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Title	Characterizing risk for type 2 diabetes in First Nations people living in First Nations communities in Ontario, Canada using population-based survey data
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Reviewer 1	Stephanie Kulhawy-Wibe
Institution	Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, Alta.
General comments (author response in bold)	<p>I am pleased to know that knowledge of traditional language and partaking in traditional foods seems to be correlated with less risk of DM2. Of course, this could be confounded by age.</p> <p><b>Thank you for this observation. In the Interpretation section, we have now added an additional sentence around our results for age to aid the interpretation of these findings in context:</b></p> <p><b>“A large proportion of new cases were predicted to occur among younger individuals, in agreement with previous research that has shown that First Nations people tend to develop diabetes at younger ages (Turin et al, 2016).”</b>  <b>Turin TC, Saad N, Jun M, Tonelli M, Ma Z, Barnabe CCM, et al. Lifetime risk of diabetes among First Nations and non-First Nations people. CMAJ. 2016; 188(16):1147–53.</b></p> <p>I would suggest describing your predicted incidence in the context of reported incidence in order to show validity of your model compared to historical data. As we know, DM2 in FN populations is a growing issue and if this model is accurate I would expect it to predict higher incidence than historical data.</p> <p><b>Thank you for this suggestion. The most recent study on diabetes in First Nations people in Ontario estimated that diabetes incidence was 0.80% in 2014, which aligns with the 10-year diabetes risk of 9.6% between 2015/16 and 2025/26 predicted by DPoRT in this study. We have added the following sentence to the Interpretation Section:</b></p> <p><b>“Using a validated population risk tool, DPoRT, and risk factor information from the RHS, we predicted that between 2015/16 and 2025/26, type 2 diabetes risk will be 9.6% in this population, which aligns with the annual diabetes incidence of 0.80% observed in 2014 for First Nations people in Ontario (Green et al, 2019).”</b>  <b>Green ME, Jones CR, Walker JD, Shah BR, Jacklin K, Slater M, Frymire E, eds. First Nations and Diabetes in Ontario. Toronto, ON. ICES; 2019.</b></p> <p>Reference list is very thin. I know this is a limited area of the literature, but not that limited.</p> <p><b>We agree with this comment, and have now added the following additional references to better frame the introduction and interpretation sections:</b>  <b>Crowshoe L, Dannenbaum D, Green M, Henderson R, Naqshbandi M, &amp; Toth E. Type 2 diabetes and Indigenous Peoples. Canadian Journal of Diabetes. 2018;42 Suppl 1:S296–S306</b>  <b>Dyck R, Osgood N, Lin TH, Gao A, Stang MR. Epidemiology of diabetes mellitus among First Nations and non-First Nations adults. CMAJ. 2010;182(3):249-256.</b>  <b>Turner N, Turner K. Traditional food systems, erosion and renewal in Northwestern North America. Indian Journal of Traditional Knowledge. 2000;6(1):57-68</b></p>

