Author’s response to reviews

Title: A Comparison of Medical Outcomes and Healthcare Costs in the End-of-Life Between Dialysis Patients with and without Cancer: A National Population-based Study

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Author’s response to reviews:

Rebuttal letter
BNEP-D-19-00047R1

Topic: A Comparison of Medical Outcomes and Healthcare Costs in the End-of-Life Between Dialysis Patients with and without Cancer: A National Population-based Study

Dear Editor-in-Chief:

Thank you for your review of our manuscript. On behalf of my co-author, I would like to resubmit our revised manuscript entitled " A Comparison of Medical Outcomes and Healthcare Costs in the End-of-Life Between Dialysis Patients with and without Cancer: A National Population-based Study " (BNEP-D-19-00047R1).

We have responded to each of the reviewers' comments point by point and marked the changes in the new manuscript with red text. Our responses are listed in the response to reviewers.

We confirm that the manuscript has been read and approved for submission by all authors. All authors have contributed to preparing the manuscript and/or that International Committee of Medical Journal Editors (ICMJE) criteria for authorship have been met, and that no person or persons other than the authors listed have contributed significantly to its preparation. The authors
declare that there is no conflict of interests regarding the publication of this article. There is not any part of the manuscript published or submitted for publication elsewhere, or appeared elsewhere in a format that could be construed as a prior or duplicate publication of the same or similar work.

Sincerely,

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BNEP-D-19-00047R1

A Comparison of Medical Outcomes and Healthcare Costs in the End-of-Life Between Dialysis Patients with and without Cancer: A National Population-based Study

BMC Nephrology

Reviewer reports:

Melissa Wachterman (Reviewer 1): Review of manuscript "A Comparison of EOL Quality of Care Indicators Between Dialysis Patients With and Without Cancer"

Major Comments:

1. Methods page 9, lines 32-36: See that data spans 2006-12/2012. Presumably can't get data beyond 12/2012 (at this point >6 yrs old)? Given that scope of hospice care not expanded until 2009, about half of data comes BEFORE that expansion. Since that expansion presumably was
reflective of an increasing commitment to improving EOL care outside of cancer, you both have a mix of data and also do not have 6 yrs of data. Presumably, care is getting better over time so results may under-rate quality of EOL care for dialysis patients, both with and without cancer, over the past 5 years. Not an absolute fatal flaw but certainly does weaken the conclusions and implications of the study. Not much can do other than state in Limitations section (unless can add more recent data, which would significantly strengthen study.

Response: Thank you for your advice!

We had added sentences in the part of Limitation.

Page 22 lines 6-10

Fourth, in September 2009, the bureau of the NHI amended the fee-charging standard to expand from patients with cancer to terminally ill patients without cancer including ESRD. So, dialysis patients received palliative care were limited before September 2009.

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2. Methods page 12 lines 30-33 - say examined survival probabilities with KM methods, but then I don't see anything in Results? This would be important b/c if survival very different between D and DC groups, one with longer survival has longer period of time within last month of life to have long stays, >= hospitalizations, ICU stay etc.

Response: Thank you for your advice!

We had added Figure 2, and sentences in the part of Results.

Page 14 lines 14-16

The survival probabilities of dialysis patients between DC and D groups were not significantly different (p = 0.300). (Figure 2)

We had revised Table 1

Table 1. Comparison of demographic characteristics between dialysis patients with cancer (DC group) and without cancers (D group) during 2006-2011

Figure 2. the survival probabilities of the dialysis patients with and without cancer
3. Table 4: Quite confusing, difficult to digest to have all of the OR’s in the Table. Seems like main point is not to conduct an analysis of all independent predictors of quality indicators but rather to compare between dialysis patients with and without cancer. So would focus Table on that and modify Methods last line page 12 first line 13 to say that is the focus of the modeling. (could include what is currently Table 4 as an Appendix table)

Response: Thank you for your advice!

We had revised the Table 4, and added a Table (original Table 4) in Additional file 2

4. Results page 14-15 lines 56-10: Technically incorrect to say "RISK", it is ODDS. Calling it risk generally overstates the findings.

Response: Thank you for your advice!

We had replaced the “risk” with “odds” in the manuscript as you suggested.

