Consent2Share: an integrated broad consenting process for re-contacting potential study subjects

Peter Iafrate, Gloria P Lipori, Christopher A Harle, David R Nelson, Timothy J Barnash, Patricia T Leebove, Kathleen A Adams, Debbi Montgomery

Corresponding author:
Peter Iafrate
Institutional Review Board, University of Florida, Gainesville, Florida, United States

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

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Ref.: Ms. No. JCTRes-D-16-00023
Consent2Share; an Integrated Broad Consenting Process for Re-contacting Potential Study Subjects
Journal of Clinical and Translational Research

Dear Dr. Iafrate,

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 point-by-point response to the comments and/or a rebuttal against each point which is being raised when you resubmit your work.

Your revision is due by Sep 10, 2016.

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

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

Reviewers' comments:

Dear authors,

Three reviewers with different levels of expertise in the field have critically appraised your paper and found the study to be interesting and useful. I have perused over the paper in light of the reviewers' comments, would like you to address the following points.

1. Reviewer 1 stated that the text should be made more accessible to a broader readership. While the level of detail is certainly appreciated, perhaps the authors should opt for placing the most technical aspects in a supplemental section (which JCTR will publish as online data supplement). Interested readers could get more in-depth information by consulting the supplemental information.

2. It is imperative that readers can understand the figures on their own without having to consult the text. Please make sure you explain the figures in the legend and define all abbreviations used in every figure in the final part of the legend.

3. Please consider making a list of abbreviations that we will place at the beginning of your article.

4. In anticipation of actual implementation of the system at your institute, I would like your paper to act as a template for other universities that aim to adopt a similar system. In order to make all the processes and key elements clear, feel free to include more illustrations that demonstrate the most important features of your system and exemplify its utility. JCTR does not have a figure limit, and you may choose to include figures in the supplemental information.

Thanks for implementing these points as well as those of the other reviewers.

Kindest regards,

Michal

Reviewer #1: 1. This is a very interesting and important topic in clinical research. One of the major bottlenecks in clinical research at academic hospitals is completing the patient cohort. This is particularly a challenge in medical institutions with relatively low number of patients where many clinical studies are conducted. The present study essentially arose from 3 main bottlenecks frequently encountered in clinical research (p. 5, lines 28-46): 1) the effort expended to recruit patients is disproportional to the yield in terms of patient numbers and diversity; 2) subjecting patients to multiple informed consent forms is time-consuming, repetitive, and most likely associated with large variability in study quality; and 3) researchers often lack the infrastructure to maintain a good patient database that is up to date. This study addresses how the common bottlenecks could be resolved more effectively. The initiative to develop an infrastructure to optimally manage inclusions certainly deserves praise, and accordingly the study should be published. However, I do have several comments to help the authors improve the paper and make the

work more accessible to readers across all relevant disciplines.

2. The paper addresses the complete infrastructure needed to streamline medical research in a hospital or academic medical center. The subject matter is complex in that various distinct features are addressed in technical detail, including 1) the ICT infrastructure; 2) infrastructure to manage and secure patient privacy; 3) the role of the researchers; and 4) the implementation and testing of the system. It is at times difficult to keep track of the bottom line because the different elements are insufficiently consolidated. The authors should make an effort to link the various components of the approach in the text or to place parts of the text in a supplemental section.

3. Figure 1 is unnecessarily complex because of the detailed illustrations embedded in the figure. The artistic touch comes at the expense of clarity. Please revise the figure and make it more mechanical.

4. The section on technological foundation (p. 8-10, l. 54-51, respectively) is a good example of a section that textually steers away from the intended audience (i.e., doctors and researchers), who have limited knowledge about the rules regarding clinical research. Please write the story up chronologically where you, so to say, take the reader by the hand and guide him/her through Figure 1. It is further important that every term in the text is retrievable in the figure. Other points that should be focused on include: what are the data comprised of; which data can be retrieved from the ib2b segment by the researcher; and how can the researcher obtain the full dataset after the initial query. And how can all these be achieved in a privacy-secured setting.

