BMJ Open Diabetes Research and Care

Utility of current obesity thresholds in signaling diabetes risk in the James Bay Cree of Eeyou Istchee

Priya Manjoo,1 David Dannenbaum,2,3 Lawrence Joseph,4 Jill Torrie,3 Kaberi Dasgupta4

ABSTRACT

Objective: The anthropometric thresholds signaling type 2 diabetes risk have not been well defined for Aboriginal communities. This study examined current thresholds in terms of ability to capture diabetes risk in the Cree of Eeyou Istchee in northern Quebec, Canada.

Research design and methods: The study cohort for this analysis included adult participants from the Nitishischaayituhtaau Aschii Multi-Community Environment and Health Study with complete data on anthropometric measures, fasting glucose, and insulin. Diabetes risk was defined as Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) value >2. Positive and negative likelihood ratios (PLR, NLR) of existing obesity thresholds were evaluated (WHO; International Diabetes Federation, IDF; Adult Treatment Panel III, ATP III). Receiver operating curves were examined to estimate optimal thresholds. In a sensitivity analysis, diabetes risk was defined as HOMA-IR >2.7.

Results: The WHO 30 kg/m² body mass index (BMI) threshold performed well in women (PLR 5.56, 95% CI 3.2 to 9.5; NLR 0.28, 95% CI 0.19 to 0.37) and men (PLR 7.51, 95% CI 3.3 to 17.1; NLR 0.33, 95% CI 0.27 to 0.41). It was close to the estimated optimal threshold (28.5 kg/m²). The ATP III waist circumference threshold (102 cm) performed well in men (PLR 4.64, 95% CI 2.47 to 8.71; NLR 0.21, 95% CI 0.16 to 0.28) and was close to the estimated optimal threshold (101 cm). With diabetes risk defined at HOMA-IR >2.7, PLR values were slightly lower with narrower 95% CIs and optimal thresholds were slightly higher; PLR values remained above 3. For other current thresholds, estimated optimal values were higher and none had a PLR above 2.

Conclusions: A BMI of 30 kg/m² in women and men, and a 102 cm waist circumference in men, are meaningful obesity thresholds in this Aboriginal population. Other thresholds require a further evaluation.

INTRODUCTION

Worldwide, Aboriginal populations consistently demonstrate high type 2 diabetes risk; a recent review, for example, highlighted a twofold to threefold risk increase in Australia, New Zealand, and the USA.1 Obesity is a key driver.2 The body mass index (BMI, weight in kg/height in m²) is the metric most frequently used to capture obesity, defined by the WHO at 30 kg/m².3 There may, however, be some ethnocultural differences in what constitutes a meaningful BMI threshold. At a given BMI, some studies indicate that Aboriginal groups, Asians, and South Asians, have a greater burden of cardiometabolic risk factors.4–7 Although not a WHO recommendation, there is some evidence that in Asians, the obesity threshold should be below 27 kg/m².8 The BMI threshold signaling diabetes risk has not been specifically defined for individual Aboriginal communities or among Aboriginal communities in general.

Similarly, Aboriginal group-specific diabetes risk thresholds have not been defined for other anthropometric measures of obesity, including waist circumference (WC) and waist to hip ratio (WHR). These measures are indicators of abdominal, central, or visceral adiposity. Visceral adipose tissue liberates proinflammatory cytokines such as interleukin 6, tumor necrosis factor α, free fatty acids and resistin,9 which promote a state of insulin resistance, a precondition for type 2 diabetes. WC has a closer correlation with visceral adiposity than BMI.10–12 In the large European Interact study, WC and BMI demonstrated independent associations with diabetes incidence.13 WHR has also

Key messages

- Being at or above the WHO obesity body mass index threshold of 30 kg/m² or more signals elevated insulin resistance in Cree women and men.
- Being at or above the Adult Treatment Panel III abdominal obesity waist circumference of 102 cm or more signals insulin resistance in Cree men.
- The relevance of other obesity thresholds to insulin resistance in the Cree is not clear.
demonstrated associations with diabetes. Ethnocultural differences have been described for relationships of WC and WHR with cardiometabolic risk factors. For example, South Asian individuals have higher glucose levels than European individuals at an equivalent WC. In a study comparing anthropometric risk factors in terms of ability to predict cardiometabolic risk factors in Aboriginal Australians, WHR demonstrated the greatest predictive power. The International Diabetes Federation (IDF) does specify different visceral adiposity-defining anthropometric thresholds for some ethnocultural groups, but none are specific for Aboriginal populations.

