PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Informed Consent, Shared-Decision Making and a Reasonable Patient's Wishes Based on a Cross-sectional, National Survey in the United States Using a Hypothetical Scenario
AUTHORS	James, John T.; Eakins, Darwin; Scully, Robert

VERSION 1 – REVIEW

REVIEWER	Marilyn Hammer The Mount Sinai Hospital / Icahn School of Medicine at Mount Sinai, New York, USA
REVIEW RETURNED	21-Jan-2019

GENERAL COMMENTS	This is an important and well appreciated study. The following would strengthen this manuscript. 1. Please provide a definition for a "Reasonable Patient". 2. It is unclear why formal statistics were not conducted. When developing a survey, factor analyses are needed. Please analyze the data appropriately. 3. The link that was provided to view the questionnaire was not accessible with the log-on information provided. Please include the survey questions in the manuscript. 4. 43% is a good return rate for a survey; it's unclear why this was stated as poor. 5. A statistical analysis to compare surveyed groups is needed. 6. In the discussion section, please discuss other studies that have evaluated informed consent (e.g., Kraft, S. A., Cho, M. K., Constantine, M., Lee, S. S., Kelley, M., Korngiebel, D., . . . Magnus, D. (2016). A comparison of institutional review board professionals' and patients' views on consent for research on medical practices. Clin Trials. doi:10.1177/1740774516648907). Overall, this manuscript would be greatly strengthened with the conduction of factor analyses, more formal descriptive statistics, and a more in-depth discussion section with comparisons to other instruments that have evaluated informed consent and ethics.

REVIEWER	Lise Aagaard Havemann Law Ltd, Amaliegade 27, DK 1256 Copenhagen K
REVIEW RETURNED	22-Feb-2019

GENERAL COMMENTS	The aim of this manuscript was to discern the information needs of a hospitalized, "reasonable patient" during the informed-consent process. The topic is interesting and have been discussed previously in both legal and medical literature. The conclusions in the paper are based on data from a national US survey.

	Before publication some changes and improvements of the manuscript must be done. Introduction: In this section links to the different international human rights instruments must be added, including the reference: Aagaard L, Kristensen K. Off-label and unlicensed prescribing in Europe: implications for patients' informed consent and liability. Int J Clin Pharm. 2018 Jun;40(3):509-512. doi: 10.1007/s11096-018-0646-4. Methods: It is unclear whether statistical analysis were made. Results: Table 1: Were there any statistical significant differences between the two groups? Table 2 is very difficult to read. Could data be presented in a more proper manner? Figure 1 and 2: Could these data be presented in a table instead of? Discussion: Limitations: Could you have studied the objective by using other methods? Pros and cons? This section should also discuss the general limitations when using survey data, e.g. limited memory, missing data, etc. References: Direct references to relevant Court decisions should be added to the manuscript.

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1
Reviewer Name: Marilyn Hammer

Institution and Country: The Mount Sinai Hospital / Icahn School of Medicine at Mount Sinai, New York, USA

Please state any competing interests or state ‘None declared’: None declared.

Please leave your comments for the authors below
This is an important and well appreciated study. THANK YOU!
The following would strengthen this manuscript.
1. Please provide a definition for a “Reasonable Patient”.
At the end of the second paragraph in the introduction, pg 6, we have added a sentence pointing out that ‘reasonable patient’ has not been well defined, and it is the intent of our study to partially rectify that problem.
2. It is unclear why formal statistics were not conducted. When developing a survey, factor analyses are needed. Please analyze the data appropriately. Although the results of the study do not depend on formal statistical analysis, we have completed that and have added an author (Dr. Scully) to the