5. The ib2b system was developed for researchers to determine whether a clinical trial could in fact be completed. To reiterate, the initiative is commendable because the system will solve problems and improves the quality of the research. Nevertheless, what is missing from the text is a detailed account of what can exactly be retrieved from ib2b, and what cannot be retrieved. Also, Figure 2 does not illustrate what the system looks like when a query is run. Again, guide the readers through the motions, both in the main text and in the legend of Figure 2. It is also questionable what Figure 2 contributes to the text; i.e., what is its complementarity to the reading material? The textual explanation is essentially sufficient to relay the message. Figures could be included to illustrate other points not elaborately explained in the text.

6. The entire development trajectory of the consent2share module, designed to reach the subjects rendered by the query, should be described in a separate (supplementary) section, as this is an important feature of the solution but perhaps too elaborate for the main text.

7. In extension of the previous point, the digital consent pathway (p. 21, l. 1-32) could then be addressed more elaborately. I would like to know whether patients were involved in the development of the digital consent module. Also, it may be useful to expand textually on this module to inform the potential participants about 1) why clinical research is being conducted; 2) why is it important to perform clinical studies; 3) why you are asking for their 'generic consent' and which problem does this solve; etc. This will make the patient understand why the iPad was handed to them. Some patients will sign without this information, but other may not, which is why it would be useful to include such text. This does not have to be in the main text, but should be reachable through drop-down menus, pop-up balloons, or deep links.

8. The authors address the testing of the paper variant and identify the bottlenecks. Consequently, on p. 20, l. 4-8 the authors indicate that the researchers will have to validate the consent furnished by the patients. Will this still apply to the digital consent forms? If yes, please specify how this will be done (which in my view defeats a major part of the purpose of the consent2share module) and under which circumstances the verification step will no longer be necessary. If no, please specify this in the text.

9. In terms of the Discussion section: it would be useful to include a future perspective on the utility of the system. Will you automate research information such that patients that comply with the input criteria will be automatically selected for a given study? Is it possible to expand this system to other hospitals and set up an inter-hospital infrastructure (which will enable multi-center trials)? What are the next steps to follow?

10. There should also be a validation study to determine whether the system indeed meets its targets such as faster recruitment of suitable patients, reduction in logistical procedures for the researcher, improvement in study quality, etc. Please include these facets in your future outlook.

Reviewer #2: The article is interesting and combines adequate analysis of the logistical challenges that can be encountered regarding the consent procedure of various studies together with an sophisticated and implementable new instrument.
The core element of Consent2Share, asking permission to contact rather than content, is an elegant solution. The iterative developmental approach has proven to be a strong method for implementation.

Reviewer #3: Reviewer report 9-8-2016

Dear Editor,

This paper on the implementation of the "Consent2Share" tool in clinical practice beautifully illustrates the difficulties researchers face in the area of recruitment of study participants, and offers an integrated and seemingly efficient solution. However, I have several remarks:

GENERAL / MAJOR COMMENTS

1. In line 12 of the Introduction the authors contend that an incent for the "Consent2Share" program is that "patients often want to be involved in clinical research but do not know what studies are available or how they can be accessed." The concept of the "Consent2Share" program, however, does not validate this statement, because it does not create a platform for patients to enable them to search for a specific study concerning their condition. It might even create a false sense of security, inhibiting a patient to look further. For example: if a patient is suffering from a specific (oncological) condition, but there are no ongoing trials in the connected hospitals, the patient might not look further for trials, although there might be suitable recruiting trials in the country. The "Consent2Share" is therefore a feasible tool for researchers than patients, which should be addressed more clearly in the Introduction. Another solution could be addressing the issue in the Discussion. You could then argue that the "Consent2Share" tool would become more feasible for patients when more hospitals are connected, increasing the chances for a patient to find his or her trial.
2. It would be very interesting to know how "Consent2Share" improved the inclusion of patients in trials. Data on patient inclusion in comparable trials before and after the introduction of "Consent2Share" is necessary to evaluate the efficiency of the tool. Please provide these if available.