5. Another sizeable limitation of this study that is not acknowledged is that the only predictors/covariates that you have come from administrative data. Presumably variables like patient treatment preferences play a very big role in affecting the 'quality' markers that you measure and I would argue that the true measure (or at least one very important measure) of the quality of EOL care is "goal concordant care" - in other words, do patients receive care consistent with what they want. Preferences may vary between dialysis patients with vs. without cancer. There is nothing you can do about this (quite usual to not have data on patient preferences), but you do need to talk about how this substantially limits your ability to say that your study reports on true quality of EOL care.

Response: Thank you for your advice!

We had added sentences in the Part of Limitations.

Page 21 line 17 to page 22 line 3

Second, patients’ and family members’ preferences may have influenced some outcomes. Previous study reported that patients wanted to discuss over advance care planning with their family rather than physicians.[53] As a previous study showed that the current EOL failed to
meet the needs of patients with advanced CKD, [54] future research is warranted to investigate the effectiveness of advance care planning for dialysis patients in Taiwan.

New references:


Minor Comments:

1. Introduction page 6 line 19: Not sure what this sentence means. Are they saying that using quality indicators focused on the last month of life is generally accepted as a good evaluation of the quality of end-of-life care? I agree with that statement but as written it's not clear.

Response: Thank you for your advice!

We had revised and added sentence in Page 6 Line 18 to page 7 line 1 as below:

Investigations into EOL care in the last month of life was reasonable [13, 14]. So, in current study, we explore the quality indicators of EOL care in the last month of life for dialysis patients.

2. Introduction page 7 lines 10-20: They write "numerous benefits from hospice care", but then all of their citations about reduction in symptom burden, improvement in QOL and mood, survival, caregiver outcomes are actually benefits from PALLIATIVE care, not hospice. Will want to clarify this and add citations supporting benefits of HOSPICE care.

Response: Thank you for your advice!

We had replaced “hospice care” with “palliative care” in the manuscript.

3. Introduction page 7, lines 42-45: Meaning of the following sentence is unclear to me: "Dialysis is also associated with higher risk of cancer in patients with ESRD”. Higher risk
relative to who? Are they saying that of all patients with ESRD, those who do dialysis (relative to those who choose conservative management) have higher rates of cancer? Or that those with ESRD bad enough to require dialysis (relative to those whose ESRD is not quite as severe such that they don't need dialysis) have higher rates of cancer? I am not a nephrologist, but my understanding is that once you categorize someone as ESRD they fall into one of the following buckets: 'dialysis', 'transplant' or 'conservative management' so it seems that only the former explanation would make sense here… OR are they trying to say that those with ESRD have higher risk of cancer than the risk of cancer in the general population (in which case they should say "Patients with ESRD have a higher risk of cancer than the risk of cancer in the overall Taiwanese population.”

Response: Thank you for your advice!

We had revised sentence in Page 7 Lines 15-16 as below:

Patients with dialysis are associated with a higher risk of cancer than patients without dialysis [22].

4. Introduction, page 7, lines 45-52: Then the next sentence (that starts "In Taiwan, most patients…"), while relevant, seems a little out of place since it does not make a connection to hospice. It raises another, broader question/issue I have which is I think an important point to clarify/make is whether, as is true in the U.S. under Medicare criteria, patients who would qualify for hospice via a hospice diagnosis of ESRD cannot receive hospice until they discontinue dialysis. HOWEVER, if they have a hospice diagnosis of cancer, then they CAN get dialysis. Is that true in Taiwan? If that policy is similar in Taiwan, I think that point needs to be made somewhere. I have done a quick re-write of the paragraph just to give authors sense of what I'm thinking (note I also include an Attachment with Track Changes of the paragraph):

"In Taiwan, the use of hospice care has gradually progressed since 1983, and the first hospice ward was established in 1990 [21]. In Taiwan, the hospice care system includes both inpatient hospice care, which is the predominant type, and home hospice care, and both are covered by Taiwan's National Health Insurance (NHI) program. Since 2009, the scope of hospice care was extended beyond cancer to another eight serious illnesses, which includes ESRD. However, the majority of hospice care continues to focus on treating patients with advanced cancer. [As you will see in Attachment with track changes, not sure what to do with following sentence…] Dialysis is also associated with a higher risk of cancer in patients with ESRD [22]. To qualify for hospice, patients must discontinue life-extending treatments directed at their hospice diagnosis, which includes dialysis for those with a hospice diagnosis of ESRD”. In Taiwan, most patients with ESRD choose dialysis until death because
there are minimal financial barriers to health insurance access, convenient medical access, and high-quality dialysis [23]. Thus, these patients are not eligible for hospice unless they have another hospice diagnosis such as cancer. Therefore, we compared the quality of EOL care between chronic dialysis patients with and without cancer."

