the “-” indicates that the response is summarized in the answer of the other check item, or could not be evaluated.”

#7: Table 4: were the last two items referring to flexibility in the display format?
The items seems a bit too restrictive and there could alternative ways for the same feature.

Our response:
We have added the following sentences to the Results section:
“The purpose of the JPRN portal site is to be accessible to all people, including disabled people. Therefore, for this purpose, these items were set as one of the improved fields regarding web accessibility. In addition, improved accessibility of the website is likely to make a good impression on all users.”

Minor Essential Revisions

#8: Discussion: “excluding the 20 minimum data elements in WHO”. It is not clear what this refers to. Please give a reference.

Our response:
We have provided the following reference:
10. **WHO Trial Registration Data Set (Version 1.2.1).**
   [http://www.who.int/ictrp/network/trds/en/]

#9: Table 2-4, change “Partly yes” to “Partly”
**Our response:**
This has now been changed.

Reviewer 2

**Reviewer's report:**

1. **Major Compulsory Revisions**

Methods, paragraph 1: There is no description of how the ‘survey’ was developed or undertaken. The term ‘survey’ is usually used when researchers ask others for information. It is assumed that in this case the 14 registries were not actually surveyed, but rather the researchers themselves assessed / analysed the information on each of the registries by just accessing each website. Was there any correspondence with the administrators of any of the registries to clarify, supplement and/or verify the information extracted?

**Our response:**
We have added the following sentences to the Methods section:
“There was no correspondence with the administrators of any of the registries to clarify, supplement, and/or verify the information extracted. We ourselves assessed the information on each of the 14 registries by accessing each website.”

Results, paragraph 1: How did the researchers determine who and how many ‘users’ were appropriate? They have identified two potential users: patients and health professionals. This assumes that everyone who is not a patient is a professional, but there may be many different types of professionals, all with differing needs: clinicians, funders, journal editors, journalists, systematic reviewers, other researchers etc. If the premise is that this dichotomous categorisation of users is appropriate, the authors should at least allude to this in the Background section and provide a supporting reference.

**Our response:**
We have changed “patients” and “health professionals” to “people who needed the information in lay terms and any other professionals such as clinicians, funders, journal editors, journalists, systematic reviewers, or other researchers”
Results, paragraph 3: Regarding “Four websites included “clinical trial” in the global navigation, five websites facilitated easy access to clinical trial information, and four websites had breadcrumb navigation features.”: this sentence contains terminology with which most readers of the journal would not be familiar and which has not been previously introduced in the manuscript. The authors should outline what is meant by ‘facilitated easy access to clinical trial information’. Does this mean there was a search facility in the website? Does it mean a record contained a specific link? The other italicised words above need further explanation for the reader.

Our response:

We have added the following sentences to the Results section:

“Global navigation is one of the beneficial usability items. The global navigation system collects the links to the main content of the website, and functions as a shortcut to the content of the website. Global navigation can understand a complete picture of the website or the user’s current position in the website. The breadcrumb navigation displays the guides as showing the hierarchy of websites and the position of the current page in the website. It can easily determine where the user is located within the website and it is also possible to jump to the hierarchy view by the link; this makes the website easier to navigate.”

(Same answer for previous reviewer's report 5)

We have added the following sentences to the Methods section:

“The definition of “easy access” followed NCI recommendation 7 in the Website Usability Test Report [9]. This recommendation was “Redesign the home page to reduce the amount of text and make links to important topics on third-level pages visible.” We assessed each website in terms of what was displayed on the part of the banner area on the home page, and the global navigation system by which users can move around the site.”

Results, paragraph 6: Regarding: “Six websites attached an “Alt” attribute almost perfectly. “Image” was not used much on three websites. Seven websites created their layout using Cascading Style Sheets (CSS), and eliminated the layout by using <table> tag”. The terminology used in these sentences would only be understandable to readers with a strong Information Technology background.

General readers of the journal would not understand this language. These sentences need to be re-written to be understood by a general readership.
Our response:
We have added the following sentences to the Results section:
““Alt” attribute, Cascading Style Sheets (CSS), and “eliminated the layout by using
<table> tag” are terms used to refer to web accessibility. “Alt” attribute means the
alternative text attached to the image. For users who need a voice browser, it is the
string that can be read by a text-to-speech browser and can be displayed when the image
is not found.”
“The CSS layout (for elimination of table layout), and the <table> tag for representing
the data in a table format, avoids the use of tables as a basis for layout (which was a
feature of earlier web browsers). For users who need a voice browser, it is not possible
to distribute the information contents accurately because the structure of the content is
dependent on appearance.”

Discussion, paragraph 1: It is not clear how the study results as presented support the
claim that most of the websites surveyed were not easily accessible to the public. The
authors have not defined what they believe ‘easy access’ constitutes, making it difficult
to support this claim with the data presented.

Our response:
The definition of “easy access” followed NCI recommendation 7 in the Website
Usability Test Report. This recommendation was “Redesign the home page to reduce
the amount of text and make links to important topics on third-level pages visible.” We
assessed each website in terms of what was displayed on the part of the banner area on
the home page, and the global navigation system by which users can move around the
site.

