Author's response to reviews

Title: Consenting the Vulnerable: The Informed Consent in Advanced Cancer Patients in Mexico

Authors:

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Version: 3 Date: 18 May 2006

Author's response to reviews: see over
Reviewer's report

Consenting the Vulnerable: The Informed Consent in Advanced Cancer

Title: Patients in Mexico

Version: 1 Date: 2 March 2006

Reviewer: Neema Sofaer

Reviewer's report:

Verastegui presents the results of a survey designed to assess the quality of informed consent in five pharmaceutical-sponsored international clinical trials in Mexico City. The author argues that the quality of informed consent is inadequate and that therefore the process of informed consent does not -- contrary to what has been argued -- guard against the commission of moral wrongs in clinical trials conducted in the developing world. Several studies have already shown that subjects in the developing world cannot understand informed consent forms as they are written. This paper adds valuable data from a new research context to support this consensus.

Major Compulsory Revisions

There are, however, two major flaws to argument. First, the author infers that the quality of informed consent is low from data that indicates that the informed consent form is not written in a form that the subject can understand. This inference fails: the quality of informed consent can be high even if the subject does not understand the consent form when she reads it if someone explains its contents to her in terms that she can understand. Second, the author draws ethical conclusions from the alleged fact that the quality of informed consent is low. It is unclear what these conclusions are and how her data supports them. If the author wishes to draw ethical conclusions, she should take more time to explain and support them. My other objections concern particular passages or claims. I have listed them below under the titles of the sections in which they occur.

I agree with the arguments.

I was not trying to question the “Ethical” aspects of the Informed Consent, or the quality of the original documents. My argument purpose is to show that the patients require better ways to be informed about a clinical trial. That the purpose of the informed consent should not be a legal instrument, but rather a document or process to ensure the well being of the patients.

Results (p. 2)

It is unclear who considered the consent “lengthy and complex to understand”. It is unclear what is meant by the claim that “only the doctor was considered to consent”.
Re written the section, lengthy was described as more that 6 pages. A better methodology section was written.

Conclusion (p. 3)

It is unclear what is meant by “ethical panacea”. One possible interpretation is “effective means to avoid exploitation”, but the author does not seem concerned only with the prevention of exploitation.

In clinical practice to have an informed consent is becoming the only way to have an “ethical procedure-research-treatment”. I tried to outline the complexity of the procedure, because of the patients’ characteristics, and as a consequence the limitation of the consent procedure.

Background

P. 4 The author should state which the four moral principles are.

I footnote was included; I wanted to focus in the autonomy, because of the difficulties to achieve it in countries like mine.

p. 5 The first sentence of first full paragraph “According with…” is incomprehensible.

The paragraph was changed

Discussion

P. 10. It is unclear what the author means by a “fine line” and why the situation she describes is an instance of a fine line. Earlier discussion suggests that the fine line divides acts or situations that are morally acceptable from those that are not. However, both coercion and lack of opportunity seem morally unacceptable. Perhaps the author means, instead, that there is a dilemma: either the subject participates in the trial without giving her adequate informed consent, in which case she is coerced,

My understanding of “a fine line” is clear from the patients’ perspective. The ultimate goal is to give the patient the opportunity to get better. I the informed consent procedure follows the international “Good Clinical Practice” guidelines, none of the patients from the hospital would understand the consent forms; therefore, without the consent the patient would not be included in the trial.

On the other hand by being paternalist you could “suggest” what is best for the patient according with the conditions in which he or she lives.

or she is excluded from the trial, in which case she lacks a crucial opportunity. Furthermore, it is contentious to claim that recruitment without informed consent is always coercive. Several recent articles in bioethics have presented refutations of this view, for instance, Hawkins JS and EJ Emanuel ‘Clarifying Concerns about Coercion’, Hastings Center Report 35 (5), 16-19.
Also: the author often refers to Bioethicist. It is unclear whether this is a particular or typical bioethicist or the journal Bioethicist; consequently, the text is often unclear.

