Author's response to reviews

Title: Factors associated with the designation of a health care proxy and writing advance directives for patients suffering from haematological malignancies

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Author's response to reviews: see over
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Authors' response to reviews: see over
Thank you for considering our manuscript for publication in your journal. We are grateful for your interest in our work and for the opportunity to resubmit our manuscript.

We have reviewed the above manuscript, point by point, according to your reviewers’ comments. All the revisions are written in italic and blue.

On the advice of our language editor and Reviewer 2 we have modified the title of the manuscript and changed “health care representative” to “health care proxy” and “malignant haemopathies” to “haematological malignancies”, throughout the manuscript.

Reviewer 1 (C. Schulz)

Major compulsory revisions

1. The Quality of written English is not suitable for publication at this stage.
   • Done: the article has been reviewed by a language editor.

2. I found it hard to understand parts of your manuscript.
   • We have made several changes to the language of the previous version and have changed the headings and subheadings to facilitate the reading of the manuscript.

3. Methodology:
   a. There is no mentioning of "mixed-methods" in your methods section, neither in terms of methodological considerations, nor on pitfalls and potential problems with such an approach.
   • We have now further developed the mixed-methods approach in the Methods section “We used a mixed-methods approach to collect the data and combine the quantitative and qualitative methods to integrate the various relevant perspectives to study HCP and ADs.” We also discuss the potential limitations of the method in the limitations paragraph: “Furthermore, similar to other mixed-method studies, the qualitative and quantitative approaches took place in a sequential order thus limiting the integration of both data forms under a unified process of data analysis. However, the mixed-method approach is highly relevant when dealing with current public health issues which typically cover multiple disciplines. It allows researchers to combine the strengths of qualitative and quantitative methodologies and can reveal which variables are related, the predictive nature of one variable over another and the characteristics of this predictive relation.”

   b. Description qualitative methodology. Please explain which concrete steps of analysis you have undertaken, how you developed your categories, etc.
   • We have added in the abstract that “A thematic analysis of the advance directives was performed by two researchers.” Furthermore, we now explain the analytical steps under subheadings in the Methods:
“Qualitative analysis
Data collection
Qualitative data was collected from written ADs available in the patient information form.

Data analysis
The aim of qualitative analysis was not to be exhaustive but rather to provide an overall understanding. All data were collected from the patients’ medical records and listed on a spreadsheet. No specific qualitative data analysis software was used. Data was analysed according to qualitative content analysis as introduced by Paillet et Mucchielli [18]. More specifically, we performed a thematic analysis of the content of the ADs after identifying the main messages and keywords and assessing recurrence.

The analytical process was conducted by a multidisciplinary research team consisting of a senior haematologist and a clinical research engineer trained in qualitative research, medical law and clinical ethics. Initially, both researchers read the six ADs independently to familiarize themselves with the data. Then they independently analysed each AD and coded data according to the rules. Codes were subsequently compared, contrasted, and grounded in data before being abstracted to related categories. During the analysis there was an ongoing discussion of emerging themes and keywords, and variance of interpretation in the study was resolved through communicative validation.”

4. In your introduction, please try to establish in more explicit terms why your research question and study is relevant to a palliative care audience.
   • We have modified the abstract accordingly: “During the last few decades, patients’ rights have been reinforced in many countries by acts of law. Measures now include health care proxies to uphold the doctor-patient relationship and advance directives for end-of-life patients. These could be relevant tools as early as the initial diagnosis of haematological malignancies because of the uncertain disease course.”

Minor essential revisions

5. Please clarify how the data abstraction process was performed.
   • We have further developed the sample selection as required: “Two hundred medical records of patients presenting with an HM and treated in the Haematological Unit of a University Hospital (Limoges, France) from June 1, 2008 to April 30, 2012 were randomly drawn. Data was extracted by a clinical research engineer using an abstraction protocol to perform a retrospective descriptive quantitative analysis [17]. Demographic and study data were collected from a specific document called the “patient information form”, which is completed by all patients on their first visit to the centre and kept in their medical records. (…) Any medical record without this patient information form filled in by the patient or his legal representative was not retained for analysis. Study data included: whether an HCP had been designated, whether an AD had been written and was available, mention of a wish to meet a religious representative or a volunteer. The survival data of the patients was updated on July 5, 2013.”

   • We have added the article cited by the reviewer in the references: “17. Gearing RE, Mian IA, Barber J, Ickowicz A: A methodology for conducting retrospective
6. You mention "fear of death" as an underlying cause for the low number of dedicated ADs in your cohort. Although this seems to be a highly interesting point from a psychological and existential philosophical perspective, you do not substantiate your claim and give no references pointing at the relevant body of literature around this topic.

