Author’s response to reviews

Title: Timing of palliative care referral and aggressive cancer care toward the end-of-life in pancreatic cancer. A retrospective, single-centre observational study

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Author’s response to reviews:

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154 Wattletree Road, Malvern, Victoria, Australia, 3144
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Dear Reviewers,

Re: Manuscript no PCAR-D-18-00089

Thank you kindly for your welcomed comments on our manuscript.
Response to Reviewer 1

1. In page 4 we have removed reference [26] and the preceding sentence “Finally, an Australian study of pancreatic cancer patients found that higher quality of care scores and improved survival were associated with those who lived in cities (adjusted difference, 11%; 95% CI 8-13%), were socio-economically advantaged (most disadvantaged areas: 8% higher; 95% CI 6-11%), and first presented to hospitals with a high pancreatic case volume” as suggested by the Reviewer.

2. The Reviewer correctly states that the definition of early palliative care can be defined as the referral within 30 days after the diagnosis of advanced cancer or first relapse for haematology. We suggest there are additional definitions that can be also used. We base this on a systematic review of randomized trials of palliative care which assessed the benefits of early palliative care. Davis et al. reported on 15 randomized trials of outpatient palliative care and 13 randomized trials of palliative home care [1]. Studies were found to be heterogeneous in terms of definition of early palliative care. “Early” palliative care was defined as the following: referral occurring at the time of diagnosis of advanced cancer [2], less than 3 months after diagnosis of advanced cancer [3] or as being seen by a palliative care specialist greater than 3 months before [4]. “Early” palliative care can also be linked to the presence of certain prognostic signs and symptoms as well as the duration of continuity of palliative care (i.e. greater than 90 days, 31-90 days, 11-30 days or 1-10 days) before death. We chose the definition linked to the duration of palliative care, defining early palliative care as a referral being initiated >90 days before death.

Based on Davis et al. systematic review which highlighted heterogeneous definitions of early palliative care, we have amended n page 5 line 142-144, to state: “We choose to define early palliative care based on the duration of continuity of palliative before death. Thus early and late PCR were defined as more than 90 days and less than or equal to 90 days before death respectively.”

3. The Reviewer correctly highlights the point that the use of futile treatment is not justifiable at the end of life.

We have amended our statement (page 10 line 265-268) to now state from “Finally, the use of chemotherapy in situations that are deemed futile remains common in cancer, particularly in cohorts with grave outcomes where ongoing treatment reinforces hope in a dire situation [45]. With uncertainty of prognosis, the compassionate use of chemotherapy may be considered ethically acceptable whilst patients and families come to terms with a new diagnosis and inevitable outcome.” to “Finally, the use of chemotherapy in situations that are deemed futile remains common in cancer, with its use sometimes being justified as a means to reinforce hope in dire situations [45]. This collusion of hope may be unnecessary if honest conversations and
early involvement of palliative care service are used to assist patients and families come to terms with the inevitable outcome.”

4. The Reviewer questions our comments on the need to de-emphasize the use of indicators for aggressive care at the end-of-life.

   We have amended this sentence (page 10 line 279-281) with the appropriate reference as requested from “We suggest that in modern cancer care, there is a need to de-emphasize the use of some of the indicators for ‘aggressive care’ at the EOL in certain circumstances and possibly even consider indicators that are based on ‘appropriateness of care’ based on physical and psychosocial needs” to “We suggest that in modern cancer care, there can sometimes be a need to reconsider the use of the term ‘aggressive cancer care’ at the EOL when the care is appropriately based on an individual patient’s presenting physical and psychosocial needs.”

Response to Reviewer 2

1. We thank the Reviewer for comments and queries questioning the use of the term ‘aggressiveness’ of end of life care and potential confusion it may cause with our simultaneous use of the term ‘aggressive cancer care’.

   The Reviewer correctly states that the term aggressive cancer care is well defined as the following: “the use of chemotherapy in the last 14 or 30 days of life, emergency department (ED) presentation, acute hospital/intensive care unit (ICU) admission within 30 days of death or death in ICU, and late referral to hospice/palliative care services (≤3 months from referral to death)” (page line).

