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Legal challenges for the implementation of advanced clinical digital decision support systems in Europe

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Legal challenges for the implementation of clinical digital decision support systems
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 15, 2018.

To submit a revision, go to https://jctres.editorialmanager.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,

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

Reviewers' comments:

Reviewer #1: The aim of the paper is to outline key legal issues in the implementation of healthcare decision support systems (DSS). The authors do a good job of outlining several key issues including liability for injury due to DSS, whether DSS is considered a medical device, regulatory oversight of DSS, the use of sensitive healthcare information from some patients in order to produce a viable DSS system.

The paper is well written and has no major grammatical mistakes/errors.

The paper's key topic is decision support systems in healthcare. Although the authors mention tools based on artificial intelligence and machine learning in facilitating healthcare decisions, they do not explicitly define DSS in this way, which causes ambiguity for the audience. The paper would be improved with the authors providing a definition for DSS that is scoped correctly for their intent. DSS takes many forms -- not only AI/ML based software tools.

I believe the author's intend DSS in their paper to mean DSS that utilizes machine learning (a form of AI) based on diagnostic and therapeutic maneuvers done on other patients retrospectively. If so, they should explicitly state this, as it is a very specific form of DSS that indeed is controversial and for which current laws may not adequately cover.

For example, drug-to-drug interaction alerts are considered 'decision support'. Providing biomedical knowledge at the point of care through computerized guidelines can also be considered DSS. Best practice alerts (BPAs), often used in EHR systems, either reminding a clinical user about a patient status (screening, for example), or alerting them as to a potential clinical maneuver not substantiated by the clinical context (ie, transfusing a patient with a hemoglobin over 9g/dl), are also decision support.

An significant bulk of the paper covers issues relevant in Europe and the European Union, yet the paper does not reflect such in the title or the abstract. Authors should consider explicitly stating the European context in the title and the abstract. There is very little in the paper that highlights US legal conventions. For example, the authors mention DSS suppliers might be liable "because it would be forseeable that healthcare providers would rely on the results of the analysis". In the US, there is case law regarding "errors and omissions" in biomedical reference information (textbooks, for example), that makes the provider ultimately responsible for any clinical decision regardless of poor or incorrect advice from a colleague, book, or other (ie, DSS system). The authors also mention privacy issues with one country's citizens data stored in another country (the paper has an example of data from a European country stored in the US). The reverse (US citizen data stored outside the country) is illegal per the US HIPAA law. Yet, this is not mentioned. I believe the same is the case in France -- medical data from French citizens cannot be stored outside France.

Overall, the paper highlights important aspects of clinical decision support systems (CDSS) based on machine learning that utilizes the retrospective data of real patients.

I would recommend the authors consider the following three changes, which are not major, but will place the paper in the correct frame and improve it significantly:

1. Authors should provide a definition of "DSS" for the paper, and examples of the "types" (alerts, reminders, drug-drug interactions, providing specific guidelines at the point of care, systems that provide suggested courses of action -- like those based on machine learning, etc..).
2. Consider further scoping the definition and paper around clinical decision support systems based on machine learning utilizing retrospective data from real patients, which is seems to be the focus of the paper
3. Consider modifying the title and abstract to reflect the largely European context for the legal key issues discussed
4. Make sure to "connect" 'translational research' to the key topics they discuss by highlighting that DSS research is needed to 'translate' the use of AI-based/machine learning DSS into clinical practice. Although research is mentioned as necessary, there is no direct connection made int he manuscript between that and the relevance to a translational research journal.

Reviewer #2: Attached

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.