SPECIFIC / MINOR COMMENTS

INTRODUCTION

1. Page 5, line 40, point 3) "researchers do not have the infrastructure to appropriately maintain a database integrated with patients' electronic health record (EHR) to ensure that up-to-date information is maintained on potential study subjects". First, your hospital uses EPIC, which allows data managers and trial coordinators to maintain specific lists for researchers of included patients, in which all clinical data are automatically updated. This would make your argument invalid. Secondly, in case I misunderstood and up-to-date information on potential subjects is a problem, how does "Consent2Share" change this problem? "Consent2Share" seems to be limited to expanding the availability of patient data for researchers, and does not necessarily ensure that it is up-to-date and integrated.
2. Page 6, line 30. Please explain the terms study-by-study consent and tiered consent to enable a broader readership, and include the following reference for study-by-study: PMID 23660530. Also please explain why you chose broad consent over tiered consent, especially since the review by Garrison et al., which you cite, claims that tiered consent is considered to be superior to broad consent by patients.

IRB APPROVAL OF THE IDR

1. Page 10 line 22. The researcher has the ability to see how many patients are applicable for his or her study, which means there is access to the baseline characteristics of patients who gave consent. The following step is approval of the IRB to access and use patients' data. This is slightly confusing, since the researcher readily had access to the patients data (?). Moreover it seems like you state that a researcher determines the feasibility of a study based on the current amount of patients within a cohort. Can you please elaborate on how this works in a situation with recruitment during a longer period of time, inclusion of new registered patients (for example, does the researcher estimates an amount of patients per year, or does he/she only look at the total amount?), and multi-center studies?

PILOT
Initial Consent Capture Process (Consent2Share)

1. Page 12 Line 28-33, You state that the pilot was executed in a clinical setting where most patients were competent to consent for themselves. Understandably, this creates some healthy-patient selection bias, which is acceptable considering protection of vulnerable patients in a pilot setting. However it would be interesting to know how you are dealing with these patients now that you expanded the pilot. Especially since recruitment of for example children or patients with dementia for trials is challenging, it would be interesting to know if "Consent2Share" is applicable in those cases, and whether it improves inclusion of these patients in trials.

RESULTS

1. Line 48 page 16. Please provide information on how this random audit was conducted, the methodology is now unclear.
2. line 50 page 18. You removed a question on approval of usage of left over tissue. Does eliminating this question implies there is no consent to use leftover tissue anymore, and left over tissue will not be used, or is tissue still used without permission?
3. Line 48 page 19. You refer to a "much smoother and simpler process." More practical information on the time efficiency and costs of the project would be interesting for the readers, assuming your message is directed at clinical practitioners.
4. Line 23 page 21. With the introduction of the eConsent, does the patient still receive a copy of the

consent?

DISCUSISION & CONCLUSIONS

1. Line 13 page 22. Please write out what "these" refers to, the sentence is unclear now.
2. Perhaps add a section on feasibility of "Consent2Share" for patients as suggested in point 1 of the major 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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******Authors response******

Reviewer #1:

2. The paper addresses the complete infrastructure needed to streamline medical research in a hospital or academic medical center. The subject matter is complex in that various distinct features are addressed in technical detail, including 1) the ICT infrastructure; 2) infrastructure to manage and secure patient privacy; 3) the role of the researchers; and 4) the implementation and testing of the system. It is at times difficult to keep track of the bottom line because the different elements are insufficiently consolidated. The authors should make an effort to link the various components of the approach in the text or to place parts of the text in a supplemental section.

Response: The technical foundation for Consent2Share has been removed from the body of the article and placed in a supplemental section at the end.

3. Figure 1 is unnecessarily complex because of the detailed illustrations embedded in the figure. The artistic touch comes at the expense of clarity. Please revise the figure and make it more mechanical.

