Article details: 2017-0144	
Title	The economic burden of cancer care in Canada: a population-based cost study
Authors	Claire de Oliveira MA PhD, Sharada Weir MA DPhil, Jagadish Rangrej MSc MMath, Murray D. Krahn MD MSc, Nicole Mittmann MSc PhD, Jeffrey S. Hoch MA PhD, Kelvin K.W. Chan MD MSc, Stuart Peacock MSc DPhil
Reviewer 1	Christine Leopold PhD MSc
Institution	Senior Research Fellow, Division of Health Policy and Insurance Research (HPI), Harvard Medical School & Harvard Pilgrim Health Care Institute, Landmark Center, Boston, MA
General comments (author response in bold)	Your approach to first estimate patient-level costs in Ontario and then extrapolating these to nation-wide costs sounds reasonable. In addition, your attempt to approach the calculation of the economic burden of cancer care from a more holistic systems perspective by including other costs such as costs for diagnostic tests, chemotherapy and radiotherapy is much appreciated. However, I have a few questions and remarks to be considered by the authors. Background It would be important to mention, that in order to estimate the real economic burden of cancer care one needs to consider costs along the entire care continuum from screening, diagnosis, treatment, survivorship, rehabilitation to palliative care and pain management. This study attempts to take this holistic approach (maybe mention why you did not take costs for screening or pain management into account). **We have added a sentence in the limitations section on why we did not account for the costs of screening. While we agree these costs are important, it was not feasible to do this for all cancer sites (this would only be possible for those with organised programmes). However, our estimates did include, to the extent possible, costs of pain management.** Methods: To increase readability, I would suggest to rearrange the order in which the methods are described. If I understand the authors correctly, there are two main analyses including the following steps: **We thank the reviewer for this suggestion. We have rearranged the methods section as suggested below. In addition, we have addressed all other comments mentioned below (see below for more details on what we did).** Patient-level analysis on the example of Ontario 1) Identification of patients with cancer and in remission in Ontario over a 10-year period based on the ICD-9 and ICD-10 codes listed in Table A2 - source Ontario Cancer Registry (second paragraph on page 7) 2) Selection of non-cancer patients (controls) - source Registered Persons Database Did you use any specific selection criteria? **We did use specific selection criteria for both cancer patients (cases) and non-cancer patients (controls). In particular we included all patients with cancer but excluded those with missing data on sex and those that were ineligible for public healthcare insurance. We applied the same criteria to controls; in addition, we excluded all controls that had a diagnosis of cancer (with the exception of non-melanoma skin cancer) before or during our analysis period. This is included in the revised manuscript.** 3) Matching of cancer and control groups based on age, sex and comorbidity In the text, the authors mentioned that the adjustment for age was +/- 1 years, but in the note under Table A4 and A5 it is mentioned +/- 2 years. Please specify. The authors mentioned that death data was also collected. Is the death data included in both sources or was another source used? **We apologise for this typo; we have corrected this so that it reads +/- 2 years where applicable. The date of date was obtained from the Registered Persons Database, a population-based registry in Ontario. We have clarified this in the revised manuscript.** 4) Estimation of patient-level cost data (first and second paragraph on page 8 and 9) Please specify, how the selected patients under point 1) and 2) were linked to the cost data as defined in an algorithm by ICES as well as the cost data for chemotherapy and radiotherapy (e.g. the Ontario Drug Benefits claims database). Is there a unique patient identifier number? **Cases and controls were linked to the administrative healthcare records using a unique encrypted identifier; we have clarified this in the revised manuscript.** Please describe what the number of doses and unit costs means. Are the authors referring to price the hospital or the Ontario Ministry of Health and Long-term Care had to pay for the drugs (including margins, taxes or accounting for any discounts received?) **We have clarified that the number of doses are doses of chemotherapy and that unit costs refer to unit drug costs. In addition, we have clarified that the cost of parenteral chemotherapy is incurred by the hospitals where it is provided and the cost of oral chemotherapy is incurred by the Ontario Ministry of Health and Long-term Care.** Acknowledging that the authors mentioned in the 'limitation section' more information on how the outpatient drug costs were estimated, I would suggest more information in the methods section on how the outpatient drugs were calculated. Did the authors take the outpatient prescription drug price (including any margins, discounts, dispensing fees?). It was mentioned, that the public outpatient drug costs only referred to patients over 65, was these same costs then applied to all patients, independent from age? Please describe in more detail. **As clarified above, the outpatient prescription drug price was the one in the Ontario Drug Benefit (ODB) program, which was incurred by the public third-party payer. In Ontario, the ODB program covered all patients 65 and older and special cases (such as, social assistance). We used these costs to extrapolate to the rest of the country. We understand that this generalisation is not entirely correct as some provinces have different coverage, such as British Columbia. We have highlighted this as a limitation in the limitations section.** If I understand the authors correctly, they had access to per patient prescribed drugs as well as to per patient unit costs for each year. However, in this study the authors present only aggregated total costs for each cost category. Please specify. **We have clarified that, although we use patient-level data, we present aggregate costs for each cost category.**

