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Title	Cancer incidence attributable to alcohol consumption in Alberta, Canada in 2012
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General comments (author response in bold)	This is a well written manuscript that provides estimates of the proportion of cancers attributable to alcohol consumption. 1. The authors assess the potential bias of their estimates due to under-reporting of alcohol consumption, but do not provide measures of uncertainty associated with the input parameters, nor assess how this uncertainty could impact the PAR. For example, the latency is unlikely to be exactly 8-9 years; rather, it likely has a fairly long-tailed distribution. Is the distribution of the latency period distribution important? Perhaps not if the rates of alcohol assumption are relatively constant. **Response: As we described in our response to the latency comment (comment 1 from reviewer 1) in reference to the methods paper, we are recommending a point estimate for estimates of latency. The rationale for this choice is that all estimates of population attributable cancer risk for alcohol were conducted with the intention of applying the resulting population attributable risk values to cancers diagnosed in Alberta in 2012. Therefore, the intention of the latency aspect of our calculations was to address the specific issue that cancers diagnosed in 2012 would be attributable to past alcohol exposure. As such, the selected latency period was intended to assist us in determining when the most appropriate past exposure time-window would be for estimates of prevalence of alcohol consumption that would be associated with cancers diagnosed in 2012.** **As we described in our previous response, our decision to use the average latency period suggested by cohort studies was influenced by the fact that previous work that has attempted to quantify appropriate latency periods has used less rigorous methods for determining the appropriate latency period (Parkin, 2011). We agree that our methods to assess latency remain somewhat imprecise but further sensitivity analyses examining the choice of latency period for alcohol were difficult to conduct due to limited availability of exposure prevalence data. Specifically, the Canadian Community Health Survey which is the source of our alcohol consumption data only includes data from the year 2000 onwards. In response to this comment, we have added an additional discussion of issues related to our choice of latency period to the limitations section on p. 10.** 2. The following statement taken from the abstract and others like it should be qualified "Overall, 5.4% of alcohol-associated cancers and 1.7% of cancers overall in Alberta were attributable to alcohol consumption in 2012." The main study output is model calculations rather than statistical estimates. For statistical estimates, it is customary to add the word 'estimated' and include 95%CI. In this case, the following wording could be considered: "Using estimates of alcohol consumption from the CCHS, we calculated that 5.4% of alcohol-associated cancers could be attributed to alcohol consumption, while adjusting for reported alcohol consumption, increased the PAR to 12%." **Response: We have amended this section of the abstract as suggested.** 3. The results section does not include a Tornado diagram which is often used in health economic studies to illustrate the input parameters most responsible uncertainty. **Response: We thank the reviewer for this suggestion. We were previously unfamiliar with the concept of a Tornado diagram, since it is not commonly used in epidemiology. We have investigated this technique and believe that it is more appropriate for health economic analyses than for the epidemiologic analyses presented in our manuscript. While investigating the economic components of the population attributable cancer risks for alcohol presented in our paper is a direction for future research, we believe this type of analysis is beyond the scope of the current work.** 4. I'd recommend at least some discussion of the impact of uncertainty in all model inputs on the PAR. The difficulty in expressing uncertainty is a general limitation of modelling studies, and this should be added to the limitation section. **Response: We have previously included substantial discussion of sources of uncertainty in the prevalence of alcohol consumption patterns in the limitations section on p. 10. We have also added confidence intervals to our estimates of population attributable risk in Table 4 and Supplementary Tables 1 and 3. A description of the Monte Carlo methods used to estimate these confidence intervals has been added to the methods on p. 6.** 5. As the objective of the study is to provide evidence for public health policy decisions, I'd recommend that the authors review methods used to grade the level of evidence. Work is ongoing to provide structure to this process. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach provides a system for rating quality of evidence and strength of

	recommendations. A series of articles on GRADE published in the Journal of Clinical Epidemiology (http://www.gradeworkinggroup.org/publications/JCE_series.htm) provides a comprehensive introduction. Adaption to the modelling environment is still ongoing. For those of us tasked with evaluating model outputs for public health guidelines, it helps if some attempt has been made to grade all the model inputs and to translate these into uncertainties in the outputs. **Response: We thank the reviewer for this recommendation. We have reviewed the GRADE material and following this review, but do not think this system is appropriate for our project. Specifically, in the introductory article to GRADE (Guyatt *et al.*, 2011), the authors note that the GRADE system is designed to assess the quality of evidence related to alternative management strategies, interventions or policies. Specifically, the proposed evaluation system automatically rates observational studies as lower quality evidence. While we understand that this may be an appropriate approach for the evaluation of interventions, in an the epidemiological context utilized in our population attributable risk project, many of the associations will have only been evaluated in observational studies as alternative study designs such as randomized clinical trials are either impractical or unethical.** Minor Points for clarification: 7. When ranges are provided, the interpretation of the range is not provided. (For example, "Proportions of cancers attributable to alcohol consumption ranged from 5.1-19.9%..."). I would limit the use of ranges to the three scenarios (self-reported, reported, and adjusted to include unreported alcohol consumptions). I think you are trying to say is that the PAR varies by cancer site. **Response: This sentence in the results section of the abstract has been rephrased to clarify that we are indeed trying to illustrate that the PAR varies by cancer site.** 8. Table 1 is full, however, it would be helpful to assign the equivalent drinks per week for each category in table format. The textual description in the methods section may not be needed. **Response: A new table summarizing the number of grams per day of alcohol used in the analysis has been added to the new Table 2. We believe this approach is a more direct method of demonstrating the quantity of alcohol consumed in each category than assigning equivalent drinks per week. The calculation of number of grams per day of alcohol in each category was a somewhat complex procedure, as evidenced by the somewhat lengthy textual description in the methods. In the interests of transparency for our methods such that other investigators might replicate our work, we think it is important to leave the textual description in the methods section.** 9. Table 1 : What are the numbers in the brackets? 95% CI? **Response: Yes, the numbers in brackets are 95% confidence intervals. A footnote has been added to Table 1 to clarify this issue.** 10. Table 2: What is the uncertainty associated with the risk estimates? **Response: The risk estimates were obtained from the previous publication by Parkin (2011) to facilitate comparison of our results both with the Parkin analysis (2011) and the analysis by Cancer Care Ontario (2014) that used the same method as our paper and also used these risk estimates. No confidence intervals were included in these estimates in the Parkin (2011) paper. As such, our initial analysis did not include confidence intervals for the risk estimates and thus no confidence intervals for the PAR estimates could be produced. However, we have returned to the original publications cited by Parkin (2011) and have obtained the corresponding confidence intervals associated with each risk estimate. As such, we have been able to add confidence intervals to our population attributable risk estimates in Table 4 and Supplementary Tables 1 and 3. A description of the Monte Carlo method used to generate these confidence intervals has been added to the methods section on p. 6.**