

Article details: 2014-0044	
Title	Effects of Pediatric Palliative Care Programs for Children with Life-Threatening Conditions in Healthcare Resources Utilization and Costs: a Systematic Review of Comparative Studies
Authors	Conte, Tania; Mitton, Craig; Trenaman, Logan; Chavoshi, Negar; Siden, Harold
Reviewer 1	Donna Johnston
Institution	Children's Hospital of Eastern Ontario, Pediatric Hematology/Oncology
General comments	<p>This is a well written review of studies of pediatric palliative care programs for children with life-threatening conditions, examining the health care resource utilization and costs. There are a few changes that would strengthen the review.</p> <p>Abstract: 1) The methods section of the abstract needs to be expanded as from the this section it is not clear how the authors carried out the study. Perhaps more specifics on what they reviewed would make it clearer.</p> <p>Methods: 1) Under the inclusion criteria the authors state that they included children up to the age of 22 years but did not explain why they chose this age as the cut off. It is not an age generally accepted in the literature as defining a child and thus they need to justify this inclusion criteria. 2) The data sources say that the search is limited to articles but the authors have included a presented abstract. They need to clarify this in the methods section if they are including abstracts, and if they are, they should define how the abstract was found and ensure there are not other abstracts that they should include in the review.</p> <p>Results: 1) Line 58 of page 7 has a typographical error (Table and not Tables). 2) On page 8, line 45 the authors describe a study of "three patients who were cared for one day" – this is unclear and more description of the study would be helpful. 3) On page 9, line 10, do the authors mean no PC code or no PC service? 4) On page 10, line 29, it is not clear what the authors mean by "deprivation category" – this needs to be defined.</p> <p>Interpretation: 1) On page 11, line 7, small typographical error: should read "who were discharged".</p>
Reviewer 2	James Downar
Institution	University of Toronto, Medicine
General comments	<p>Review of CMAJOpen-2014-0044 James Downar, University of Toronto</p> <p>Reviewer's self-perceived bias: I am a strong supporter of Palliative Care and firmly believe that palliative care programs generally improve resource use (hospital admission, length of stay and costs) even though some studies do not support this.</p> <p>Major Comments: The authors must be congratulated for trying to make sense of a confusing body of literature. That said, I am still confused after reading this review. I hope that my comments will be helpful. The authors cannot be faulted for the numerous limitations and heterogeneity in the literature, but please help the reader make sense of it all. I would suggest categorizing the literature into higher and lower quality studies (based on objective evaluations of bias, and strength of methodology), and more comprehensive vs. less comprehensive PPCP interventions. This could make it easier to interpret contradictory results (for example, if all of the high quality studies of comprehensive PPCP interventions show a benefit, while the lower quality, less comprehensive studies do not). Otherwise, the authors' conclusion (i.e. that there is a benefit to PPCP) is hard to justify- the interventions are too different, the endpoints are not well tracked, and the results vary too much between studies.</p> <p>Minor Comments: 1. Study characteristics-I am confused about the definition of PPCPs used in the analysis of observational studies- this is variously defined as hospice provider, PC billing or planned location of death. These are not equivalent- does a planned location of death really indicate the existence of a PPCP? Is "access to PPCP" the same thing as receiving PPC? 2. The results section of the abstract and the first paragraph of the conclusion section</p>

