Reviewer's report

Title: Reduction in Cervical Cancer Incidence and Mortality in Canada: National Data from 1932.

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Reviewer: Leonardo Simonella

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The aim of the analysis was to assess the change in cervical cancer incidence and mortality trend over time by age group and birth cohort to better understand the effect of screening. The authors observed that over time, age-standardised incidence and mortality fell from around 1952 and 1970, respectively. Moreover, age-specific mortality and incidence fell across all age groups by sequential 5 year periods. Figures 2A and B are a nice illustration of this effect. The analysis also illustrates the incidence and mortality trend in each 5 year age group by calendar year.

Major Compulsory Revisions

Aims:

In the last paragraph on page 5, the term ‘such screening’ appeared to refer to policies encouraging starting screening early in life and repeated frequent screening. While I understand the intent of the authors’ analysis, the aims need to be stated more explicitly. The current wording of the aim of the analysis suggests that changes in trend are to be related to cervical screening organization and policies. For clarity, it would be good if the authors could state how assessing changes in trend is related to the cervical screening in Canada.

Methods:

For the population denominators, the authors indicate that between 1932 – 1970 the censal estimates were not adjusted for undercount. I would have liked to seen this described more clearly and an outline of the implications for this effect. Does this affect the reported incidence and mortality rates in anyway? If so, this probably needs to be raised as a discussion point.

Is the calculation for the probability of dying from cancer a standard method as well? One of my concerns about calculating the two probabilities (probability of developing cervical cancer and probability of dying from cervical cancer) is that would the probabilities significantly differ if different years were used? Would if it be better to use a combination of time points (if this is a feasible option)? I’m not familiar with this method, but it would nonetheless be good sensitivity analysis to see if this were the case.

Other points about methods:

Screening not addressed: The aim of the analysis was to assess trends in light of
screening. However, there is no mention of analysis with respect to cervical screening policies or screening uptake. I think this needs to be included or addressed in the analysis. Otherwise, one could argue that the reduction in cervical cancer mortality was due to better treatment of CIN and/or invasive cervical disease. This point is raised in the discussion, but there is no attempt at distinguishing the effect of screening from the effects of improved treatments. For example, the authors could look at the participation rate for screening in Canada over time? Did this differ by province? What were the screening policies for each of the provinces? Reference was made to screening in younger age groups as well? What is the evidence for screening in this age group? Any discussion of trends need to be made in light of timing of a particular policy and how the target population were engaged in screening behavior (where information about behavior is available).

Use of mortality data for years where death certificates could be inaccurate: I think this is a real concern of the analysis. The change in the trends before 1970 for certain again groups (Figure 3a) and in general (Figure 1) are compelling. A reader could mistakenly assume that the increase in the trend before 1950 could be due to cohort effects as opposed to the quality of death certification (as pointed out by the authors). To address this issue, the authors might want to present a trend analysis by calendar year on the trend of uterine cancers NOS as backdrop to the cervical cancer mortality trends. Alternatively, to account for the uterine cancers NOS, the authors may want to reallocate these to cervical cancer using methods proposed by Arbyn et al. 2009 (Eur J Cancer 45(15):2640-8)

Calculation of 95% confidence intervals for the percent reduction: There seems to be large reductions in incidence and mortality reductions. Confidence intervals would indicate whether the reduction in each of the age groups differed significantly from each other (or not).

Results:
In general the analysis provides a broad overview of the change in trends by calendar and age group. However there is no assessment of change in trend with respect to screening policy, uptake, changes in treatment for cervical cancer, or availability of healthcare for the population. Given the strength of the paper is in the availability of incidence and mortality data, if would be good if the above stated factors could be incorporated into the analysis. As an example, the authors may want to look at a paper by Taylor et al. 2006 (Cancer Causes and Control; 17(3): 299-306).

Discussion:
The discussion is generally well written as it provides as summary of overview of findings and the limitations. However, a very brief mention was made on the impact of HPV vaccination, and the potential use of primary HPV testing or HPV triage. The authors state in the abstract that ‘we analyzed national data... and provide data for revising the national recommendations on screening for cancer of the cervix’. I could be wrong, but I interpret this objective to mean that any assessment in trends would assess the potential implications for new cervical screening technologies in light of HPV vaccination. For example, given the
intensity of screening in countries like the US and certain provinces in Canada, the use of primary HPV testing or HPV triage may reduce the rate of overtreatment of CIN2, as well as potentially increase the screening interval.

HPV vaccination is going to also affect the cost-effectiveness of cervical screening. To ensure cervical screening remains cost-effective in the context of HPV vaccination in Canada, HPV screening may need to be introduced to enable the use of longer screening interval. An additional point that probably needs to be considered is the impact of HPV vaccination on incidence and mortality trends. This will be affected by uptake. A section in the discussion probably needs to be included to address the above points on HPV screening and HPV vaccination and the potential implications on cervical cancer incidence and mortality trends.

Discretionary Revisions

In general, I found it a little hard to follow the analysis section. To address this, it might be worthwhile for the authors to provide an example of how an age-group midpoint was added to a birth cohort midpoint to assess birth cohort midpoint mortality and incidence.

In terms of data sources, these were generally well described. I would have liked to have seen more detail on exactly what codes were used to define incidence and mortality cases.

The authors should state the percent reductions with respect to the changes in the age-standardised rates. One could infer the large changes in percent reductions could relate to large changes in rates.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
'I declare that I have no competing interests'