

Article details: 2016-0045	
Title	Cancer Incidence Attributable to Lifestyle and Environmental Factors in Alberta, Canada in 2012: Summary of Results
Authors	Anne Grundy PhD, Abbey E. Poirier MSc, Farah Khandwala MSc, Xin Grevers BSc, Christine M. Friedenreich PhD, Darren R. Brenner PhD
Reviewer 1	Dr. Agnihotram Ramana-Kumar
Institution	McGill University, Epidemiology and Biostatistics, Montréal, Que
General comments (author response in bold)	<p>1. Methods, first para, authors need to write couple of sentences regarding individual exposures (though reference was given).</p> <p><b>Response: As we also describe in response to comment #2 from reviewer 2, this summary manuscript used population attributable risk estimates calculated in exposure-specific manuscripts to estimate the summary values for Alberta. As such, in our opinion it would be overly repetitive to describe all exposure-specific data in the summary manuscript. A citation for all exposure-specific manuscripts has been added to the first sentence of the second paragraph of the methods section on p. 4 to more clearly refer readers to the exposure specific manuscripts.</b></p> <p>2. Results, first para, need to mention about source (Registry etc.) data and completeness and reliability (or) some reference about the the source data is required.</p> <p><b>Response: Additional Information about the Alberta Cancer Registry has been added to the results on p. 5. The Alberta Cancer Registry has a Gold Rating from the North American Association of Central Cancer Registries for "completeness of the data, timely reporting and other measures that judge data quality." (<a href="http://www.albertahealthservices.ca/assets/healthinfo/poph/hipopph-surv-cancer-appendix-2012.pdf">http://www.albertahealthservices.ca/assets/healthinfo/poph/hipopph-surv-cancer-appendix-2012.pdf</a>)</b></p> <p>3. Interpretation, since most of this section has compared the Alberta results with results based on the UK population (2012). An appendix table comparing the prevalences and populations of UK and Alberta study populations may be very helpful to understand the attributable risks of cancer in general.</p> <p><b>Response: Comparisons between the UK and Alberta populations at an exposure-specific level are presented in each of the exposure-specific manuscripts (cited in the first paragraph of the introduction), where the exposures we considered were also considered for the UK. In our opinion repeating these comparisons in an appendix would be unnecessary duplication. Thus, we have added a sentence to the interpretation on p. 7 referring readers to the exposure-specific manuscripts for these comparisons.</b></p>
Reviewer 2	Dr. Lawrence Svenson
Institution	Alberta Health and Wellness, Surveillance & Environmental Health, Edmonton, Alta.
General comments (author response in bold)	<p>The authors describe the role of a number of modifiable risk factors and estimate the proportion of cancer cases in Alberta that may be attributed to these factors. The authors conclude that approximately 40% of cancers diagnosed in Alberta can be attributed to these factors.</p> <p>The authors refer to other papers they have written to rationale the need for this paper. The introduction comes across weak and even includes reference to Table 1, which would be better referenced in the methods section.</p> <p><b>Response: The sentence referring to Table 1 has been moved to the first paragraph of the methods section on p.4 and a list of the full set of exposures considered in this manuscript has been added to the final paragraph of the introduction on p. 3. We have added some information concerning the total cancer burden in Alberta to the beginning of the second paragraph of the introduction on p. 3 to provide some additional context to our population attributable risk work. Finally, we have also added details concerning comparable population attributable risk work conducted in Australia where approximately 32% of cancers were attributable to causal factors on p. 3, which provides further context to our Alberta-specific efforts.</b></p> <p>The methods section primarily indicates that the details are to be found elsewhere. While this is fine, the description that was provided could have been strengthened by providing more detail on how the risk factors were attributed to specific cancers. The calculation of PAR was nicely described, but not how the authors used, for example, CCHS data to derive their estimates.</p> <p><b>Response: This summary manuscript used population attributable risk estimates calculated in exposure-specific manuscripts to estimate the</b></p>

summary values for Alberta. As such, the use of data sources such as the CCHS is described in detail in the exposure-specific manuscripts. In our opinion, it would be overly repetitive to describe all exposure-specific data sources in the summary manuscript. A citation for all exposure-specific manuscripts has been added to the first sentence of the second paragraph of the methods section on p. 4 to more clearly refer readers to the exposure specific manuscripts.

The method section also appears to be presenting results, which should be better placed elsewhere in the paper.

**Response: While we understand the reviewer's perspective here, we respectfully disagree that the mention of Table 2 in the methods section is inappropriate. Specifically, the interior cells of Table 2 present the individual exposure-cancer site estimates of population attributable risk that form the input data for our overall estimates of population attributable risk. As such, in order to clearly explain the methods we are utilizing to generate our overall estimates, we believe it is important to point the reader to a clear summary of these individual population attributable risk estimates. While Table 2 also contains the estimates of overall population attributable risk by exposure, cancer site and all cancers combined that form the results for this manuscript, these numbers are not discussed in the methods section (other than in the context of the approach used to generate them). In our opinion presenting all of this data together in Table 2 makes it easier for readers to understand where our estimates come from and potentially replicate our methods. We have removed the reference to Table 2 at the end of the first paragraph on p. 5 as we agree with the reviewer that citing the table in this sentence was indeed inappropriate for the methods section.**

The limitation section states "While our summary estimates of population attributable risk did make an effort to account for the fact that some cancers are caused by multiple risk factors, they did not include a formal analysis of potential interactions between risk factors." This is a significant limitation that needs further exploration. The role of risk factors for any chronic condition represent a complex dynamic system. Dynamic systems often self correct when one factor is reduced or removed so that the end result is not simple subtraction. While the authors have not stated that the removal of one factor would reduce the incidence of cancer by a fixed amount, the final interpretation of the results implies just such a simplicity. To state that 40% of cancers are attributed in some form to the factors examined could be open to misinterpretation. The analysis would have been strengthened by presenting a conceptual model of the interactions that may be in play across the risk factors. Maybe factors will co-exist and be highly correlated (e.g. smoking and drinking; obesity and physical activity). As such, there is a complex dynamic at play that needs to be discussed in the paper. The consistency with the UK study is a strength and helps to support the claim, but the claim may be best tempered given the analysis did not look at the complexities of the interplay across the factors explored.

**Response: We agree with the reviewer that it is worth noting that our analytical approach to combine the attributable burden across risk factors does not account for the potential complex interactions between the factors. Given the multi-factorial causation of most cancer sites, this is certainly an oversimplification of the associations meant to provide a relative estimate of cumulative cancer burden. In a project currently underway we and colleagues are beginning to address the impact of interactions between risk factors on cancer burden in Canada, for example, physical activity and body size or tobacco and alcohol consumption. Furthermore, we are assessing the impact of potential interventions beyond a hypothetical complete removal of the risk exposure from the population. We have added language to the end of the first paragraph of the limitations section on p. 8 noting that caution is warranted when interpreting our population attributable risk estimates and the directions of our ongoing work.**

References:

1. Parkin DM, Boyd L, Walker LC. 16. The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010. Br J Cancer 2011;S77-81.