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Title	Use of patient reported outcomes in regional cancer centres over time: a retrospective study
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Reviewer 1	David Stock
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General comments (author response in bold)	<p>This paper presents important and interesting work and has potential to make a needed contribution to the literature.</p> <p>Please justify your research question and your selection of characteristics of interest: The reason to conduct the research should be clearly justified in the introduction. It is unclear what the utility of identifying characteristics associated with uptake is. I am presuming you want to use the characteristics information to create a targeted intervention to increase uptake of PROMS in vulnerable groups; If so, I can't really see the place for some of the characteristics/covariates you selected if interventions are the end goal (e.g. Charlson or RUB). It also seems odd to me that cancer center is not included in the model. I suspect there would be overlap with region of residence. It seems identifying the cancer center would be more meaningful if the end goal was to create interventions and if I had to choose one or the other, I would select this indicator. Also, why look over time? Is there a reason to assume uptake will change over time, e.g. an intervention; more wide spread roll out.</p> <p>There is every reason to expect uptake over time will change. This is a massive scale change management project and to our knowledge, nothing of the kind has been attempted elsewhere. Because of the scope and scale of the program, uptake would vary widely by region and would change slowly over time.</p> <p>Our primary interest was changes in uptake over time and by region. For this reason we wanted to control for patient, tumor and system factors, using administrative data, that might have confounded differences among the regions.</p> <p>How do you define success? There are several places where the authors indicate they are interested in "success" of implementation (e.g. Page 3, line 37; page 4, line 54; page 13, line 27). Success is a loaded word - what does it mean. Is 67% people completing really "successful"? Suggest finding a different descriptor.</p> <p>In this context of this study success is based on the ESAS rate. We have removed all uses of the word success.</p> <p>Study design: I am not clear why this is a cohort study? How are you using information from the same person over time?</p> <p>We have created annual cohorts based on eligibility criteria at the start of each year. By doing so, the same individual can be followed year-to-year. In each year, we are measuring ESAS uptake which is why we have longitudinal information on patients over time. This has been clarified in the methods.</p> <p>PROM roll out: Has the PRO program been active in all cancer centres during the entire study period? In the introduction you mention there was a wide spread implementation in 2010, yet study starts in 2007. I am concerned both about internal and external validity. Internal validity: did you include patients that had no opportunity to be "exposed" to PROMS; is so, is the % completing really saying what you want it to say? The reported low uptake shown on page 10, lines 5-6 could be a result of no PROMS at certain centres. Could the "low uptake" of PRO in early years be the result of an inappropriate denominator?</p> <p>The denominator is reasonable for all years. The program launched in all centres in 2007. Each centre had a different capacity to manage the change required to implement ESAS. The early years also reflect a pilot phase where implementation started with lung cancer patients and patients attending palliative care clinics.</p> <p>External validity: if the PROM was only available at some centres (and you excluded those without), do you think the changes over time can be generalizable?</p> <p>The PROM was available at every centre. These results are generalizable to any system implementing in a similar context.</p> <p>Objectives/Analysis: I think the rate of PROM uptake over time is an interesting finding and one that should be an overall study objective and clearly stated. You don't mention any interest in rates in your introduction (Page 5; Lines 3-8) but discuss in your outcome definition section (Page 6, Line 50-52) and also in your analysis section (Page 8, line 21).</p> <p>We have re-worded the last sentence of the introduction.</p> <p>Moreover, I am not clear about total follow-up time (Page 7, lines 6-8) and how the offset variable was created. When does follow-up time start and when does it end, e.g. If I receive radiotherapy 8 times over 2 weeks, then I have a single follow-up appointment 2 weeks later, I would have 7 person-days "at risk" but over the course of 21 calendar days. Would you use 7 or 21? I think 7 is the most accurate.</p> <p>As mentioned earlier, we have created annual cohorts based on eligibility at the start of each year. In each year, an individual is considered to be "at risk" for ESAS for the entire duration of the year, unless they had a subsequent cancer diagnosis or they died at some point during the year or the study ended. If none of these events occurred, then the follow-up time for this individual would be 1.0 years during that specific year. As a result the individual's ESAS uptake rate in any given year is the number of ESASs occurring in that year divided by the duration of time in that year over which ESASs may have occurred.</p> <p>Please justify your use of a multivariable model since the end goal is not to provide an overall, unbiased estimate of effect or to build a clinical prediction model. I think a univariate presentation would lend to more practical application/interpretation and be just as interesting.</p> <p>In addition to understanding the univariate or crude relationships between the characteristics and ESAS rate, it is very important to understand if these relationships hold under the presence of confounding. Thus a complete picture is required, both univariate and multivariable. Based on requests by 2 reviewers, we have now provided an additional figure showing the univariate and multivariable results for the entire cohort, overall.</p> <p>Figures: Suggest using tables instead. The figures, as is, are problematic for several reasons. The font is so small and you cannot make out any results; the separation of the results from a single model into multiple graphs is confusing; the graphs are multiplicative but they are plotted on the linear scale; a relative rate of 0.0 is not possible and should not be included in the figures; labels on the tables/figures are redundant.</p> <p>After again taking a look at the large volume of output from the original tables, we have kindly elected to keep Figures 2 and 3, as we feel it is a convenient way to illustrate the results and the corresponding trends. There was no relative rate point estimate of 0.0 - this is simply used as a marking on the scale rather than saying "0.01" for example.</p>