	<p>give different impressions of the data, and both conclude that there is benefit although this is not clear to me from the data (see above).</p> <p>3. Outcomes- One study showed that PC was associated with a LOWER likelihood of sedatives and analgesia prior to death. Is that correct?</p>
Reviewer 3	Simone Stenekes
Institution	CancerCare Manitoba, Symptom Management and Palliative Care
General comments	<p>Thank you for this important summary of literature evaluating key aspects of program resource utilization related to pediatric palliative care.</p> <p>Overall, the analysis of the 11 articles included in this review is broad. The inclusion criteria and process for the review is clear. The various evaluation techniques are outlined and the tables are detailed and comprehensive. The summary included within the text of the review is straight forward and to the point. Future recommendations are valid and timely.</p> <p>Overall comments: Using PPC, PC or PPCP within the document does not provide consistency for the reader.</p> <p>I have detailed information below regarding some suggestions for changes/modifications to specific text.</p> <p>p. 5, line 39-40: "Evidence suggests PPCPs decrease resource use". Based on what is included in this review, this is likely too strong of a statement to make. I would suggest softening it a bit to the realities of the studies included.</p> <p>p.6, line 18: grammar "potentially compromising the continuity of care and lacking critical ..." Add the word "of"</p> <p>p. 6, line 26: "to those who rely exclusively on hospital care". Standard care likely includes home care in many pediatric programs. Home care usage is not exclusive to PPCP's.</p> <p>page 7, line 57: remove the "s" from "Tables", to read instead : "..presented in Table 1"</p> <p>p.10 – first paragraph – When stating that enrollment in PPCP often requires a referral by a healthcare professional, I think that pediatric programs are much more open than adult programs. Families could refer themselves and have a discussion about program criteria directly with the PPCP. In line 7, the statement about "not often carried along with curative treatments" should be removed. Often treatment aimed at prolongation of life may continue to be chosen by families whose children are enrolled in PPCP. Many pediatric disease are not curable, and many children are followed by PPCP who are admitted to ICUs and pursue very aggressive care while also being very involved with PPCP. Can you support these statements about the differences between the 2 groups with literature?</p> <p>p. 10 – line 19 "overtime" should be two words "over time".</p> <p>p.10, line 37 – "and costs observes in the PPC was a consequence" – should be past tense to be consistent with the rest of the sentence.</p> <p>p.10 – lines 55-56 – It is too strong of a statement given the information provided in the sentences preceding this (lines 48-54). The sentence is also quite weak in how things are stated (i.e.: "it is likely reasonable"). This is one of the most important sentences in your paper. I would suggest this sentence be modified to reflect that this review supports that PPCP do not increase healthcare utilization and costs.</p> <p>p. 11, line 3 – change "literature" to "systematic review"</p> <p>p. 11, line 4 – "included only included children" - remove first 'included'</p> <p>p.11, line 7 – ""or those who were discharged to die at home" – add the word 'were'</p> <p>p.11, line 23 – change to "types of inpatient resource utilization" – remove 's' in inpatient and add 'resource'</p> <p>p. 11, line 52-55 – sentence difficult to understand. Consider re-wording.</p>

	<p>p.12, line 28+29 – I would suggest removing “policies and procedres” and replacing with “funding models”</p> <p>p.12, lines 31-33 – sentence requires revision</p> <p>p.12, last sentence – “Noting these limitation, this review” change ‘study’ to ‘review’</p> <p>p.13, line 5 – remove “and a proxy for quality of end-of-life care for children and families”</p> <p>p.13 – funding and affiliation – you might want to provide this information in the order the authors are listed.</p> <p>Table 1 – keep tense the same throughout – suggest use of past tense – this will require numerous changes, which I have not listed.</p> <p>Table 1 – p. 15 – Dussel article info</p> <ul style="list-style-type: none"> • check “participants” box – unclear language and structure of this box. • Check “comparator” box – should read “did not plan” (remove “-ed) <p>Table 1 – p.16 – Arland article info</p> <ul style="list-style-type: none"> • “Intervention” box – “program carried by a “, should probably read “program provided by a” <p>Table 1, p. 17 – Smith article info</p> <ul style="list-style-type: none"> • list as “Smith A et al 2013” – the ‘A’ is forgotten as all other first authors have their first initial listed in this table (This is a consistent issue in all of the other tables as well) • “participants” box – ‘decile’ - ? incorrect spelling or word • “funding” box - “by the hospital where the research” – change ‘were’ to ‘where’ <p>Table 2 – no explanation provided on what this table means. I have no idea what low risk, moderate and high risk are attempting to convey. Provides a description of the type of research design, but the rest of it means nothing to the reader.</p> <p>Table 3 – unknown what “follow-up” refers to regarding the studies listed in this table</p> <ul style="list-style-type: none"> - Fraser – decrease or increase in these admissions listed? - Dussel (p. 20) – “did not planned” – change to “LOD not planned” or “did not plan” - Arland (p.21) – “the authors stated a 46% fewer hospital”, change to “the authors state 46% fewer hospital” (remove ‘a’) - Pascuet (p.21) – “monthly” should read “month” <p>Table 4 - Pascuet (p.22) – “monthly” should be “month”</p> <ul style="list-style-type: none"> - Dussel should be “Did not plan LOD”, instead of “Did not planned LOD” <p>Appendix B – Numerous spelling and grammatical errors. Too numerous to list all of them. Please revise and pay attention to these details.</p>
<p>Author response</p>	<p>Abstract:</p> <p>1. Please shorten the background section to two sentences: Explain the problem or issue (the reason you decided to conduct your study) in the first sentence and state the objective of your study (the question you set out to answer) in the second sentence. (i.e., “Pediatric palliative care is a young and evolving field and the cost of these pediatric palliative care programs (PPCPs) is unclear. We conducted a systematic review to compare inpatient healthcare resource utilization and costs among children with LTCs who have accessed a PPCP with those who have not accessed a PPCP.”)</p> <p>ACTION/ANSWER: corrected as required. Page 1, l28-31</p> <p>Introduction:</p> <p>2. Please rephrase the statement that, “In particular, administrators in both hospital and hospice settings in British Columbia were requesting the type of review” with something more generic. For example, “this information will be useful to hospice and hospital administrators”.</p> <p>ACTION/ANSWER: corrected, yet later removed to meet the word count required.</p> <p>3. Why did you choose to focus your review on resource utilization? Did you consider including studies of cost-effectiveness analysis (i.e., costs/QALY)?</p> <p>ACTION/ANSWER: This systematic review is one part of a project looking at health care</p>

