PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of palliative home care support on the quality and costs of care at the end of life: a population-level matched cohort study
AUTHORS	Maetens, Arno; Beernaert, Kim; De Schreye, Robrecht; Faes, Kristof; Annemans, Lieven; Pardon, Koen; Deliens, Luc; Cohen, Joachim

VERSION 1 – REVIEW

REVIEWER	Viktor von Wyl University of Zurich, Switzerland
REVIEW RETURNED	06-Sep-2018

GENERAL COMMENTS	This is a well-performed study on health care use over the last 14 days of life, compared by palliative care use status up to 15 days prior to death. The analysis is methodologically sound and state-of-art. Nevertheless, I would be hesitant to state that the observed lower costs and generally more favorable inappropriateness of end-of-life care indicators are entirely due to palliative care. Despite the impressive database for this study, residual (unknown) confounding may play a substantial role; a fact that is also adequately acknowledged in the limitation section. As it is unclear (and unmeasured) what factors were taken into account when deciding about palliative care use, it remains likely that - despite propensity score matching - the palliative care group may still not entirely be comparable to the control group. For example, the diagnostic categories employed in this analysis are very broad, and expectations regarding remaining life time or cure rates differ widely (e.g. across different cancer types). Looking at intensity of care trajectories in the period prior to death may be instructive in that regard. Moreover, the dominance of neoplasms in the palliative care group also suggests that certain diseases may be more apt for palliative care planning and intervention than others. However, these limitations do not diminish this study's value, and the conclusions are very balanced. In my view, this analysis also clearly demonstrates that the circumstances of palliative care decisions clearly warrant further investigation, as they are still only partially understood.

REVIEWER	Dr Nikki McCaffrey Deakin University, Victoria, Australia
REVIEW RETURNED	25-Sep-2018

GENERAL COMMENTS	Please note, the views expressed below belong solely to this reviewer. The comments are intended to be constructive and the feedback aims to improve the quality of the manuscript. This matched cohort study provides a useful contribution to the field of research on the costs and benefits of community-based palliative care services. Generally, this is a well written and well-structured manuscript. The manuscript would benefit from further, minor editing for grammar. The title adequately describes the study. The abstract is a fair summary of the study. The introduction clearly states the objective of the study. Overall, the methods chosen appear robust and appropriate for the stated objective based on the information provided. Sufficient data are provided to support the overall presentation of results. Additional data on the statistical significance of the incremental costs would add value to the information provided (including tests for differences between the mean costs and presenting the 95% confidence intervals). Good use is made of tables and figures to summarise findings. The discussion and the conclusion are justified by the research reported in the manuscript. The conclusion covers the main points. Major points 1. Abstract: given the results state the average costs of care were lower for those using palliative home care support, please include the increment and 95% confidence intervals. 2. Abstract: suggest the context for the analysis needs including in the conclusion, i.e. ‘Palliative home care support use positively impacts quality of care and reduces total costs of care at the end of life in Belgium (or a Belgium population).’ 3. Abstract: add in the data for use of palliative home care support to support the final sentence. 4. Background: line 71, did the four retrospective studies use matching? If so, please make this clear in the text. 5. Methods: why was the exposure group selected from people who had received at least one type of palliative home care support up to 720 days? Why was this time frame chosen? Particularly given seriously ill patients with a short life expectance is defined by law as “more than 24 hours and less than three months.” Of course, this is expected life expectancy (and therefore may not be accurate1), but even so, two years appears somewhat inconsistent with three months. What are the implications of the differing time horizons? Please include discussion. 6. Methods: how were the baseline covariates chosen? How was relevance determined? Literature? Expert opinion? Both? Please include more details about how these decisions were made. 7. Results: are the differences in mean inpatient, outpatient and total costs statistically significant? What are the 95% confidence intervals? 8. Results: the data in supplementary table 1 seem to suggest there was a difference for the risk of home death for the cohort using multidisciplinary palliative home care teams. Please comment on this finding in the results and discussion sections. 9. Discussion: please discuss the implications of accessing the services at different times during the possible 15-720 day period and the implications of receiving home-based palliative care services for different durations. 10. Discussion: what proportion of home-dwelling adults who died in Belgium in 2012 used palliative home care supports in the last three months of life?