	<p>Minor Suggestions: Abstract Page 3, Line 40: Change "variables" to "characteristics" Done.</p> <p>Introduction: Page 4, Lines 6-14: Providing a bit more context on the use of PROMS in other settings/countries would strengthen the introduction (e.g. Sweden, UK; length of time PROMS collected in these settings). Done.</p> <p>Page 4, Lines 28-49 The description of ESAS seems more appropriate in the methods section under "outcome measures". This has been moved.</p> <p>Methods: Page 5, Line 17: Is this really a cohort study? Someone could be enrolled on December 31, 2015 (also study end date). Persons are not really followed forward and individual trajectories do not seem to be of interest here. Moreover, it seems there are really 6 annual cohorts; this should be clearly laid out in the study design/setting. The cohort population derived by creating annual cohorts. By doing so, the same individual can be followed year-to-year. In each year, we are measuring ESAS uptake which is why we have longitudinal information on patients over time.</p> <p>Page 5, Line 39-41: Page 5, Line 44: Partner hospitals are not the focus or not included? They are not included. The language has been clarified.</p> <p>Page 6, Line 21-23: What is the activity level reporting database? Can you please provide more context - what information does it routinely collect? Done.</p> <p>Page 6, Line 33: Why exclude men and women with a non-first cancer diagnosis? It simplifies attribution of cancer type.</p> <p>Page 7: Did you check to see if age was linear in your models? Yes – quadratic and cubic terms for age were explored. They were not significant, and thus not further discussed.</p> <p>Page 8, Line 3: Missing a period between sentences. Done.</p> <p>Results: Figure 1: There is a lot of information in this graph and it is well thought out. I am not sure if the counts per person per year is really that interesting for this article. If you are using this distribution to justify negative binomial regression, perhaps it can be placed in the appendix? As suggested, we have now placed this Figure in the Appendix.</p> <p>Table 2: Suggest placing this in the appendix and not as a main result. I agree with you; the characteristics seem fairly stable over time and the data is very similar to table 1. As recommended, we have now placed Table 2 in the Appendix.</p> <p>Figure 3: Assuming that age is linear in your models. Suggest providing a more meaningful estimate (e.g. decrease every 5 years) Thank you for this comment. It is unclear whether age every 2 years, 5 years, or 10 years would be a meaningful way to present the estimate. We have thus elected to keep age as continuous and use the basic "per year" interpretation. This way, a reader is also able to easily calculate the corresponding "multi-year" age effects.</p> <p>Discussion: Page 12: line 16-20: Unclear what CCO performance management system is. How do you know it was effective decreasing variation across regions? We agree that this statement should be tempered. We have added details regarding CCO's performance management system and have modified the wording of the statement in the discussion</p> <p>Page 12: Line 47: What is a deprived individual? I am not clear how Basch et al study relates to this; can you elaborate. Computer inexperience is likely related to age, education level and income which are all indications of socio-economic status. It may be that those from lower socio-economic stand to benefit most from routine patient reported outcome use, even if it is collected electronically.</p> <p>Page 13, Line 8: I would not call administrative data comprehensive, especially since in the same paragraph you note it is not (e.g. language spoken was not available). The wording has been modified.</p>
Reviewer 2	Bryan Stirling
Institution	School of Population and Public Health, University of British Columbia, Vancouver, BC
General comments (author response in bold)	<p>My initial question, relating to the objectives, is how context-specific the results might be? The data were collected in Ontario and specific to CCO, and so I fear that any key findings might not have relevance in other clinical and jurisdictional settings. This point is underlined by the authors when they indicate that "each center has implemented in ways that suit local context". This comment makes me wonder whether a mixed methods approach might be more likely to answer the question. A full understanding of why some centres have moved forward to collect such data and others have not is likely best answered, in part, through qualitative investigation, in addition.</p> <p>The main goal of the paper is to understand factors associated with ESAS use over time at a system level. This is meant to help understand if there are differences in access. The paper is not meant to evaluate or compare the efficacy of different methods of implementation. A mixed method approach would help understand this problem better but this is beyond the intended scope of the manuscript under consideration. CCO has previously collected</p>