Response: A significantly revised and simplified figure has replaced the initial one.

4. The section on technological foundation (p. 8-10, l. 54-51, respectively) is a good example of a section that textually steers away from the intended audience (i.e., doctors and researchers), who have limited knowledge about the rules regarding clinical research. Please write the story up chronologically where you, so to say, take the reader by the hand and guide him/her through Figure 1. It is further important that every term in the text is retrievable in the figure. Other points that should be focused on include: what are the data comprised of; which data can be retrieved from the ib2b segment by the researcher; and how can the researcher obtain the full dataset after the initial query. And how can all these be achieved in a privacy-secured setting.

Response: This section has been integrated into a better description of the process, what i2b2 contains, and the sequence of events the researcher goes through.

5. The ib2b system was developed for researchers to determine whether a clinical trial could in fact be completed. To reiterate, the initiative is commendable because the system will solve problems and improves the quality of the research. Nevertheless, what is missing from the text is a detailed account of what can exactly be retrieved from ib2b, and what cannot be retrieved. Also, Figure 2 does not illustrate

what the system looks like when a query is run. Again, guide the readers through the motions, both in the main text and in the legend of Figure 2. It is also questionable what Figure 2 contributes to the text; i.e., what is its complementarity to the reading material? The textual explanation is essentially sufficient to relay the message. Figures could be included to illustrate other points not elaborately explained in the text.

Response: Figure redone, more explanation added in revised pages 11 and 12.

6. The entire development trajectory of the consent2share module, designed to reach the subjects rendered by the query, should be described in a separate (supplementary) section, as this is an important feature of the solution but perhaps too elaborate for the main text.

Response: A simplistic explanation added into the body of the text, pages 11 and 12.

7. In extension of the previous point, the digital consent pathway (p. 21, l. 1-32) could then be addressed more elaborately. I would like to know whether patients were involved in the development of the digital consent module. Also, it may be useful to expand textually on this module to inform the potential participants about 1) why clinical research is being conducted; 2) why is it important to perform clinical studies; 3) why you are asking for their 'generic consent' and which problem does this solve; etc. This will make the patient understand why the iPad was handed to them. Some patients will sign without this information, but other may not, which is why it would be useful to include such text. This does not have to be in the main text, but should be reachable through drop-down menus, pop-up balloons, or deep links.

Response: We did not involve patients in the development of this consent form. The digital version is exactly the same as the paper one. Since UFHealth provides other efforts to inform patients about the benefits of research, and since we had to balance providing enough information but not too much, we focused merely on informing them that this consent only allowed researchers to contact them about a future project. Ideally we would educate folks more; we had discussed running an informational research loop on TVs in waiting rooms, but have not moved forward with that effort. When the electronic system can support pop-ups, etc., more will be done with this electronic consent form.

8. The authors address the testing of the paper variant and identify the bottlenecks. Consequently, on p. 20, l. 4-8 the authors indicate that the researchers will have to validate the consent furnished by the patients. Will this still apply to the digital consent forms? If yes, please specify how this will be done (which in my view defeats a major part of the purpose of the consent2share module) and under which circumstances the verification step will no longer be necessary. If no, please specify this in the text.

Response: Addressed on revised page 20.

9. In terms of the Discussion section: it would be useful to include a future perspective on the utility of the system. Will you automate research information such that patients that comply with the input criteria will be automatically selected for a given study? Is it possible to expand this system to other hospitals and set up an inter-hospital infrastructure (which will enable multi-center trials)? What are the next steps to follow?

Response: Agree, text added to this section at the end.

10. There should also be a validation study to determine whether the system indeed meets its targets such as faster recruitment of suitable patients, reduction in logistical procedures for the researcher, improvement in study quality, etc. Please include these facets in your future outlook.

Response: Agree, thanks for this feedback!

