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Title	Prenatal screening rates across healthcare regions in Ontario, Canada: A retrospective cohort study
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Reviewer 1	Amanda Shane MSc
Institution	Field Epidemiologist, Public Health Agency of Canada *located at* Toronto Public Health
General comments	While the majority of my comments are minor (see below), I have identified some major comments in the Materials and Methods section as follows:

1) Univariate analysis: Specifically describe methods used for the descriptive/univariate analysis. Further, the statistical test used to assess differences in key characteristics was not specified, therefore it is difficult to determine whether the interpretation of the results is accurate.

2) Multivariate analysis: Include specific details on the model building process. Describe how you arrived at the final predictor set. Was confounding or effect modification considered? If so, which variables and how were they addressed? If not, explicitly state.

3) General: In the Results, there is an emphasis on the geographic distribution of PNS, however, geography was not stated as an important variable *a priori* in the Materials and Methods. Ensure that all variables used in the analysis are summarized in the methods. Further, provide clarification/rationale for suppressing the actual geographic locations in the text and figure (currently, without this information, the figure is unnecessary and does not add value to the paper, given the geographic locations are masked).

MINOR COMMENTS

There are a few relatively minor changes from the Introduction, Materials and Methods and Results that I would recommend prior to publication in CMAJ Open:
1) Introduction. Overall, I felt there was a clear and concise summary of the issue, and a clear statement of the study objectives. However, the following recommendations should be considered:
- Paragraph 2. The reference to Table 1 may be misplaced; the table does not summarize differences in screening practices and performance across jurisdictions, as suggested in the text. Recommend moving the in-text table reference to the second sentence in Paragraph 2.
- Paragraph 2. Recommend including brief description of how screening practices vary across jurisdictions within Ontario and Canada, specifically.
2) Materials and Methods. This section is generally comprehensive: however, please consider the following:
- Paragraph 1. Discrepancy between length of gestation between this section and the abstract (>16 vs. >=16 weeks). Clarify throughout.
- Paragraph 1. Include reference for sentence 2, "...most women should be offered PNS by this point in their pregnancy.".
- Paragraph 5. The rationale for selection of most predictors was provided. This section would be strengthened by including the rationale for: parity; previous spontaneous or therapeutic abortion; prior delivery of a child with congenital malformation; and immigration status.
3) Results. There were some concerns regarding the interpretation of the statistical tests as well as suggested clarifications. Specifically:
- **Paragraph 1. For completeness, consider including the "total" cohort size, and** then provide the number of excluded pregnancies in order to arrive at the study cohort.
- Paragraph 2. Second sentence, confirm age groupings: change "over 21 years a delivery" to "21 years and over" (or similar). |

- Paragraph 2. Change "65%" to "66%" (not recent refugee immigrant – as per Table 2).
- Paragraph 2. Last sentence: it is not clear where the data to support this statement come from. Recommend adding to Table 2, or including the statement "(data not shown")".
- Table 2. For Previous delivery or a stillborn child and previous abortion in the past 5 years, what is the statistical test applied to? The clarification requested to the univariate methods should address this comment.

4) Discussion.
- Throughout: Suggest removal of italicized font for emphasis.

STROBE CHECKLIST
The STROBE criteria were met for the Abstract, Introduction and Interpretation. However, there were some criteria not met for Methods and Results, as follows:

1) Materials and methods
- Bias. Recommend an assessment of potential sources of bias, and how these were addressed in the study design *a priori*, or how they were addressed in the analysis.

2) Results
- Descriptive data. Include details on how missing data were handled, and what (if any) impact this may have on the interpretation.

As stated by the authors, this is the first population-based study to examine the uptake of prenatal screening in Canada. Despite the potential contribution to the literature, the suggested revisions above should be considered before publication in order to strengthen this study.

Reviewer 2	Kimberley Garbedian
Institution	Obstetrics and Gynecology, Mount Sinai, Toronto, Ont.
General comments	Overall an excellent paper. My only comment would be that the NIPT discussion seems out of place. You do not have any data looking at access/% opting for NIPT or provider knowledge regarding NIPT. The paper is based on prenatal testing covered by OHIP. There are a lot of confounding variables associated with NIPT discussion ie. patients that opt to pay $1000 for this test often have had a difficult past pregnancy experience ie. down syndrome, still birth etc. So, reasons other than just location and socioeconomic status.
Author response	*Response to Reviewer #1's MAJOR Comments (Amanda R. E. Shane, MSc, Field Epidemiologist, Public Health Agency of Canada)* 1. As suggested, we have specified that chi-square tests were used to compare the timing of screening (1st vs. 2nd trimester) among women who received prenatal screening. 2. As suggested, we have included additional details on the multivariate model building process. Specifically, all screening predictors identified a priori were entered into the multivariate model after checking these variables for collinearity. We were explicit about not doing additional analyses focused on confounding by individual variables apart from their inclusion in the multivariable model. 3. As suggested by the Editor (above), we have included a map that illustrates screening rates by regions 1-14 screening laboratory locations. As we have better articulated in the Methods section, Local Health Integration Network was used descriptively and not included in the multivariate model. Rather the RIO score was used as a measure of geography given its more meaningful representation of rural/urban status. Response to Reviewer #1's MINOR Comments (Amanda R. E. Shane, MSc, Field Epidemiologist, Public Health Agency of Canada) 1. Introduction, Paragraph 2. • Thank you for pointing out that Table 1 does not summarize differences in screening practices and performance across jurisdictions. We have added a sentence to specify the Ontario context and relocated the in-text Table 1 reference to the end of this sentence. • As suggested, we have included an additional sentence (and citation) that refers to

how screening practices vary across Ontario.

2. Materials and Methods.
• We have corrected the discrepancy between length of gestation (>16 vs. >16 weeks) throughout. Pregnant women > 16 weeks gestation were included.
• As suggested, we have included a reference for Paragraph 1, sentence 2, "...most women should be offered PNS by this point in their pregnancy."
• The rationale for including parity, previous spontaneous or therapeutic abortion, prior delivery of a child with congenital malformation, and immigration status is that these predictors have all been shown to be associated with uptake of prenatal screening in other jurisdictions. We have made this explicit in the Methods and provided references accordingly.

3. Results.
• We appreciate your suggestion to include the "total" cohort size and the number of excluded pregnancies to arrive at the study cohort. Since establishing the cohort required several steps, we have provided these details in Appendix 1; our preference would be to include this flowchart as Supplementary content to the manuscript.
• As suggested, we have changed "over 21 years a delivery" to "21 years and over."
• As suggested, we have changed "65%" to "65.9%" to align with Table 2 and with CMAJ Open's decimal place convention.
• As suggested, for the last sentence of Paragraph 2, we have included the statement "data not shown".
• Table 2. For Previous delivery or a stillborn child and previous abortion in the past 5 years, what is the statistical test applied to? The clarification requested to the univariate methods should address this comment.

4. Discussion.
• As suggested, we have removed italicized font throughout.
Response to Reviewer #2's comments (Dr. Kimberley Garbedian, Mount Sinai, Obstetrics and Gynecology)
1. Thank you for your comment regarding non-invasive prenatal testing. Indeed the paper focuses on prenatal testing covered by OHIP and indeed there are many factors other than location and socioeconomic status that might be associated with uptake of NIPT. However, our rationale for including a reference to NIPT in the introduction and in the discussion is to flag the fact that barriers to accessing recommended prenatal screening services (identified by our findings) will only be exacerbated with the arrival of market-driven NIPT. This adds urgency to our existing need to attend to provincial (and national) policy strategies for assuring universal access to gold standard prenatal screening tests for all pregnant women.