data on barriers to implementation (Pereira 2016 JPSM).

The primary variable in the analysis is a rate of ESAS assessments, calculated overall and annually. I would have expected the number of scheduled visits would vary by patient and centre and so I would have thought that a simple proportion of visits with an ESAS assessment would have been a better measure of uptake. Perhaps the justification for the use of rates would be helpful. **Please see earlier comments above. A visit based indicator would also be a reasonable approach. However, the rate used in the analysis is similar to the metric that CCO uses for performance management and public reporting. The outcome measure as it is defined in the paper provides a reasonable measure of ESAS uptake. Our methods do account for duration of follow up, as some patients may die or experience another cancer during the study period.**

No rationale is given for the choice of explanatory variables in the model. I would like to see some explanation for the inclusion of each explanatory variable, drawing on past evidence or some theoretical construct. This would then lead naturally into statements of the hypothesis being tested.

The variables used broadly fall into patient, tumor and system factors. They are variables commonly used in analyses of health services utilization, and can be important for understanding uptake of PROs such as ESAS. We have clarified this in the methods.

Table 1 has N=525,409 patients with at least one visit to a CCO cancer centre between 2007 and 2015. A total of 5908 were excluded due to missing covariate information or invalid visit type. Some more detail on the exclusions would be helpful. Could imputation have been used for the sub-group where data were missing?

While this is technically possible to do, the proportion of patients excluded is very small and not enough to influence the results of the analysis. Imputation methods also have their own set of limitations. An appropriate relationship between the missing variable and the remaining information needs to be found in order to have meaningful results from the imputation. For these reasons, especially due to the low percentage of missing information, we have not pursued this further.

Figure 1 is very difficult to interpret. Some further work to clarify what is being presented would be helpful. I would suggest that all years are presented in Figures, where possible. This might need to be provided as an appendix but the selection of just some years when the authors have fuller data raises concerns.

There was too much data to show every year in a manageable format. The years chosen are a fair representation. However, given other comments, we have now moved this figure to the appendix.

The results from the modelling analysis, presented on page 11, are very mixed and difficult to interpret clearly. This highlights the absence of a priori hypotheses, and makes much more challenging the results interpretation. This especially important given that so many exploratory analyses are reported.

As per prior comments, we have clarified the intent of the analysis and reasons for variables chosen.

In summary, I would want to indicate support for CCO's leadership on the routine collections and use of PRO data, especially in the context of routine care. However, the questions being addressed in this paper, on factors associated with uptake of such data collection, might best be conducted using a mixed methods approach and may be a challenge to generalize from when using data only from CCO.

This comment has already been covered with prior responses. The only novel issue regards generalization. CCO's experience is unique in its scope and scale. However, there is tremendous interest world wide for cancer programs (and non-cancer programs) to administer PRO measures in routine care and on larger scales. It is difficult to be certain about how generalizable the results are, but the novelty of the experience is sufficient ground for reporting, in our opinions. We have added one statement regarding the possibility of limited generalizability.