11. Table 3: please include the 95% confidence intervals for the increment.
Minor points
1. General: suggest ‘full’ is redundant when describing population-level data. Alternatively, perhaps use ‘complete’ rather than ‘full’.
2. General: for an international audience, please consider alternative phrases for ‘palliative supportive measures’. Maybe ‘palliative support services’, ‘community-based palliative support services’ or ‘home-based palliative support services.’
3. Abstract: results: please highlight the time period, i.e. ‘those using palliative home care support in the last 720 to 15 days of life…’
4. Strengths and limitations of the study: suggest add, ‘given ethical and practical concerns’ to the second bullet point as per the main body.
5. Strengths and limitations of the study: whilst the operationalisation of palliative home care support does indeed increase the reproducibility of the study in other countries, the findings are largely generalisable to countries with similar health care service delivery models and funding. For example, the findings may be somewhat different in the US setting.
6. Background: line 59, why were costs lower in the intervention group? Please elaborate.
7. Background: suggest start a new paragraph starting with the sentence, ‘However, traditional experimental study designs…’ to aid flow of the information.
8. Background: perhaps provide an example of ‘ethical and practical concerns’ to help the reader’s understanding.
9. Background: suggest reword lines 67-9, ‘A matched cohort study design with robust matching of a group receiving home care support and a group not receiving this support is the best level of evidence for evaluating this impact at a population level.’
10. Methods: what does ‘matched to a control cohort from the same pool’ mean? Please clarify.
11. Methods: please explain what is meant by ‘fiscal data’. Perhaps provide a few examples in brackets.
12. Methods: providing a brief summary of the properties of the RAND/UCLA quality indicators in addition to the citation would be very helpful for the uninformed reader.
13. Methods: please provide a brief description of how health care services are funded in Belgium and how services are costed. For example, are DRGs used to determine payment for hospital services?
14. Methods: what were the sources of the unit costs?
15. Discussion: whilst the findings are more easily translated to other jurisdictions due to the population-wide analysis and inclusion of multiple models of home-based palliative care service delivery, the generalisability of the results is still limited to jurisdictions with similar health care delivery and funding systems. Please clarify this in the text.
16. Conclusion: line 337, suggest insert ‘matched’ before cohort as this highlights one of the strengths of this study.
17. Conclusion: ‘remains widely underused’ is a very strong statement based on the evidence presented. Suggest soften to, ‘appears widely underused.’
18. Supplementary table 1: please include the results from the aggregated services from Table 2 to facilitate easy comparison with the three subgroups.
19. Supplementary table 2: please include the increment and 95% confidence intervals.

	References 1. White N, Reid F, Harris A, et al. A Systematic Review of Predictions of Survival in Palliative Care: How Accurate Are Clinicians and Who Are the Experts? PLOS ONE 2016;11(8):e0161407.

VERSION 1 – AUTHOR RESPONSE

	Reviewer comments	**Response**	**CHANGES MADE** [all references to **pages and lines** are related to the resubmitted revised manuscript **("track changes" version)]** *New text,* original text, with referral page and line number of the revised manuscript and supplementary appendix.
	EDITOR COMMENTS		
1	Please edit your title so that it is not declarative		We changed the title: p.1, line 1: *Impact of palliative home care support on the quality and costs of care at the end of life:* a population-level matched cohort study
2	Please provide another copy of your figures with better qualities and please ensure that figures are of better quality or not pixelated when zooming in. NOTE: They can be in TIFF or JPG format and make sure that they have a resolution of at least 300 dpi and at least 90mm x 90m of width. Figures in PDF, DOCUMENT, EXCEL and POWER POINT format are not acceptable.		Figure 1 was saved as a high-resolution JPEG format.
3	Please re-upload your supplementary files in PDF format.	OK	
4	Please embed the following statements to your main document just before your reference list: A. contributor ship statement B. competing interests	We believe all necessary information was included, but changed the titles of the headings as requested.	We changed the titles of the headings under "Declarations" on p.20, lines 501, 511, 517: "*Contributorship statement*", "*Declaration of competing*

