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)	End-of-life cost and its determinants for cancer patients in urban China: A population-based retrospective study
AUTHORS	Li, Zhong; Pan, Zijing; ZHANG, LIANG; He, Ruibo; Jiang, Shan; Xu, Chengzhong; Lu, Fangfang; Zhang, Pei; Li, Boyang

VERSION 1 – REVIEW

REVIEWER	Ilaria Massa Istituto Scientifico romagnolo per lo Studio e la Cura dei Tumori IRST IRCCS, Meldola (FC) Italy
REVIEW RETURNED	23-Nov-2018

GENERAL COMMENTS	The paper is interesting and the work is well done. Some observations: the introduction is not so focused on the research question which needs to be clarified in the last sentence of the introduction. The actual last sentence in the Introduction is not appropriate for it , but it must have been shifted to Mat and Meth. Usually, the end of an introduction must contain the aim of the research. In the Introduction at line 11 the referral to "death" is not clear: what do you intend with " EOL in-home care can improve patients satisfaction, thereby reducing......death"?Please explain Discussion: line 29 the comparison with Obermayer et al is not clear, the findingd by Obermeyer seems to be similar and not different from the results reported here. Please clarify

REVIEWER	Diana Zuckerman National Center for Health Research, USA
REVIEW RETURNED	10-Dec-2018

GENERAL COMMENTS	The authors did an excellent job of explaining why this study is important. However, some of the results were difficult to understand. For example, when the authors compared the costs of the last 6 months of care for those who only lived 3-6 months, I could not make sense of it. Wouldn't those who only lived 3 months be studied for only 3 months? There were times when I didn't understand what the authors were referring to, such as the 5/80 cancer disequilibrium mentioned in the Introduction. There were a few minor language problems, such as the term "decedents" was used incorrectly. Also, I don't think the authors meant to only provide marital status for male patients (see page 6). The authors refer to Table 4 but it is missing.

	We can all agree that too much money is spent at the end of life, but I think the authors need to better explain why aggressive end of life care is bad for the patient and not just because of cost. Overall, I think this is an important article that needs some tweaking to make it easier to understand.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1
Point 1: the introduction is not so focused on the research question which needs to be clarified in the last sentence of the introduction. The actual last sentence in the Introduction is not appropriate for it, but it must have been shifted to Mat and Meth. Usually, the end of an introduction must contain the aim of the research.
Response 1: Thank you very much for this valuable suggestion, we have revised the last paragraph as you suggested and added the aim of the research in the end of this paragraph as followed:
A population-based study examining EOL healthcare expenditure and its determinants has not been explored, especially in terms of the real-world data of the regional health system in China. Therefore, in this study, we aimed 1) to define the EOL healthcare utilisation and its cost among cancer patients, 2) to investigate the determinants of EOL healthcare cost, and 3) to inform related policy making and implementation in China.
Point 2: In the Introduction at line 11 the referral to "death" is not clear: what do you intend with " EOL in-home care can improve patients satisfaction, thereby reducing......death"?Please explain
Response 2: Thank you very much for pointing out this mistake, we have revised it as followed:
Several systematic reviews have noted that in-home EOL care can improve patient satisfaction, thereby reducing inpatient hospitalisation utilisation and hospital death.
Point 3: Discussion: line 29 the comparison with Obermayer et al is not clear, the findingd by Obermeyer seems to be similar and not different from the results reported here. Please clarify
Response 3: Thank you very much for this kindful suggestion, we have clarified the findings of Obermayer et al's studies and compared it with our results as followed:
One study by Obermeyer Z et al. [53] revealed that Medicare fee-for-service beneficiaries with poor-prognosis cancer, which were enrolled in the hospice care programme, used less hospitalisation, intensive care unit admissions, and invasive procedures with a lower total cost than the non-hospice group. Hence, there is great potential for the development of hospice care programmes in China.
Reviewer 2
Point 1: The authors did an excellent job of explaining why this study is important. However, some of the results were difficult to understand.
For example, when the authors compared the costs of the last 6 months of care for those who only lived 3-6 months, I could not make sense of it.
Response 1: Thank you very much for this valuable suggestion, and it really helped a lot in the improvement of our manuscript In the Table 3, we meant to describe the population-level EOL cost. In the Table 4, for the “Wouldn't those who only lived 3 months be studied for only 3 months?”. We are sorry for this mistake, we have re-conducted the four generalized linear regression model and re-wrote the Statistical analysis section. Moreover, we have added the number of observation into the Table 4 to help readers better understand this study. For example, in the Model 1, we took all the patients who survived than more than six months (Number of observation=398). In addition, we checked the Results and Discussion section and modified the language expression for better understanding.