Reviewer #2: The article is interesting and combines adequate analysis of the logistical challenges that can be encountered regarding the consent procedure of various studies together with a sophisticated and implementable new instrument.

The core element of Consent2Share, asking permission to contact rather than content, is an elegant solution. The iterative developmental approach has proven to be a strong method for implementation.

1. Abstract front page "all aspects of this process are electronic and done in a de-identified manner". How can an investigator review medical records in a de-identified manner, is this guaranteed with the i2b2 tool?

   Response: We have attempted to better clarify the sequence of events. Via i2b2, the researcher has no access to any data. The query they construct uses the limited data set to provide the researcher with the number of potential subjects that meet the criteria entered. They also receive de-identified demographics for the group identified (eg. age ranges, gender). Once IRB approved, the query is run again by the IT honest broker against the identifiable data based to provide the researcher with the approved information.

2. Abstract front page "all aspects of this process are electronic and done in a de-identified manner." Can the patient limit to what extend the investigator can access his/her medical record? E.g. when screening whether patient can be included in a study about diabetes, records of psychiatry can be excluded from consent2share?

   Response: Once they agree to Consent2Share, the subject cannot limit what is included in the limited data set that is queried in i2b2. For example, psychiatric information can certainly be an important co-morbidity. Thus the number of potential subjects the system determines includes all EHR information. However, when that researcher submits their protocol to the IRB, the IRB may determine not to allow a researcher that has no clinical need to know, access to identifiable data that contains sensitive information.

3. Abstract use of abbreviations. EHR? IRB? UF? IDR?

   Response: All abbreviations have been clarified.

4. Introduction overall. It might be beyond the scope of this article but the authors use broad terms like integrity and governance to emphasize the importance of Consent2Share. The axiom and starting point of the article is the assumption that asking consent is the best way to inform a patient about the attributive burden research will impose on him/her. However, Daniel Kahneman and his colleagues have proven in several landmark experiments (see book Thinking Fast and Slow) that information only moderately influences our decisive behavior. A paragraph might be added to explain the value if the concept of giving consent is still relevant regarding these novel insights.

   Response: Although an important discussion, we believe this is beyond the scope of this article.

5. Introduction l36 'approaching patients with multiple consent forms.' In general, the inclusion of patients in multiple studies is less desirable. How does Consent2Share foresee this problem?

   Response: Agreed, however in an institution that has some 12,000 protocols and several hundred investigators, coordinating efforts to minimize some patients being approached by multiple investigators is not something the institution nor the Consent2Share process addresses.

6. Technological foundation l54 "the Consent2Share program relies on the institution's underlying clinical and research data infrastructure". Does this mean that the Consent2Share program cannot be used in other hospitals?

   Response: The process of a general consent to develop a research contact registry is certainly done in other institutions. Those that use EPIC as their EHR could develop the same Consent2Share effort. This does take a unique collaboration and desired from all the stakeholders to make this as seamless as possible.

7. Pilot. What is the percentage of patients who agreed in Consent2Share but denied to participate in future studies? If the rate is <5%, one can question the additional value of Consent2Share.

   Response: This is a good question, but at this point in the evolution of this effort, we have not followed up with the many researchers who have used patients that were contacted via Consent2Share. This is now described as a future enhancement at the end of our discussion section.

8. "Honest Brokers". How are they defined?

   Response: Added to revised page 12, but an Honest Broker in clinical research is defined as a neutral intermediary (person or computer system) between researchers, the individual whose tissue and data were collected, and the healthcare provider who obtained the tissue and/or data and thereby has a responsibility to protect personal identifiable information (which must be separated from the original clinical data). At UF, 8 individuals that are part of the IT informatics group, have been trained and certified as Honest Brokers; they have access to the identifiable clinical data, and provide the minimum

9. Discussion. Is the Consent2Share consent only applicable to medical information from one hospital? E.g. Patient has given consent2share at hospital A, is referred to hospital B, investigator of hospital B is allowed to approach patient?

