

| Article details: 2016-0039 | |
|--------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Title | Cancer Incidence Attributable to Excess Body Weight in Alberta, Canada in 2012 |
| Authors | Darren R. Brenner PhD, Abbey E. Poirier MSc, Anne Grundy PhD, Farah Khandwala MSc, Alison McFadden BSc, Christine M. Friedenreich PhD |
| Reviewer 1 | Dr. Carolyn Gotay |
| Institution | University of British Columbia, School of Population & Public Health, Vancouver, BC |
| General comments (author response in bold) | <p>This paper provides a useful analysis of the relationship between excess weight (overweight and obesity) and cancer in Alberta residents. There are a number of strengths to this report, including its population-based rates of cancer and overweight/obesity, the use of best current estimates of relative risk for various cancers due to excess weight, incorporation of latency periods following exposure in the analysis, and correction of self-report bias in reports of height and weight.</p> <p>While linear trends were used in analysis, in at least two areas, this may not be the best approach. There is considerable evidence that obesity has been increasing rapidly over time, such that many individuals are likely exposed to changing and increasing rates of overweight and obesity over a 10-year period. It has also been shown by several investigators that the relationship between obesity and some cancers - i.e., endometrial and pancreatic - is not linear. It is not clear if nonlinear models might affect the cancer rates observed.</p> <p>We appreciate the reviewer's comment and agree that particularly for endometrial cancer the risk has been shown to be non-linear. We attempted to apply a standardized analytical framework for this manuscript series which did not include estimating/modeling non-linear (log-linear) risk associations. As part of future work, we are attempting to apply more complex non-linear risk and non-linear exposure prevalence trends to project the future avoidable burden of disease. This work will be able to address the reviewers comment on whether non-linear models might affect the cancer rates observed.</p> <p>It is surprising that the largest paper in this area - a global analysis reported by Arnold, et al. in the Lancet in 2015 - was not referenced. This sophisticated analysis looked at rates in WHO regions, which combine Canada and the United States to comprise the "North America" region. This paper found much higher attributable cancer risk for excess weight, such as 47.8% for post-menopausal breast cancer, 48.2% for esophageal adenocarcinoma in women, and 53.4% for gallbladder cancer in women. Given that the current study seems to be consistent with other Canadian analyses, why does the Lancet paper differ so much in its estimates?</p> <p>The Arnold et al., 2015 paper is now referenced in the discussion and compared to the results of the current analysis (starting on line 224). However, it should be noted that the 'North American' region in the Arnold et al. analysis does not include any prevalence data from Canada. All BMI prevalence estimates were from the U.S NHANES database.</p> <p>An important point to be considered is whether overweight and obesity should be combined as a single cancer risk factor. Evidence continues to accumulate indicating that overweight and obesity have different effects on mortality: notably, Aune, et al.'s just published BMJ report that showed overweight was actually protective. It would be useful for the authors to indicate why they do not consider overweight and obesity separately, or as a continuous rather than categorical variable.</p> <p>As outlined in the response to reviewer comment #1, we chose to use the standard BMI cut-points in these analyses for two reasons. First, we wanted our results to facilitate interpretation from a public health standpoint. From a policy and public health perspective it is more straightforward to communicate a meaningful message based on BMI cut-offs rather than continuous variables. In addition to interpretability, several assumptions are required to calculate the PAR on a continuous scale, mainly the distribution of BMI and the relative risk function. Defining the change in prevalence distribution and associated parameters as well as the pattern of relative risk for shifts in BMI is beyond the scope of this project.</p> <p>Finally, the implications of the findings are quite brief and would be enhanced by more discussion. For example, what are the implications of reducing obesity on other outcomes, such as economic burden? (See Krueger, et al., CJP, 2015.)</p> <p>Reference to the economic burden of excess weight has been added to the conclusion (lines 267-268).</p> <p>What evidence do we have that reducing obesity (by itself or in conjunction with increasing physical activity) would impact cancer rates?</p> <p>Evidence on the avoidable burden of cancer has been added to lines 231-233.</p> <p>The paper notes that obesity has been increasing markedly. Given that obesity has been going up for more than a decade (the latency period used here), do time trends for cancer incidence show increases in cancer rates? If not, what are possible explanations, and how might these affect the interpretation of the findings reported here?</p> <p>The cancer rates for the sites associated with overweight/obesity have also been rising for over a decade. Therefore, we do not feel as though it is necessary to include any additional explanations.</p> |
| Reviewer 2 | Dr. Jennifer Kuk |

| | |
|--------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Institution | York University, School of Kinesiology and Health Science, Toronto, Ontario |
| General comments (author response in bold) | <p>Were individuals with prevalent or past cancer excluded? How does your inclusion/exclusion compare with the population from which you used the risk estimates?</p> <p>Estimates from the Canadian Community Health Survey were used for the prevalence of overweight/obesity. The survey did not exclude those with cancer or a history of cancer. Relative risk estimates were obtained from a comprehensive meta-analysis (see methods and the footnote in Table 2). The meta-analysis included 28 studies from North America.</p> <p>Are there age specific risk estimates? I would assume that cancer risk varies by age. Also, it is not clear that the RR for overweight and obesity should be taken together as most health factors are exponentially related with obesity.</p> <p>Unfortunately, age-specific risk estimates were not available. An explanation as to how the risk estimates were used for overweight and obesity can be found on lines 111-115.</p> <p>Risk estimates for 5 kg/m² increase would translate to a 15.3kg difference for a man of average height in Canada. This is a fairly large value and would be much larger (~2-3x) than what is typically observed with lifestyle weight loss. Thus, I feel that the risk estimates are unfairly over-inflated due to the largeness of the unit chosen.</p> <p>We agree with the reviewer's comment that a 5 kg/m² increase is larger than has been generally observed in interventions of diet or physical activity. The objective of this analysis was to provide an estimation of how many cases of cancer in Alberta are attributable to being overweight or obese i.e. if an intervention could move the population to normal body weight. For our future analyses we will be modeling the impact of known interventions on body weight on current and future cancer burden in Canada. These complex analyses are, however, beyond the scope of this manuscript and the related manuscript series.</p> <p>It is unclear what is meant by the 'the square of this values was used for the obese category'. Was a different unit for expressing RR used in the obese group? If so, Why? And was it 5 kg/m² squared or square root?</p> <p>The wording has been changed on lines 114-115 to better reflect how the risk estimates were modified for use with obesity prevalence.</p> <p>The methods could be more clear by speaking to cancer first and then the latency period for body weight after as the years used were in reference to the cancer measure.</p> <p>The cancer incidence sub-section of the methods has been moved to a section before the latency period sub-section.</p> <p>From the supplementary table, I am not clear on how the correction factors were applied and how the estimates were adjusted. It would be helpful to put the self-reported and adjusted prevalences.</p> <p>The original estimates have been added to Supplementary Table 1 for comparison.</p> <p>The discussion is very short and could be expanded. The authors devote more than half the discussion to limitations and topics that are not directly relevant to the current topic of obesity and cancer.</p> <p>The discussion section has been expanded based on editor and other reviewer comments.</p> <p>Minor comments</p> <p>Please add units to numbers such as BMI and age throughout the manuscript text.</p> <p>These revisions have been made.</p> |