5) Calculation of 'net cost'

National-level analysis
1) Identification of person-based cancer prevalence (first paragraph on page 7) - source Statistics Canada and the Canadian Cancer Society
2) Calculation of the national-level costs (first paragraph on page 10) - source NHEX

Was the prevalence data linked to the NHEX costs data?
No, prevalence data were not linked to NHEX cost data; this is not possible.

3) Calculation of 'net costs"
The results of both studies are presented for two year groups (group 1: 2005-2008 and group 2: 2009-2012) and all costs are adjusted to 2015 constant dollars.

Results
I would suggest to start with a short paragraph in which the baseline characteristics of the patient-level cohort in Ontario as well as the national-level cohort is described (total number of patients per year, average sex, average age etc.) for both year groups.
We did not include this information as this was not the goal of the analysis per se. However, we included the numbers of patients by age/sex in the Appendix.

In addition, it would help the reader to explain why some of the costs in tables 2 and 3 are negative, e.g. for long-term care. It would be expected that these costs are high for cancer patients.
We had included this reason for this in our original manuscript. In particular, we wrote 'Subcategories of net costs, and respective confidence intervals, were negative for some years due to higher costs among matched controls.' This is not uncommon and has been found in previous work using this method.

While I appreciate the footnote in the tables explaining what is meant by 'drugs', I believe it would be helpful to change it in the table to 'outpatient drugs' as it is not self-explanatory.
We have clarified this in the revised manuscript.

On page 12 in paragraph please note, it should be referred to figure 3 and not figure 2.
We thank the reviewer for this. We have corrected this.

In addition to the increase in chemotherapy and radiation therapy costs, there is also a great increase in cancer clinic costs from $357 in 2006 to $783 in 2012.
Yes, this is true. However, there were large increases in costs for other health services, such as emergency department visits (this increase was actually larger than for cancer clinic costs). We only highlighted the increase in chemotherapy and radiation therapy costs as these health services saw the largest increases among other health services; furthermore, they are important elements of care in treating cancer patients and their rise has important implications for the third-party public payer.

Interpretation
It would be interesting to learn from the authors, what they see as possible reasons for why the costs for cancer clinics increased substantially over the last years (assuming that these cost increases cannot be linked to increases in drug costs).
We decided not to showcase this in our revised manuscript. Please see above for our rationale behind this.

Conclusion
In addition to hospital care being among the highest costs, the authors should also point to the costs of cancer care clinics which have increased substantially over time.
Another aspect to look at in future research is to understand at which point of the care continuum (screening, diagnosis, treatment, survivorship, rehabilitation to palliative care and pain management) most costs occur. Looking at the cost burden by different age groups could also be of interest for decision-makers.
Previous research done by our group has already shown at which point of the care continuum most costs occur. Costs of cancer tend to be higher in the first 6 months after diagnosis and in the last year before death. Therefore, we did not include this as an item for future research.