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Title	Community-based specialist palliative care teams reduce health system costs at end of life: a pooled-analysis of 11 teams
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Reviewer 1	Kieran Quinn
Institution	Department of Medicine, University of Toronto, Toronto, Ont.
General comments (author response in bold)	<p>MAJOR POINTS:</p> <p>1) Measuring costs as the primary outcome is informative but serves as a surrogate outcome for other important aspects of care that were not reported here, which would help explain some of the principle findings. Is the reduction in costs due to lower use of acute care services such as visits to the ED or hospitalizations? Or did access to community-based palliative care shorten length of hospital stay instead? This should be reported as a secondary outcome or discussed as a limitation in the interpretation of these findings.</p> <p>Reduction in costs was largely attributable to lower hospitalization costs not ED costs. We have included healthcare sector specific costs differences as a secondary outcome, as requested. This is stated in the RESULTS "Costs by healthcare sector" section. As can be seen in Figure 2, ED cost differences are negligible to the other sectors. We also have replaced "acute care" with "hospital care" in reference to our findings to avoid confusion. We added the LIMITATION that we did not differentiate multiple visits within hospital costs or look at length of stay; We do add a citation that shows that among cancer patients who die in hospital in Ontario, the majority only have a single visit in the last month of life.</p> <p>2) The costs measured and saved are those incurred by the healthcare system, and not out-of-pocket patient/family costs as the authors point out. Are we simply downloading increased homecare costs from those paid for by government-funded health insurance plans to individual families? Further discussion on the existing literature (including the average additional costs measured using the Ambulatory and Home Care Record – Guerrier et al. J Aging Res 2011) around this potential phenomenon should be discussed in more depth to support the study's principle findings and its potential limitations.</p> <p>We have replaced "overall costs" with "health system cost". We noted in LIMITATIONS that we did not account for other indirect costs borne by informal caregivers. We now state in CONCLUSIONS that further research is needed to examine these informal costs in relation to specialized palliative care teams.</p> <p>3) The choice of a paired t-test as an unadjusted statistical model (despite the use of a propensity score for up front matching) without accounting for clustering by individual care teams may bias the primary estimates of cost differences. Reanalysis of the primary outcome using GEE and adjusting for other measured factors that may impact upon EOL costs (e.g. urban versus rural team geography, number of decedents) should be performed or specifically discussed as a limitation to the findings.</p> <p>With respect, we do not believe that a clustered analysis is appropriate given that the study was not a multilevel regression design. (We also consulted two independent statisticians to be sure). If our research question was to ascertain the independent effect of having a specialist team on the costs in the last month of life (so regression would show the effect of team is \$X less than reference group, controlling for other covariates)—then we would require a GEE regression (and we could account for clustering). However, our research questions was to describe the cost difference among those who got a specialist team vs a comparable group who did not. Thus, our study design was a paired analysis from propensity score matched pairs. Here it is critical that we analyse the outcomes by matched-pairs... since we are matching pairs on the propensity score to get a specialist palliative care team (compared to usual care)... which is what we did. And thus we looked at mean cost differences on matched pairs (paired differences)—since we have a within-paired study design. Moreover, since our matches were excellent on virtually all the covariates between exposed and unexposed, we did not need to further adjust using regression. This study design was not intended to look at the differences within teams—or the independent effect of various aspects of each team (e.g. roster size) on cost outcomes, though this is noted as future work in the CONCLUSION.</p> <p>4) The most challenging aspect to palliative care research using administrative data is the presence of confounding by indication. While the authors have attempted to minimize this using a propensity score matching process, it is difficult to know whether the primary results were simply a result of unmeasured preferences for more intensive (and often more expensive) care. This should be discussed as one of the principle limitations of the study.</p> <p>The reviewer is correct that confounding by indication is one of the most challenges aspects of using administrative data. To be clear, we are not accessing cost savings among those who got any palliative care vs not (where there are very likely major confounders among those who do not choose any palliative care). We are assessing costs savings among (mostly) those who are already receiving end-of-life homecare, but exposed got also specialist palliative care team as well, whereas unexposed (usual care) just got end-of-life homecare only. We have added more detail in Table 2, which shows how much bias there is if we did not use propensity score matching (e.g. 79% of exposed group has cancer, whereas only 35% of usual care patients have cancer). Perhaps the most important confounder is the use of homecare: 78% of the exposed group was receiving end-of-life homecare for a mean of 87 days before death; whereas only 15% of usual care patients received end-of-life homecare for a mean of 15 days. The access to end-of-life homecare (and time using it before death) is a major confounder, as it is often a gateway to specialist community palliative care services. If we did not include home care as a covariate (both home care intent type and length of time on homecare), then we would have a major confounding issue, as shown in the before – after data in Table 1. Fortunately, in our propensity score matching methods, we are controlling for these homecare factors, as well as prior hospital and emergency department, comorbidity (using the Johns Hopkins Adjusted Clinical Groups), among other factors. After the matching, pairs are 78% using end-of-life homecare for a mean of 79 days before death... but the exposed also received community-based specialist palliative care team, whereas the unexposed did not.</p> <p>So we are matching on the propensity to receive palliative care among those who already have the same use of end-of-life home care; the pairs have the same likelihood/ propensity to get community-based speciality palliative care team (although only one group did). This is a strong study design to adjust for confounding by indication. But the reviewer is correct, that we cannot adjust/match on for unmeasured variables, like patient preferences. This is included as a LIMITATION. We believe it is partially minimized due to the two groups willingness to receive end-of-life homecare for almost 3 months in the first place, but is still a limitation.</p> <p>MINOR POINTS:</p> <p>Introduction: - The authors should provide further background and rationale as to the opportunity for cost savings near end of life as there appears to be an emerging controversy over the potential cost savings that can be had for care provided as individuals approach death. It can be difficult to predict when death will occur for many individuals, so knowing after the fact that costs can be saved makes it challenging to know when to implement palliative care (Einav et al. Science 2018).</p>