   Response: At UF, any hospital or clinic that is under UFHealth is included in the IDR and thus included in any i2b2 query. Those using i2b2 can link information through a web-based software network called SHRINE (Shared Health Research Informatics Network) to allow researcher from one institution query information from multiple other institutions. Although the University of Florida is involved with a SHRINE effort, we hope in the future other institutions develop a similar Consent2Share effort which could then allow cross institutional contacting of potential study subjects. This has been added in the text on the revised page 22.

10. Discussion l13 'the awareness of these data is increasing'. Which data?

Response: Clarified in the text.

11. Overall. Is it possible to include some screenshots of the consent2share and i2b2 tools? Most illustrating would be a short case of a patient presenting at a clinic.

Response: This could be added, but would add significantly to the length of this manuscript.

Reviewer #3: Reviewer report 9-8-2016

GENERAL / MAJOR COMMENTS

1. In line 12 of the Introduction the authors contend that an incent for the "Consent2Share" program is that "patients often want to be involved in clinical research but do not know what studies are available or how they can be accessed." The concept of the "Consent2Share" program, however, does not validate this statement, because it does not create a platform for patients to enable them to search for a specific study concerning their condition. It might even create a false sense of security, inhibiting a patient to look further. For example: if a patient is suffering from a specific (oncological) condition, but there are no ongoing trials in the connected hospitals, the patient might not look further for trials, although there might be suitable recruiting trials in the country. The "Consent2Share" is therefore a feasible tool for researchers than patients, which should be addressed more clearly in the Introduction. Another solution could be addressing the issue in the Discussion. You could then argue that the "Consent2Share" tool would become more feasible for patients when more hospitals are connected, increasing the chances for a patient to find his or her trial.

Response: The reviewer is correct, and on the revised pages 5 and 12, the goal of the Consent2Share effort is better described “The original goal of this effort was to give patients who wanted to be considered for future research protocols a way to provide their name to researchers to let them know they are interested, and to potentially improve recruitment into research studies.” UF has other methods to allow patients to search on line for current research studies that they may be interested in.

2. It would be very interesting to know how "Consent2Share" improved the inclusion of patients in trials. Data on patient inclusion in comparable trials before and after the introduction of “Consent2Share" is necessary to evaluate the efficiency of the tool. Please provide these if available.

Response: We agree with the reviewer that this type of information would be great; we have added this as a future goal of this program at the end of the article.

SPECIFIC / MINOR COMMENTS

INTRODUCTION

1. Page 5, line 40, point 3) "researchers do not have the infrastructure to appropriately maintain a database integrated with patients' electronic health record (EHR) to ensure that up-to-date information is maintained on potential study subjects". First, your hospital uses EPIC, which allows data managers and trial coordinators to maintain specific lists for researchers of included patients, in which all clinical data are automatically updated. This would make your argument invalid. Secondly, in case I misunderstood

and up-to-date information on potential subjects is a problem, how does "Consent2Share" change this problem? "Consent2Share" seems to be limited to expanding the availability of patient data for researchers, and does not necessarily ensure that it is up-to-date and integrated.

Response: The reviewer is correct that within EPIC, an investigator can, by hand, add study subjects into a list. However, the value added by having subjects electronically added, and the ability to then query all patient data within EPIC and other databases to identify those that meet certain research criteria is not attainable by any individual investigator. We have edited this statement to be more accurate.

2. Page 6, line 30. Please explain the terms study-by-study consent and tiered consent to enable a broader readership, and include the following reference for study-by-study: PMID 23660530. Also please explain why you chose broad consent over tiered consent, especially since the review by Garrison et al., which you cite, claims that tiered consent is considered to be superior to broad consent by patients.

Response: A brief definition was added.