	C. funding D. data sharing statement		*interests*", "*Data sharing statement*".
5	We have implemented an additional requirement to all articles to include 'Patient and Public Involvement' statement within the main text of your main document. Authors must include a statement in the methods section of the manuscript under the sub-heading 'Patient and Public Involvement'. This should provide a brief response to the following questions: How was the development of the research question and outcome measures informed by patients' priorities, experience, and preferences? How did you involve patients in the design of this study? Were patients involved in the recruitment to and conduct of the study? How will the results be disseminated to study participants? For randomised controlled trials, was the burden of the intervention assessed by patients themselves? Patient advisers should also be thanked in the contributorship statement/acknowledgements. If patients and or public were not involved please state this.		We added the 'Patient and Public Involvement' statement in the method section, p.6-7. lines 151-166: "We used *previously* validated quality indicators (QI) for end-of-life care to measure appropriateness and inappropriateness of end-of-life care on an aggregated level. *Patients were not directly involved in the design of the study or development of the QIs. The design of the study, using population-level decedent data, did not allow to disseminate results to or involve observed patients in the development of the research questions or outcome measures.*"
	REVIEWER 1		
0	This is a well-performed study on health care use over the last 14 days of life, compared by palliative care use status up to 15 days prior to death. The analysis is methodologically sound and state-of-art.		
1	Nevertheless, I would be hesitant to state that the observed lower costs and generally more favorable inappropriateness of end-	We agree with the comments of the reviewer about the need to carefully interpret the results, and we did so by stating clearly the	We added in the limitations section on p.18, lines 470-472: "*Although the circumstances of palliative care decisions clearly warrant further investigation, as*

	of-life care indicators are entirely due to palliative care. Despite the impressive database for this study, residual (unknown) confounding may play a substantial role; a fact that is also adequately acknowledged in the limitation section. As it is unclear (and unmeasured) what factors were taken into account when deciding about palliative care use, it remains likely that - despite propensity score matching - the palliative care group may still not entirely be comparable to the control group. For example, the diagnostic categories employed in this analysis are very broad, and expectations regarding remaining life time or cure rates differ widely (e.g. across different cancer types). Looking at intensity of care trajectories in the period prior to death may be instructive in that regard. Moreover, the dominance of neoplasms in the palliative care group also suggests that certain diseases may be more apt for palliative care planning and intervention than others. However, these limitations do not diminish this study's value, and the conclusions are very balanced. In my view, this analysis also clearly demonstrates that the circumstances of palliative care decisions clearly warrant further investigation, as they are still only partially understood.	limitations of the study and the propensity score method that was used.	*they are still only partially understood, our findings are* relevant information…”
	REVIEWER 2		
0	This matched cohort study provides a useful contribution to the field of		

	research on the costs and benefits of community-based palliative care services. Generally, this is a well written and well-structured manuscript.		
1	The manuscript would benefit from further, minor editing for grammar.	We had the manuscript language checked by a professional, native English language editor. We reread the manuscript to edit remaining grammar mistakes.	
2	The title adequately describes the study. The abstract is a fair summary of the study. The introduction clearly states the objective of the study. Overall, the methods chosen appear robust and appropriate for the stated objective based on the information provided. Sufficient data are provided to support the overall presentation of results. Additional data on the statistical significance of the incremental costs would add value to the information provided (including tests for differences between the mean costs and presenting the 95% confidence intervals). Good use is made of tables and figures to summarise findings. The discussion and the conclusion are justified by the research reported in the manuscript. The conclusion covers the main points.		We added data from the t-test to compare difference between the mean costs: p-values for the incremental costs and 95% confidence intervals, p.14-15 lines 349-357 (including edits in Table 3)
3	Abstract: given the results state the average costs of care were lower for those using palliative home care support, please include the increment and 95% confidence intervals.		We added this information in the abstract.
4	Abstract: suggest the context for the analysis needs including in the conclusion, i.e. ‘Palliative home care support use positively impacts quality of care and reduces total costs of care at the end of		We added the suggestion.p.2 line 43: “…*in Belgium*.”

