Author’s response to reviews

Title: Advance directives as a tool to respect patients' values and preferences. Discussion on the case of Alzheimer's disease.

Authors:

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Version: 1 Date: 24 Jul 2017

Author’s response to reviews:

Dear Editor,

I am submitting the revised version of my manuscript that is now entitled “Advance directives as a tool to respect patients’ values and preferences. Discussion on the case of Alzheimer’s disease”.

Revisions in the text are in bold. Sentences slightly moved are in italic.

I would like to thanks you and the three reviewers for reading and commenting the work.

I hope the work will now be suitable for publication.

Best regards,

Corinna Porteri

Brescia, 24.7.2017

EDITOR COMMENTS:

1. Competing interests

Please include a statement to say that you are an Associate Editor with BMC Medical Ethics.

I included the statement.
2. Please ensure no supplementary files are attached with your revision. The Response to reviewers should appear in the relevant section on the submission system.

I did.

REVIEWER REPORTS:

Esther Lee Marcus (Reviewer 1):

I have some comments and suggestions that may enrich this discussion.

In the Background section the author presents an excellent brief summary on the change in diagnostic criteria for Alzheimer's disease and early diagnosis at the mild cognitive impairment (MCI) or predementia/prodromal stage, including the role of various biomarkers. Apart from the issue of the role and appropriateness of advanced directives in the early stages of Alzheimer's disease, a related medical ethical issue is the potential effects of diagnosis disclosure on the patient. For example, in a review article titled "To know or not to know: ethical issues related to early diagnosis of Alzheimer's disease (Mattsson et al. International Journal of Alzheimer's Disease 2016;Article ID 841941) the authors discuss the various aspects of this issue ""A test result indicating AD may bring extended followup and stigmatization resulting in feelings of hopelessness, agony, and despair" (Page 2). The diagnosis can cause depression, and maybe an increased risk of suicide. (Although the link between increased risk of suicide and the stigma of diagnosis is not clear). The article mentioned above also addresses the issue of advanced directive and can be added to the reference list. Another excellent review of this subject is the article by Gauthier S et al "Diagnosis and management of Alzheimer's disease: past, present and future " (Progress in Neurobiology 2013;110:102-113): "Those arguing against the practice of disclosure also evoked the potential for adverse psychological reactions, including anxiety, depression (Maguire et al., 1996), and catastrophic thinking (Thompson et al., 1990). Suicidal ideation (Rubin and Kinscherf, 1989 ; Draper et al., 1998) as well as suicide (Markle, 1993; Frierson, 1991 ; Draper et al., 1998) were also cited as concerns, though a growing body of evidence suggested that comorbid depression, as opposed to AD, was the driving factor in the case of reported suicides (Rohde et al., 1995). Moreover, despite the association between the transmission of diagnostic information—and consequent "confrontation with cognitive deficits" (Meyers, 1997)—and depression, the claim was made that the argument for long-term psychological sequelae was empirically unfounded with the risk of lasting psychological damage mitigated by the use of psychological defense mechanisms—including externalization, displacement, and somatization (Bahro et al., 1995)—and neuropsychological deficits in the form of anosognosia (Michon et al., 1994)". I think that the author should refer to this issues in the Background section since diagnosis disclosure is the first step before considering advance directive in this population." (Page 104).
I agree that the disclosure of the diagnosis is a key ethical issue when discussing the use of biomarkers in AD and comes before any consideration regarding the offer to execute an advance directive. Although I did not elaborate the subject in depth not to lose the focus of the article, I have now included a reference to the topic in the background section and added the suggested papers (p.3 lines 15-19).

Another issue is the statements about the value of biomarkers in early diagnosis. The author should emphasize more the limitations of those biomarkers and the predictive role of MCI and that there is still a possibility of an erroneous test as discussed by Mattsson et al "However, even a test with ad diagnostic accuracy of 90% results in a large number of misdiagnosed persons if the disease prevalence is 50%, which is the typical prevalence of AD in MIC cohorts"(page 2).

This is in fact another topic of paramount importance: I stressed the fact that biomarkers are not yet validated for the use in clinical practice and I recalled the concept of uncertainty of the diagnosis (on which my colleagues and I have also written extensively in other papers) (p.3 lines 14-19).