Authors'rebuttal

Rebuttal letter
Responses to Reviewers Comments

Comment	Response
Reviewer 1	

1. Authors should provide a definition of "DSS" for the paper, and examples of the "types" (alerts, reminders, drug-drug interactions, providing specific guidelines at the point of care, systems that provide suggested courses of action -- like those based on machine learning, etc..). For example, drug-to-drug interaction alerts are considered 'decision support'. Providing biomedical knowledge at the point of care through computerized guidelines can also be considered DSS. Best practice alerts (BPAs), often used in EHR systems, either reminding a clinical user about a patient status (screening, for example), or alerting them as to a potential clinical maneuver not substantiated by the clinical context (ie, transfusing a patient with a hemoglobin over 9g/dl), are also decision support.	We have amended the introduction to provide a broad definition of DSS as suggested.
2. Consider further scoping the definition and paper around clinical decision support systems based on machine learning utilizing retrospective data from real patients, which is seems to be the focus of the paper The paper's key topic is decision support systems in healthcare. Although the authors mention tools based on artificial intelligence and machine learning in facilitating healthcare decisions, they do not explicitly define DSS in this way, which causes ambiguity for the audience. The paper would be improved with the authors providing a definition for DSS that is scoped correctly for their intent. DSS takes many forms -- not only AI/ML based software tools. I believe the author's intend DSS in their paper to mean DSS that utilizes machine learning (a form of AI) based on diagnostic and therapeutic manoeuvres done on other patients retrospectively. If so, they should explicitly state this, as it is a very specific form of DSS that indeed is controversial and for which current laws may not adequately cover.	Thank-you for very helpful comments and we have refined our introduction to specify our focus on AI-based DSS as you identify. We have also amended the title to make this clearer.

Overall, the paper highlights important aspects of clinical decision support systems (CDSS) based on machine learning that utilizes the retrospective data of real patients.	

3. Consider modifying the title and abstract to reflect the largely European context for the legal key issues discussed An significant bulk of the paper covers issues relevant in Europe and the European Union, yet the paper does not reflect such in the title or the abstract. Authors should consider explicitly stating the European context in the title and the abstract. There is very little in the paper that highlights US legal conventions. For example, the authors mention DSS suppliers might be liable "because it would be forseeable that healthcare providers would rely on the results of the analysis". In the US, there is case law regarding "errors and omissions" in biomedical reference information (textbooks, for example), that makes the provider ultimately responsible for any clinical decision regardless of poor or incorrect advice from a colleague, book, or other (ie, DSS system). The authors also mention privacy issues with one country's citizens data stored in another country (the paper has an example of data from a European country stored in the US). The	We are focused on the European context and we have amended the title and abstract to reflect this.

reverse (US citizen data stored outside the country) is illegal per the US HIPAA law. Yet, this is not mentioned. I believe the same is the case in France -- medical data from French citizens cannot be stored outside France.	
4. Make sure to "connect" 'translational research' to the key topics they discuss by highlighting that DSS research is needed to 'translate'. Although research is mentioned as necessary, there is no direct connection made in the manuscript between that and the relevance to a translational research journal.	Thank-you, we have emphasised this connection where we discuss research in the manuscript and abstract. In particular at the end of Sections 1 and 2.1, where we explain why discussing legal issues is important in the process of introducing AI-based/machine learning DSS into clinical practice.
Reviewer 2	

General comments: • Timely subject and mostly a well-written manuscript. However, (some of) the revisions mentioned below are needed before I would recommend publication. • The authors demonstrate a reasonable level of insight into the legal framework and the related challenges that arise from the implementation of DSS. • At points where the manuscript gets interesting, because issues or challenges are mentioned, authors often tend to (only) raise questions that still need to be answered. Since the aim of the article also is to identify issues, this is not problematic to me.	Many thanks for helpful and detailed comments. We have amended the article where possible to address your comments.
Specific comments	
P. 3, lines 19-28: the interpretation of the Dutch professional standard by our Supreme Court is indeed similar to the UK standard. I recommend referral to the	We have added this reference (fn. 10).
following standard case: HR 09-11-1990, ECLI:NL:PHR:1990:AC1103 (Speeckaert/Gradener)	
P. 3, line 40-41: Not all medical decisions are the responsibility of a(n) (individual) physician. Not all professional insights are based on guidelines.	We have deleted this sentence
P. 3, lines 42-45: I would not say that professional standards are absent. Many of the norms as discussed in the manuscript are part of the current professional standard. Do the authors mean that there is a lack of specific codes of conduct or other forms of self-regulation related to DSS?	We have amended to specify that specific codes of conduct for advanced DSS are yet to be developed.

