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Patients To Learn From: On the Need for Systematic Integration of Research and Care in Academic Health Care

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Patients To Learn From: On the Need for Systematic Integration of Research and Care in Academic Health Care
Journal of Clinical and Translational Research

Dear authors,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you resubmit your work.

Your revision is due by Jun 28, 2017.

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

Yours sincerely,

Joost Huiskens
Editorial Board Member

Journal of Clinical and Translational Research

Reviewers' comments:

Dear authors,

Thank you for submitting your work to the JCTR special issue on ICT in health care.

Three reviewers and two editorial board members have critically appraised your work, based on which we encourage you to resubmit a revised version of the paper. The main issue of the present draft is that your work needs more elaboration on certain critical points as addressed below. This is a viewpoint that is shared by us. Some of the questions can be addressed in a summarizing table, such as the questions raised by reviewer 1. Others require in-text elucidation and exemplification, such as the initiatives alluded to by reviewer 3.

We therefore ask you to consolidate these comments into a revised draft, using track changes in the main text and a point-by-point response to every comment in a separate document. You don't have to agree with everything, but please explain why you chose to veer from the recommendation.

Please don't hesitate to contact us in case something is not clear.

Kindest regards, also on behalf of the JCTR editorial board,

Joost Huiskens,
Martijn van Oijen,
Michal Heger

Reviewer #1: In general this article seems to spend a little too much time painting the picture, the generalities leaves one without a clear picture of what is needed to allow the use of clinically derived tissue and data to further the research mission. As one reads, there is a build up that at the end, the PSI example will provide all the answers, but the PSI leaves one wanting for many more details, what dose the consent looks like, how the process to consent occurs, where is the data stored, can people opt out later, how does the subject find out they are in another study, how do results come back to the patient and by whom, etc. Perhaps closer to the beginning of the article, you could describe the PSI, then in the context of the paper, you could provide examples of something concrete that has been developed at the PSI, or various options in your experience, for each of the 6th areas discussed. Many unanswered questions regarding the PSI, how do you deal with the volume of left over tissue? How is the laboratory or location where the clinically required tissue is collected informed on which patients have agreed to have their tissue used for research and thus the left over tissue is placed in the bio-repository? Although some of this is covered in the original article referenced, there are just too many unanswered questions that will frustrate the reader.

There is an on and off reference to rare diseases. Is it that in rare diseases you need to involve a lot of patients to accumulate rare disease data? It just isn't clear the connection between tissue and data collection from all patients, and how that relates to the rare diseases.

The issue of obtaining consent for patients might need to be expanded. The issue of having some type of "universal" consent is much easier said than done. How is it kept track of, how long does consent last? Although you state in various places that the burden is less on the subjects, many want that burden if it means they have a say in what research they are involved in. The decrease in burden seems to be more on the researchers end. Again, adding a little to this discussion, with perhaps how the PSI solved this problem would be helpful. How do researcher access the data or tissue? What information

comes with it? Is each subsequent research effort approved by an ethics board?

At the bottom of page 8, you state, "Establishing these novel routines and infrastructures has led to rapid improvements in patient care throughout participating institutions, by stimulating inter-institutional comparison and learning processes for all kinds of aspects of clinical procedure, by driving the uptake and diffusion of clinical best practice, as well as by facilitating ongoing comparison and improvement of clinical outcomes." This is an impressive statement, but is not supported by any reference or data; are there either if so, it should definitely be added.

Reviewer #2: The authors discuss the interesting development of integration of research and care that is currently ongoing, and describe the Dutch Parelsnoer Institute as an example. Points to consider when integrating research and care are stated.
The authors focus on academic health care, but don't describe why integration of research and care in non-academic hospitals is not desireable or feasible.
It would be of added value when the authors would also describe the benefits for non-exceptional patients. Could this approach help answer clinical questions in a wide variety of patient populations?
The parelsnoer Institute is described as an example of a national research infrastructure; standardisation has led to improvements in patient care. Examples of improvements in patient care and clinical outcomes would be appreciated. Likewise a description of developments after the initiation/standardization phase. How do they facilitate the ongoing comparison that they describe?

Reviewer #3: The authors focused on Systemic Integration of Research and Care in Academic Health Care, an interesting and promising concept gaining more attention with several new initiatives. The authors mentioned the Dutch Parelsnoer Institute (PSI) as example and focused on core concepts that has to be done to achieve this Systemic Integration of Research and Care.

MAJOR: The authors need to provide more information about the study design and the methods. The research question has to be more specific.

MAJOR: Methods and results sections are described in the abstract, but not included in the manuscript. Please add conformity in paragraphs in abstract and manuscript.