My concerns and the purpose of this work are to highlight what happen in practice. A limited knowledge of “bioethics” is common in medical practice. My concern is not the coercive actions. My proposal and concern are that the informed consent as it is given now is not helping us, physicians in charge of “vulnerable” patients to protect the patients’ rights. I think there must be a consent procedure that informs the patients of the purposes of the clinical trials, their rights and duties.

Consent procedures focused in the patients and not focused in accomplish what the regulatory agencies need to protect their interests.

Bioethicist, (as a theoretical figure). But I changed the text

Questionnaire

1. It’s unclear how either set of data establishes the subjects’ quality of informed consent for the reason given above.

2. For each question, the author should say how many subjects answered it and which proportion of subjects gave each answer. It is insufficiently informative merely to list the different answers given.

3. Some of the questions are badly designed. For instance the question “did you read the questionnaire by yourself at the hospital?” requires a “yes” or “no” answer. However, “no” could mean that the subject did not read the questionnaire by him/herself or that he/she did not read it at the hospital.

[EV1]Minor Essential Revisions

The author should run a spell-check and ask a native English speaker to edit the paper. Here is an (incomplete) sample of the major types of spelling and grammatical errors. The author often uses a comma where a full-stop or semi-colon would be more appropriate. Her use of tense is often inconsistent or incorrect (for instance, the first sentence of Results reads “answer”, but should instead read “answered”, and the last sentence of the questionnaire should have “decide” not “decided”). Some words are missing (e.g. “form” is missing after “consent” in the second sentence of Results on p. 2). Some sentences have extra words that do not fit into the grammatical structure (e.g. it is wholly unclear what the word “intent” is doing in the first sentence of Discussion on p. 3.) The choice of words is sometimes wrong. Example 1: “a giving population” in Discussion, p. 3, instead “a given population”. Example 2: “According with” (p. 5) instead of “according to”. Example 3: P. 9 lines 1 and 4 say “though” where the author clearly means “thought”.

The manuscript was reviewed.

Unable to decide on acceptance or rejection until the authors have
What next?: responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.
Reviewer’s report

Consenting the Vulnerable: The Informed Consent in Advanced Cancer Title: Patients in Mexico

Version: 1 Date: 9 March 2006

Reviewer: Catherine M Slack

Reviewer’s report:

General

This study describes cancer trial participants’ experiences of consent forms.

Investigation of aspects of consent and recommendations for improving consent experiences for volunteers remains a timely and critical ethical concern.

In conclusion, this is a potentially useful study in a critical and timely area.

The authors should respond to the major compulsory revisions before a decision is taken around publication. I recommend that if a revised paper is submitted it should be sent back to reviewers, if this is an option.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The paper as it stands, however, requires major compulsory revisions before it can be considered for publication. These are as follows:

1. Background. Some review of literature that examines how to improve understanding by enhancing consent forms would be valuable given the scope of the study. See Flory J, Emanuel E. Interventions to improve research participants’ understanding in informed consent for research: A systematic review. JAMA 2004;292:1593-1601.

There are many ways to improve the understanding of the procedure, as mention in the recommended review, and changes should be made. However, at the present time; it is difficult for me to understand why to enforce a procedure that is known to be wrong for this population in its present format.

Several international clinical trials, are not interested in new ways to improve consent procedure, they are interested in the documents that backup the defined procedure, for regulatory purposes.
I think this paper could make a contribution for Latin American physicians’, acknowledging the need to play an active role in the design and procedures to obtain the informed consent according to the population they are in contact with.

2. The aim needs to be revised to consistently represent that the purpose of the study is to assess participants’ experiences of consent forms.

a. At present, the abstract states that the aim is “to evaluate the validity of the consent procedure” (perhaps too broad a statement as process aspects of consent are not examined in any detail); “to evaluate if the informed consent procedure fulfils the purposes that are meant to be achieved (these purposes are not spelled out and the design of the study could not support such an exploration) and that the study “assess(ed) their comprehension of the consent forms” (p2: Abstract). (the study did not assess understanding of trial concepts contained in forms at all!).