	life in Belgium (or a Belgium population).’		
5	Abstract: add in the data for use of palliative home care support to support the final sentence.		We added in the data in the abstract, p2 line 33-34: “*In the unmatched cohort, 11,149 (13.5%) people received palliative home care support in the last 720 to 15 days of life.*”
6	Background: line 71, did the four retrospective studies use matching? If so, please make this clear in the text.	Three of the four studies used matching, the other was a retrospective cohort study without matching.	We deleted the reference to study not using matched controls, and added information in the text, p.5 line 102-104: “~~Four~~*Three* retrospective cohort studies *using matched controls* found … in Canada, England, ~~Italy~~ and the US.”
7	Methods: why was the exposure group selected from people who had received at least one type of palliative home care support up to 720 days? Why was this time frame chosen? Particularly given seriously ill patients with a short life expectance is defined by law as “more than 24 hours and less than three months.” Of course, this is expected life expectancy (and therefore may not be accurate1), but even so, two years appears somewhat inconsistent with three months. What are the implications of the differing time horizons? Please include discussion.	We wanted to include as many persons who received palliative home care support in the analysis, while also aiming to have a “prospective” look at the data to reconstruct a trial the best as possible with retrospective data. Our choice for the 720 day time-frame is in that sense a pragmatic choice: we had data available for up to 720 days before death.	We added this point in the methods section, p.7 lines 169-172: “*We included all persons receiving palliative home care support for the longest time-frame available in our data, i.e. up to 720 days before death. We did not want to exclude persons on the basis of a (retrospectively) predefined timeframe, as this information (time before death) would not be known using a prospective design.*”
8	Methods: how were the baseline covariates chosen? How was relevance determined? Literature? Expert opinion? Both? Please include more details about how these decisions were made.	We added references to support the relevance of the chosen baseline covariates.	p.10 lines 269-271: “*To calculate* the propensity scores, *relevant predictors for receiving palliative home care, based on previous research findings, were used* as baseline covariates [13]. *The following baseline covariates were used*: …”
9	Results: are the differences in mean inpatient, outpatient and total costs statistically significant?	Please see comment 2 of this reviewer for the answer to a similar comment.	

	What are the 95% confidence intervals?		
10	Results: the data in supplementary table 1 seem to suggest there was a difference for the risk of home death for the cohort using multidisciplinary palliative home care teams. Please comment on this finding in the results and discussion sections.	We already mention in the results that: "We performed sensitivity analyses on each supportive measure separately (shown in appendix) with no substantial differences between these measures in the impact on the quality and cost outcomes." (p.11 lines 291-293). We feel that this is sufficient information, since the direction and size of the effect is largely similar among all types of support, despite differences, and that this is not the scope of the article.	
11	Discussion: please discuss the implications of accessing the services at different times during the possible 15-720 day period and the implications of receiving home-based palliative care services for different durations.		We added this as a discussion point for further research, p.17 lines 433-435: "…removing it could increase the use *and timely initiation* of palliative home care support. *Further research should also be done to investigate the implications of accessing support at a different period in the disease trajectory on the quality and costs of care at the end-of-life."*
12	Discussion: what proportion of home-dwelling adults who died in Belgium in 2012 used palliative home care supports in the last three months of life?	We did not calculate the use of palliative home care support only in the last three months of life. However, many people receive this support late in life; in the population of home-dwelling people, the median number of days before death of first use is 41 days (unpublished result). We mention this as a limitation on p.17-452-454. Also, we describe the	

		choice for our inclusion period in the methods section on p.7 lines 162-165.	
13	Table 3: please include the 95% confidence intervals for the increment.	Please see our answer to comment 2 of the same reviewer.	
14	General: suggest ‘full’ is redundant when describing population-level data. Alternatively, perhaps use ‘complete’ rather than ‘full’.		We followed this comment and removed “full” in “population-level data” throughout the manuscript.
15	General: for an international audience, please consider alternative phrases for ‘palliative supportive measures’. Maybe ‘palliative support services’, ‘community-based palliative support services’ or ‘home-based palliative support services.’		We did not change the terminology to those proposed, since not all types of palliative home care support included were services (ie the allowance for palliative home patients). Instead, we deleted “measure” where possible and replaced it with “support”, “support type”, or “policy measure”.
16	Abstract: results: please highlight the time period, i.e. ‘those using palliative home care support in the last 720 to 15 days of life…’		We added this in the results section of the abstract., p.2 line 32: “Those using palliative home care support *in the last 720 to 15 days of life* had…”
17	Strengths and limitations of the study: suggest add, ‘given ethical and practical concerns’ to the second bullet point as per the main body.		We added the suggestion “given ethical and practical concerns” to the second bullet point in the strengths and limitations box, p.3.
18	Strengths and limitations of the study: whilst the operationalisation of palliative home care support does indeed increase the reproducibility of the study in other countries, the findings are largely generalisable to countries with similar health care service delivery models and funding. For example, the findings may be somewhat different in the US setting.		We added this point to the fourth bullet point in the strengths and limitations box, p.3: “…, *especially in countries with similar health care service delivery models and funding.*”
19	Background: line 59, why were costs lower in the intervention group? Please elaborate.	The authors of the Cochrane review did not go into detail about reasons for	