MAJOR: The Parelsnoer Institute (PSI) is mentioned as example of systemic integration of research and care. Are there any other initiatives? Please add an overview (for example presented in a table) of other initiatives if available (PLCRC?)

MAJOR: Start this manuscript with PSI as example, evaluate and eventually criticize this concept and then provide general information about the concept of integration of research and care. This layout seems more logical.

MAJOR: What is the reason for only focusing on 'exceptional' patients? What do 'not exceptional' patients have to expect from systemic integration of research and care? And why only focusing on academic centres with academic patients? Please explain these concepts in more detail in the introduction.

MINOR: There are two statements called 'fifth' in the section: 'Integrating academic care and research: aspects to consider'

MINOR: Please add more specific future recommendations in the conclusion section instead of 'rethinking' issues. What has to be done to improve integration of research and care? What are the first steps?

In general, English text and grammar is of moderate quality and has to be improved in a new rewritten version.

********Authors response********

Reply to reviewers' comments

Dear editors,

Thank you for providing us with the opportunity to improve on our paper and reply to reviewers' comments. Attached you'll find an improved version of our paper. Below is a point-by-point reply to reviewers' comments. We hope to have sufficiently addressed all points made and await your decision.

Kind regards, on behalf of the authors,

Martin Boeckhout

Reviewer #1

In general this article seems to spend a little too much time painting the picture, the generalities leaves one without a clear picture of what is needed to allow the use of clinically derived tissue and data to further the research mission. As one reads, there is a build up that at the end, the PSI example will provide all the answers, but the PSI leaves one wanting for many more details, what dose the consent looks like, how the process to consent occurs, where is the data stored, can people opt out later, how does the subject find out they are in another study, how do results come back to the patient and by whom, etc. Perhaps closer to the beginning of the article, you could describe the PSI, then in the context of the paper, you could provide examples of something concrete that has been developed at the PSI, or various options in your experience, for each of the 6th areas discussed. Many unanswered questions regarding the PSI, how do you deal with the volume of left over tissue? How is the laboratory or location where the clinically required tissue is collected informed on which patients have agreed to have their tissue used for research and thus the left over tissue is placed in the bio-repository? Although some of this is covered in the original article referenced, there are just too many unanswered questions that will frustrate the reader.

As suggested, we have moved the exposition of PSI up front and have included a summary table listing the general features of PSI. Moreover, we have moved and expanded on aspects of PSI in the section on further aspects to consider. We have opted against expanding on the specific questions listed above as these would lead us into a lot of detail without added value to the overall argument. For more details we now also point to the PSI website at which model protocols, regulations etc are available for download.

There is an on and off reference to rare diseases. Is it that in rare diseases you need to involve a lot of patients to accumulate rare disease data? It just isn't clear the connection between tissue and data collection from all patients, and how that relates to the rare diseases.

We have changed the build-up of the article slightly and now discuss the focus on particular patients as one of the aspects to consider. The point we wish to make is that patients suffering from rare diseases, along with other 'exceptional' patients, merit particular attention when pursuing integration of research and care, both because of reasons having to do with their (lack of) care options as well as with the opportunities these afford for research. This is an argument for having academic health care focus on these patients as well.

The issue of obtaining consent for patients might need to be expanded. The issue of having some type of "universal" consent is much easier said than done. How is it kept track of, how long does consent last? Although you state in various places that the burden is less on the subjects, many want that burden if it means they have a say in what research they are involved in. The decrease in burden seems to be more on the researchers end. Again, adding a little to this discussion, with perhaps how the PSI solved this problem would be helpful. How do researcher access the data or tissue? What information comes with it? Is each subsequent research effort approved by an ethics board?

We have addressed this point in the section on aspects to consider by adding the following: 'Consent need not be project-specific. Instead, consent can be 'broad', pertaining to research in a particular area or research programme. A crucial component of such broad consent is that it involves consent for governance; consent, that is, to a particular way of managing resources and deciding on proper use (23,24). Consent provided for PSI, a template of which is available on the PSI website, provides an example of this.'

Details of the consent provided for PSI can be found in the template.

At the bottom of page 8, you state, "Establishing these novel routines and infrastructures has led to rapid improvements in patient care throughout participating institutions, by stimulating inter-institutional comparison and learning processes for all kinds of aspects of clinical procedure, by driving the uptake and diffusion of clinical best practice, as well as by facilitating ongoing comparison and improvement of clinical outcomes." This is an impressive statement, but is not supported by any reference or data; are there either if so, it should definitely be added.