The group studied was the Cree of the eastern James Bay region (Ekoyou Ischhe) in Canada. In this population, diabetes prevalence rose 10-fold from 2.4% in 1983 to 22.1% in 2011 (non-standardized rates). Between the 1940s and 1970s, geographic displacement was imposed to allow natural resource exploitation (eg, forestry, mining, and hydroelectric development). In these Cree communities, there was a shift in food procurement methods from hunting, fishing, and berry picking, until at least the 1970s, to a high intake of processed foods and beverages. A nomadic way of life was supplanted by permanent year-round settlement within nine communities. Snowshoeing and canoeing activities were replaced by snowmobiles and motorboats. As recently documented by the Truth and Reconciliation Commission, until 1969, Aboriginal Canadians children were forced to leave their families and attend boarding schools where many were physically, sexually, and psychologically abused; mortality rates were high in what has been described as cultural genocide. All of these factors have likely contributed to the diabetes epidemic faced by Aboriginal communities in Canada.

Insulin resistance, as measured using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), signals an increased risk for type 2 diabetes. The present analysis addresses a knowledge gap in the relevance of current anthropometric thresholds for signaling diabetes risk in the James Bay Cree, as captured by elevated HOMA-IR.

METHODS

Data sources

Data were collected as part of the Multi-Community Environment and Health (Nituuchishaayihitaau Aschii) Study, which aimed to provide assessment and surveillance of health status of the Cree in a context of hydroelectric dam projects with potential environmental impacts. Procedures were approved by Research Ethics Boards of Laval, McGill, and McMaster Universities, and the Cree Board of Health and Social Services of James Bay; community level consent for procedures was obtained through Band Council Resolutions. Individual participants also provided informed consent. Large scale hydroelectric dam projects and concerns about increasing mercury contamination led to the 1986 and 2001 Mercury Agreements between the Grand Council of the Cree (GCC) the government of Quebec, and Hydro-Québec, the government body responsible for dam construction. Part of the agreement included assessment of health impacts (eg, risk of consumption of contaminated fish, risks of avoiding fish consumption). There was a direct planning and consultation process between the Cree Health Board and the Cree communities for a comprehensive environment, and health study with the Mercury Agreement funds.

Simple random sampling without replacement was performed within each age stratum in order to build a list of participants who were then contacted by local recruiters. The overall participation rate (adults and children) was 48%. Demographic variables, and items relating to lifestyle factors and medical histories, were obtained through interviewer-administered questionnaires in either Inuktitut or English. Medical chart reviews were conducted to obtain additional medical history and details of medication use.

Weight was measured on a beam scale and height to the nearest cm. WC to the nearest 0.5 cm was determined at the end of exhalation using a measuring tape horizontally placed between the last floating rib and the iliac crest. Hip circumference to the nearest 0.5 cm was assessed at the level of the pubic symphysis and the point of greatest posterior extension of the buttocks. Blood pressure was assessed following a 5 min rest period, using mercury sphygmomanometers and appropriately sized cuffs, in accordance with Canadian Hypertension Education Program (CHEP) guidelines. Three measurements were taken, and the final two systolic and diastolic measurements were separately averaged. Following an overnight fast, venous blood was sampled for measurements of glucose (spectrophotometric assay, Vitros 950, Vitros Chemistry, Ortho-Clinical Diagnostics, Rochester, New York, USA), insulin (immunoassay with chemiluminescent detection, Bayer Health Care, Advia Centaur), and total cholesterol, high-density lipoprotein (HDL) and triglycerides (Vitros 950 Chemistry Station, Ortho-Clinical Diagnostics, Raritan, New Jersey, USA). Low-density lipoprotein (LDL) was computed. Some participants additionally underwent an oral glucose tolerance test (OGTT, 75 g oral glucose load).

Cohort for present analysis

We retained adults (≥18 years) with data on all three anthropometric parameters (BMI, WC, WHR), and...
fasting glucose and insulin measurement, permitting computation of HOMA-IR. We excluded individuals with type 1 diabetes and those without a medical chart review. Medical chart review procedures were implemented only after data collection in two of the nine communities had been completed; these two communities were thus not included in the present analysis.

