Author’s response to reviews

Title: Eliciting meta consent for future secondary research use of health data using a smartphone application - A proof of concept study in the Danish population

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Author’s response to reviews:

Editor:

The paper has support by two reviewers and another one is instead highly critical. Two of the reviewers highlight the need for further development of the paper - i.e., that it is too focused on the proof-of-concept aim.

I agree with them that there is a lot unsaid and a shortage of engagement with recent developments. For example, when you claim that “It introduces and tests a completely new model of informed consent” that seems to depend on whether it is the electronic nature of the process or the "meta aspect" that is meant, but recent options such as Secure Consent, WCG eConsent, iCONS, or the Penn one (see https://www.pennmedicine.org/news/news-releases/2011/october/penndeveloped-online-informed) all use a electronic format and sometimes incorporate elements of what could be called meta consent.

Also the on-going ethical and legal discussions are largely missing from the paper.

I believe the paper could be developed in either of two directions.

1) Focus the paper even more strongly on the empirical study and state more strongly the limitations. Some of the remarks by reviewer 3 are then highly relevant to take into consideration for the revision of the paper and to make clear its fundamental soundness,

or

2) Follow the lead of reviewer 2 and develop the discussion further. Reviewer 3 have some important remarks that should be addressed then as well. I believe you should then go deeper into the recent literature (many sources are now old or consist your own papers). In addition to those mentioned in reviewer's comments could be added for example:
Use of mobile devices and the internet for multimedia informed consent delivery and data entry in a pediatric asthma trial: Study design and rationale.

Teleconsent: A novel approach to obtain informed consent for research, Brandon M. Welcha, Elizabeth Marshalla, Suparna Qanungob, Ayesha Aziza, Marilyn Lakenb, Leslie Lenerta, Jihad Obeida

Orri M, Lipset CH, Jacobs BP, Costello AJ, Cummings SR, Web-based trial to evaluate the efficacy and safety of tolterodine ER 4 mg in participants with overactive bladder: REMOTE trial, Contemporary Clinical Trials 38/2 (2014), pp. 190-197


You could then more clearly state what contribution your paper make to the body of knowledge.

RESPONSE:

We have chosen primarily to revise the paper according to your suggestion 1, but have included a section on issues in recent research on informed consent in which we reference the suggested articles and electronic implementations of informed consent mentioned above.

The reviewers' reports, together with any other comments, are below.

Reviewer #1:

This is a nice proof of concept study and the results reflect the objectives. It demonstrates feasibility and sets the stage for further research and exploration on the innovative use of mobile devices to obtain research consent. I look forward to ongoing research by the investigators on the topic.

Were any major changes made to the prototype through the prototype testing? Did you do any qualitative user testing? If so, were there any notable comments?

RESPONSE:

Only minor design changes were made after the prototype testing. No qualitative user testing was made.
Though not critical, I suggest using visual charts to represent the results as opposed to data in tables. It's much easier for the reader to see trends when represented graphically.

RESPONSE:

We are oldfashioned and prefer tables.

Also, a minor comment related to the questions in Table 2. The question was framed by "How easy was it to..." with the possible options ranging from "Very difficult" to "Very Easy". The question might have been better framed as "I found understanding X to be..".

RESPONSE:

We agree but cannot now change the wording. We do not think that it is likely that a change of wording would have led to different results.

Reviewer 2:

This is a well written, well structured, and interesting investigation.

There are several points, that if addressed, would significantly enrich this manuscript:

Is the distribution of education levels seen in the sample representative of the Danish population as a whole? Were there any differences in responses by education level?

RESPONSE:

Numbers now included

Was socioeconomic status used to target recruitment for this study? If not, why not? Was SES a factor in who participated (e.g., in ownership of a suitable device for participation)? What are the potential implications of this for the conclusions reached?

RESPONSE:

No, SES was not one of the stratification variables. Device ownership is very widespread in Denmark (on average more than 2 devices per adult), and varies more by age than by SES.
What work might be done to assess participant understanding of the concepts presented within this consent framework? Why would this be an important next step in this investigative pathway?

RESPONSE:

Good point. We have added a section explaining our choice of a subjective standard of testing but also why an objective standard should be included in any future studies.