We indeed do not have extensive data to back up these points in this article; instead, we point to Douglas & Scheltens 2014 from which the example is drawn. We have also added one element of evidence mentioned in that article: 'A tangible outcome of such improved care is evidenced by the fact that the diagnostic protocol for PSI has remained in wide use in most UMCs by participating clinicians.'

Reviewer #2

The authors discuss the interesting development of integration of research and care that is currently ongoing, and describe the Dutch Parelsnoer Institute as an example. Points to consider when integrating research and care are stated. The authors focus on academic health care, but don't describe why integration of research and care in non-academic hospitals is not desireable or feasible.

It would be of added value when the authors would also describe the benefits for non-exceptional patients. Could this approach help answer clinical questions in a wide variety of patient populations?

We have expanded slightly on our argument, adding the following:

'Furthermore, patients with extreme, contrasting clinical features (such as either a very poor or very favourable response to therapy) are likely to yield novel insights into and understanding of basic underlying pathological and biological mechanisms involved in health and disease (11,12). Patients suffering from similar, less pronounced symptoms may also profit from these insights.'

The parelsnoer Institute is described as an example of a national research infrastructure; standardisation has led to improvements in patient care. Examples of improvements in patient care and clinical outcomes would be appreciated. Likewise a description of developments after the initiation/standardization phase. How do they facilitate the ongoing comparison that they describe?

See below – we refer to Douglas & Scheltens 2014 for this. (We conceed that more evidence for this point would be preferable.)

Reviewer #3

The authors focused on Systemic Integration of Research and Care in Academic Health Care, an interesting and promising concept gaining more attention with several new initiatives. The authors mentioned the Dutch Parelsnoer Institute (PSI) as example and focused on core concepts that has to be done to achieve this Systemic Integration of Research and Care.

MAJOR: The authors need to provide more information about the study design and the methods. The research question has to be more specific.

As the paper is an essay/perspective, there is not really a way in which we can truly improve on study design and methods here. We did, however, try to refocus the argument by (a) backgrounding the point about the kinds of patient populations as a point to consider and by (b) providing a summary table of our main example, PSI.

MAJOR: Methods and results sections are described in the abstract, but not included in the manuscript. Please add conformity in paragraphs in abstract and manuscript.

We have removed the mention of this in our abstract.

MAJOR: The Parelsnoer Institute (PSI) is mentioned as example of systemic integration of research and care. Are there any other initiatives? Please add an overview (for example presented in a table) of other initiatives if available (PLCRC?)

It seemed beyond the scope of our article to provided an exhaustive overview of the kinds of initiatives that do so. However, we now more explicitly mention of initiatives trying to achieve similar objectives, in particular patient registries and cohort studies serving as research platforms (such as PLCRC).

MAJOR: Start this manuscript with PSI as example, evaluate and eventually criticize this concept and then provide general information about the concept of integration of research and care. This layout seems more logical.

Done.

MAJOR: What is the reason for only focusing on 'exceptional' patients? What do 'not exceptional' patients have to expect from systemic integration of research and care? And why only focusing on academic centres with academic patients? Please explain these concepts in more detail in the introduction.

See above: the point we wish to make is that patients suffering from rare diseases, along with other ‘exceptional’ patients, merit particular attention when pursuing integration of research and care, both because of reasons having to do with their (lack of) care options as well as with the opportunities these afford for research. This is an argument for having academic health care focus on these patients as well.

MINOR: There are two statements called 'fifth' in the section: 'Integrating academic care and research: aspects to consider'

OK

MINOR: Please add more specific future recommendations in the conclusion section instead of 'rethinking' issues. What has to be done to improve integration of research and care? What are the first steps?

We have rewritten the conclusion in order to address this concern.

In general, English text and grammar is of moderate quality and has to be improved in a new rewritten version.

We have revised and hopefully improved the text throughout.

2nd editorial decision

Date: 21-Jul-2017

Ref.: Ms. No. JCTRes-D-17-00003R1
Patients To Learn From: On the Need for Systematic Integration of Research and Care in Academic Health Care
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 Aug 20, 2017.

To submit a revision, go to http://jctres.edmgr.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,

Joost Huiskens
Editorial Board Member
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #3: No further comments except for some suggestions for textual and grammatical improvement attached to this comments.

There is additional documentation related to this decision letter. To access the file(s), please click the link below. You may also login to the system and click the 'View Attachments' link in the Action

column.
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3rd editorial decision
Date: 25-Aug-2017

Ref.: Ms. No. JCTRes-D-17-00003R2
Patients To Learn From: On the Need for Systematic Integration of Research and Care in Academic Health Care
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,

Joost Huiskens
Editorial Board Member
Journal of Clinical and Translational Research

Comments from the editors and reviewers:

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