Reviewer’s report

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

Version: 0 Date: 10 Feb 2017

Reviewer: Deborah Mascalzoni

Reviewer's report:

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.

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.

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.

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.

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.

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.

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.

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)

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

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.

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.
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?

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?))

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).

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

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 forsee several confounding and/or mediation effects here.

Were the table included tested for readability?

The tool:

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

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?

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).

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.

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?

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.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No
Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

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I am able to assess the statistics

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