**Statistical analyses**

Statistical analyses were conducted using R (R V.3.0.2. (Copyright (C) 2013 The R Foundation for Statistical Computing). BMI was calculated by dividing the weight (kg) by the squared height (m²). WHR was calculated by dividing the WC (cm) by the hip circumference (cm).

The β cell function was estimated using HOMA-β= \( \frac{20 \times \text{insulin}}{\text{glucose} - 3.5} \)%. We computed the HOMA-IR (fasting insulin (µunits/mL)×fasting glucose (mmol/L)/22.5). The constant 22.5 is derived from the HOMA-IR formula: \( \frac{\text{fasting insulin (µunits/mL)} \times \text{fasting glucose (mmol/L)}}{22.5} \). The β cell function was estimated using HOMA-β= \( \frac{20 \times \text{insulin}}{\text{glucose} - 3.5} \)%. We computed the HOMA-IR (fasting insulin (µunits/mL)×fasting glucose (mmol/L)/22.5).

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HDL ratio and LDL-C differed little across groups, HDL was lower and triglycerides higher in the upper two HOMA-IR categories. HOMA-β increased with HOMA-IR.

Body mass index

In women, the WHO BMI obesity threshold of 30 kg/m² had a sensitivity of 79% (95% CI 75% to 83%) and specificity of 86% (95% CI 64% to 97%) for HOMA-IR >2 (table 2). The PLR was 5.56 (95% CI 1.95 to 15.9) and NLR was 0.24 (95% CI 0.19 to 0.31). In men, this threshold performed similarly with a sensitivity of 70% (95% CI 64% to 75%) and a specificity of 91% (95% CI 78% to 97%), PLR of 4.64 (95% CI 2.47 to 8.71) and NLR of 0.21 (95% CI 0.16 to 0.28). With an HOMA-IR threshold of 2.7, a WC of 102 cm or more in men had a PLR of 2.61 and NLR of 0.17. The optimal ROC-defined threshold for WC in men was very similar to the ATPIII threshold at 101 cm (see online supplementary figure S2D). With an HOMA-IR threshold of 2.7, the optimal threshold was higher at 105.5 cm.

Waist to hip ratio

In women, the WHO 0.85 threshold was sensitive (92%, 95% CI 89% to 95%) and moderately specific (48%, 95% CI 26% to 70%) with a PLR of 1.76 (95% CI 1.17% to 2.65%) and an NLR of 0.16 (95% CI 0.09% to 0.29%) (table 2), similar to the test characteristics of the WHO 0.90 threshold in men. PLR values were also below 2 with an HOMA-IR threshold of 2.7. The optimal ROC-defined threshold for WHR in women was 0.87 (see online supplementary figure S2E) and the optimal value in men was 0.98 (see online supplementary figure S2F).

In women (table 2), the WHO 0.85 threshold was sensitive (92%, 95% CI 89% to 95%) and moderately specific (48%, 95% CI 26% to 70%) with a PLR of 1.76 (95% CI 1.17% to 2.65%) and an NLR of 0.16 (95% CI 0.09% to 0.29%) (table 2), similar to the test characteristics of the WHO 0.90 threshold in men. PLR values were also below 2 with an HOMA-IR threshold of 2.7. The optimal ROC-defined threshold for WHR in women was 0.87 (see online supplementary figure S2E) and the optimal value in men was 0.98 (see online supplementary figure S2F).
Table 1  Characteristics, by degree of hepatic insulin resistance, in women and men