Point 2: There were times when I didn't understand what the authors were referring to, such as the 5/80 cancer disequilibrium mentioned in the Introduction.
Response 2: Thank you very much for this valuable suggestion, Several studies had estimated that only 5% of global resources for cancer are spent in low and middle countries. However these countries account for almost 80% of the disability-adjust life-years lost worldwide to cancer. That is “5/80 cancer disequilibrium”. we have revised it as followed:
Given the considerable share of the total health expenditure on cancer (approximately 6% in European countries [3], 9.2% in Taiwan [4 5]) and the great gap in the cancer healthcare delivery system between developed and developing countries [2], evaluating the end-of-life (EOL) cost and identifying its key determinants have been a worldwide concern [6].
Point 3: There were a few minor language problems, such as the term "decedents" was used incorrectly.
Response 3: Thank you very much for this valuable suggestion, we have revised it.
Point 4: Also, I don't think the authors meant to only provide marital status for male patients (see page 6).
Response 4: Thank you very much for this valuable suggestion, we have revised it as followed:
Over half (66.78%) of these patients were male, and 83% of the 894 patients were married.
Point 5: The authors refer to Table 4 but it is missing.
Response 5: Thank you very much for this valuable suggestion, we have attached the table at the end of the article as we submitted the manuscript in August 2018.
Point 6: We can all agree that too much money is spent at the end of life, but I think the authors need to better explain why aggressive end of life care is bad for the patient and not just because of cost.
Response 6: Thank you very much for this valuable suggestion, We have realized that aggressive end of life care is bad for the patients and not just because of cost. Several studies had indicated that high-intensity treatments may not be associated with better patient quality of life, outcomes, or caregiver bereavement. Aggressive medical care of cancer patients at the end of life stage is associated with radiation therapy, which may impact patients’ quality of life near death. Palliative care has a positive effect on many clinical outcomes, including symptom distress, quality of life, satisfaction and survival. As for patients’ family carers, aggressive treatment not only brings them heavy economic pressure, but also physical and emotional strains. Therefore, we revised the last paragraph of the Discussion section as followed:
The abovementioned results indicated that numerous health resources in China might be irrationally used, similar to other countries [54]. Studies have noted that patients receiving hospice care or early palliative care intervention could experience better palliation of pain and symptom management [55] and improved the likelihood of the place of death they preferred [12, 52]. The overuse of aggressive care during the EOL period can be harmful from the perspective of the patient, including care-related financial strain [14] and the inability to palliate the bereavement of the families [18]. Given the potential benefits of hospice care and early palliative care intervention, the healthcare need of patients should be satisfied. The timely initiation of hospice or home care may reduce the low-value cancer healthcare services in China.
Point 7: Overall, I think this is an important article that needs some tweaking to make it easier to understand.
Response 7: Thank you very much for this valuable suggestion, we have tried to simplify the paragraph, including removing the methodology-related paragraph into the Method section, removing some repetitive statements and adding some necessary information. We also conducted a deeper discussion combining the results with the latest research as you suggested. Moreover, the manuscript was sent to be modified by American Journal Experts (https://secure.aje.com/cn/researcher/) to help readers better understand this paper.

VERSION 2 – REVIEW

REVIEWER	Diana Zuckerman National Center for Health Research
REVIEW RETURNED	13-Jan-2019

GENERAL COMMENTS	I remain confused about the measure of cost of the last 6 and 3 months. What if the patient doesn't live that long? Are they only included for the categories of the length of time they lived? Doesn't that bias the results? I suggest that percentages etc be presented with only one decimal point rather than 2 (e.g. 66.8% rather than 66.78%) And refer to that as two-thirds rather than more than half. As noted in my previous review, there are some language difficulties. The article needs a good editor at BMJ. Here are some examples of sentences that I edited, but there are many others. There are many examples where the wording is slightly off or needs to be more logically organized, such as: ADD "ineffective" to this sentence: Timing palliative care is urgently needed to address irrational healthcare utilisation and to reduce costs. Reorganize this 1st sentence to read: Cancer is the leading cause of mortality and accounts for 14.1 million new cancer cases, 32.6 million individuals living with cancer,and 8.2 million deaths worldwide in 2012, [1]. Several systematic reviews have noted that in-home EOL care can improve patient satisfaction, as well as reducing inpatient hospitalisation utilisation and hospital death [78]. Based on the International Statistical Classification of ... including additional care-related financial strain e [14], no reduction in the bereavement of the families [18]. Patients receiving hospice care or early palliative care intervention could experience better management of pain and other symptoms [55], and an improved likelihood of dying at home if that was preferrred [12, 52]. Given the potential benefits of hospice care and early palliative care intervention, the timely initiation of hospice or home care may reduce low value cancer healthcare services in China

VERSION 2 – AUTHOR RESPONSE

Reviewer 1

Point 1: I remain confused about the measure of cost of the last 6 and 3 months. What if the patient doesn't live that long? Are they only included for the categories of the length of time they lived? Doesn't that bias the results?

Response 1: Thank you so much for this question. In table 3, we used the population-level estimation of end-of-life cost. The patients were not only included for the categories of the length of time they live. In table 4, we aimed to explore how the included factors will impact on the different end-stage cost. Hence, patients were only included for the categories of the length of time they lived. In Model 1, the number of observation was 398, 629, 807 and 868 in model 1, 2, 3 and 4, respectively.

Point 2: I suggest that percentages etc be presented with only one decimal point rather than 2 (e.g. 66.8% rather than 66.78%) And refer to that as two-thirds rather than more than half.

Response 2: Thank you so much for this suggestion. We have revised it.

Point 3: As noted in my previous review, there are some language difficulties. The article needs a good editor at BMJ. Here are some examples of sentences that I edited, but there are many others. There are many examples where the wording is slightly off or needs to be more logically organized, such as:

1) ADD "ineffective" to this sentence: Timing palliative care is urgently needed to address irrational healthcare utilisation and to reduce costs.

2) Reorganize this 1st sentence to read: Cancer is the leading cause of mortality and accounts for 14.1 million new cancer cases, 32.6 million individuals living

with cancer, and 8.2 million deaths worldwide in 2012, [1].

3) Several systematic reviews have noted that in-home EOL care can improve patient

satisfaction, as well as reducing inpatient hospitalisation utilisation and hospital death [78].

4) Based on the International Statistical Classification of ...

5) including additional care-related financial strain e [14], no reduction in the bereavement of the families [18].

6) Patients receiving hospice care or early palliative care intervention could experience better management of pain and other symptoms [55], and an improved likelihood of dying at home if that was preferrred [12, 52]. Given the potential benefits of hospice care and early palliative care intervention, the timely initiation of hospice or home care may reduce low value cancer healthcare services in China.

Response 3: Thank you so much for these suggestion. We have revised as you suggested and checked the other parts of our manuscript.