study because he performed that for us. He also performed factor analysis on the surveys. The analyses are summarized on ppg 14-16, and details are provided in the additional files.
3. The link that was provided to view the questionnaire was not accessible with the log-on information provided. We added a better link at the bottom of pg 4.
Please include the survey questions in the manuscript. The survey's hypothetical scenario and respondents' choices are in the methods section and the 10 questions are in table 2 of the results section. The two forms of the survey have been added to the 'additional files' in our re-submission. These should be readily accessible.
4. 43% is a good return rate for a survey; it's unclear why this was stated as poor. It was stated as 'low,' which is our opinion. In general, a response rate of at least 60% is desirable.
5. A statistical analysis to compare surveyed groups is needed. That is unnecessary to support our conclusions; however, detailed statistical analyses of our data has been completed and added as requested. Summaries on ppg 14-16 and details in 'additional files.'
6. In the discussion section, please discuss other studies that have evaluated informed consent (e.g., Kraft, S. A., Cho, M. K., Constantine, M., Lee, S. S., Kelley, M., Korngiebel, D., . . . Magnus, D. (2016). A comparison of institutional review board professionals' and patients' views on consent for research on medical practices. Clin Trials. doi:10.1177/1740774516648907).
In the introduction, we briefly mentioned a study (reference 6) showing that in the case of possible PCI, cardiac patients do not get complete information to make an informed decision. The study by Kraft, et. al (above) addresses the different views of researchers on IRBs and patients who participate in research studies. Kraft's study found important differences in the views of researchers and participants when it comes to how informed consent is pursued. However, the study does not directly apply to survey studies like ours that address a clinical setting rather than a research setting. The PCI study is a fine example of the difference between what patients should know and what is actually told to them when informed consent is undertaken in a clinical setting.

Overall, this manuscript would be greatly strengthened with the conduction of factor analyses, more formal descriptive statistics, and a more in-depth discussion section with comparisons to other instruments that have evaluated informed consent and ethics.
Factor analysis was performed on each of the surveys. Findings are reported on ppg 14-16, and details are in additional files.'
Descriptive statistics. Descriptive statistics have been added in summary in ppg 14-16 and 'paired test of proportions' to table 1 (pg 14) and to the 'discussion' section of the paper, ppg 16 1nd 17.
Informed consent and ethics. In methods we pointed out that our literature search was unable to identify any general survey like ours on informed consent. There were two focused studies (references 12 and 13) that surveyed patients' opinions in constrained situations – one evaluated anesthesia informed consent and another asked patient's impressions following surgery in a Jamaican hospital. We added a sentence about the results of the latter study where it is mentioned in the 'methods' section (pg 7). The new reference (8) describes the difficulty of meeting the ethical dimension of patient autonomy and the practical delivery of informed consent in a clinical setting. This is now reflected in the introduction (pg 6).

Reviewer: 2
Reviewer Name: Lise Aagaard

Institution and Country: Havemann Law Ltd, Amaliegade 27, DK 1256 Copenhagen K

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

The aim of this manuscript was to discern the information needs of a hospitalized, "reasonable patient" during the informed-consent process.

The topic is interesting and has been discussed previously in both legal and medical literature. The conclusions in the paper are based on data from a national US survey.

Before publication some changes and improvements of the manuscript must be done.

Introduction:
In this section links to the different international human rights instruments must be added, including the reference: Aagaard L, Kristensen K. Off-label and unlicensed prescribing in Europe: implications for patients' informed consent and liability. Int J Clin Pharm. 2018 Jun;40(3):509-512. doi: 10.1007/s11096-018-0646-4.
We addressed this issue by adding a paragraph at the beginning of the introduction (pg 5) that ties together information from the United Nations pertaining to human rights and the right of patients to know the risks and benefits of medical care (ref 1-3). We have added the Aagaard et. al. study to the introductory paragraph (ref 4).

Methods:
It is unclear whether statistical analyses were made. No formal statistical analyses were performed in our original paper because these were not necessary to achieve the goals of our study and the conclusion that reasonable patients consistently want more information than is imparted during informed consent. However, we have performed a more detailed statistical analysis), which is presented in the discussion section (summarized pg 14-16 and details in additional files).

Results:
Table 1: Were there any statistical significant differences between the two groups?
We performed a '2-sample test of proportions' on the data in table 1. We have added p values in a last column (pg 11).
Table 2 is very difficult to read. Could data be presented in a more proper manner?
We have added a verbal description of table 2 into the discussion to orient the reader to its contents (pg 12). we feel that the table, as is, allows the reader to get a complete overview of our results in one place. We have also added in bold red in the header, a phrase explaining the meaning of the bold red percentages in the columns.