Response: Thank you for your advice!

We had revised the sentences as suggested.

Page 7 line 10 to page 8 line 7

In Taiwan, the palliative care system includes both inpatient palliative care, which is the predominant type, and home palliative care, and both are covered by Taiwan’s National Health Insurance (NHI) program. Since 2009, the scope of palliative care was extended beyond cancer to another eight serious illnesses, which includes ESRD. However, the majority of palliative care continues to focus on treating patients with advanced cancer. Patients with dialysis are associated with a higher risk of cancer than patients without dialysis [22]. To qualify for palliative care, patients must discontinue life-extending treatments directed at their hospice diagnosis, which includes dialysis for those with a hospice diagnosis of ESRD. In Taiwan, most patients with ESRD choose dialysis until death because there are minimal financial barriers to health insurance access, convenient medical access, and improvement in dialysis care [23]. Thus, these patients are not eligible for palliative care unless they have another diagnosis such as cancer, which meets the criteria for palliative care. However, the use of palliative care had significantly increased for patients with cancer due to the NHI’s reimbursement in Taiwan regarding palliative services since 2000, of which, two national policies fostering palliative services for terminal cancer patients were held in 2011[24].

5. Methods page 9, lines 23-27, should include the ICD-9 procedures codes used to identify HD and PD (could go in an appendix)

Response: Thank you for your advice!

We had added sentence in the part of Methods.

Page 10 lines 3-4

We used ICD-9-CM code and charge master code to identify cases of HD and PD. (Additional file 1)

We had added the file to identify HD and PD in the Additional file 1.
Additional file 1. ICD-9-CM code and charge master codes to identify HD and PD cases.

Patients with ERSD (ICD-9-CM code 585) that received hemodialysis (HD) or peritoneal dialysis (PD). Then we used charge master code in NHIRD to identify HD and PD. The charge master codes for HD included 58001C, 58002C, 58003C, 58007C, 58014C, 58018C, 58019C, 58020C, 58021C, 58022C, 58023C, 58024C, 58025C, 58027C, and 58029C. The charge master codes for PD included 58009B, 58010B, 58012B, 58011C, 58017C, and 58028C.

6. Should define "major episodes in the last month of life"? Not explained in 'Definitions' section - I had to dig into Table 3 to find it’s things like having an MI, sepsis etc right?

Response: Thank you for your advice!

We had revised the sentences in the part of Methods, and revised the Table 2.

Page 13 line 12-14

We compared patients’ demographic and clinical characteristics (Table 1), and major episodes in the last month of life (Table 2), and quality indicators in EOL dialysis care (Table 3) between DC and D groups.

Devika Nair (Reviewer 2): Strengths of this study include the patient-centeredness and economic relevance of the topic, and the fact that the time period studied was adequate to measure the authors' outcomes of interest. A known limitation of using claims data and retrospective cohort analyses that the authors acknowledge is the inability to include unmeasured confounders and covariates (medication adherence, coexistent major depressive disorder, etc.) that may have otherwise influenced the outcomes in this study. The manuscript contains useful information but would benefit from more precise wording and slight alterations clarify and unify the authors' overall message to readers. I have included the following general and specific comments and questions to hopefully help the authors further strengthen their contribution:

Major comments
- Patients who receive chronic peritoneal dialysis often have different clinical and personal characteristics as compared to those who receive chronic hemodialysis, such as prolonged maintenance of their residual renal function and better self-efficacy (Ueda et al Adv Perit Dial 2017, Tong et al Am J Kidney Dis 2013). These and other characteristics may have influenced some of the outcomes the authors were interested in measuring, such as hospitalization rate. If possible with the claims data, would consider restricting analyses to just hemodialysis patients. Otherwise can state this as a limitation.

Response: Thank you for your advice!

We had added sentence in the part of Result.

Page 16 Lines 14-17

In current study, we found 20 patients (1.7%) received peritoneal dialysis, and only 1 case belonged to DC group. The results for restricted patients with hemodialysis were similar.

We had added sentence in the part of Limitation.

Page 22 Lines 9-10

Fifth, the results were not extended to peritoneal dialysis patients in current study.

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- The authors define 'quality of end-of-life care' only in terms of objective measures associated with higher healthcare costs. Quality of end-of-life care should ultimately be based on whether outcomes at the end of a patient's life were in concordance with his or her wishes leading up to that moment. Would suggest that the authors replace 'quality of end-of-life care' with 'medical outcomes at the end of life and associated healthcare costs' or a similar phrase.