		cost differences found in the studies.	
20	Background: suggest start a new paragraph starting with the sentence, ‘However, traditional experimental study designs…’ to aid flow of the information.		We inserted the sentence as a new paragraph on p.4 line 90.
21	Background: perhaps provide an example of ‘ethical and practical concerns’ to help the reader’s understanding.		We added an example in parenthesis, p.4 line 91-92: “…*e.g. it would illegal to refrain patients from receiving any palliative home care in a trial*)
22	Background: suggest reword lines 67-9, ‘A matched cohort study design with robust matching of a group receiving home care support and a group not receiving this support is the best level of evidence for evaluating this impact at a population level.’		We reworded the sentence, p.5 lines 99-100: “A matched cohort study design with a high-quality matching *on the propensity of receiving palliative home care* is the best possible technique to evaluate this impact.[15]”
23	Methods: what does ‘matched to a control cohort from the same pool’ mean? Please clarify.		We edited this sentence on p.5-6 lines 122-131 to: “~~A cohort~~*An individual* that used at least one type of palliative home care support *was matched to* ~~a cohort from the same pool~~ *an individual* that used no palliative home care support.”
24	Methods: please explain what is meant by ‘fiscal data’. Perhaps provide a few examples in brackets.		We added clarification in brackets, p.6 lines 148-149: “Additionally the data include demographic data, fiscal data (*i.e. net taxable annual income*),…”
25	Methods: providing a brief summary of the properties of the RAND/UCLA quality indicators in addition to the citation would be very helpful for the uninformed reader.		We described the RAND/UCLA method and added a citation to this method on, p.9 lines 206-209: “We used quality indicators for appropriate and inappropriate end-of-life care that were developed using the RAND/UCLA Appropriateness method, that aims “to combine the best available scientific

			evidence with the collective judgment of experts to yield a statement regarding the appropriateness of performing a procedure at the level of patient-specific symptoms, medical history, and test results" [25]."
26	Methods: please provide a brief description of how health care services are funded in Belgium and how services are costed. For example, are DRGs used to determine payment for hospital services?		We added a description of how healthcare services in Belgium are funded on p.8 lines 185-188: "*The Belgian health system is primarily funded through social security contributions and taxation, with a compulsory national health insurance, which covers the whole population. Compulsory health insurance is combined with a private system of health care delivery, based on independent medical practice, free choice of service provider and predominantly fee-for-service payment*." Additionally, supplementary box 1 describes the Belgian health care system in more detail.
27	Methods: what were the sources of the unit costs?		We added in the methods section that the nomenclature codes include identification of the reimbursed health-insurance cost.
28	Discussion: whilst the findings are more easily translated to other jurisdictions due to the population-wide analysis and inclusion of multiple models of home-based palliative care service delivery, the generalisability of the results is still limited to jurisdictions with similar health care delivery and funding systems. Please clarify this in the text.		We added this to the discussion section on p.17-18 lines 451-453: "*It should be noted however that the generalizability of the results remains largely limited to countries or regions with similar health care delivery and funding systems.*"
29	Conclusion: line 337, suggest insert 'matched' before cohort as this highlights one of the strengths of this study,		We inserted matched before cohort as suggested, p. 18 line 459.

30	Conclusion: 'remains widely underused' is a very strong statement based on the evidence presented. Suggest soften to, 'appears widely underused.'	We agree with the suggestion to soften the statement and changed "remains widely underused" to "appears widely underused" (p.18 line 465).
31	Supplementary table 1: please include the results from the aggregated services from Table 2 to facilitate easy comparison with the three subgroups.	We added the results in Supplementary table 1.
32	Supplementary table 2: please include the increment and 95% confidence intervals.	We included the increment and 95%CI in Supplementary Table 2 (not in track changes)

VERSION 2 – REVIEW

REVIEWER	Viktor von Wyl University of Zurich, Switzerland
REVIEW RETURNED	31-Oct-2018

GENERAL COMMENTS	No further comments