Figure 1 and 2: Could these data be presented in a table instead of?
These provide a refreshing, visual overview of key demographic data as they pertain to participants' responses. We want to keep these figures.

Discussion:
Limitations: Could you have studied the objective by using other methods? Pros and cons? We do not see how anything other than a survey instrument could have addressed the broad scope of the intent of our study. The fact that the final survey was nationally based precludes any other practical approach to answering the question, 'what does a reasonable patient want?' Furthermore, it is only through a survey instrument such as ours, that two diverse groups (nurse students and HPESS) may be directly compared.

This section should also discuss the general limitations when using survey data, e.g. limited memory, missing data, etc. Our survey method relies only on the immediate response to each question in the context of the hypothetical scenario. There is no chance for memory limitations. We had very little missing data in the national and 'nurse student' groups. In the discussion, we speculate on why our

43% response rate in the 'HPESS' group was lower than we had hoped. Also, see additional thoughts on hypothetical surveys vs. surveys in the 'real world.'

References:
Direct references to relevant Court decisions should be added to the manuscript.
we have two references in our paper to pertinent court rulings as related to the reasonable patient, one of which was added in response to reviewer comments (ref 4 and 7). We have added a couple of paragraphs at the end of 'discussion' (ppg 18-19) outlining the history of informed consent in the U.S. as relevant rulings reflect on the questions in our survey. The review we cite (ref 19) contains direct references to the pertinent court decisions. Our plan is to engage lawyers in writing about the findings of the present study for a law journal. It is unlikely that lawyers will read a study published in BMJ Open. Would you like to partner with us Dr. Aagaard in creating such a paper?

VERSION 2 – REVIEW

REVIEWER	Marilyn Hammer Mount Sinai, USA
REVIEW RETURNED	22-Apr-2019

GENERAL COMMENTS	Although the authors addressed most of the major concerns from the original submission, there continue to be areas that need to be addressed, as follows: 1. It is appreciated that the vagueness of "reasonable patients" was addressed, however, the term "reasonable clinicians" was not addressed. It is recommended to either explain this in the background or just use the term clinicians. 2. On page 5, line 42, please change "…based on PubMed citations…" to "…based on the peer-reviewed literature…." 3. Page 39, line 5/6 – the use of the term "additional files" is unusual. Please use the terminology of "supplemental material" and remove the quotes. Please also provide this supplemental material for review. 4. The added material on the history of informed consent and court cases would be more appropriately placed in the background. Please provide citations. 5. Having students in a class complete a survey for research could be considered coercive. Please explain how they were informed about the survey and if they were given a choice to complete it. Please include this sample bias as a limitation. 6. Limiting survey questions for response burden considerations is only appropriate if the study questions can adequately be answered. The notation that this would be inadequate for actual patients diminishes the significance / clinically meaningful applicability of this study. Please clarify this.

REVIEWER	Lise Aagaard Havemann Law Firm Ltd.
REVIEW RETURNED	24-Apr-2019

GENERAL COMMENTS	The authors' have revised the manuscript according to previous review comments. It would be a pleasure to work together with the authors on a new article for a law journal.

VERSION 2 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Marilyn Hammer

Institution and Country: Mount Sinai, USA

Please state any competing interests or state 'None declared': None declared. As above.

Please leave your comments for the authors below

Although the authors addressed most of the major concerns from the original submission, there continue to be areas that need to be addressed, as follows:

1. It is appreciated that the vagueness of "reasonable patients" was addressed, however, the term "reasonable clinicians" was not addressed. It is recommended to either explain this in the background or just use the term clinicians. In our opinion, 'reasonable clinician' will be understood by readers as the average amount of disclosure a typical clinician would give the patient. In the end, this concept varies and is also vague, but is clearly distinct from the wishes of a 'reasonable patient."

2. On page 5, line 42, please change "…based on PubMed citations…" to "…based on the peer-reviewed literature…." I did the suggested change.

3. Page 39, line 5/6 – the use of the term "additional files" is unusual. Please use the terminology of "supplemental material" and remove the quotes. Please also provide this supplemental material for review. Wording was changed as suggested, and 'supplemental files' are now accessible by reviewers and carefully numbered, corresponding to numbers in the text.