I notice the apparent reluctance of participants to sharing of their data for private commercial research and international research and, to some extent, for private commercial research (Table 3). Although the ongoing ethical conversation about secondary use of data in research is alluded to in the Background, the implications of this type of approach to consent for research are not discussed despite presenting data -- like that in Table 3 -- that has very real implications for research. It appears that the authors are keeping a very tight focus on this work as a pilot of usability, yet I feel strongly that there is more that can be said here (and that additional thought/reflection would bring the article more in line with the other papers within this journal.)

RESPONSE:

We have added a section in the Discussion on these implications.

Reviewer 3:

Approach of the paper: At present there are several points where the reader must guess the assumptions behind the sentences which makes reading the paper more difficult. The paper somewhat implies that the reader already studied the papers written previously by the authors. To clarify the message would be important to follow sentences such as "we have elsewhere argued " by a concise and clear explanation of the argument.

Regarding Meta Consent and the critique to traditional consent:

On the theoretical level, meta consent is presented very briefly and as an accepted concept.

The author's refer only to their own literature (line 21-32, Ref. 13-14) to suggest that repeated consent may lead to habitual consent, or refusal to consent and from there they follow that therefore offering meta-consent (with no consent options) is ok and by doing that they overrule what has been regarded as a right with a sentence. While the author's consideration on "bad habit of asking all the time bad consent" can be an argument to introduce the need for better organization of consent procedures and communication it can hardly, from a logical point of view imply the need to cancel the need for consent.
The reviewer apparently misinterprets the notion of meta consent. Meta consent does not cancel the requirement of consent. It does not in any way overrule the rights of the individual. It simply asks people how they would like to exercise their right to provide consent. We have added a single line in the introduction to make this clear for all readers.

Meta consent here is presented as it, on the theoretical level, does not present any ethical challenge or problems. There does not appear to be a balanced use of references, the literature reported in the paper appears to be one-sided and does not mention nor discuss other existing literature and how the model relates to it.

Meta consent is presented as the only alternative to super-specific repeated consent, and this is so far not the only alternative as represented broadly in the last 5 years of literature on the topic.

A lot of the literature on patient's preferences, for instance, lean towards transparency and dynamic interactions in many instances. One time meta-consent, as presented in the paper, is not offering a clear or informative choice as it is not offering information about possible current uses of information, nor meta-consent can account for future uses or the possible development of technologies that may lead to completely unexpected outcomes in the use of information.

In fact the type of information provided at the time of meta-consent (if offered) is not presented in this paper, rendering it impossible to assess it.

RESPONSE:

We have added a section on some of the recent issues in the discussion of informed consent and added a number of references to aid the reader with a general interest in recent developments on informed consent.

We have also, however, made it entirely clear that this is an empirical study of one specific model of consent. It is not supposed to discuss the pros and cons of different models of consent.

We have also clarified that meta consent is not ‘one time’ but continually modifiable.

The authors suggest that meta-consent can be beneficial for science since it is allowing "blank consent". Regardless of the critique to blanked consent in the literature (not mentioned), at the same time the tool is also allowing blank refusal (which may be very detrimental for science), introducing a bias in the presentation of the choices. As it is phrased the test, without further explanation of sort, it is inducing the patients towards a certain answer.

RESPONSE:
The reviewer is mistaken here. If we require informed consent for research, then the possibility of blanket refusal is not more or less detrimental to research than the possibility of specific consent. In either case there is a risk of people refusing consent. We cannot see how the phrasings used induce people towards a certain answer.

The emphasis in the alternatives provided is placed on how many times you want to be "contacted" ("affect them in terms of consent requests", line 46) implying the burden of re-contact with no mention of benefits or reasons why you should be re-contacted (such as meaningful results for the patient). This approach seems biased, as assumes (without discussion reported) that consent is only a burden for patients (as bad consent is). The whole literature on re-contact for incidental findings, or multistep consent or layered or staged consent in the US and elsewhere (see for instance Applebaum 2015) suggest how a qualitative re-contact may greatly benefit the patients and it is wished for. Something as "Should we contact you if something relevant for your health should arise?" is not asked in this exercise, nor proposed as possible choice, and potential benefits of re-contact (for patients) are not mentioned elsewhere, rendering a balanced choice very difficult.

RESPONSE:

The reviewer is conflating issues here. We are suggesting and testing a model of consent – we are not investigating a system for recontacting research participants in the course of a research project. The answer to a meta consent request is entirely independent of an answer to a question about recontact.