Regarding the issue of personhood in dementia (Pages 4-6, the argument of personal identity) I would add referring to the reports in the literature about people with advanced dementia who respond to music, and are able to use artistic and creative skills (For example: Crutch and Rossor "Artistic changes in Alzheimer's disease" International Review of Neurobiology 2006;74: 147).

These are interesting reports which may add insight into the issue of personhood: I added a reference to the topic in the section on personal identity (p. 6 lines 6-8).

In " Ethics of the Fathers 2:4 it is claimed "Do not judge your fellow until you have stood in his place". In the case of a patient with dementia one may claim: do not judge yourself until you have stood in your place when you suffer from dementia. On page 8 the author claims "On the contrary, although the disease may appear in slightly different ways and time of progression in different patients, AD has a quite well known course that can be communicated to the patients". Although the course can be communicated to the patient, we do not really know what are the feelings and emotions of people in advance dementia, do they suffer, and as a consequence it is difficult for a patient with pre-dementia or mild dementia to know and anticipate what he/she will want when they are in advanced stage of dementia. (See discussion about that gap of knowledge about the feelings and what is the live experience of being in advance dementia in an article we recently published  (Marcus EL et al. Ethical issues related to end of life treatment in advanced dementia: The case of artificial nutrition and hydration. Diametros 2016; 50: 118-137).
This is an important issue: I included a reference to the argument in the section “Advanced directives are especially advisable in dementia” (p.9 lines 10-13).

On page 15 the author suggests "Nevertheless, as we have argued, current interests should not override the indication of a clear and not too broad advance directives, and the values of others should not prevail over the patient's values, as they do not prevail in the case of a competent person”. However in the Abstract and also in the text the author supports advanced directives that contain the appointment of an attorney. It has been shown that surrogate decision-making is complex and in many times reflects the attitude and opinion of the attorney and not the wishes and attitudes of the person. I think that the author should clarify this issue further.

I made clearer in the paper that I am supporting an advanced directive that includes both decisions regarding health care and the appointment of an attorney. I recognized that there are data showing that surrogates’ judgements about patients’ preferences both in the clinical (Shalowitz 2006) and research setting (Ciroli 2007) are often discordant. Nevertheless, I regard as reasonable, although evidence is lacking, that those data could be corrected by prior written and not too broad communication of preferences by the patients themselves. I made this explicit in the paper (p.10 line 16; p. 11 lines 13-17).

Page 12, line 17 "May wish to terminate life-saving treatments including nutrition and hydration”. Do you mean artificial nutrition and hydration? or even oral feeding?

Yes, I meant artificial nutrition and hydration: I corrected the point (p. 14 line 1).

Another issue that may be discussed in barriers to implementation of advanced directives. In the article by Spoelhof and Elliot (Implementing advance directives in office practice (American Family Physician 2012;85:461) the authors discuss barriers to implementation of advanced directives. Among those barriers are: health literacy (which may be more prevalent among patients with pre-dementia or early stages of dementia), difficulties in understanding end-of-life terminology and spiritual, cultural and racial traditions. I think that the author should refer to these barriers, in brief, with emphasize on specific issues relating to patients with AD.

As suggested, I included in the paragraph related to the “Difficulties of implementation of advance directives in dementia” the discussion of other important barriers related to the individual with dementia (p. 16 lines 8-17).
To the general discussion about the role of advanced directives in Alzheimer’s disease I would suggest that the author can refer also to the article by Burla et al. "Alzheimer, dementia and the living will: a proposal (Med Health Care and Philos 2014;17:389-395).

I included a reference to the suggested paper in the background section (p.4 lines 13-14).

Another issue related to advanced directives in general in in dementia patients specifically is that patients change their mind with time. Jongsma et al in their article "The implausibility of response shifts in dementia patients (J Med Ethics 2015) discuss the differences in wishes of dementia patients that do not conform or contradict earlier expressed preferences. This may lead us to sometimes disregard prior preferences even when expressed in advance directives. The authors (Jongsma et al) argue that because of the loss of cognitive capacity this change in preferences is not a result of change in perception and evaluation of quality of life that caused a "response shift", and therefore a change in expressed wishes should not be followed blindly. The author may add to her discussion those concerns.