   The term aggressive end-of-life care is also well described in the literature. We provide references from 4 palliative care articles published this year that use the term in the Reference list at this end of this Response to the Reviewers [6-9]. However, we agree that our use of this term in this manuscript adds confusion. The Reviewer’s comments suggest that we need to reconsider how we use the word ‘aggressive’ in the end of life context. We have now used the term ‘aggressive treatments toward the end of life’ to allow a more careful distinction from the term ‘aggressive cancer care’. We have thus made adjustments to the manuscript as follows:

   a) Title has been changed to

   Timing of palliative care referral and aggressive treatments toward the end of life in pancreatic cancer. A retrospective, single-center observational study
b) Page 3 line 69 has been changed from “Quality EOL indicators to evaluate treatment aggressiveness towards the EOL” to “Quality EOL indicators to evaluate the use of aggressive treatments towards the EOL”

c) Page 3 line 72 has been changed from “Traditionally, aggressive cancer care at the EOL” to “Traditionally, aggressive cancer care received toward the EOL”

d) Page 3 line 75-76 has been changed from “Studies have shown that patients experience more aggressive EOL care” to “Studies have shown that cancer patients experience more aggressive treatments toward the EOL”

e) Page 4 line 90-91 has been changed from “Data relating specifically to aggressiveness of EOL” to “Data relating specifically to the use of aggressive treatments toward the EOL for pancreatic cancer patients remain limited.”

f) Page 4 line 97-98 has been changed from “PCR was associated with less aggressive EOL care, including less chemotherapy treatment (OR 0.34, 95% CI 0.25-0.46)” to “PCR was associated with less chemotherapy treatment (OR 0.34, 95% CI 0.25-0.46)”.

g) Page 4 line 108-109 has been changed from “aimed to examine associations between timing of PCR and aggressiveness of EOL care received by pancreatic cancer patients in the last 30 days of life.” to “aimed to examine associations between timing of PCR and aggressive cancer care received by pancreatic cancer patients in the last 30 days of life.”

h) Page 6 line 149 has been changed from “measures of aggressive care” to “measures of aggressive cancer care”

i) Page 8 line 220 has been changed from “instances of aggressive care near death, with the minimum number of palliative care contacts” to “instances of aggressive treatments used near death, with the minimum number of palliative care contacts”

j) Page 9 line 251 has been changed from “These contradictory findings of seemingly aggressive care supports the findings of Wijnhoven” to “These contradictory findings of seemingly aggressive cancer care supports the findings of Wijnhoven”

1. The Reviewer seeks clarification in our concluding statements.

Page 10 line 275-279 has been changed from “Our findings reaffirm the benefits of early referral to palliative care, especially for those with aggressive illnesses and limited prognoses. We
however question the ongoing benchmarks for aggressive care at the end of life, based on our findings that patients with significant symptoms and whose caregivers lack support or resilience appropriately require acute hospital service utilization or care in a supported environment” to:

“Our findings mirror the results of a small number of international studies and reaffirm the benefits of early referral to palliative care for pancreatic cancer patients to avoid futile treatment and inappropriate care toward the EOL [10,23,25]. We however question the current benchmarks for aggressive cancer care at the EOL, based on our findings that patients with significant symptoms and whose caregivers lack support appropriately require acute hospital service utilization or care in a supported environment.”

2. The reviewer seeks that the paper is strengthened to ensure generalizability beyond Australia. We have made the following amendments to the manuscript:

Page 3 line 64-66 has been changed from “Despite pancreatic cancer being the fourth and fifth leading cause of cancer death in the United States of America [7] and Australia [8] respectively” to “Despite pancreatic cancer being the fourth leading cause of cancer death in the United States of America [7] and Europe [8] and the fifth leading cause of cancer death in Australia [9],”

Page 10 line 275-277 has been changed from “Our findings reaffirm the benefits of early referral to palliative care, especially for those with aggressive illnesses and limited prognoses” to “Our findings mirror the results of a small number of international studies and reaffirm the benefits of early referral to palliative care for pancreatic cancer patients to avoid futile treatment and inappropriate care toward the EOL”

References