The purpose of the study was rephrase:

**With the purpose to assess the clinical research participants’ experiences during the informed consent process in the setting of a cancer centre in Mexico we conducted a qualitative the analysis of the procedure. The study design included the evaluation of ten different consent forms provided by international sponsors, and the use of questionnaires to asses patients’ and doctors’ knowledge about the meaning of the consent forms.**

b. Another aim should be added in order to justify the presentation of results of a survey of researchers’/ doctors’ opinions of consent.

Done

3. Method:

a. Evaluation of random selection of consent forms: The author must provide more detail of how this evaluation was done. Given the present detail, this part of the study could not be replicated. It only states that use of technical words, language difficulty, accuracy of translation and “intelligibility” were “qualitatively analysed”. How were technical words defined and recognised? How was language difficulty assessed? To what extent did raters agree with each other? If the methodology cannot be rigorously detailed, perhaps the paper would be strengthened if this section were omitted altogether.

Changes were made in the methodology presentation, and appendixes were added to improve understanding of the text.

b. Participants’ experiences:

i. It would be helpful if the paper described early on that all persons approached to participate in the survey accepted.
Done

ii. More detail should be provided on the structure of the patients’ survey questionnaire in the text and it should be included as an Appendix. It is currently not clear whether participants in this consent survey answered questions in an open-ended fashion and whether these were qualitatively coded; or whether they selected responses to statements, e.g. “To free the institution and doctors and doctors of responsibility in case something bad happens” (agree – disagree). If this latter format was used, were participants free to select more than one statement or only one? It would not be possible to replicate the study from the information currently provided.

Done

iii. More detail should be provided on the structure of the doctors survey questionnaire in the text and it should be included as an Appendix. Currently it is not clear how questions were posed and in what format doctors were required to answer.

Done

4. A section on scoring and analysis (for both the patient and doctors’ results) must be inserted into the paper. Currently this is absent.

A section was added

5. Ethics: There should be some discussion of the ethics of this study itself. Currently this is absent. What were participants in this study told about it? How was consent obtained to take part in this consent study and from whom was ethical review obtained?

The study was accepted by the REC of the hospital and the statement has been added to the text

6. Sample: The paper should describe clearly how many participants took part in this consent survey. There is a discrepancy between the number provided in the text of 55 (page 8) and the number provided in the table of 50.

In order to have a uniform criterion for the analysis, only those patients that complete the whole survey were included in the revised document.

All the information provided has been double checked.

7. Results:

a. The narrative text describing the results should describe in an even-handed manner all 10 questions posed to participants. (At present only 4 out of 10 questions are described).
b. Statements in the narrative text of the results section should be more adequately supported by and linked to specific data. At present there are some ambiguities:

E.g., (1) It states that the consent form was too long according to all, however I can only see that 25 participants stated this from the summary table.

E.g., (2) It states that those patients who read the consent form thought the explanation from their doctor was clearer, however I cannot see this from the summary table of results.

E.g., (3). It states that most patients thought that consent was not needed, whereas I cannot see the data that support this assertion in the summary table of results.

c. A section in the text must be inserted describing the results of the doctors’ survey in an even-handed manner. At present there are only 3 lines devoted to this. These results should be clearly supported by and linked to actual results presented in the summary table.

d. SEE TABLES (POINT 12 BELOW)

8. Discussion:

a. The discussion section should stay closer to the actual results identified in the study and relate these to other empirical investigations of consent experiences, and to conceptual literature on how to improve understanding via enhancing consent forms. At present the author largely makes general objections against compliance with international regulatory requirements for consent that are insensitive to socio-economic and cultural characteristics, as she does in the background section. It would be of more value for readers to hear her thoughts on how the consent forms and processes should respond to the impoverished, poor, largely rural patients in this study and how her data supports such recommendations.

b. The discussion section should discuss all the major results more critically and consistently. E.g.,

(1) 50% of participants did not read the consent form! This is an extremely interesting result, given the effort made on translation and the esteem with which forms are held by review and regulatory authorities.

E.g., (2) Question 2 elicited the result that every participant was consented by their doctor. What could this say about power differential between the 2 parties and what impact might this have on social desirability responses by the participant?