We have included in our INTRODUCTION and INTERPRETATIONS section more text about how access to specialist team might lead to health system cost savings.

- The references provided regarding the improvement of QOL for EOL care in those accessing palliative care are for patients with cancer and should be highlighted. Is there evidence for the same effect in those with terminal illness but without cancer?

The INTERPRETATION section now includes 2 systematic review references that describe noncancer and cancer populations about home-based palliative care and effect on costs. And how it relates to our study.

Methods: - Is the exposure to palliative care an individual's first exposure? Having individuals in either group with prior exposure may bias the results so this should be clarified.

We matched on time from first exposure to homecare... matching both on type of homecare intent (end-of-life, supportive, etc) and on time on homecare before death. This is mentioned in the METHODS - Propensity score matching section. The at which the exposed group got the specialist team almost always occurred after homecare initiation.

- What are the reasons that the unexposed group did not receive palliative home care (for teams 7 to 11 that were matched to "similarly resourced regions")? Do the cost differences observed merely reflect the inability to access other services as well? Providing a measure of specialist visits and other measures of healthcare utilization (beyond prior ED visits and hospital admissions) may help to illuminate this. Alternatively, this could be discussed as a potential limitation.

To be clear, the unexposed teams did in fact receive end-of-life homecare services (as this is an free accessible public healthcare service), but in the "similarly resourced regions"—a community-based specialist palliative care team did not exist at that time. So both exposed and unexposed teams were getting homecare (80% getting end-of-life homecare for a median of 90 days before death), but the exposed only got palliative care teams. The "similarly resourced regions" did not have an existing specialized team during the study period.

- How are "palliative care unit admissions" determined using admin data? Has this been previously validated?

We stated that "Costs for both hospital and inpatient palliative care unit admissions came from the same database [the Discharge Abstract Database (DAD)] so they are reported together." We did not mean to imply that the palliative care unit admission could be separated or has been validated independently (it has not—as it is complicated to accurately count palliative care unit beds). However, a stay in a hospital—as an inpatient for palliative care purposes, inpatient bed for non-palliative care purposes, or in a dedicated palliative care unit—would all show up in the DAD—and all costs from these were counted as hospital costs. We removed this sentence to avoid confusion.