I added this interesting argument to my discussion (p.14 lines 21-24).

Lionel Pazart (Reviewer 2): The subject of this article is in the news. The situation of demented persons is very specific and the article rightly highlights a number of these specificities.

The title "Advance guidelines as a tool to respect patients' values and believes" could imply an original work. In fact, this paper is the expression of an opinion rather than an original study or a review.

I revised the title to make it clear that this is not an original study: now the title is “Advance directives as a tool to respect patients’ values and preferences. Discussion on the case of Alzheimer’s disease”.

The introduction (like the summary) addresses the subject in terms of progress in diagnosis, with in particular the emergence of biomarkers allowing early diagnosis of the disease. However, the development of the argument does not mention the impact of this progress on the previous situation. The author should logically analyze the consequences of "biotechnological" progress and its impact on ethical, moral and legal considerations, if any.

I tried to make it clearer what does it mean – with regard to advance directives – to receive a diagnosis at a prodromal stage versus to receive a diagnosis late on in the disease process, and why an early diagnosis makes the ethical and legal discussion on advance directives in dementia
even more important. The focus here is more on the time of the diagnosis than on the use of biotechnology (from p.3 line 23 to p. 4 line 3; from p. 4 line 23 to p. 5 line 2).

A reminder of the concept and application of advance directives by country would be appropriate at the beginning of the article. Similarly, the factors (in particular socio-cultural factors) influencing the adoption or not of a regulation in this field could be mentioned.

I included a few lines to recall the point (p. 4 lines 15-16).

Finally, the scope of these guidelines seems to be limited to care, could reflection be opened on more general aspects of quality of life?

I clarified that health care planning includes both medical treatments and choices related to quality of life (p.10 line 6).

The stated purpose of the paper is to discuss the value of advances directives in dementia. The reader's legitimate expectation would therefore be to find an analysis of the studies on the intrinsic value of advance directives and their impact in the context of dementia in relation to other pathological situations.

I tried to show that questioning the value of advance directives in dementia – as many scholars do- is not correct and that, on the contrary, advance directives are particularly valuable in dementia. I believe I have shown this in many parts of the work and specifically when I have referred to: i) the time where the disease is already detected, although symptoms are absent or very mild; ii) the possibility to communicate a quite well known disease course; iii) the fact that the directive would be eventually executed not too much in advance of future incapacity; iv) changes in personality and interests as an additional reason to promote advance directives and make people more confident about their future; v) the lack of effective treatments for the disease.

I have now added just a brief reference to studies results on the effectiveness of advance directive in patients with severe cognitive impairment, affirming that data are few and not conclusive (p.16 lines 11-15; p.17 lines 1-7). Anyway, in my view, this do not weaken the value of advance directives in AD, but ask for concrete policies and actions to make directives known and effective (p. 17 lines 8-14).
Moreover, in accordance with the title "enticing", the reader would expect some confrontation between the "patients' values and believes" and the content of the advance directives. Could the author elaborate on what it encompasses in patients' values and believes?

I changed the expression “values and believes” (that can be considered as one) in “values and preferences”, where values (including believes) form the foundation for decision making and refer to patients’ view on themselves and life, and preferences are based on and guided by values and express the patients’ elective way to better promote and preserve that view. I added a clarification into the text, along with a reference to a values history document that could be appended to an advance directives to guide difficult medical decisions (p. 8 lines 19-20; p. 10 lines 12-14).

Could very practical questions concerning advance directives be highlighted ? when, how, where they can be drafted ? who can be the depositary? how to know that they exist (especially for an "incompetent" or demented person )? what should be its content? what are the difficulties of possible formulations and interpretation ? etc.

Following this and the other reviewers’ suggestion, I completed the paragraph related to “Difficulties in implementing advance directives in dementia” with very practical concerns that are in fact important and were lacking in the first version of the manuscript, and I enriched the paragraph “Conclusion” with some suggestions on the role that family physicians could play (p. 16 lines 8-17; p. 17 lines 1-14).