Informed consent requires informed decision at least to a certain extent if you still want to call it consent. Even more if people are asked to make a "meta" decision about future undetermined uses. What are those possible uses even broadly described? What are the implications even broadly? And a big question: what was the information provided to the study participants, what was included, who provided it and how? This piece of information is not provided. In the paper authors assume the user's are provided with information, but do not mention the categories of information that should be included, see current literature.

RESPONSE:

We have included an appendix with a translation from Danish of all the information provided to the study participants.
On the legal aspects of meta consent would be worth at least mentioning the 2016 published EU GDPR, as it seems that meta-consent clashes greatly with it and with the principles outlined i.e. the notion of transparency, affirmative action (when referring to consent) and in general the idea of proper information as represented in the GDPR.

RESPONSE:

The reviewer is mistaken here. A meta consent model does not clash with the EU GDPR: Article 89 in EU GDPR allows for national derogation from consent requirements for use of data for scientific research purposes. This obviously entails the possibility of a meta consent model, as well as for research without any consent.

The "concept study": methodology issues

How was the "study " designed? The authors provide a short description of the study design which is not sufficiently informative. Most information that is essential to understand, appraise and judge the methods and results of this paper is completely missing. Besides the fact that such information is needed in the review process, it is highly relevant for peers reading the paper (they need to be able in sense to reproduce the study).

Methods:

Pilots: How were the pilot experiments designed? It is reported that Likert scale was used to measure patient's expectations: running from where to where? What are the categories? Which question was asked to which the respondents replied on this Likert scale

How did the experiment took place? this part is completely missing and the reader has to try to reconnect bits and pieces

1) We recruited (how)

2) We asked questions etc…….

Questionnaire (unclear is this was part of the study but based on the results I assume there was some kind of questionnaire): what questions were asked, what were the answering categories, are these validated questions, how were the answers coded etc.?? All this information is missing.

RESPONSE:
We have added information on the Likert scale and the recruitment process and the questionnaire.

Sample description is unclear: what data was collected and how?

(line 18) Here authors say that the background panel consists of 53,000 persons. Then they sent out 1000 emails. Why? How were they selected? How did they get the emails? (Recruitment is only shortly described and privacy considerations missing)

RESPONSE:

This is already in the text. We write “A stratified sample of 1000 potential respondents, representative of the adult Danish population was drawn from TNS Gallup’s Danish panel. The sample was stratified according to gender, age and residential region. The background panel consists of approximately 53,000 persons. Potential respondents were contacted by e-mail, with further reminders by e-mail and SMS to those who had not either 1) stated that they did not have a suitable smartphone or tablet, or 2) declined participation.”

We have, however, added a line clarifying that Gallup sent the e-mail, and that therefore there are no privacy issues.

Regarding the analysis: what tables and regression was used? What is the significance level? None of this is reported.

RESPONSE:

We have clarified this in the text.

Ethics: this is a highly sensitive topic. Even if ethical approval may not be mandatory in the author's country by law, it would be in most EU countries. We wonder if this should really be accepted. In ethical terms, there are reasons why elsewhere this types of studies are conducted inside proper ethical review framework. This has also to do with scientific aspects such as assessing selection bias, potential flaws, generalizability etc. This aspects are not mentioned in the results section and they constitute a bias, especially for studies that aim at proposing possible policies solutions.

RESPONSE:

The reviewer is mistaken here. In many countries social science studies collecting anonymous data are not legally subject to evaluation by research ethics committees. Moreover, it is not at all
clear that hypothetical consent preferences are highly sensitive information. Finally, none of the publication ethics guidelines (WAME, COPE, ICMJE) requires research ethics evaluation of such studies. It would also be impossible to obtain such an evaluation in Denmark, precisely because the Danish REC system is based in law and therefore only evaluates those projects that fall within the legally specified criteria for REC submission.

Results:

The first full application was measured with a method (ref. 17) that is called "quick and dirty usability scale" that is at least problematic.

RESPONSE:

This is an industry standard, well validated scale for the evaluation of user interfaces. The publication currently has 4536 citations on Google Scholar. We of course apologise for the reviewer being mislead as to the appropriateness of the scale from the title of the publication, but it is standard in the app development field, including in relation to health apps, see for instance https://www.usability.gov/how-to-and-tools/methods/system-usability-scale.html.

