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Title	Trends in prostate cancer incidence and mortality in Canada during the era of PSA screening
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Reviewer 1	Lawrence Paszat
Institution	Institute for Clinical Evaluative Sciences, Cancer research programme
General comments (author response in bold)	The paper contains excellent reviews and discussion of existing knowledge about prostate cancer. 1. However, there is one huge flaw and another significant omission, in the research design. The PSA utilization data referenced in 2 papers do not support the claim of a turning point in 1990-1991. The Bunting reference explains that the private lab data (one of multiple larger community lab providers in Ontario) did not start contributing data until 1992. It is impossible to describe the trend in utilization prior to 1992 from either publication or from other sources. The data for utilization trends are incomplete and non-representative of the Ontario population. **The reviewer is incorrect. Levy (2) specifically says this. We are now referencing a more recent paper by Bunting, which is more complete, but regardless of slightly incomplete data the relative changes are so massive that they swamp such errors. Sakatchewan had similar contemporaneous increases, and indirect references about Alberta and Quebec suggest similar changes at that time.** 2. In addition, the reasonable hypothesis that treatment might explain mortality reduction was not investigated: LHRH therapies can be described by volumes of sales per province per year, and may be obtained from the Ottawa based office which compiles such data. **We have raised this hypothesis. To test it in detail would require work beyond the scope and length of this paper.** **These two flaws would discredit the conclusions, which are probably correct, but this study does not provide appropriate data to support the conclusions.**
Reviewer 2	Maria Ramos
Institution	Balearic Islands Health Department, Spain, Public Health Department
General comments	(There are no comments.)
Reviewer 3	Isra Levy
Institution	Ottawa Public Health
General comments (author response in bold)	This is a thorough review of the descriptive epidemiology (person and time trends only) of prostate cancer incidence and mortality in Canada, and is a useful contribution to the field. 1. The authors do, however, seek to draw conclusions that are qualitatively more definitive than the study design merits - this is evidenced most vividly in the inappropriate and scientifically meaningless use of the words "are" and "largely" in the last sentence of the abstract, in which it is asserted that "other factors such as improved medical treatments are largely responsible for reducing prostate cancer mortality". At best, from descriptive epidemiology reports, one could deduce the hypothesis generating conclusion that other factors such as medical treatment may explain some or all of the observed rate changes. The paper needs to be revised to address this minor, but important, element traces of which are present in several areas. **This reviewer appears to have misunderstood our meaning. We have changed the sentence to prevent such misunderstanding. We have referenced other authors who reach similar conclusions from other evidence.** **The Introduction and Methods sections are clear and concise.** 2. The second sentence of the Results section refers to a "gradual" increase in rates. This is a value laden word, and is arguably incorrect in any event. Many would accept an annual % change in

observed rates of 3%, or a doubling of observed rates in 20 years, as "large". In the field of descriptive cancer epidemiology these are certainly not gradual. Perhaps some similar time trend comparators with other cancers would help. In any event, the choice of the word "gradual" implies the possibility for a non scientific bias to creep into the interpretation of the simple data.

This reviewer is reading more into the words than was stated: we think that comparative adjectives direct the reader to the difference in gradients.

3. The Discussion section starts by raising a similar sense of possible preconceived bias in the interpretation of the results, with the use of the word "apparent" in the first sentence - the rates were observed. Unless the assertion is that data quality was suspect, this is not an "apparent incidence" rate. It is the "observed incidence".
The word apparent was used to emphasise that the incidence rates are an artifact of extra testing that over-diagnoses and finds non-disease.

4. Page 5 - lines 43-47; would it be possible to calculate or estimate what effect size would have been expected? In other words, quantitatively, what proportion of the 30% mortality reduction could, conceivably, be attributed to a screening effect?
WE have discussed this in more detail.

5. Page 6 - lines 29-34; there is a flaw in logic in this sentence. The question is why there has there been a reversal in the upward trend, but the fact of the reversal is presented as a possible contributory explanation.
We have deleted this part.

6. Page 7 - line 29; the word "earlier" is missing. ie secular changes in incidence......"started EARLIER and peaked higher..."
WE have made this change.

7. Last sentence of the Discussion - again, this is a true statement; but it presumes more than the study can truly bear; it behooves the authors to acknowledge the plausibility of a contributory role of screening too.
We have substantially rewritten the discussion and conclusions section.