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th></th>
<th>Men</th>
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<tr>
<td></td>
<td>HOMA-IR &lt;2</td>
<td>HOMA-IR 2–3</td>
<td>HOMA IR 3–4</td>
<td>HOMA IR &gt;4</td>
<td>HOMA-IR &lt;2</td>
<td>HOMA-IR 2–3</td>
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<td>Age, years, mean (SD)</td>
<td>37 (18)</td>
<td>36.5 (16.3)</td>
<td>36.4 (14.3)</td>
<td>39.7 (14.9)</td>
<td>32 (16)</td>
<td>38 (15)</td>
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<td>Tobacco use, N (%)</td>
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<td>42 (64)</td>
<td>152 (47)</td>
<td>27 (62)</td>
<td>31 (56)</td>
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<td>BMI, kg/m², mean (SD)</td>
<td>25.1 (4.4)</td>
<td>29.2 (5.3)</td>
<td>32.7 (5.6)</td>
<td>37.4 (6.8)</td>
<td>24.8 (3.3)</td>
<td>28.9 (3.5)</td>
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<td>Waist circumference, cm, mean (SD)</td>
<td>89.4 (12.8)</td>
<td>99.6 (12.5)</td>
<td>106.2 (12.6)</td>
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<td>93.9 (11.1)</td>
<td>102.5 (9.9)</td>
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<td>Hip circumference, cm, mean (SD)</td>
<td>102.7 (9.1)</td>
<td>108.2 (11)</td>
<td>114.3 (10.1)</td>
<td>122.1 (13.1)</td>
<td>102.3 (7.1)</td>
<td>108.6 (3.3)</td>
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<td>WHR, mean (SD)</td>
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<td>0.92 (0.07)</td>
<td>0.91 (0.13)</td>
<td>0.96 (0.07)</td>
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<td>Fasting glucose, mmol/L, mean (SD)</td>
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<td>15.4 (2.4)</td>
<td>31.7 (18.9)</td>
<td>7.4 (1.3)</td>
<td>10.5 (1.3)</td>
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<td>HOMA-IR, mean (SD)</td>
<td>1.6 (0.3)</td>
<td>2.6 (0.3)</td>
<td>3.5 (0.3)</td>
<td>10.2 (10.4)</td>
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<td>HOMA-B, mean (SD)</td>
<td>155 (109)</td>
<td>162 (75)</td>
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<td>Total cholesterol, mmol/L, mean (SD)</td>
<td>4.9 (1.2)</td>
<td>4.4 (0.9)</td>
<td>4.6 (0.8)</td>
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<td>LDL-C, mmol/L, mean (SD)</td>
<td>2.7 (0.9)</td>
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<td>HDL-C, mmol/L, mean (SD)</td>
<td>1.6 (0.5)</td>
<td>1.6 (0.4)</td>
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<td>Triglycerides, mmol/L, mean (SD)</td>
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<td>1.0 (0.4)</td>
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<td>Cholesterol-HDL ratio, mean (SD)</td>
<td>3.3 (1.7)</td>
<td>2.9 (0.7)</td>
<td>3.5 (0.7)</td>
<td>3.8 (1.0)</td>
<td>3.3 (1.0)</td>
<td>4.0 (9.8)</td>
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<td>Blood pressure</td>
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<td>Systolic, mm Hg, mean (SD)</td>
<td>109 (15)</td>
<td>114 (13)</td>
<td>119 (14)</td>
<td>120 (15)</td>
<td>115 (9)</td>
<td>121 (11)</td>
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<td>Diastolic, mm Hg, mean (SD)</td>
<td>67 (10)</td>
<td>70 (12)</td>
<td>72 (11)</td>
<td>73 (11)</td>
<td>71 (9)</td>
<td>75 (10)</td>
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<td>Medication Use</td>
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<td>Antihypertensive, N (%)</td>
<td>0 (0)</td>
<td>6 (12)</td>
<td>12 (18)</td>
<td>110 (34)</td>
<td>3 (7)</td>
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<td>Lipid-lowering, N (%)</td>
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<td>2 (4)</td>
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<td>51 (15)</td>
<td>1 (2)</td>
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<td>Oral antihyperglycemic, N (%)</td>
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<td>2 (4)</td>
<td>6 (9)</td>
<td>82 (25)</td>
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<td>Insulin, N (%)</td>
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<td>0 (0)</td>
<td>0 (0)</td>
<td>34 (11)</td>
<td>0 (0)</td>
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</table>

BMI, body mass index; HDL, high-density lipoprotein; HOMA-IR, Homeostatic Model Assessment-Insulin resistance computed as (fasting serum insulin (μU/mL)× fasting plasma glucose (mmol/L))/22.5; HOMA-B, Homeostatic Model Assessment computed as (20×fasting serum insulin (μU/mL))/(glucose (mmol/L)−3.5); LDL, low-density lipoprotein; WHR, waist-to-hip ratio.
### DISCUSSION