utilization and cost of the PPCP in BC (including a cohort study and a cost analysis). During the screening of the articles, we were mindful in looking for any type of comparative studies approaching costs or utilization; therefore, cost/QALY studies were considered yet not found.

Methods:

4. In support of your decision to limit your search to studies of children up to 22 years of age, you reference Canuck Place. According to their website, "Canuck Place is open to all British Columbia children up to and including the age of 19 with a progressive, life-threatening illness". Please clarify.

ACTION/ANSWER: Twenty two years of age is an arbitrary cut off we chose to "control" for adult acquired diseases, but still capture children diagnosed with an LTC in the late teens where death may occur at 19+, or for conditions where the diagnosis is made during childhood but death usually occurs after 19 (e.g. certain neuromuscular conditions).

Cancer is the main mortality cause in the hospice cohort. According to the Canadian Cancer Statistics leukemia, lymphomas and cancer of central nervous system (CNS) are the most common cancers in children and youth (0-19 years) with a 5-year Observed Survival Proportion of 84%, 89% and 71%, respectively.¹ More specific data from UK on youth and young adults (15-24 years) showed a 5-year survival for these types of cancer from 50%-80%² which predicts a important proportion of this population going through the transition phase and, therefore, impacting in the utilization and cost. While children cannot enter the program at Canuck Place (CP) if they are 19+, if they were enrolled in the program before 19, they are still involved in the transition/bereavement phase that usually last 1-2 years. Children in the transition no longer has access to respite, but for an additional year or two, they can still access end-of-life care or fully migrate to adult palliative care. Although this program feature is not available in the website is a part of the internal trend, confirmed through personal communication (Chavoshi, N; Siden, H., e-mail communication, September 2014).

5. Please clarify which study designs were included in your search: "As ethical concerns surround the randomization of children to different approaches of care in Randomized Control Trials (RCTs), the inclusion criteria for studies included all types of comparative studies (experimental or observational studies, and secondary administrative databases analysis), regardless of length of observation period. The review included published articles or abstracts from conference procedures, retrieved through the automatized search strategies and grey literature review." For example, "We included published articles and abstracts describing comparative studies (experimental or observational studies, and secondary administrative databases analysis), regardless of length of observation period."

ACTION/ANSWER: Corrected. We were following the Cochrane Handbook Chapter on non-randomized studies³ which requires a justification for the inclusion of non-randomized studies. If CMAJ's editorial does not require it, we agree that removing it increases the readability. Page 2, 132.

6. It is not clear from your response whether study selection was conducted in duplicate. That is, did both TC and LT review the full list of 3765 abstracts?

ACTION/ANSWER: Yes, both authors reviewed the full list of 3765 abstracts. TC identified 84 abstracts while LT identified 41 abstracts for inclusion to full paper review. Of the 84 and 41, 16 papers were in common. See level of agreement on comment 10.

7. Please re-order the paragraph on data extraction, analysis and quality assessment so that the methods are reported in that order [(1) data extraction, (2) analysis and (3) quality assessment].