- At what time point were baseline variables used to propensity match individuals "prior to exposure"?

We have tried to make this clearer in the METHODS. Age, sex, cancer/noncancer, rurality, income quintile is from death; homecare service type and time in homecare is from when first exposure to homecare occurred; and comorbidity score (ADG) and prior hospital/ED use was 6-18 months before death.

- The primary outcome is reported as total costs within regional teams. Seven of these teams reported cost savings, while 4 did not. How is one to interpret this as the primary outcome? Is the cost savings in the 7 teams significantly different than the other 4 teams? Clarification on the primary outcome and how it is measured should be made

Based on reviewer comments, we have clarified in our METHODS that our primary outcome has been changed to: "the paired-difference in total health system costs between the matched-pairs of exposed versus unexposed groups in the last 30 days of life across the overall aggregated pooled cohort". We also made Table 3 into Figure 1, as a forest-plot, which is perhaps more typical for a meta-analysis-type study, and this includes 95% CI to indicate significance. Table 3 containing the data is now included as a supplement.

About how it is measured: We also explain in the METHODS how the pooled cohort was determined: "The pooled cohort was comprised of the matched-pairs, considered independently, pooled into an aggregate total cohort, akin to a meta-analysis of 11 separate studies." The meta-analysis pools data together to understand the broader trend beyond any one individual study or, in this case, individual team.

Results:

- How many individuals were assessed for eligibility in the study (relative to the 3,109 individuals that were ultimately matched)? A study flow diagram would help clarify this, unless this would constitute a copyright issue from Dr. Seow's referenced BMJ publication.

We have added the before-matching values to (now) Table 2. It is much clearer. We also explain in the text of the RESULTS the differences before and after for clarity.

- It would be interesting (but not necessary for this study) to describe the amount of variation in costs that are attributable to variation between teams. This could be mentioned as an opportunity for future research in the discussion if the authors agree.

Thank you for the suggestion. We do show in Figure 1 (now a forest-plot) the variation in costs within team, including 95% CIs within team. We also add some sentences in the RESULTS that describe the variation.

Discussion: - The language of the interpretation of the primary outcome should be modified. Using the term "results" implies causality which cannot be determined from this study.

We replaced "results in" with "associated with".

- In the limitations section, it is mentioned that the study does not adjust for unmeasured covariates. The statistical model does not adjust for any measured covariates either and this should be highlighted as outlined above.

We have included this in our LIMITATIONS.

- The authors report an ~10% savings of the absolute costs. What is a meaningful (i.e. from a policy-maker's or even patient perspective) reduction in costs per patient?

We attempt to discuss this. We interpret that the differences are from higher homecare, but offset by much lower hospital costs in Figure 2, where we show paired-differences by health care sector. Moreover, we state that though significantly different in ED, sub-acute care, and physician services, this cost difference is so negligible and is not clinically significant. The study did not attempt to address what is a "meaningful reduction in costs," which is more aligned with Cost Utility Analysis or trade offs using Health Economics research.