4. The added material on the history of informed consent and court cases would be more appropriately placed in the background. Please provide citations. I'm unclear what is specifically indicated by 'background." In our opinion, such material is appropriately placed in the discussion section of the paper with some portion in the introduction to create interest in the reader without excessively drenching her in details. As indicated in responses to Reviewer 2's original suggestions, we cited a review paper on court decisions. Please also note that Reviewer 2 has indicated interest in adapting our findings for publication in a legal journal where a more thorough discussion would be appropriate.

5. Having students in a class complete a survey for research could be considered coercive. Please explain how they were informed about the survey and if they were given a choice to complete it. Please include this sample bias as a limitation. The students attended an invited lecture by Dr. James that had nothing to do with the student's class work. There was absolutely no coercion, nor any mechanism by which they could be coerced; therefore, there is no need to consider this as a limitation. I have clarified this on page 8.

6. Limiting survey questions for response burden considerations is only appropriate if the study questions can adequately be answered. The notation that this would be inadequate for actual patients diminishes the significance / clinically meaningful applicability of this study. Please clarify this. As best I understand this comment, it is referring to the added part on page 20 dealing with the limitations of surveys relative to the real clinical world. We never indicated that our study questions cannot be adequately answered, only that a frightened patient may not be aware that they should be asked and fully answered. Some questions may be difficult for the clinician to answer, but as we indicated in 'limitations,' clinicians can get support for the answers requested by a reasonable patient. One purpose of our study was to impel clinicians to be prepared to answer all our reasonable questions as part of shared-decision making. Are they fully prepared now? No. Can they get prepared? Yes, if they are sharing decisions with an empowered and wise patient.

Reviewer: 2

Reviewer Name: Lise Aagaard

Institution and Country: Havemann Law Firm Ltd.

Please state any competing interests or state 'None declared': None. I have now done this on page 4 of the submission, explaining why there are no competing interests beyond improving patient safety.

Please leave your comments for the authors below

The authors' have revised the manuscript according to previous review comments.

It would be a pleasure to work together with the authors on a new article for a law journal. I'll contact you via email to get the ball rolling. I'd like to add a respected U.S. lawyer with expertise in informed consent and possibly a clinician with similar expertise. I have a clinician in mind, do you know of such a lawyer in the States?

VERSION 3 – REVIEW

REVIEWER	Marilyn Hammer Mount Sinai, USA
REVIEW RETURNED	09-Jun-2019

GENERAL COMMENTS	The overall premise of this study to better define a "reasonable person" in the context of informed consent is important and significant. The use of a large, heterogeneous sample and conducting factor analyses to establish validity and reliability with a newly developed questionnaire are commendable. However, there are a number of challenges with how this manuscript is written.

	Addressing these concerns would strengthen this manuscript tremendously. 1. The study design is mislabeled ("survey" is not a study design) – this was a cross-sectional study to develop an instrument and better define the term “reasonable person” in relation to informed consent. 2. It is inappropriate to insert opinions in the background section 3. The background lacks the needed discussions related to the protection of human subjects (e.g., the tenets of medical ethics, the Belmont Report) 4. Many statements are lacking citations and have opinions inserted instead (e.g., pg 12, lines 15-18, “….because it is likely lay readers will understand this more readily….”). If this is important, cite research studies that have evaluated average reading levels. It is also unclear why the authors are focused on having lay readers evaluate the results of this study. 5. All descriptions of the methods and analyses belong in the methods section. 6. Only state the findings in the results section; avoid inserting opinions here. Opinions and comparisons of findings to other studies belong in the discussion section. 7. Using the direct statistical output from the software program instead of putting it into manuscript-ready tables is inappropriate. 8. One of the objectives of this manuscript was to better define a “reasonable person”, yet setting parameters to define a “reasonable person” based on findings were not included. Overall, the manuscript as written does not present as an expected scholarly document with the exception of the statistical material, likely written by a statistician. It is recommended that the authors seek the support of a professional healthcare editor to put this manuscript into proper format with a more professional writing style.