Discussion, paragraph 2: Why is there reference to duplicate registration here? There
is nothing in this study’s aims, data collection or results that contribute to the duplicate
registration issue discussion. Where are the data that supports the statement that “there
are only a few items that pertain to patients and the general population, who are asking
for specific and prioritized information.”? People wanting more information regarding
clinical trials would surely be interested in a trial’s inclusion/exclusion criteria,
condition of interest and many of the other of the minimum 20 data items. Again, how
do the data presented support such a statement? There are then comments about the
need for website usage logs, user satisfaction and evaluation surveys. Again, as this
study contains none of these type of data, it is difficult to see how these comments add
to the discussion of the results presented.
We have added the following sentences to the Discussion section:

“The problems (such as duplicate registration, new items, lay terms) were identified by the clinical research/trial activation committee and so these issues were discussed [6]. One problem is that people cannot find information such as the clinical research/trials related to their own diseases, e.g., how many clinical research/trials are being conducted, or if they are taking place at a nearby location. It is a problem that the total number of clinical research/trials that have been conducted in Japan cannot be calculated (some clinical research/trials have been conducted in Japan which have been registered to overseas organizations, excepting JPRN).”

“We did not have much opportunity to ascertain the user opinions about the JPRN portal site. There is a need to continuously improve the website with only a limited personnel and budget, and to evaluate the contents of the website by methods such as satisfaction surveys.”

“A big challenge is the data format in JPRN, which has a different Japanese format and system in each of three organizations. Therefore, it is necessary to reform the legal system to account for new data items; it should be mandated that lay terms be provided at registration to enable patients and the general public to understand them more easily.”

We have made suggestions regarding improvement, citing examples of good practice, in our discussion of website problems.

Conclusion, paragraph 1: There is an overall assumption in this paper, that trial registry websites should be providing data that is in a format that is accessible/suitable for public consumption. As the authors did not actually survey (i.e. did not contact) the trial registries themselves to verify this, it may be a false assumption. Many registries take the position of being a national repository of trial activity, and then feed their data to consumer-friendly websites that are often disease and/or country specific, rather than themselves attempting to be both consumer- and professional-relevant simultaneously. Thus, by saying that “concerning the distribution of their information services to patients and the public, we discovered room for improvement in many organizations’ content and website systems”, the authors are assuming that each of these trial registries is intending to have a patient/public focus, which they may not. The conclusions should be tempered to reflect this limitation of the study.

Our response:

We have changed the statement “concerning the distribution of their information services to patients and the public, we discovered room for improvement in many
organizations’ content and website systems” to “concerning the distribution of their information services to patients and the public, we discovered room for improvement in JPRN’s content and website systems.”

We have added the following sentences to the Conclusion section:
“There may be some organizations that have similar challenges, apart from our registered members in JPRN.”

2. Minor Essential Revisions

Background, paragraph 2: The first sentence needs re-phrasing as it is not grammatically correct.

Our response:
The sentence “From the “Clinical research/trial activation five-year plan 2012” from the MHLW Ministry of Education, Culture, Sports, and Science, the assumed goal is that patients and the public should be able to access the website and use the clinical research/trial information, and the clinical research/trial information effectively used for originating innovation from Japan such as creation of new drug [5]” has been changed to “According to the “Clinical research/trial activation five-year plan 2012” in the MHLW and Ministry of Education, Culture, Sports, Science, and Technology (MEXT), the assumed goal is that patients and the public should be able to access the website and use the clinical research/trial information, and the clinical research/trial information effectively used for originating innovation from Japan such as creation of new drug [5].”

Background, paragraph 3: The terminology “the current state of distribution regarding clinical research/trial information” suggests some sort of statistical distribution was calculated. As this was a descriptive study, this terminology sounds odd and thus might be improved with different wording.

Our response:
The sentence “the current state of distribution regarding clinical research/trial information” has been changed to “the pattern of current distribution of regarding clinical research/trial information.”

3. Discretionary Revisions

Methods, paragraph 2: The term ‘distribution’ seems incorrect for the analyses done within this study. Perhaps a better term would be to ‘determine the pattern of ….’?
Our response:
The sentence “The survey results were analyzed to determine the distribution of clinical research/trial information” has been changed to “The survey results were analyzed to determine the pattern of clinical research/trial information.”

Reviewer 3
Reviewer's report:
Major Compulsory Revisions:
This is a useful summary of the current situation regarding publicizing trial information in 13 primary registries and clinicaltrials.gov. It helps to get an overview of the situation globally.

#1: In the last paragraph of the method section it states: “Based on the results of this survey, a system prototype could be built and evaluated that could be easily accessed by patients and the general public to find information, and which would also be useful for medical professionals.” Clearly finding out that current websites are not satisfying the public need for easy access to trial information is not enough to address this problem. Discussing different ways of providing information in lay terms and its pros and cons could to some extent reveal the practical difficulties in achieving this goal and is a valuable addition to the discussion.

Our response:
We have added the following sentences to the Discussion section:
“A big challenge is the data format in JPRN, which has a different Japanese format and system in each of three organizations. Therefore, it is necessary to reform the legal system to account for new data items; it should be mandated that lay terms be provided at registration to enable patients and the general public to understand them more easily.”

#2: The paper provides information on whether or not there is information regarding institutional review board in the registry websites. It concludes that IRCT does not have such information. However, IRCT has information regarding the ethics committee that has given approval to the trial. I believe ethics committee and IRBs are different names for a single function. Therefore the author should make sure that similar conclusions have not been made with other websites.

Our response:
We have added the following sentences to the Methods section:
“In this study, we surveyed only the English versions of websites, with the exception of
the JPRN portal site, in Japanese; the native-language versions of these websites may offer more functions or different content than the English versions. For the presence of the display of the Institutional Review Board (IRB), the subject of website is only written in English, but there also maybe describe the other name of the non-IRB. The IRB website may contain information regarding overlap with ethics committee information. We recognize a limitation here, in that we cannot check in native language whether the item has not been evaluated since the websites are written in English. We excluded websites that were either not active or had not joined the registry at the time of our survey.”