Article details: 2013-0025	
Title	A snapshot of breast cancer surgery in Canada
Authors	Geoff Porter MD, Brandon Wagar PhD, Heather Bryant MD PhD, Maria Hewitt PhD, Elaine Wai MD MS, Kelly Dabbs MD, Anne McFarlane MSc, Rami Rahal BSc MBA
Reviewer 1	Biniam Kidane
Institution	Department of Surgery, Western University, London, Ont.
General comments	The authors present a study with an important message. They are cognizant of the limitations of their data and analyses. However, it would help to include some more discussion around why this methodology was used as opposed to others. (see below for examples) 1) The authors state "A logistic regression model was estimated for the mastectomy rate...". Perhaps they meant "for the predicted mastectomy rate"? This should be clarified. It would also be helpful to describe how this predicted mastectomy rate was calculated in more detail. 2)The authors calculated predicted mastectomy rates using logistic regression and then used this to calculate an adjusted mastectomy rate (adjusted for presumed confounding predictors). Then, chi-square analysis was used to determine whether significant interprovincial variation existed. There are likely many other factors confounding the relationship between province and mastectomy rate (as aptly mentioned by the authors). The use of a univariable inferential test like chi-square in this case is thus a significant limitation. It is unclear why the authors did not perform GEE/GLM modelling with mastectomy rates (or "increase in mastectomy rates", etc.) as the continuous outcome variable and allowed for adjusted analyses right from the outset.
Reviewer 2	M.F. Bakker
Institution	UMC Utrecht, Julius Center for Health Sciences and Primary Care, The Netherlands
General comments	Comments for the authors: The study describes the contemporary surgical treatment of invasive breast cancer in Canada, specifically trends in use of breast conserving therapy and mastectomy. In general: - The aim as stated right now in the introduction is rather wide and expansive. My suggestion is to try to make it more concise. Right now there are so many endpoints that it doesn't make it clear what the main aim of this manuscript is. - The number of exclusions is rather high (about 16.000 of all 57.840 included patients). This cannot be easily neglected. At least sensitivity analyses should be investigated and more in depth as well as more detailed information should be given. E.g. a table showing the characteristics of these group of patients in comparison to the group as taken into account in the analyses. - The fact that a lot of known breast cancer risk factors and information about the tumor itself are missing is a rather huge limitation. These variables are probably confounders of the type of surgery and have their influence on the found results. It is stated that only the "stage of cancer" was not available, how receptor status, lymph nodes or BRCA for example? Abstract: - Please add some information about the crude and adjusted (which variables?) analyses in the methods section. - The number (or %) of exclusions should be mentioned here as well. Introduction: - I would suggest to give here more background on what is already known about surgical treatment, e.g. based on guidelines or data from other (western) countries. How is the situation in Canada in comparison with other countries? - What are the expectations of the descriptive trends stated in the aim that will be examined? Do the authors expect variation by province (if so, based on what kind of information, literature)? Methods: - What do the authors mean with "…and a related surgical intervention indicated

	anywhere on the abstract"? - Age group, neighborhood income, and travel time were right now included as the only co-variates. I think the authors might need to include more confounders in the analyses (like know risk factor for severity of disease). - Please provide references for the sentence: "Age was categorized into approximately quartiles, using ranges that aligned with existing literature". Please mention in methods section already the categories used, same for the other two co-variates. - Please provide more background of the patients who were excluded from the analysis (see comment above as well). Were they different (or comparable) compared to the patients who were included in the study? They could be selective drop outs. Results: - Please provide already in methods section the number of provinces. - Not take into account the bilateral cases due to small number should be mentioned in the discussion section as well. Discussion: - I'm not sure whether the improvement of care can be based on this manuscript (as is stated right now). Good insight can be given in the differences, but further research is definitely necessary to explore how improvements can be made. - The geographic variation should be explained in more detail in the introduction already (What are the expectations? Is this seen in other countries as well?). - The last paragraph of the manuscript seems to stray off from the original aim. This makes it a bit confusing. Tables: - Please provide some footnotes like based on all cases or only on part of cases. (e.g. seems like in table 3 not all were included?) - Table 3: is it possible to add p-trends for all co-variates? - Table 4: please provide information on "adjusted" - Table 5: "data suppressed due to small size": this has not been mentioned in methods/results section of manuscript?
Author response	Dr. Biniam Kidane 1. The authors state "A logistic regression model was estimated for the mastectomy rate...". Perhaps they meant "for the predicted mastectomy rate"? This should be clarified. It would also be helpful to describe how this predicted mastectomy rate was calculated in more detail. a. We agree that the term "estimated" is confusing, and we have expanded upon this issue in the methods (page 7, first paragraph). b. Calculation of predicted mastectomy is expanded upon in more detail in the methods (page 7, first paragraph) 2. The authors calculated predicted mastectomy rates using logistic regression and then used this to calculate an adjusted mastectomy rate (adjusted for presumed confounding predictors). Then, chi-square analysis was used to determine whether significant interprovincial variation existed. There are likely many other factors confounding the relationship between province and mastectomy rate (as aptly mentioned by the authors). The use of a univariable inferential test like chi-square in this case is thus a significant limitation. It is unclear why the authors did not perform GEE/GLM modeling with mastectomy rates (or "increase in mastectomy rates", etc.) as the continuous outcome variable and allowed for adjusted analyses right from the outset. a. Estimation of variation for crude rates requires a univariable inferential test like chi square. b. Chi-square analysis of variation among adjusted rates was performed to assess variation among adjusted rates. While we agree that there are limitations associated with this test, and there are likely many other factors confounding the relationship between province and mastectomy rate, we were unable to measure any of these variables in our data. However, we do not consider use of GEE/GLM modeling as a solution. This approach would not differentiate between sources of inter-provincial variation we would hope to deal with (e.g., stage), and sources of inter-provincial variation we would not want accounted for (e.g., practice variation). DR. M.F. Baker's comments: 1. The reviewer requests that the Aim within the Introduction be made more concise.. a. We agree with the reviewer that the aim, as currently stated in the Introduction, may be too wide. We have thus revised it to be more concise and focused (page 4, last