- We have now developed the notion of "fear of death" as suggested: “The Terror Management theory argues that human understanding of mortality creates an existential anxiety that must be kept under constant control. Defences are erected to keep thoughts about death as far removed from the consciousness as possible[42, 43].”


Referee 2 (J. Gaertner)

General comments

1. a. The research question as conveyed in the title is relatively concise. Further on (abstract, ll 29-31) this question is much broader: “The aim of this research was to assess the appropriation of health care representatives and advance directives by the patients in a clinical hematology department.

- We have taken into account your remark and corrected this point in the abstract: “The aim of this research was to assess the factors associated with the designation of a proxy and the writing of advance directives by patients in an haematology department.” and in the background “The main goal of this study was to assess the factors associated with the designation of HCP and the writing of ADs by patients presenting with HM both quantitatively (how many patients) and qualitatively (content of ADs).

b. Then, throughout the manuscript I found it hard to follow the main scope of the document. I became confused which findings the authors really considered relevant and what messages they want to convey at the most. This perception steadily increased when reading the different sections of the manuscript until the „conclusion“paragraph. For example, though I strongly agree with the authors statements in the „conclusion“, these cannot be supported by findings of the study. For example: „A true appropriation of HCR and ADs requires time and accompaniment“. Or: „These two tools are a potential ground for starting up a dialogue and listening space with the patient“ Or: „More than just the formality of writing, potentially awkward for part of the population, oral communication with carers about wishes discussed with relatives represents an occasion to build up a good doctor/patient relationship.“ I share the authors´ opinion and underlying attitude, but from the scientific point of view, the statements are out of place in the conclusion section for this study. Much more compelling and clearly relevant is he following statement from ll 341-343: The findings of our study emphasize that, despite an advance care planning
program to assist the patients, and training of the caregivers, few people chose to write down ADs.

- We understand the point that the reviewer is making here and have modified the manuscript to bring the key messages into clearer focus.
- We have developed how advance care planning could affect the designation of health care proxy and writing of advance directives.
- We have reworked the headings and subheadings and the conclusion: “The findings of our study highlight that, despite an advance care planning programme to assist patients and the training of caregivers, few people choose to write ADs. Accompanying a patient through the process of designating an HCP and writing ADs requires time and allocation of support personnel. Both tools are a potential opportunity for starting up a much needed dialogue with a patient facing a life-threatening disease. The fact that only a few patients presenting with severe HM write ADs, would indicate that the need remains to be better defined by French patients. Furthermore, as some patients could find the formal approach of writing difficult, informal oral communication about wishes with carers and relatives should also be encouraged as it represents an opportunity to develop a good doctor/patient relationship.

2. In different sections, the authors write that they have identified “predictive factors for...” I suggest careful reassessment of these statements. Due to the retrospective nature and the inevitable sources of bias of this study wouldn’t it be better to say that these factors “were associated with...”?

- Done: we have modified these statements: L.44 “Patients who wrote an advance directive were more likely to have expressed a wish to meet a religious representative (p<0.001) or a volunteer (p=0.003).”
- “The main findings of this mixed method approach to better understand which factors influence patients with an HM in using end-of-life tools (…)”
- L.52 / 184 and in the Tables "predictive factor(s)" has been replaced by "factor(s) associated with ...."

3. The discussion section starts with the limitations of the study. Better move this downward to the end of the section.

- We have now moved the limitations of the study towards the end of the Discussion section.

4. The manuscript is far too long for the amount of relevant information provided. Strongly consider substantial shortening of the manuscript. Suggestion for general improvement. Yet, before publication, I strongly suggest the authors should have a critical look at the main scope of their findings and focus on these. To me, even the sole provision of the information that despite the implementation of the advance care program only few people wrote ADs is clearly relevant and worthwhile sharing. Substantial shortening and sharpening of the manuscript may be painful for the authors, since may feel like wasting large amounts of information gathered. In this case, it could be an option to intensify the valuable qualitative analyses and publish this separately.

- We examined your advice carefully and considered substantial shortening of the manuscript as you suggest. However, we have decided to keep the research as a whole. Very few articles are available on health care proxies and advance directives in France. Despite the bias mentioned in the manuscript, the results of the research and discussion are valuable at a national and at an international level. However, we have improved readability by adding subtitles to focus on the main key messages.