P. 3, lines 46-47: research on efficacy, safety and risks would, in my opinion, only be a first step towards establishing professional norms and answering the (major) question raised by the authors.	We have qualified this point to emphasise translational research is necessary but not sufficient.
P. 4: consider deleting or changing footnote 10. I don't see any added value in the current content.	We have deleted this footnote.
P. 4, lines 2-13: I would not raise this as a question and be more decisive and clear on this matter. Do the authors agree that, according to current principles and rules, DSS cannot fully replace the decision by medical experts? If so, please substantiate this view while referring more explicitly to relevant norms. In addition, it could be valuable to reflect on the potential relevance of Art. 22 GDPR on automated individual decision-making.	We agree that this would seriously challenge existing norms and have amended this point, removed the question and added a reflection on the relevance of Article 22 GDPR on this point.
P. 6, lines 14-23: this touches upon a key issue, but misses an important point. Related to the duty of medical confidentiality is the privilege of non-disclosure of physicians. Do DSS suppliers who process personal data of patients have a (derived) privilege of non-disclosure? When this is not the case, they cannot ensure the same level of confidentiality and privacy as health care providers, as is regarded essential by the authors. When a big data pool containing personal data is created in the interest of (personalised) medical treatment of future patients, it is questionable whether sufficient safeguards are in place to protect (medical) confidentiality, in particular in relation to access by public authorities. The importance of such safeguards (in general) is emphasized by the ECHR: "*Without appropriate safeguards against the disclosure of medical information, those in need of medical assistance may loose confidence in the medical profession, and in the health services in general; they may be deterred from seeking medical assistance and this may be to the detriment of their*	Thank-you for this good point, we tried to do justice to this comment by amending the text (in S.2.3), with reference to *Z v Finland*.

health." (Z. v. Finland, 22009/93, 25-21997).	

P. 6, lines 24-31: Is it currently allowed at all, according to Dutch law and guidelines, to store the data of Dutch patients using such cloud services?	We think that this depends on the specific circumstances. Because we don't want to go into the specifics of this matter, we deleted 'Dutch'.
P. 7, lines 28-30: although the general tenor of the data protection principles will largely remain the same in the GDPR, I would not claim that the *application* of these principles will not alter.	Amended accordingly, altering to emphasise that the effect of the principles will remain the same.
P. 7, lines 36-38: Please add a reference and clarify the exact scope of this new law. The law does for instance not cover push messages between caregivers from different (health) care providers.	We have inserted a reference to this new Dutch law and amended text to make this clear.
P. 8, lines 2-11: when special categories of personal data are processed, such as data concerning health, Article 9(2a) GDPR applies in addition to Article 7 GDPR, and introduces a stricter consent requirement.	We have amended to make this clear.
P. 8, line 12: Or: One of the exceptions to this rule is…	Amended.

P. 8, lines 12-22: this exception needs to be implemented in national law, according to the conditions as set out in Article 9(2j) GDPR. Without such implementation in national law, there is no research exception.	Amended to clarify this.
P. 8, lines 22-26: This explanation of the additional requirements from the Dutch Medical Contract Act is incomplete and incorrect. Two different exceptions are possible from the rule that informed consent should be obtained to use personal data from patient records for research purposes. Only one exception is displayed here in an incomplete manner, and it is conflated with the other exception. It is not impracticable to obtain consent from deceased patients. This is impossible and therefore this situation falls under the other exception. My advice would be to just mention that additional requirements could result from norms related to medical confidentiality, with a referral to the relevant article in Dutch law, as an example.	This is clarified.
P. 8-9, 'International transfers of patient data': Article 9(4) and 49(5) GDPR may be relevant. Some EU countries may not allow the transfer of medical data on the basis of explicit informed consent to the proposed transfer when an adequacy decision and/or appropriate safeguards are absent. I heard that Denmark is one of the countries where explicit consent will not suffice, but did not check this myself.	Thank-you for this point, we have added it but are unable to confirm if individual countries, e.g. Denmark, have implemented such limitations.
P. 9, line 19: the manuscript does not really discuss the challenges from an ethical perspective.	We have deleted 'ethical'.
P. 9, 41-44: please clarify whether this only applies to the processing of personal data for the purpose of providing care to the individual data subject, or for the purpose of providing care in general.	We have clarified that this applies to the processing of personal data for providing care to the individual data subject.