Response: Thank you for your advice!

We had revised the topic as below:

A Comparison of Medical Outcomes and Healthcare Costs in the End-of-Life Between Dialysis Patients with and without Cancer: A National Population-based Study

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- Would be interested in data re: differences in healthcare costs between patients in this study who received hospice vs. those who did not, if this information is available.

Response: Thank you for your advice!
We had added sentences in the part of Results.

Page 15 line 15-19

We further calculated the healthcare costs between dialysis patients with and without palliative care in the last month of life. The mean health care costs per person during the final month of life for dialysis patients receiving palliative care were slightly less than those without palliative care, but it did not reach statistically significant (US$1967 ± 55 vs. US$2832 ± 108, p = 0.786).

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- An interesting finding in this study is that a high percentage of dialysis patients had high healthcare utilization during the last month of life but low hospice utilization. Would highlight this in the Abstract. Readers may be interested in learning more about barriers to hospice utilization in Taiwan (if the authors are aware of any literature that explains this), especially since hospice is covered by the national health insurance program. The authors begin to describe some of this in the Discussion on page 18 - would expand upon this.

Response: Thank you for your advice!

We had added the sentences in the part of Abstract.

Page 4 line 7-8

Conclusion: The dialysis patients without cancer had higher healthcare utilization during the last month of life but lower palliative care utilization than those with cancer.

We had added the sentences in the part of Discussion.

Page 20 lines 17 to page 21 line 6

Although palliative care is covered by the NHI program in Taiwan. The barriers to palliative care and withdrawing dialysis for patients with advance renal failure in Taiwan included patient-related (e.g. variations in goals and values, lack of efficient communication with physicians, lack of advance care planning, and others), physician-related (e.g. medical ethics uncertainty, not familiar with the law and regulation, fear of legal issues, and others), and system-related (e.g. not addressing preferences for dialysis, transition of care, lack of community-based palliative care systems, family-centered decision-making model, special culture considerations, and others). [51]
- Overall, this work would also be strengthened if the authors can a) more explicitly justify why analyses were stratified by presence or absence of cancer, and b) more clearly explain what question they were aiming to answer using their multiple regression analyses.

Response: Thank you for your advice!

a) We had added and revised sentences in the part of Introduction.

Page 9 lines 4-9

A previous study reported that more than 80% of the terminal cancer patients with renal failure received HD, and almost 20% of terminally-ill cancer patients in palliative care received HD. [30] The aim of current study is to compare EOL care quality indicators between chronic dialysis patients with and without cancer and to examine survival and health care costs in the last month of life.

b) We had added and revised sentences in the part of Methods.

Page 13 lines 12-18

We compared patients’ demographic and clinical characteristics (Table 1), and major episodes in the last month of life (Table 2), and quality indicators in EOL dialysis care (Table 3) between DC and D groups. All factors listed in Table 1, 2 and 3 were included in multivariate logistic regression models. A multivariate analysis was conducted by the stepwise variable selection procedure to determine vital predictors of quality indicators during the final month of life. (Table 4) Collinearity between all collected variables was checked.

New reference:

- Background:

  o The authors should revise or exclude the first sentence of this abstract, as end-of-life care for dialysis patients is being increasingly investigated in their home country (Wu et al J Palli Med 2019, Kang et al J Palli Med 2019) as well as around the world. Would also include that survival was investigated in this study.

  Response: Thank you for your advice!

  We had revised the sentence in Page 3 Lines 2-3 as below:

  End-of-life (EOL) care for patients with dialysis is an important issue to investigate.

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- Methods:

  o If word count allows, would include what variables were used to measure quality of end-of-life care

  Response: Thank you for your advice!

  We had added the sentence in the part of Methods.

  Page 3 lines 8-10

  The patients’ demographic, clinical characteristics, and major episodes in the last month of life were included to measure the quality indicators in the multivariate analyses.

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- Conclusions:

  o Would consider adding the finding that a high percentage of dialysis patients had high healthcare utilization during the last month of life but low hospice utilization

  Response: Thank you for your advice!

  We had added the sentence in the part of Conclusion.

  Page 4 lines 7-8
Conclusions: The dialysis patients without cancer had higher healthcare utilization during the last month of life but lower palliative care utilization than those with cancer.