	<p>Oster RT, Grier A, Lightning R, Mayan MJ, Toth EL. Cultural continuity, traditional Indigenous language, and diabetes in Alberta First Nations: A mixed methods study. <i>Int J Equity Health</i> 2014;13:92.</p> <p>Chronic Disease Surveillance and Monitoring Division, Centre for Chronic Disease Prevention and Control. <i>Diabetes in Canada: Facts and figures from a public health perspective – First Nations, Inuit, and Metis</i>. Ottawa, ON: Public Health Agency of Canada, 2015 <a href="https://www.canada.ca/en/public-health/services/chronic-diseases/reports-publications/diabetes/diabetes-canada-facts-figures-a-public-health-perspective/chapter-6.html">https://www.canada.ca/en/public-health/services/chronic-diseases/reports-publications/diabetes/diabetes-canada-facts-figures-a-public-health-perspective/chapter-6.html</a></p> <p>Green ME, Jones CR, Walker JD, Shah BR, Jacklin K, Slater M, Frymire E, eds. <i>First Nations and Diabetes in Ontario</i>. Toronto, ON. ICES; 2019</p> <p>Turin TC, Saad N, Jun M, Tonelli M, Ma Z, Barnabe CCM, et al. Lifetime risk of diabetes among First Nations and non-First Nations people. <i>CMAJ</i>. 2016; 188(16):1147–53</p> <p>Grammar - Page 9, line 18: should that read FN persons? or people? <b>Thank you for noting this, we have reviewed the paper carefully and corrected the grammatical errors.</b></p>
<b>Reviewer 2</b>	Constantine Samaan
Institution	Division of Pediatric Endocrinology, McMaster Children's Hospital, Hamilton, Ont.
General comments (author response in bold)	<p>The authors of this paper used the First Nations Regional Health Survey (RHS) data from 2013 phase 3 to assess the risk and risk factors for type 2 diabetes (T2D) in Indigenous communities in Ontario. This is an important area of research as there are limited data on the Indigenous population of Canada. The questions asked are crucial for Indigenous communities as they plan their own T2D prevention strategies. It also helps Indigenous decision-makers and those who deal with government to advocate the assignment of finite resources to areas of impact and need. The inclusion of representation from the Chiefs of Ontario is bringing the most important stakeholder voice, the Indigenous people, to the table.</p> <p>Major comments: -It is not clear in the introduction how with a response rate of 78% that only 993 people were included in this analysis. I think there is some explanation missing here as to how this number was arrived at. I do see better clarification in the results which should be moved up to explain the weighted measures in the methods section even briefly at this early point (Page 4, paragraph 2).</p> <p><b>Thank you for this comment. For more clarity, we have added additional details in the methods section to describe the sampling frame and weighting system of the RHS. Briefly, the RHS Phase 3 sampling design used complex sampling that incorporated a two-stage sampling strategy. The first stage involved the selection of communities and the second stage pertained to the selection of individuals within each community sampled. The sampling rate within each community was determined as a function of the overall sub-region probability (within regions) and the probability of community selection (within a sub-region). In all, 5.5% of the target population was sampled in the RHS, and the response rate was 76.1%. Individual responses were weighted using sampling weights provided by the First Nations Information Governance Centre to reflect the representation of the population by the sample. The sampling weights were based on registry counts for the year 2014 from Indigenous and Northern Affairs Canada.</b></p>

-One issue is whether the DPoRT tool has been validated in Indigenous communities to predict diabetes risk. It is noted that the authors report the validation of the tool in Manitoba. Was this an Indigenous cohort? Are there other papers or reports validating this tool in Indigenous communities (Page 4, paragraph 3).

**In the methods section we have clarified the description about the validation of DPoRT. DPoRT was originally validated in Ontario and Manitoba in cohorts that were representative of the provincial general populations, including Indigenous people living off-reserve. The appropriateness of using DPoRT to estimate risk in First Nations people living in First Nations communities (on-reserve) was assessed in this study by applying DPoRT to the RHS Phase 3 data and examining the model's predictive performance for those with self-reported type 2 diabetes. The results are presented in the second paragraph of the results section. We found that predicted risk corresponded with diabetes risk at baseline (ie., 90.2% of individuals with diabetes were classified as high or moderate diabetes risk). In comparison, in the Ontario general population, 94.8% of individuals with diabetes were classified as high or moderate risk at baseline (estimated with the Canadian Community Health Survey, cycle 2013/14). We are unable to carry out a formal validation with prospective data because the RHS data are not linked to outcome data. This type of analysis would have to be a future direction of the Chiefs of Ontario and would involve several important discussions with the community to discuss if these data should be linked and how that linkage will be analyzed according to their priorities.**

-It is not clear how physical activity was reported and measured. Please provide further clarification (Page 5, paragraph 1).

**Thank you, in the methods section we have clarified the calculation for physical activity: "Physical activity level was measured using the physical activity index in the RHS, which calculates total energy expenditure by multiplying the number of times engaged in each activity in the past three months, average duration of participation in minutes, and metabolic equivalent (MET) value assigned to each activity." A citation to the RHS survey has been provided for further details about the specific activities that were assessed.**

-It is also not clear how the knowledge of the Indigenous languages is a protective factor against diabetes. This needs further clarification as it is not elaborated on in the methods or discussion sections (Page 5, paragraph 1; Page 9, paragraph 2). Language is only one factor of culture, so were data collected on participation in traditional practices such as ceremonies, dances, community activities, sports, hunting, or any other parts of culture?

**Thank you for this important comment. We captured aspects of participation in First Nations culture from two RHS questions that assessed consumption of traditional foods and knowledge of a First Nations language. We have clarified in the methods section that First Nations language was measured by the RHS question, "Do you have any knowledge of a First Nations language, even if only a few words (yes, no)". We also agree that these variables are only a proxy measure of Indigenous culture, and have now recognized this important point in the Interpretation section, limitations paragraph:**

**“Our study included only proxy measures of Indigenous culture, namely traditional foods and language, which does not capture all aspects of First Nations culture and traditional activities.”**

-The authors need to consider and address the following issues in their interpretation of the data:

**We appreciate the opportunity to strengthen the discussion of our findings, and thank the reviewer for sharing this reference and insightful comments. We note below how we have addressed each point.**

A link is included to help the authors understand the currently available data by the Government of Canada that can frame this discussion in this context. In addition, there are other considerations when it comes to the reasons why Indigenous peoples are at risk of diabetes that include in-utero exposure (epigenetic mechanisms) in addition to all the other factors noted in this paper:

<https://www.canada.ca/en/public-health/services/chronic-diseases/reports-publications/diabetes/diabetes-canada-facts-figures-a-public-health-perspective/chapter-6.html>

**We have incorporated this point and reference into the revised background section:**

**“In addition to genetic susceptibility, socioeconomic determinants, and risk behaviours that are common diabetes risk factors in all populations (3), First Nations people have unique experiences that contribute to diabetes risk, including intergenerational effects of colonization, loss of culture and language, epigenetic mechanisms, and disproportionate experiences of low income, food insecurity, and risky behaviours compared to other populations in Canada (4-7).”**

a-It is obesity that drives diabetes and being obese is the main driver of diabetes in all populations including Indigenous ones. However, the impact of obesity is more devastating on the Indigenous communities. This needs to be highlighted.

**We have highlighted this point in the Interpretation section with the following sentence:**

**“Remote northern First Nations communities in particular experience unique food security challenges in accessing healthy and inexpensive foods (11, 23), and changes from traditional lifestyles and diets have contributed to the high prevalence of obesity and physical inactivity in First Nations people (21, 24).”**

b-As reported, physical activity halves the risk of developing diabetes. This is an important recommendation for communities even in the presence of food insecurity. This needs to be elaborated on.

c-The conclusion that eating traditional foods few times per week is successful at preventing diabetes is not quite reflective of the data and is likely related to the food insecurity issue (9.5%, CI 8.1 to 10.9 and 10.4%, CI 7.8 to 12.9). This needs to be reported based on the data available. The consumption of traditional foods by the Indigenous communities makes a lot of sense for many reasons but does not seem to be very protective against the development of diabetes. This has implications for what to recommend for this population especially urbanized Indigenous people where access to traditional foods is difficult. It is also likely that getting traditional foods in sufficient quantities to feed all indigenous communities

	<p>to maintain health will require significant planning and resource allocation, as sourcing these foods is not easy even for those who live on their territories and may not offer a practical strategy to prevent diabetes.</p> <p>It is important to consult Indigenous partners on this issue, and word things carefully to ensure that support continues for traditional foods consumption but noting that this is only one piece in preventing type 2 diabetes and may be having healthy food choices that are not traditional foods may offer health benefits. The wording has to be measured and supportive of all Indigenous peoples having a healthy future. Also note that off-reserve Indigenous peoples seem to have less obesity rates when compared to on-reserve people, and it is likely that they are not necessarily consuming traditional foods although this is hard to prove.</p> <p><b>We fully agree with this comment and recognize the importance of working in collaboration with Indigenous partners throughout the research process. Our research was conducted in full partnership with the Chiefs of Ontario, which represents the 133 First Nations communities located within Ontario. This included presenting the research proposal to the Chiefs of Ontario Health Coordination Unit, comprising of Chiefs and other representatives of First Nations communities, for feedback and approval, as well as presentations prior to the dissemination of results to allow shared interpretations of the findings. The Senior Author of this manuscript is the Chiefs of Ontario Director of Health, Carmen Jones, who is a contributing co-author on this paper. We have now explicitly recognized our partnership with the Chiefs of Ontario in the methods section:</b></p> <p><b>“The study was conducted in partnership with the Chiefs of Ontario.”</b></p> <p>Minor:</p> <p>-please add a reference to clarify the calculation of the BMI in the methods section (Page 5, paragraph 1).</p> <p><b>We have added the following reference to the methods section to clarify the BMI calculation and categories:</b></p> <p><b>World Health Organization. Obesity: preventing and managing the global epidemic. Geneva: WHO; 2000.</b></p> <p>-the last line on page 5 needs editing with a grammar issue</p> <p><b>Thank you for noting this, we have reviewed the paper carefully and corrected the grammatical errors.</b></p>
<b>Reviewer 3</b>	M.E. Pavkov
Institution	Centers for Disease Control and Prevention, Atlanta, Ga.
General comments (author response in bold)	<p>Rosella et al. estimated the 10-year risk of type 2 diabetes in First Nations people living in Ontario using a validated population risk tool based on the distribution of a number of risk factors. Their finding that adherence to traditional diet and culture reduces the risk of type 2 diabetes in these communities confirms previous studies among indigenous people.</p> <p>I offer the following comments for consideration:</p> <p>1. This is a paper that makes use of self-reported data for diabetes prediction. This reader would have liked to see more information about how the prediction tool works and if the model underwent any improvements since 2011. At that time, the c-statistic indicated an AUC of maximum 0.8, which indicates fair prediction, and didn't appear to add predictive value to the cohort-specific risk factors.</p> <p><b>Thank you, we agree that further details about DPoRT's development,</b></p>

validation and information about previous model updates that were undertaken would be informative to readers. We have added the following text to the methods section:

**“DPoRT is a statistical model based on the Weibull survival distribution and is validated to calculate up to 10-year type 2 diabetes risk in any population-based data that contains self-reported risk factor information, including age, sex, body mass index, education, smoking status, heart disease and hypertension. The original risk algorithm was based on a cohort of 19,861 individuals  $\geq 20$  years of age without diabetes followed between 1996 and 2005, and validated in two external cohorts in the provinces of Ontario ( $n = 26,465$ ) and Manitoba ( $n = 9,899$ ) which were representative of the general population, including Indigenous people living off-reserve (8). The algorithm was updated with more recent data including individuals from the original 1996 Ontario cohort and Ontario respondents of CCHS Cycle 1.1 (2001) and 2.1 (2003), and externally validated in Ontario respondents to the 2005 CCHS, with follow-up until 2011 (10). DPoRT was demonstrated to have good discrimination and calibration ( $c$ -statistic = 0.77; HL  $X^2 < 20$ ), which was informed by linkage to administrative databases that identified observed diabetes cases during the prediction period (10).”**

2. In the 2011 publication (citation #8) the authors predicted the 9-year diabetes risk in 2005. It would be interesting to indicate how that prediction compares with real data, i.e., the model predicted about 1.7 million new cases by 2014 based on the Canadian Community Health Survey – how many cases occurred in reality? This type of comparison certainly benefits the prediction tool. It would also help interpret the current analysis.

**Thank you, we have provided additional details about DPoRT’s validation (described above) which we believe addresses this comment.**

**The original and updated DPoRT algorithm were validated by linkage to provincial administrative databases that were used to identify observed diabetes cases during the prediction period. Measures of calibration were assessed to determine agreement between observed diabetes cases and predicted diabetes cases across different risk groups, and the model was found to be appropriately calibrated (HL  $X^2 < 20$ ).**

3. In table 2 it is not clear what adjustment was used for risk prediction. Is each risk parameter adjusted for the others?

**Table 2 shows results for predicted diabetes risk and number of new cases, which were calculated by applying the DPoRT algorithm to the population groups specified in the table. To increase clarity about DPoRT’s model specification, we have now included DPoRT’s algorithm formula in an Appendix.**

4. The authors may wish to structure the presentation of the results to more clearly convey the differentiation between relative and absolute risks. For example, in their interpretation of results the authors only focus on the number of cases predicted for each risk category, which may be misleading. For example, on page 8, first paragraph under Interpretation, it is stated: “We also found important reductions in diabetes risk among First Nations adults that reported connections to Indigenous culture, specifically, eating traditional vegetative foods and knowledge of a First Nations language” The DPoRT predicted risk, however, is similar among those with and without traditional food consumption and among those with and

without knowledge of First Nation language (largely overlapping 95% CI). Similar for food security categories, both the predicted risk and the predicted cases are similar, suggesting that this variable – at least as self-reported – is not a particularly good predictor of future diabetes risk.

**We have chosen to present the results with consideration that both diabetes risk and number of new cases are important for understanding the diabetes burden in First Nations communities. Diabetes risk and number of new cases are influenced by the level of risk associated with the risk factors for diabetes and the prevalence of those risk factors within the population. Although diabetes risk was similar between food secure and food insecure groups, it is important to acknowledge that almost half of the new diabetes cases will occur among food insecure individuals, suggesting that this is an important target group for diabetes prevention. Similarly, for consumption of traditional vegetative foods and knowledge of a First Nations language, although a small reduction in diabetes risk was observed, we believe it was important to acknowledge the absolute risk reduction to transcend the deficit-focused approach that is common in Indigenous health literature. We agree that the distinction between diabetes risk and expected cases can be made more clearer in the text to better convey this message. To address this, we have added the following sentence to the results section to contextualize our presentation of the findings:**

**“Given that diabetes incidence is influenced by the level of risk associated with the factors that contribute to diabetes and the prevalence of those risk factors within the population, Table 2 presents results for both 10-year diabetes risk and number of new cases by important subgroups.”**