ACTION/ANSWER: re-ordered. Page 3, 27-32

8. As you have now assessed the quality of included studies using the NOS, there is no need to reference the Cochrane Collaboration's tool for assessing risk of bias: "Bias was also assessed independently by two the reviewers using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions and ranked according to the Newcastle-Ottawa Scale (NOS)".

ACTION/ANSWER: corrected. Page 3, 20-21

9. You note that studies were ranked/categorized according to the NOS. How was this done? The studies in Table 2 do not appear to be ordered from highest number of stars to lowest.

ACTION/ANSWER: Actually they are. We rated them by the overall number of stars (not by item). The first study has an overall rate of 6 stars and gradually decreases to an

overall rate of 3 stars.

Results:

10. In your description of the results of the study selection process, please add a sentence describing the exclusion of 3656 abstracts. If this was conducted in duplicate, please provide the level of agreement.

ACTION/ANSWER: We can provide the kappa statistics for the level of agreement in the selection for full text analysis according to the editor's request ($\kappa = 0.25$, 95% CI 0.22–0.28, $p < 0.001$, indicating fair agreement). However, at the first stage a higher level of agreement was not expected due to a broad question and learning process on how the topic was being published worldwide. At the inclusion process the level of agreement was ($\kappa = 0.83$, 95% CI 0.64–1.00, $p < 0.001$, indicating almost perfect agreement). It is the second kappa statistic that we believe relevant information for the reader. However, as advised by the editor we included both scores. Due to a word count constrain we provided kappa statistics, confidence interval and interpretation in squared brackets without further debating the results. Page 3, l 27-32.

11. According to your methods, your search was not designed to find RCTs. If this is the case, please delete the statement, "No RCTs were found". If your search strategy did allow for the inclusion of RCTs, please move this statement to the 'Study Characteristics' sub-section and clarify the methods section.

ACTION/ANSWER: Corrected. We moved the statement to the 'Study Characteristics' sub-section and clarify the methods section by adding randomized control trials (RCT) besides experimental studies. Page 3, l35; Page 2, l32-33.

12. Please rename the 'Risk of bias' sub-section 'Quality assessment'.

ACTION/ANSWER: renamed. Page 4, l27

13. As your reporting of outcomes is characterised according to study quality, please move the 'Risk of bias' subsection earlier in the results section (i.e., after the 'Study characteristics' sub-section).

ACTION/ANSWER: moved. Page 4, l27

14. Some of the text under the 'Risk of bias' sub-section (i.e., the description of the NOS) would be more appropriately placed in the 'Data extraction, analysis and quality assessment' sub-section in the methods section.

ACTION/ANSWER: moved. Page 3, l21-23

Table 5:

15. Please further summarize the outcome data for the Knapp study. For example, "Total mean expenditures (all causes of death): Hospice users: \$83,719; Non-hospice users: \$36,597"

ACTION/ANSWER: Changes applied. Page 14

Appendix D:

16. Please review this Table. Some sections do not appear to have any boxes ticked.

ACTION/ANSWER: Some boxes are not ticked because this is a feature of the NOS tool. If an article meets a criterion followed by a ★ in the checklist, then the box will appear as a ★. If the article meets a criterion that is not followed by a ★, then the box will appear ticked. In the "Comparability" section there is only 2 questions, both followed by a ★, the articles did not meet either criteria and, therefore, did not received a ★. References and manual on how to use the scale were extracted from the Ottawa Hospital Research Institute.⁴ We have added a note below the table so the reader will know exactly how to interpret this presentation. Page 50-51

General:

17. The acronyms should be defined in table footnotes. This is not done consistently.

ACTION/ANSWER: reviewed and corrected. Page 10-14

18. Please ensure your final word count is below 3000 words (excluding abstract, figures, tables and references).

ACTION/ANSWER: We did our best to incorporate all applicable changes required by the reviewers/editors and reduce word count, managing to get down to 3259 words (excluding abstract, figures, tables, references and titles). Taking into consideration the complexity of the topic and that the included studies are not straightforward RCTs, we feel that suppressing further details will compromise the quality of the systematic review and the reader's ability to interpret the results. Kindly provide advice on where

further word cuts can be made without compromising readability.

19. Please supply Figure 1 as an editable Word or PowerPoint file.
ACTION/ANSWER: provided editable Word. Page 9

20. Please list each author's degree(s) and affiliation(s) on the title page.
ACTION/ANSWER: moved. Page 1