Manuscript

- Background:

  o Page 5 Line 9 - remove comma after 'diseases.'

Response: Thank you for your advice!

We had removed the comma after diseases.

- Page 5, Line 41

  - "The mortality of dialysis patients decreased by 26% from 2001 ... to 2015... in the United States; however, the mortality did not significantly change from 2000...to 2012 in Taiwan. These data indicate that the quality of dialysis has improved."

Response: Thank you for your advice!

We had revised sentence in Page 5 Line 13-15 as below:

These data indicate that the mortality rate of dialysis patients in Taiwan was comparable to that in the United States.

- Page 7, Line 14-15 - "Dialysis is also associated with a higher risk of cancer in patients."

Response: Thank you for your advice!
We revised the topic as below:

Page 7 line 15-16

Patients with dialysis are associated with a higher risk of cancer than patients without dialysis [22].

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o Page 7, Line 1 - would replace 'hospice' with 'palliative'

Response: Thank you for your advice!

We had replaced the “hospice care” with “palliative care” in the manuscript.

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o Page 7, Line 17 - what is meant by 'high quality dialysis’?

Response: Thank you for your advice!

We had revised the sentence as below:

Page 7 line 18 to page 8 line 2

In Taiwan, most patients with ESRD received dialysis until death because there are minimal financial barriers to health insurance access, convenient medical access, and improvement in dialysis care [23].

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o Page 7, Lines 17-19 - Presumably the authors hypothesized that 'DC' patients who used hospice would have better quality of end-of-life care and decreased healthcare costs during the last month of their life? An explanation of the authors' hypothesis would help readers better understand the reasoning behind comparing quality of end-of-life care and healthcare costs between 'DC' vs 'D' patients. If no hypothesis was pre-specified, then the authors can state that this was mainly exploratory

Response: Thank you for your advice!

We had added sentence in Page 8 Lines 8-9 as below:
A previous study showed that family-reported quality of EOL care was better for cancer patients than for patients with ESRD. [25]

New reference:


Page 7, Lines 17-18 - would include why the use of hospice increased during this time (ie due to policy changes as the reference suggests, etc.)

Response: Thank you for your advice!

We had revised and added sentence in Page 8 Lines 2-7 as below:

Thus, these patients are not eligible for palliative care unless they have another diagnosis such as cancer, which meets the criteria for palliative care. However, the use of palliative care had significantly increased for patients with cancer due to the NHI’s reimbursement in Taiwan regarding palliative services since 2000, of which, two national policies fostering palliative services for terminal cancer patients were held in 2011[24].

Page 9, Line 8 - replace 'ERSD' with 'ESRD'

Response: Thank you for your advice!

We had revised the word as ESRD.

Page 10, Line 10 - would specify whether 'potassium imbalance' refers to hyperkalemia or hypokalemia, or both, if this data is available. Appears to be specified in Table 4.
Response: Thank you for your advice!

In this study, the numbers of hyperkalemia or hypokalemia are 43 (3.9%). So, we used potassium imbalance as a variable.

We had revised sentence in Page 11 Lines 4-5 as below:

Therefore, we added the following comorbid conditions for analysis: MI, CHF, PAOD, COPD, pneumonia, sepsis, and potassium imbalance (hyperkalemia or hypokalemia).

We had added footnote in the Table 2 and 4.

* Potassium imbalance includes hyperkalemia or hypokalemia

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o Page 11, Lines 1-4 - was the presence of cancer only ascertained at one time-point?

Response: Thank you for your advice!

We had added sentence in Page 11 Lines 18-19 as below:

The NHIRD and catastrophic illness database were used to identify patients with cancer.

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o Page 12, Line 16 - was this truly a regression analysis? (if the authors are referring to the analyses used to obtain data in Tables 1-3)

Response: Thank you for your advice!

We had revised and added sentence in Page 13 Line 12-17 as below:

We compared patients’ demographic and clinical characteristics (Table 1), and major episodes in the last month of life (Table 2), and quality indicators in EOL dialysis care (Table 3) between DC and D groups. All factors listed in Table 1, 2 and 3 were included in multivariate logistic regression models. A multivariate analysis was conducted by the stepwise variable selection procedure to determine vital predictors of quality indicators during the final month of life. (Table 4)
o Page 12, Line 19 - did the authors pre-specify which variables they thought would be most predictive of particular outcomes? Was there any collinearity between any of these variables? Would like more information on the reasoning behind doing this

Response: Thank you for your advice!