IRB APPROVAL OF THE IDR

1. Page 10 line 22. The researcher has the ability to see how many patients are applicable for his or her study, which means there is access to the baseline characteristics of patients who gave consent. The following step is approval of the IRB to access and use patients' data. This is slightly confusing, since the researcher readily had access to the patients data (?). Moreover it seems like you state that a researcher determines the feasibility of a study based on the current amount of patients within a cohort. Can you please elaborate on how this works in a situation with recruitment during a longer period of time, inclusion of new registered patients (for example, does the researcher estimates an amount of patients per year, or does he/she only look at the total amount?), and multi-center studies?

Response: We have attempted to better clarify the sequence of events. Via i2b2, the researcher has no access to any data. The query they construct uses the limited data set to provide the researcher with the number of potential subjects that meet the criteria entered. They also receive de-identified demographics for the group identified (eg. age ranges, gender). Once IRB approved, the query is run again by the IT honest broker against the identifiable data based to provide the researcher with the approved information.

PILOT
Initial Consent Capture Process (Consent2Share)

1. Page 12 Line 28-33, You state that the pilot was executed in a clinical setting where most patients were competent to consent for themselves. Understandably, this creates some healthy-patient selection bias, which is acceptable considering protection of vulnerable patients in a pilot setting. However it would be interesting to know how you are dealing with these patients now that you expanded the pilot. Especially since recruitment of for example children or patients with dementia for trials is challenging, it would be interesting to know if "Consent2Share" is applicable in those cases, and whether it improves inclusion of these patients in trials.

Response: A clarification was added on revised page 13. We decided that we will eventually expand to include children since the software could identify when the child turned 18, and thus the now adult patient would need to be re-consented. We decided at this point we will never include incompetent adults, since

identifying if those individuals regain competency and thus would require a re-consent, would be too difficult to accomplish with the number of patients agreeing to Consent2Share. Although there is certainly a need to include incompetent patients in research, Consent2Share is currently not a method to identify those, and identify who would be contacted to obtain consent for a future study.

RESULTS

1. Line 48 page 16. Please provide information on how this random audit was conducted, the methodology is now unclear.

Response: A statistically driven selection of 700 records (10% at the time) was used to conduct the initial audit. Once we discovered the problems, we reviewed all consent forms, one by one.

2. line 50 page 18. You removed a question on approval of usage of left over tissue. Does eliminating this question implies there is no consent to use leftover tissue anymore, and left over tissue will not be used, or is tissue still used without permission?

Response: At UFHealth, we currently do not ask permission to use totally de-identified tissue for research. Investigators must submit those requests to the IRB, who determines that the tissue is in fact de-identified. Should the NPRM become a reality, that practice would have to stop, or we would include that request within the Consent2Share consent.

3. Line 48 page 19. You refer to a "much smoother and simpler process." More practical information on the time efficiency and costs of the project would be interesting for the readers, assuming your message is directed at clinical practitioners.

Response: We added a short edit to clarify our statement. We did not quantify the time it took all involved initially and after the changes made, it was a subjective assessment by those involved.

4. Line 23 page 21. With the introduction of the eConsent, does the patient still receive a copy of the consent?

Response: Yes, patients that agree are offered a copy of the consent, if they want one; it is printed at the admissions desk. Our plan is to eventually post it on the “myChart” page which all patients can log into to communicate with their physicians and review their various medical results.

DISCUSISION & CONCLUSIONS

1. Line 13 page 22. Please write out what "these" refers to, the sentence is unclear now.

Response: Clarified

2. Perhaps add a section on feasibility of "Consent2Share" for patients as suggested in point 1 of the major comments.

Response: This issue was addressed under our response to point 1 of the major comments.

Journal of Clinical and Translational Research
Peer review process file 02.201604.001

2nd editorial decision

Date: 2-Oct-2016

Ref.: Ms. No. JCTRes-D-16-00023R1
Consent2Share: an integrated broad consenting process for re-contacting potential study subjects
Journal of Clinical and Translational Research

Dear Dr. Iafrate,

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

Comments from the editor and reviewers can be found below.

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:

Reviewer #2: - Careful and detailed reviewed comments
- Promising field of research
- Satisfied with current result

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