	<p>References: - No concerns.</p> <p>Tables/Figures: - Table 1 – Why didn't the authors compare for differences between the matched exposed and unexposed groups using standardized differences? Differences >0.1 should be subsequently adjusted in the statistical models measuring the primary outcome (for example income quintiles appear to be different and could introduce residual confounding). We have modified the Table to include the before and after matching, with p-values (as suggested by the other reviewer). There were no significant differences between the groups after matching, except for income quintile (which is seen in the p-values now), and we felt this did not warrant a separate regression for this variable alone. We do note this is a limitation, as previously suggested.</p> <p>- Table 2/Figure 1 – Did the authors consider presenting only the data for the primary outcome and providing separate (possibly supplementary) tables/figures for the 30 day outcome? We agree and have now chosen the last 30 days as the primary outcome (as this is where the majority of costs are), as shown in Figure 1 and 2.</p> <p>- STROBE Statement – the addition of the specific RECORD items for studies completed We have added and completed the RECORD items to the STROBE form and resubmitted as a supplemental file.</p>
Reviewer 2	Matthias Hoben
Institution	Faculty of Nursing, University of Alberta, Edmonton, Alta.
General comments (author response in bold)	<p>Please justify why you are focussing on the 2009-2011 time period. Is no more recent data on these palliative care teams available? Please discuss to what extent these findings may still be valid today or how conditions affecting costs savings through palliative care teams may have changed since 2011. These were the most current data at the time of the original study given the admin data lag and the intensity of instating data sharing agreements between each of the teams and the admin data holder (ICES) to link the data. The cost was a secondary outcome, whereas utilization was the primary outcome (published in BMJ first); admittedly it took some time to complete the cost paper. We explain the time frame concern in the INTERPRETATION and LIMITATIONS section, and explain that we believe the data/results are still relevant since the homecare system and the death-in hospital rate has not changed much since 2011. (including references)</p> <p>The selection of clients exposed to palliative care teams and inclusion/exclusion criteria for palliative care teams is well justified - as are the variables used for propensity score matching. However, the two approaches of matching unexposed clients to exposed clients are confusing. I understand advantages and disadvantages of both approaches. Selecting clients from the same region but from a previous time period (when no palliative care service was established yet) cancels out confounders related to different regional characteristics (as long as regional characteristics did not change over time - which the authors state was not the case). However, client characteristics may have changed before compared to after 2009. This is taken care of by matching unexposed clients with exposed clients. However, if the overall population of unexposed clients is substantially different from the matched sample of unexposed clients, generalizability is limited. On the other hand, having to select unexposed clients from a different region may introduce regional confounders - again which is taken care of by using regional characteristics in the propensity matching. However, regional populations may differ from selected regional samples. Selecting two different matching approaches then makes this issue even more complex. Why did the authors not simply select matched controls from the same time period (2009-2011) from another region with similar characteristics - for both, services that started before and after 2009? Please clarify and discuss limitations of the selected matching approach in the limitations section. The a priori preferred method (with less potential for confounding) was to match to the same area at an earlier time (right before team was established). We used this method where possible. However for some older teams, to match to the same area at an earlier time before the team was established would have introduced biases due to the extent of time lapsed and changes in the region over this time (since for instance, one team started in 1979, another in 1986). As well, a major health care policy leading to regionalization of homecare occurred in 2006 (establishment of Local Health Integration Networks), and we did not want to compare prior to 2006—prior to regionalization. Therefore, for these older (more established) teams we used (what we felt was) the next best method - matching to a similar region (with similar hospital resources and rurality/urbanization) at the same time (2009-2011)—but where the similarly resourced regions did not have access to a specialist team. We added a statement to METHODS to better explain this 2 comparison method and to the LIMITATIONS as requested.</p> <p>The authors do not describe their pooling approach in the statistical analysis section. Did they simply average across the overall sample or did they use fixed or random effects models to pool the team-level estimates? We have described the approach to derive our "overall pooled cohort" in the METHODS - Statistical Analysis. We explain: "The pooled cohort was comprised of the matched-pairs, considered independently, pooled into an aggregate total cohort, akin to a meta-analysis of 11 separate studies."</p> <p>When reporting results of costs by healthcare sector, in Figure 1 as well as in the manuscript text, inclusion of 95% confidence intervals rather than standard deviations would be appreciated. By including 95% CIs as error bars in Figure 1, the reader could more easily determine whether or not the exposed versus unexposed groups were substantially different. (The standard deviations seem huge, suggesting a substantial variance of costs across clients and teams, so probably many of the differences are not statistically significant?) We have changed Figure (now Figure 2). The figure now shows the mean paired cost differences between matched pairs for each of the 5 sectors individually and the total combined health system costs, as well as the 95% confidence intervals, as suggested by the reviewer. We agree that the 95% CI bars help to better show the significant difference in hospital, homecare and total health system costs.</p>