We had revised and added sentence in Page 13 Lines 12-18 as below:

We compared patients’ demographic and clinical characteristics (Table 1), and major episodes in the last month of life (Table 2), and quality indicators in EOL dialysis care (Table 3) between DC and D groups. All factors listed in Table 1, 2 and 3 were included in multivariate logistic regression models. A multivariate analysis was conducted by the stepwise variable selection procedure to determine vital predictors of quality indicators during the final month of life. (Table 4) Collinearity between all collected variables was checked.

- Results

o Page 13, Line 5 - would replace 'with' with 'on.' Also, were these peritoneal dialysis patients as well as hemodialysis patients?

Response: Thank you for your advice!

We had revised the sentence as suggested.

o Page 13, Line 6 - would specify how death was measured in this study (ie exit from database, etc) Was data available on whether patients received a kidney transplant?

Response: Thank you for your advice!

We had added sentence in part of Result.

Page 14 Lines 3-4 as below:

Patients usually exited from insurance system after death, and the insurance system exit dates was our proxy for death.
We had added sentence in part of Result.

Page 14 Line 7 as below:

Only 1 patient who had received kidney transplant was belonged to the D group.

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o Would include results of Kaplan Meier plots or survival statistics of 'DC' vs 'D' groups. This may help explain some of the findings (ie could it appear that the 'DC' patients had more days in the hospital because they were living longer?). Would be important to include information on whether patients were transplanted in this section.

Response: Thank you for your advice!

We had added Figure 2

Figure 2. the survival probabilities of the dialysis patients with and without cancer

We had added sentence in part of Result.

Page 14 Line 7 as below:

Only 1 patient who had received kidney transplant was belonged to the D group.

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o Page 15, Line 4 - what variables were adjusted for?

Response: Thank you for your advice!

We had revised and added sentence in Page 16 Lines 7-12 as below:

…after adjusted demographic variables (e.g. history of hypertension, high social economic status, living in the northern Taiwan area, living in suburban area, and received service in the teaching hospital in the last month of life), and the major episodes in the last month of life (e.g. myocardial infarction, congestive heart failure, peripheral arterial occlusive disease, pneumonia, and sepsis) (listed in Additional file 2). (Table 4)

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- Discussion

- Page 17, Line 7-8 - "In the current study, we showed that DC patients were more likely to receive hospice care compared with D patients"

- I am not sure that the results shown in Table 3 fully suggest that 'DC' patients are more likely to receive hospice care. Would temper this to state that patients in the 'DC' group had a higher percentage of hospice care.

Response: Thank you for your advice!

We had revised sentence in Page 17 Lines 13-14 as below:

In the current study, we found patients in the DC group had a higher percentage of palliative care.

* It remains unclear why a higher percentage of 'DC' vs. 'D' patients died in the hospital despite receiving more hospice care than 'D' patients. That question may not be able to be answered in this study, but the authors suggestion of cultural influences on patients' and caregivers' views on death and dying may partially explain why a high percentage of 'D' patients in general died in the hospital

Response: Thank you for your advice!

We had revised and added sentence in Page 19 lines 2-7 as below:

In Taiwan, patients with terminal illnesses requiring palliative service must be transferred to a palliative ward in a hospital for consultation and evaluation. During their palliative care course, more hospital admissions, more hospital stays, and dying in the hospital in the last month of life for relieving pain and other symptoms are expected.

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- Figure

Would specify whether these patients are on peritoneal dialysis or hemodialysis

Response: Thank you for your advice!

We had revised Figure 1
o Replace 'Alived' with 'Alive'

Response: Thank you for your advice!
We had replaced 'Alived' with 'Alive'.

- Tables

 o Tables 1-3 may be able to be combined into one table

 Response: Thank you for your advice!
If we combine the table 1-3 altogether into one table, there might have some inconveniences including difficulty following the formatting instructions.

 o Table 4 - would group these into 'D' vs 'DC' patients and again specify whether hemodialysis or peritoneal dialysis, if that data is available

 Response: Thank you for your advice!
We had added sentence in Page 16 line 14-17

In current study, we found 20 patients (1.7%) received peritoneal dialysis, and only 1 case belonged to DC group. The results for restricted patients with hemodialysis were similar.

 o The calculation of AUCs may not add much meaningful information to this Table; would consider removing this here and in the Results section as well

 Response: Thank you for your advice!
We had deleted the sentences in the Table 4 and in the part of Results.