E.g., (3). Questions 5, 6, 9, and 10 elicited answers about how participants made decisions, finding that only the smallest minority decided by themselves. This result could be discussed in the light of some literature on decision-making, or even culture?
c. The author concludes by objecting to “informed consent in the “Western format” however the actual conditions she is objecting to are not clear. If she is objecting to lengthy, complex, boring consent forms that do not promote understanding surely these are as objectionable in a “Western” setting?

Section rephrased

9. Recommendations: As alluded to above, currently the author does not make comprehensive and concrete recommendations for how to improve consent forms (and to some extent those limited process features – like consent by the patient’s doctor – that she explores). This is a lost opportunity and would add considerable value to the paper.

The discussion is now focused in the results

10. Abstract: Once the above revisions are undertaken the abstract should be revised.

Done

11. Limitations. Some critical discussion of the limitations of the study would strengthen it, e.g., sample size, generalizability to other trials etc.

Done

12. Tables:

a. Table 2.

i. This table should be renamed: Summary of results of patient survey.

ii. There is missing data from the tables, that is, for Question 3 (reviewers numbering) 4, 5, 8, 9, 10 there is no “n” assigned.

b. Table 3:

i. This table should be renamed: Summary of results of doctor survey.

ii. The table should provide more detail and substance than it does at present. EG (1). are the readers to believe that all the doctors answered “at the request of sponsors and authorities” to the question “what is the purpose of consent”? What selection of statements did they choose from? Was this result of qualitative coding?

iii. The table has missing data, that is, for Question 1,2,3,4,5, and 7 there is no “n” assigned.

iv. The table of results should not contain references. Rather make these points in the discussion.
13. The author should clearly define “coercion” and “exploitation” in the background (p.4, 5) and discussion (p.10) sections, and more clearly delineate the relationship of these ethical concepts to her study. At present they appear to be used quite loosely and their meaning is not self-evident.

These words are used in the works referenced after every phrase.

Useful definitions can be found in Emanuel E. Ending concerns about undue inducement. Journal of Law Medicine and Ethics 2004; 32:100-105.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

References: There are a number of errors and inconsistencies in the referencing such as use of fullstop, bolding etc.

[EV5]------------------------------------------------------------------------

Discretionary Revisions (which the author can choose to ignore)

Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

What next?: responded to the major compulsory revisions

An article whose findings are important to those with closely related research interests

Level of interest: related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.
Reviewer's report

Consenting the Vulnerable: The Informed Consent in Advanced Cancer Title: Patients in Mexico

Version: 1 Date: 3 March 2006

Reviewer: Theresa Rossouw

Reviewer's report:

General

The topic of the informed consent process in general and informed consent in vulnerable populations in particular, has been widely discussed in numerous international journals. I however do believe that this article gives an important perspective from a South-American population, and therefore makes a valid contribution to the current ethical discourse.

The article aims to provide qualitative and quantitative data to assess the validity of the informed consent process in a specific vulnerable population. The methods are appropriate and the data sound, although there is room for a more comprehensive analysis with pertinent questions about the understanding of ethical terms among doctors and suggestions from patients and doctors for improving the informed consent documents and process.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. Methods: Please note whether there were sample answers or whether the patients could give their own answers in the questionnaires.

The change was made in the text

2. Discussion. Human rights language is part of ethical and legal discourses, and does not necessarily feature prominently in the discourses of patients. If patients were therefore not directly asked whether they think the informed consent process was there to protect their human rights, it can be concluded that the informed consent process is not valid.

The patients did not answer that it was, the meaning of this may not be clear since only one question was asked. After the review of the work with your comments

I was aware that the weight of this assumption may not be… real?
3. Patients' and Doctors' Questionnaires: Present data more clearly. Suggestion: 3 columns: questions, answers, and response rates. Please give responses as absolute values and percentages.

Suggestion accepted,

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Conclusion: It would be worthwhile to consider including alternative suggestions to the current informed consent process in the conclusion, rather than just saying it is not a panacea.

Changes were made

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Discretionary Revisions (which the author can choose to ignore)

Reconsider the title to include the question of validity of the process. The term "consenting" a patient, is also not widely acceptable, but can be used for effect - such as a "catchy" phrase.

That was the idea.. Do you have another suggestion?

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.