Our analyses indicate that among the Cree, an HOMA-IR >2 is consistent with a twofold greater odds of type 2 diabetes. Compared against this risk indicator, the current WHO 30 kg/m\(^2\) BMI threshold demonstrated moderately important PLR values (ie, above 5) and somewhat important NLR values (ie, 0.2 to 0.5) in women (PLR 5.56, 95% CI 1.95 to 15.9; NLR 0.24, 95% CI 0.19 to 0.31) and men (PLR 7.51, 95% CI 2.94 to 19.2; NLR 0.33, 95% CI 0.27 to 0.41). The optimal value was slightly lower (28.5 kg/m\(^2\)) than the WHO threshold. In men, the ATP III WC threshold (102 cm) had a PLR close to 5 (PLR 4.64, 95% CI 2.47 to 8.71; NLR 0.21, 95% CI 0.16 to 0.28). For WC in women, and WHR in women and men, none of the current thresholds had a PLR value above 5. The findings indicate that for diabetes risk assessment in the Cree, a BMI of above 30 kg/m\(^2\) is a risk factor to consider. In men, a WC >102 cm may also be a meaningful threshold in terms of diabetes risk. These thresholds also appeared reasonable when the HOMA-IR cut-off was raised from 2 to 2.7 in sensitivity analyses.

The analyses presented suggest that, for WC in women and WHR in women as well as in men, current thresholds are not associated with a high PLR, and our analyses suggest that optimal thresholds may be higher, although this requires confirmation. In a previous Canadian study, Lear and colleagues compared Aboriginal (at least three Aboriginal grandparents) and European-origin Canadians living in Vancouver. They measured anthropometric parameters, blood pressure, and cardiometabolic risk factors, and performed a single slice abdominal CT scan to assess visceral and subcutaneous adipose tissue. At the same BMI and WC, they identified no difference in subcutaneous or visceral adipose tissue areas between Aboriginal and European participants, nor in the prevalence of dyslipidemia, hypertension, impaired fasting glucose or metabolic syndrome. Insulin levels, however, were higher in Aboriginal Canadians, and thus HOMA-IR values, had they been computed, would likely have been higher at a given WC or BMI. It is thus possible that at-risk WC, BMI, and WHR levels, may differ between Aboriginal populations. Similarly, another previous Canadian study used factor analysis to ascertain the BMI cut-points equivalent to 30 kg/m\(^2\) in South Asian, Chinese, and Aboriginal Canadians (Six Nations, Ontario). Their analysis suggested that a much lower BMI was optimal in these groups (ie, <22 kg/m\(^2\)) including the Aboriginal Canadians studied. They included a mix of Aboriginal Canadians of Mohawk, Cayuga, Onondaga, Oneida, Seneca and Tuscarora origin, living in the Six Nations community in Ontario; they did not include the Cree. In contrast, we determined the BMI cut-point of 30 kg/m\(^2\) to be applicable in terms of risk of elevated HOMA-IR in the James Bay Cree. There is a need for population-specific thresholds to define high risk in groups that may have important cultural, genetic, and epigenetic differences.

### Table 2

<table>
<thead>
<tr>
<th>BMI thresholds</th>
<th>Waist to hip ratio thresholds</th>
<th>Waist circumference thresholds</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATP III thresholds</td>
<td>ROC-derived threshold</td>
<td>WHO thresholds</td>
</tr>
<tr>
<td>Asian</td>
<td>European</td>
<td>Asian</td>
</tr>
<tr>
<td>Sensitivity, % (95% CI)</td>
<td>79 (73 to 85)</td>
<td>96 (94 to 99)</td>
</tr>
<tr>
<td>Specificity, % (95% CI)</td>
<td>93 (91 to 95)</td>
<td>96 (94 to 98)</td>
</tr>
<tr>
<td>Positive likelihood ratio (95% CI)</td>
<td>7.51 (2.47 to 19.1)</td>
<td>4.64 (2.47 to 8.71)</td>
</tr>
<tr>
<td>Negative likelihood ratio (95% CI)</td>
<td>0.24 (0.09 to 0.71)</td>
<td>0.16 (0.09 to 0.33)</td>
</tr>
</tbody>
</table>