The response rate is really very low. Authors should reflect in the discussion on this (discuss selection bias, potential for generalizability etc.)

How was a sample efficiency of 89 calculated?

RESPONSE:

We have added a section on this in the discussion.

The school categories in which the authors place the respondents are not described and are not standard (what does medium university education mean? How to compare this to high university and low university (isn't this all higher education?))

RESPONSE:

We have added length of university degrees in the Results section. The categories are standard in Danish social science research.

Tables & analyses:
The tables are not described nor the results, some examples of what is unclear:

We have to read them as readers but this is not how it should be (both text and tables should be readable and interpretable without one another). They are also very unclear (universal scientific writing guidelines explain that table titles are place above the table).

RESPONSE:

We have moved table titles to the top of the tables.

We disagree with the more general claim here. The implication of the claim that text and tables should be readable and interpretable without one another seems to imply that all text should be recapitulated in the tables, and all of the results recapitulated in the text.

The 3 questions that authors appear to have asked of participants' (how? Where? Why?), doesn't really prove that people understood the information? Why wasn't a more objective measure of understanding used?

RESPONSE:

We agree with the reviewer that the questions asked do not prove understanding. We have added a section explaining our choice of a subjective standard in this pilot-study, and why future studies should include an objective test of understanding.

Lines 45-50: Why did you use regression analysis: what does this type of analysis tell us? What regression was performed: uni or multivariate, linear or logistic? What is the dependent variable? Authors write the are investigating relations (later they talk about correlation, this is not the same at all!), this is of course not possible using cross-sectional data, they should refer to associations.

Why do they report the R2, of course this will be low only including 1 independent variable (how I assume they conducted the analysis but this is completely unclear). Also, why not adjust for confounding factors? I can foresee several confounding and/or mediation effects here.

RESPONSE:

We have revised the relevant section in response to these queries.

Were the table included tested for readability?

RESPONSE:
No.

The tool:
The figure explaining the choices provided is unclear. Does it represent what people were seeing at the time of the choice?

RESPONSE:
Yes it shows – as described in the text – two of the main screens in the app.

The categories used are not of easy comprehension. I had problems to understand the meaning of it, having worked with registries and bio-banks for long time.

What does "always ask" mean (is it once a day, once a month, 10 times a day?)

What does "rarely "mean? What do the authors mean by "same kind of projects"? Areas of research? (cancer, metabolic? Or more restricted stroke, diabetes?) or types of investigation (genetic association studies, gene environment interactions, candidate genes etc.), or type of institutions involved (national level, consortia, Worldwide investigation)

"Always allowed" (do you provide any information about why this is a concern in the literature? Any info about familial implications?

"Never allow": Any idea about return of results and possible benefits in participating in a research project?

RESPONSE:
All of the categories are described in the text. Thus the category “Always ask” is given the definition “It means that you will be asked for consent for every research project in which your data is being used” right below the category. And this goes for all categories. We believe that this is fairly comprehensible.

I think that most people would not understand the implication of this "always or never" if applied in the context of electronic patient records (including supersensitive data such as psychiatric, gynecologic, etc.) or health care data in registries, or even tissues (completely different category,
that implies many possible uses such as derived cell-lines, CRISPR studies, IPS derived studies, the handling of genetic data with all its implications etc).

RESPONSE:

The reviewer is mistaken here. We do not ask for consent preferences for general use of tissue. We ask – as the respective category says – for consent preferences for “Data from tissue samples”.

It is unclear if information at all was provided to participants to the study about what meta consent is, what the possible consequences of decisions are, what the possible implications of such decisions. This should be described in the design.

RESPONSE:

We have added information in the design section about the information given, and include an appendice containing ALL information to study participants.

Discussion (line 34)

The discussion is in general blurry and unclear. The text is confused with regard to discussing the study outcomes, comparisons with other studies (completely missing), limitations, implications, recommendations and conclusions. For instance authors claim that "The choices made indicate that there are significant differences in consent". Do they really, according to the data provided in the paper?

RESPONSE:

Yes they do.

Regarding the presented paper conclusions:

I was unable to draw the presented conclusion from the data (as currently described (as far as I can judge) but potentially also not when fully described.

RESPONSE:

We believe they hold until proven otherwise.