VERSION 3 – AUTHOR RESPONSE

>Thank you very much for your email in regards to your manuscript under consideration at BMJ Open. We do appreciate that the last decision email would have been frustrating given the extensive work that you have already done on your manuscript. We were also disappointed that the reviewer had identified additional revisions that were required, but we felt that the suggestions would improve the paper.
>
>However, we appreciate your position and we agree that not all of the suggestions are necessary at this stage. That said, we do feel that some additional revisions are required before we can accept your paper, and so we’d be grateful if you could respond to the following points:
>
>“1. The study design is mislabeled ("survey" is not a study design) – this was a cross-sectional study

to develop an instrument and better define the term “reasonable person” in relation to informed consent.” I'VE CHANGED THE STUDY 'DESIGN' DESCRIPTION IN THE ABSTRACT TO REFLECT THIS SUGGESTION AND ADDED TO THE STUDY TITLE. PAGE 2.
>
>We agree with the reviewer that the study design can be better defined in both the title and the abstract.
>
>“7. Using the direct statistical output from the software program instead of putting it into manuscript-ready tables is inappropriate.”
>
>We agree that the supplementary analysis would be better presented in tables, but we appreciate that changing this requires a lot of work and so we leave this to your discretion.I APPRECIATE THAT YOU MADE THIS OPTIONAL. IN THE INTEREST OF GETTING THIS PUBLISHED AND MY VERY LIMITED TIME, I ASK THAT YOU GO AHEAD WITH THE STATISTICAL OUTPUT AS RECEIVED.

>In addition, please respond to the following editorial points copied from the decision email. We appreciate that further revisions should not be required at this stage, but we do feel that these changes are important:
>
>- Unfortunately, the first paragraph of the patient and public involvement section is not appropriate for this section. We require that this section of the manuscript refers specifically and only to patients and the public and so we would be grateful if you could change the title back to “Patient and public involvement” and remove the first paragraph. We are happy for you to move this paragraph to elsewhere in the methods section if you feel that this is appropriate. Please be aware that this is a mandatory editorial request and so we will not be able to proceed until it has been done. I DELETED ANY REFERENCE TO 'PROVIDERS' IN THE SECTION AND RETITLED IT TO 'PATIENT AND PUBLIC INVOLVEMENT.' SOME PARTS OF THE FIRST PARAGRAPH WERE RETAINED BECAUSE THEY MADE REFERENCE TO PATIENT ADVOCATES AS THE SOURCE OF THE STUDY. WE FEEL THIS IS IMPORTANT FOR THE READER TO KNOW. I ALSO MODIFIED THE NEXT PARAGRAPH BECAUSE SOME OPPORTUNITIES DESCRIBED THERE FOR DISSEMINATION OF OUR RESULTS HAVE EXPIRED. PAGES 9-10.
>
>- Please ensure that you have provided the information in the methods section relevant to point 6 in the STROBE checklist to fully describe how the participants were recruited. I ADDED INFORMATION AS NECESSARY TO DESCRIBE THE MEANS OF RECRUITMENT OF PARTICIPANTS FOR EACH OF THE 3 STUDY POPULATIONS. PAGE 8.
>
>- Please also ensure that you have fully discussed the issue of selection bias as highlighted by reviewer 1 in the previous round of review. Could selection bias, from the method of recruitment, have affected the results? If so, please ensure that this is discussed as a limitation in the discussion section. I HAVE ADDED A PARAGRAPH TO 'LIMITATIONS' DESCRIBING POTENTIAL SELECTION BIAS BECAUSE OF HOW PARTICIPANTS WERE RECRUITED. THIS WAS AN ESPECIALLY IMPORTANT SUGGESTION BECAUSE IT FORCED ME TO DETERMINE HOW MANY AMERICANS CANNOT READ. I WAS ASTONISHED TO FIND THAT 32 MILLION COULD NOT READ. FINALLY, I NOTE THAT THE CONSISTENCY OF THE FINDINGS BETWEEN GROUPS SUGGESTS THAT MINIMAL BIAS IS PRESENT FOR THOSE WITH ELECTRONIC ACCESS TO THE SURVEY AND CAN READ ENGLISH. PAGE 20 (ALSO ADDED TO LIMITATIONS SUMMARY, PG 4)