**Suggestion for general improvement**
Specific comments and suggestions for improvement

1. The writing requires thorough revision
   - The manuscript has been reviewed by a language editor.

2. Some sentences could be a little more unobtrusive: i.e. LL 29: “Patient’s rights have been reinforced in all countries by acts of law” (All countries, are you really sure? Maybe many would suffice).
   - We have changed “all” to “many”

3. Formatting has to be improved. Headings and subheadings are difficult to distinguish since both are formatted equally.
   - We have now formatted the subheadings by writing them in large, blue, italic font.

4. Formatting and presentation of tables could be improved, tables 2 and 5 are unacceptable. Also, be consistent with the number of decimals when reporting ratios. One (at the most) is enough, but then provide it in the other ratios as well. i.e.: Twelve patients (75%) wished to meet a religious representative and 6 (66.7%) a volunteer.
   - We have modified all the tables accordingly and standardized the number of decimals.

5. Please be consistent with capitalizations in (sub-) headings (i.e. Sample Selection vs Statistical analysis)
   - We have corrected the inconsistencies in capitalization.

6. Please revise the number of decimals, especially in the confidence intervals, percentages and ratios. (e.g. p=0.0000025)
   - We have now standardized the presentation of the numbers and revised the decimals.

7. Please be consistent in the writing of numbers <10. Sometime you write “six”, next line “6”. Writing out numbers below 10 would be best
   - All numbers below 10 are now written in full (except for reference to time, e.g. “2-year survival”).

8. Examples of syntax/wording that sounded odd (to me) or that I found hard to follow:
   a) I demand for my life not to be prolonged
      - Done: “I request that my life is not prolonged”
   b) obstinacy...?? (important as this is used very often!)
      - Done: We have replaced « unreasonable therapeutic obstinacy » by “life-sustaining care”.
   c) precocity
      - Done: We rewritten the sentence: “The fact that ADs were written after diagnosis could suggest that the wishes expressed are more the consequence of the patient’s personal experience rather than a reaction when faced with imminent death.”
   d) accompaniment. (isn’t this a term from orchestral music?)
• Done: we have removed this word and rewritten the sentence:
“Accompanying a patient through the process of designating an HCP and writing an AD requires time and allocation of support personnel.”
e) Informal ADs, done orally,
• Done: We replace « Informal ADs, done orally » by “Informal oral ADs”
f) partnered (to the patient?)
• We have changed partnered by “Married or with a partner” We wanted to distinguish between the patients who were married and others who lived in couple.
g) Pathology group
• We have changed “pathology group” to “pathologies”.
h) Awkward and far too long (beware of length of many sentences): “To the best of our knowledge, no such experience has been reported in haematology, even though the prognostic is often severe due to the risks of death along the clinical pathway for patients suffering from an advanced disease, the risk of sudden death during induction therapy or secondary to septic shock or later in palliative care for refractory disease.”
• We have modified this sentence by: “To the best of our knowledge, no such studies have been conducted in the context of haematological malignancies (HM). These diseases have a particularly poor prognosis and the risk of dying remains in the foreground throughout the clinical pathway. Moreover, septic shock or sudden bleeding can occur during induction therapy or in advanced stage disease. It is thus logical to introduce the concepts of HCP and AD to a patient in this setting.”
• l.142/145, we have also reworked the following sentence: “For this study, HCP was defined in accordance with French regulations as a person chosen by the patient for two types of missions: first, to support him/her throughout the healthcare pathway and in making decisions and second, to speak on his/her behalf for future healthcare decisions in case the patient is unable to express wishes him/herself. The HCP can never make a decision in place of the patient.”
i) Institute advance directives (ADs) (reviewer: institute correct in this context?)
• We have removed the word “institute”.
j) “In France, the implementation of health care representatives and advance directives is still very random.”
• We have now removed this sentence from the introduction and developed further why our research is relevant to palliative care (re comments of first reviewer).
k) Health care representative
• After reading several articles, we have changed “Heath care representative” to “heath care proxy”.
l) “Reports and publications show an insufficient appropriation, both for carers and the general public depends on pathologies and culture.”
• “various publications [11–13] report insufficient uptake both by carers and the general public.”
m) “Appropriation”: carefully reassess the correct use in each of the many sentence where you use it.

- Done, we now use “designation” (1.75) as advised and “allocation” (1.82).

n) “the grounded theory” (isn’t “grounded theory” enough?)

- Reference to “grounded theory” has now been removed as advised by the first reviewer.

o) Only few patient… “wrote advance directives because of their fear of death.” (? Because they felt uncomfortable with the subject or were afraid of dying when writing an AD?)