	paragraph) 2. The number of exclusions is rather high (about 16.000 of all 57.840 included patients). This cannot be easily neglected. At least sensitivity analyses should be investigated and more in depth as well as more detailed information should be given. E.g. a table showing the characteristics of these group of patients in comparison to the group as taken into account in the analyses. a. We agree that the wording is inaccurate. Residents of Quebec and the Territories were not excluded per se, but rather not included in the regression analysis (i.e., the analysis of adjusted mastectomy rates is for select jurisdictions). We have thus revised the methods to be more concise (page 7, first paragraph) 3. Similar to the Editor, the Reviewer questions the influence of other confounders such as stage, BRCA ect…. a. We agree with the reviewer that further clarification is required – see response to Editor, issue #4. 4. Please add some information about the crude and adjusted (which variables?) analyses in the methods section [of the abstract]. a. A statement to this effect has been added to the Abstract (page 3, Methods). 5. The number (or %) of exclusions should be mentioned here [in the abstract] as well. a. A statement to this effect has been added to the Abstract (page 3, Methods). 6. The Reviewer requests information regarding surgical breast cancer treatment in other developed countries a. No strong evidence exists within Canada to either support or refute the possibility of significant variation in surgical breast cancer care. A statement to this effect has been added to the Introduction (page 4, last paragraph). 7. What are the expectations of the descriptive trends stated in the aim that will be examined? Do the authors expect variation by province (if so, based on what kind of information, literature)? a. To our knowledge, this issues has not been examined at the National level. Provincial variation was expected, but based on anecdotal information rather than published research. 8. What do the authors mean with "…and a related surgical intervention indicated anywhere on the abstract"? a. Records in the databases may contain up to 20 surgical interventions. By "anywhere on the abstract" we mean that if any of the related surgical interventions occur in the record – regardless of whether it is the first or the 20th intervention coded – we included that record in the analysis. 9. The Reviewer questions whether more confounders need to be included in the analysis a. As per Editor # 4 and Reviewer #3, the lack of ability to access clinicopathologic variables is a limitation of this study – see response to Editor, issue #4. 10. Please provide references for the sentence: "Age was categorized into approximately quartiles, using ranges that aligned with existing literature". Please mention in methods section already the categories used, same for the other two covariates. a. Because the ranges adopted were similar to, but not exactly the same as, existing grey literature, we have revised the statement in the methods (page 7, second paragraph). 11. Please provide more background of the patients who were excluded from the analysis (see comment above as well). Were they different (or comparable) compared to the patients who were included in the study? They could be selective drop outs. a. See response to issue 2 above. 12. Please provide already in methods section the number of provinces. a. We have added this to the Methods (page 6, first paragraph of methods). 13. The Reviewer requests that exclusion of bilateral breast cancer be explicitly acknowledged in the Discussion a. We agree with the Reviewer and have added this to the Discussion (page 13, first paragraph)

	14. The Reviewer questions whether improvement in care can be based on this manuscript. a. We do not believe that the current manuscript states or implies that improvements in care can be based on the findings of this study, we agree completely with the reviewer that further research is required to better understand variations identified, and to inform improvements (page 12, last paragraph) 15. The geographic variation should be explained in more detail in the introduction already (What are the expectations? Is this seen in other countries as well?). a. See response to issue 7 above. 16. The Reviewer questions whether the last paragraph of the Discussion (i.e. the Conclusion) strays from the study's main aim and is thus confusing. a. We agree with the Reviewer and have revised this paragraph to better align with the study's objectives and results 17. Please provide some footnotes like based on all cases or only on part of cases. (e.g. seems like in table 3 not all were included?) a. We have added notes where this information was lacking (page 19, page 20) 18. Table 3: is it possible to add p-trends for all covariates? a. We did not add this, as significance of odds ratios ($p < 0.05$) can be inferred when CI do not overlap with 1.0. However, we can do so if requested. 19. Table 4: please provide information on "adjusted" a. We have added notes for this information (page 19) 20. Table 5: "data suppressed due to small size": this has not been mentioned in methods/results section of manuscript? a. Suppression was motivated by privacy rather than a methodological consideration. Once again we thank the editorial staff and reviewers of CMAJ Open, as we feel that this revised manuscript is greatly enhanced.