ATP III, Adult Treatment Panel III; BMI, body mass index; HOMA-IR, Homeostatic Model Assessment-Insulin resistance computed as fasting serum insulin (\(\mu\)U/mL)× fasting plasma glucose (mmol l\(^{-1}\))/22.5; IDF, International Diabetes Federation; ROC, receiver operating curve.
Our analyses are limited by their cross-sectional nature; in an ideal study, potential thresholds would be examined in terms of ability to predict the development of prediabetes and diabetes. Given the limitations of the available data, we opted to use an HOMA-IR above 2 as the diabetes risk indicator against which current obesity thresholds were evaluated, and performed a sensitivity analysis using an HOMA-IR of above 2.7. Although the HOMA IR has been extensively tested against other measures of insulin resistance,\(^3\)\(^3\)\(^2\) it is a surrogate marker, and there may be differences between the assays used to derive the HOMA IR equation and the assays of insulin resistance used in our study. However, at the HOMA-IR of >2, there is a clinically important increase in odds of prediabetes or diabetes, as confirmed by our logistic regression analyses (see online supplementary table S1).

CONCLUSIONS

Identifying participants at the stage of insulin resistance before the development of diabetes is an important window of opportunity for focused intensive lifestyle change efforts, demonstrated to be effective in large clinical trials.\(^3\)\(^3\)–\(^3\)\(^6\) Anecdotally, clinicians working in Eeyou Istchee (Cree territory) have reported to us that, given the high frequency of a BMI above 30 kg/m\(^2\) among their patients, they have started questioning what is ‘normal’ in the community, and considered the possibility that a BMI above this threshold might not have the same importance here as it has in the general population. The analyses presented do suggest that Cree women may be able to tolerate a WC above current thresholds before experiencing an important increase in insulin resistance. This remains to be confirmed in longitudinal studies. A large majority of Cree in Eeyou Istchee have a BMI above 30 kg/m\(^2\). Our findings indicate that in this Aboriginal population, a BMI above 30 kg/m\(^2\) is associated with a high HOMA-IR. Further, a BMI at this level has a moderately high PLR value for HOMA-IR >2 in women and men. Thus, the WHO obesity threshold demonstrates clinical importance in this regard for this population.

Acknowledgements

The authors thank the Principal Investigators of the Multi-Community Environment and Health Longitudinal (Nituuchischaayhtitaau Aschii) Study and the Cree Board of Health and Social Services of James Bay for permitting this data analysis.

Contributors

PM, DD, and KD formulated the study question and devised the analytic plan. PM and KD performed the literature search and summarized the literature. PM performed the data-analysis in collaboration with LJ and KD. PM and KD co-wrote the manuscript, with review and comment by DD, LJ, and JT. KD is the guarantor and, as such, had full access to all the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Funding

Data collection for the original study (Nituuchischaayhtitaau Aschii: Multi-Community Environment-and-Health Study in liyiyu Aschii) was funded through an agreement between the Grand Council of the Crees and Hydro Quebec; it was supported by the Cree people of northern Quebec, the Cree First Nations and the Cree Board of Health and Social Services of James Bay, through financial contributions from Niskamoon Corporation.

Competing interests

PM is the assistant professor of Department of Medicine at the University of British Columbia. DD is the assistant professor of Department of Medicine at McGill University and the medical advisor for chronic diseases with the Cree Board of Health and Social Services of James Bay. LJ is the professor of Department of Epidemiology, Biostatistics, and Occupational Health at McGill University. JT is the assistant director of Public Health Surveillance, Evaluation, Research, and Communication, and Clinical Preventive Practices with the Cree Board of Health and Social Services of James Bay. KD is the associate professor in the Department of Medicine of McGill University and holds a Senior Investigator award from the Fonds de Recherche en santé du Québec.

Ethics approval

The procedures were approved by Research Ethics Boards of Laval, McGill, and McMaster Universities, and from Board resolution of the Cree Board of Health and Social Services of James Bay; community level consent for the study was obtained through Band Council Resolutions.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data sharing statement

The data are owned by the Cree people of northern Quebec and the Cree First Nations, and are held by the Cree Board of Health and Social Services of James Bay. Permission to use these data must be sought from the owners of the data.

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Utility of current obesity thresholds in signaling diabetes risk in the James Bay Cree of Eeyou Istchee

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