Anyway, I agree that a separate paper focusing specifically on very practical questions concerning advanced directives in AD could be interesting and useful.

Several notions (rupture of personal identity, conflicts interests before and after disease etc.) are important to relativize in relation to the practices of the advance directives. These guidelines may be formulated on the occasion of the occurrence of a serious condition or, in general, outside of any pathological context. Could the concept of temporality and duration of validity of advance directives be underlined?

While it is true that advance directives may be executed at any time, the manuscript focuses on the execution of advance directives after having received a diagnosis of Alzheimer’s disease. Some elements regarding temporality (and at the same time the fact that late on in the disease process the patient will not be able to eventually revise the directive) were already present (p. 14 from line 14). I reinforced the point speaking about the possible role of the family physician that should include assuring ongoing revision of the directive (p. 17 lines 12-13).
It is particularly appropriate to address different circumstances such as care, involvement in research and the end of life. Can the author comment on the differences in values in these situations, and how best to approach them in practice?

I revised the first part of the paragraph “Which kind of advance directives for patients with dementia” to better organize the discourse. The differences between care, research and end of life should now be clearer. I underlined that patients should be invited to make decisions on participation in research and end of life, as they are particularly sensitive issues (p. 10 lines 5-14).

In conclusion, the title, introduction and development appear somewhat disconnected. The author could rely more on the studies already conducted, especially in The Netherlands and Germany, to present the knowledge, experiences and attitudes regarding advance directives in patients who have become mentally incompetent.

I hope the revised version of the manuscript may overcome the reviewer’s concerns. Following this and other reviewers’ suggestion, I referred to other studies and papers.

Suzanne Van De Vathorst (Reviewer 3): While I agree with the drift of your paper, I feel you should elaborate on some points and clarify some others.

On p 3 you state in line 21 that a multi-domain intervention can be effective, but in the next sentence you state there are no effective treatments. Please explain.

I have clarified the point in the text (p. 4 lines 5-8).

You state on p 10 that a proxy appointment is the preferred route. In the following sentences you claim that 'discordant preferences are likely to be corrected': could you elaborate on how this would happen? Do you really believe prior communication will correct? Is there any empirical evidence for this claim? I think you should underbuilt your argument better. Why is proxy consent superior to a first hand directive?

I made clearer in the paper that I am supporting an advanced directive that includes both decisions regarding health care and the appointment of an attorney (p. 10 line 16). It is true that we do not have empirical evidence to affirm that discordant preferences between the patient and the attorney are likely to be corrected by prior communication of preferences by the patient. I reformulated the sentence to acknowledge the lack of evidence, while affirming that this is reasonable (p 11 lines 13-17). I also added a reference to the impact on surrogate of knowing patient’ preferences (p.11 lines 7-10).
On p 11 line 8: you say an advance research directive can only work in the presence of a caregiver? I do not understand your reasoning here. Moreover earlier you said you preferred proxy consent, and here you say it is not necessary?

The text was probably not clear enough. I tried to better clarified the point (p 12 lines 16-17; p.10 line 16)

On p 13 you state euthanasia practices are problematic per se, but in the last sentence of that paragraph you state that it would be discriminatory to deny this choice to dementia patients. I get confused: what is your position?

In fact, I was not expressing a personal position on the point. Instead, I was affirming that it would be discriminatory not to apply to patients with dementia what a pluralistic society recognizes as a right for the other citizens.

Anyway, in the revised version of the manuscript, also in the light of your following comment, I decided to cut the part related to assisted suicide and euthanasia as they are not essential to the discourse and are very specific situations which probably deserve a more specific discussion.

All in all I am sympathetic to your paper. I also think your reasoning, your argumentation build-up could be stronger. You actually cover many subjects (the identity problem, critical vs experiential interests, proxy or advance directive, research, care and end-of life options) in this relatively short paper, and that leads to not all of these subjects being explored as thoroughly as they deserve.

I hope the revised version of the paper is more convincing on the points that you and the other reviewers raised. I agree that the fact that the paper cover many subjects may be regarded as a limit of the work. At the same time, I believe this has the merit to present in a unique work the key elements for a discussion on the topic.