- We have now removed reference to the fear of death in the abstract (because of word count) and further developed it in the manuscript.

p) After dedicated interventions to encourage discussions about end of life preferences, 200 patients’ medical records were selected at random and a quantitative retrospective analysis was performed, crossed with a qualitative analysis of the content of 34 advance directives. (This is from the abstract, but also in the methods section I did not quite understand the “dedicated interventions” (and wouldn’t be the better term be “specific” anyway?).

- We have changed “dedicated” to “specific” and have further described the advance care planning program to which we were referring.

9. Be consistent also with acronyms (e.g. US or USA or United States?)

- We have standardized the acronyms and chosen “US”.

10. I am not a native speaker and not a gender-expert at all, but a careful look (by an English speaking scientist at the correct use of “gender” and “sex” may be indicated, but I am not sure about it.

- We have replaced “sex” by “gender”.

11. “Comma” and “full stop” get messed up in numbers (sometimes French, sometimes English)

- We have corrected and standardized the presentation of numbers.

12. British and American English is used inconsistently (i.e. haematology and hematology)

- We have now standardized the wording and use British English throughout the manuscript (“haematology”). We have chosen key words in accordance with MeSH headings: “Haematology, Advance directives, Proxy, Ethics, Health communication, Spirituality.”

Referee 3 (R. Aubry)

Discretionary revisions or explicitations

1. Method
   a. Concerning the methodology, the authors could maybe specify how the random selection was made and how the retrospective descriptive quantitative analysis was performed.

   - We have modified the abstract as follows: “After a specific programme to encourage discussions about end-of-life preferences, we used a mixed-methods approach. We conducted a retrospective study of a random sample of 200 patients’
medical records, crossed with a qualitative analysis of the content of advance directives.”

- We have also further developed the sample selection as advised: “Two hundred medical records of patients presenting with an HM and treated in the Haematological Unit of a University Hospital (Limoges, France) from June 1, 2008 to April 30, 2012 were randomly drawn. Data was extracted by a clinical research engineer using an abstraction protocol to perform a retrospective descriptive quantitative analysis [17]. Demographic and study data were collected from a specific document called the “patient information form”, which is completed by all patients on their first visit to the centre and kept in their medical records. (...) Any medical record without this patient information form filled in by the patient or his legal representative was not retained for analysis. Study data included: whether an HCP had been designated, whether an AD had been written and was available, mention of a wish to meet a religious representative or a volunteer. The survival data of the patients was updated on July 5, 2013.”

b. Concerning the qualitative sector, the authors could specify if the analysis of verbatim was the fact of one or several researchers.

- We have accordingly completed the abstract: “A thematic analysis of the advance directives was performed by two researchers.”

- The qualitative method section has been detailed too:

  “Qualitative analysis

  Data collection
  Qualitative data was collected from written ADs available in the patient information form.

  Data analysis
  The aim of the qualitative analysis was not to be exhaustive but rather to provide an overall understanding. All the data were listed on a spreadsheet. No specific qualitative data analysis software was used. The data were analysed according to qualitative content analysis as introduced by Paillet et Mucchielli [18]. More specifically, we performed a thematic analysis of the content of the ADs after identifying the main messages and keywords and assessing recurrence.
  The analytical process was conducted by a multidisciplinary research team consisting of a senior haematologist and a clinical research engineer trained in qualitative research, medical law and clinical ethics. Initially, both researchers read the six ADs independently to familiarize themselves with the data. Then they independently analysed each AD and coded data according to the rules. Codes were subsequently compared, contrasted, and grounded in data before being abstracted to related categories. During the analysis there was an ongoing discussion of emerging themes and keywords, and variance of interpretation in the study was resolved through communicative validation.”

2. Results: Concerning the designation of a health care representative while in the abstract the authors write that 8.1% and 4.6% wished to meet a religious representative or a 41 volunteer, respectively, in this chapter it is written that: twelve patients (75%) wished to meet a religious representative and 6 (66.7%) a volunteer.

- We see your point. The figures presented in the abstract and in the results were not sufficiently explained. These numbers are different because they refer to different populations: those in the abstract are related to the total sample (16/197 patients want to meet a religious representative (8.1%) and 9/197 a volunteer (4.6%)); and
those in the results are related to the sample of the patients who designated a health care proxy (12/127 patients want to meet a religious representative (75%) and 6/127 a volunteer (66.7%).

- We have now clarified this point in the results:
  “Description of the sample of patients who designated a health care proxy

Quantitative content analysis

Among the 197 evaluable medical records, 127 patients designated an HCP (64.5%). The characteristics of these patients are summarized in Table 3. The average age was 64.8±14.2 [range: 23; 91]. The gender ratio was 1.27. Among them, only 12 patients (75.0%) wished to meet a religious representative and six (66.7%) a volunteer.”