P. 10, line 1-2: Is consent really needed in all the mentioned situations? Also for research purposes?	Amended to advise that consent is sought (rather than suggest it is necessary).
Conclusion in general: is there a need for further research?	As Reviewer 1 highlights, we believe there is a need for translational research to help set standards and we have now emphasised this in the conclusion.
P. 10, lines 5-16: Not a very strong ending of the conclusion. What do the authors try to substantiate with this reference to the lessons learned from the care.data program? Does it relate to the sentences above? In the lengthy last sentence, it seems like the authors try to provide a recommendation that covers all the issues discussed in the manuscript.	We have removed this text.
Language	
I did not in particular focus on English grammar, since I am not a native speaker myself. The manuscript could benefit from feedback by a native speaker. Nevertheless, I would recommend the following changes:	
□ P. 3, line 21: 'careful care provider' does not seem to cover the meaning of the Dutch standard of 'goed hulpverlenerschap'.	Thank-you, we changed this in standard of a 'good health care provider'.
□ P. 6, line 44: "data is" should be: "data are". Please check the whole manuscript.	Thank-you, these have been altered.

2nd editorial decision

Data: 19-Jul-2018

Ref.: Ms. No. JCTRes-D-18-00010R1
Legal challenges for the implementation of clinical digital decision support systems
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 18, 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: General comments
* In general, the authors have amended the manuscript according to the comments made.
* The manuscript would still benefit from English language editing.

Remarks related to my previous comments
* P. 8, line 10: in my previous comments, I remarked that: "although the general tenor of the data protection principles will largely remain the same in the GDPR, I would not claim that the application of these principles will not alter." The authors state in their revised manuscript that: "The GDPR does not alter the effect of these principles (..)". The effect on what? It is not clear to me what the authors try to bring forward here. In my opinion, the GDPR has a significant effect on how some of the principles are/need to be applied in practice.

Authors' rebuttal

Response to Reviewer 2's Comments

Reviewer #2: General comments In general, the authors have amended the manuscript according to the comments made. The manuscript would still benefit from English language editing.	Thank-you, we have made some edits throughout the paper to improve the English.

P. 8, line 10: in my previous comments, I remarked that: "although the general tenor of the data protection principles will largely remain the same in the GDPR, I would not claim that the application of these principles will not alter." The authors state in their revised manuscript that: "The GDPR does not alter the effect of these principles (..)". The effect on what? It is not clear to me what the authors try to bring forward here. In my opinion, the GDPR has a significant effect on how some of the principles are/need to be applied in practice.	We have altered this on p.8 to reflect the comment that the tenor of the data protection principles remain the same and to clarify that there are differences, for instance, the requirement to carry out an impact assessment: '*Although the data protection principles in the GDPR remain largely the same as the principles in the former Data Protection Directive, the new regulation is stricter on some points. For instance, it requires data controllers to carry out an impact assessment prior to processing—in particular, processing using new technologies—if it is likely to result in a high risk to the rights and freedoms of individuals*.'

3rd Editorial decision:

Date: 24-Jul-2018

Ref.: Ms. No. JCTRes-D-18-00010R2
Legal challenges for the implementation of clinical digital decision support systems
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: