



## The hypertriglyceridemic-waist phenotype is associated with the Framingham risk score and subclinical atherosclerosis in Canadian Cree

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### KEYWORDS

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**Abstract** *Background and aims:* For primary prevention of cardiovascular disease (CVD), Canadian guidelines recommend that asymptomatic Canadians with abdominal obesity undergo Framingham risk score (FRS) assessment, and that in Indigenous Peoples, indicators of metabolic syndrome also be used to identify at-risk individuals. The hypertriglyceridemic-waist phenotype (HTGW) has been proposed to be a surrogate marker of visceral obesity and a simple proxy measure for metabolic syndrome. The primary aim of this study was to evaluate whether the HTGW and the FRS associated with sub-clinical atherosclerosis.

*Methods and results:* Asymptomatic Cree participants in a cross-sectional study conducted 2005–2009 (n = 446, 18–81 y) were assessed for the HTGW using NCEP-ATP-III gender-specific cut-offs (waist circumference: for men,  $\geq 102$  cm; for women  $\geq 88$  cm) and fasting triglycerides  $\geq 1.7$  mmol/L. Sub-clinical atherosclerosis was defined by the presence of a high sex-specific common-carotid-intimal-medial-wall-thickness ( $\geq 75$ th percentile). HTGW was present in 26.7% and a 10-y FRS greater than 10% was present in 18.8% of participants. The multivariate adjusted OR (95% CI) for sub-clinical atherosclerosis associated with an FRS greater than 10% was 4.10 (2.20–7.50) while that associated with the HTGW phenotype was 1.74 (95% CI 1.61–1.88) from a model including age, body mass index, alcohol consumption, FRS and the HTGW. *Conclusions:* The HTGW phenotype is prevalent in the Cree. Our findings support further study on the utility of combining the HTGW with the FRS in the prediction of cardiovascular disease outcomes and in health screening and intervention programs among indigenous peoples.

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*Acronyms:* BMI, Body mass index; C-CAR, Common carotid intimal-to-medial arterial wall thickness; CI, Confidence interval; CVD, Cardiovascular disease; FRS, Framingham risk score; GEE, Generalized estimated equations; HDL, High density lipoprotein; HTGW, Hypertriglyceridemic-waist phenotype; IMT, Intimal-to-medial arterial wall thickness; NCEP-ATP III, National cholesterol education program adult treatment panel III; NS, not statistically significant; OR, Odds ratios.

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## Introduction

Rates of cardiovascular disease (CVD) have been rising among Canada's indigenous populations [1] which represent 4.3% of the total Canadian population [2]. The Cree, which are the largest indigenous group of North America, show high diabetes risk [3] and central fat patterning with weight gain [4–6], which is commonly associated with increased visceral adiposity and abnormal metabolic profiles over a wide range of body mass indices (BMIs) [7]. For primary prevention purposes, Canadian guidelines have recommended that asymptomatic individuals with abdominal obesity, or at-risk waist circumference (WC), be initially assessed for the Framingham Risk Score (FRS) [8,9] which uses age, sex, smoking history, systolic blood pressure, and total and high-density lipoprotein (HDL) cholesterol, to estimate the 10-year risk of developing total cardiovascular events [10]. The FRS, however, has not been validated in indigenous populations and thus its potential utility for the James Bay Cree is not known. Further, visceral obesity, in population-based subjects free of CVD, has been shown to be associated with greater adverse levels of CVD risk factors as compared to subcutaneous adipose tissue [11]. Also, visceral obesity has predicted incident CVD, after adjustments for FRS risk factors and standard obesity measures including BMI and WC in a recent study [12].

A proposed surrogate marker of visceral obesity is the hypertriglyceridemic-waist phenotype (HTGW), which combines at-risk triglycerides with at-risk waist circumference measurements [13,14]. The HTGW has received much attention over recent years for its association with CVD risk factors including risk factors used to calculate the FRS [13–19] and for its association with coronary artery disease [14,17]. Although the HTGW has been studied in Canadian indigenous populations such as the Ojée-Cree [18] and Inuit [19], it has not been evaluated for its association with carotid ultrasound measures of preclinical atherosclerosis, which has been useful in predicting CVD [20,21].

Our primary objectives were to evaluate the prevalence of the HTGW and its association with CVD risk factors and the FRS, and the association of the HTGW and FRS with subclinical carotid atherosclerosis among the James Bay Cree.

## Methods

### Study population

Data for analyses are from the Nituuchischaayihitaa Aschii, a large-scale multi-community environment-and-health longitudinal study held in Eeyou Istchee. Seven communities were surveyed over a five year period (2005–2009). All ages were eligible to participate. The Nituuchischaayihitaa Aschii study includes a random sampling strategy which has been described in detail elsewhere [22,23]. The total population sizes of the 7 communities studied ranged from 561 to 3820. The Cree

study obtained a certificate of ethical acceptability by McGill University and Université Laval and was approved by the Cree Board of Health and Social Service and by all communities. Each individual who accepted to participate in the survey signed an informed consent form. Participation rates by communities varied between 35% and 56%, for an overall participation rate equal to 50% [23].

### Study participants for analysis

Adult participants ( $\geq 18$  y) who had fasted for at least eight hours at baseline, had complete information, and were not outliers were included in the present analysis ( $n = 737$ ). We excluded participants with heart disease ( $n = 34$ ), diabetes ( $n = 188$ ), and other serious illnesses ( $n = 51$ ). We also excluded pregnant participants ( $n = 19$ ). The above-mentioned exclusions resulted in a sample which consisted of 446 study participants (226 females and 220 males).

### Anthropometric measures

Details on the measurement of anthropometry indices are described elsewhere [6]. Briefly, waist circumferences were measured at the end of exhalation with the tape placed horizontally between the last floating rib and the iliac crest. Height and weight were measured at the baseline physical health examination and BMI calculated ( $\text{kg}/\text{m}^2$ ).

### Blood collection and lipid analyses

All blood samples were taken under fasting conditions and stored frozen at  $-80^\circ\text{C}$  until time of analysis. Plasma triglycerides, total cholesterol, and HDL cholesterol were analysed using standard enzymatic methods with a Vitros 950 Chemistry Station (Ortho-Clinical Diagnostics, Raritan, NJ) including manufacturer's reagents. Analyses were carried out at the biochemistry laboratory of Laval Hospital in Quebec City as previously described [6].

### Blood pressure measurements

Blood pressures were measured using a manual mercury sphygmomanometer with the mean of the last two of three blood pressure readings used for analyses as described elsewhere [6].

### Assessment of participant chronic conditions, demographics and lifestyle factors

Medical files were used to obtain information on study participants with regards to chronic conditions and medication usage. Age, sex, and lifestyle factors (smoking, alcohol consumption) were collected by questionnaires. For the present cross-sectional analyses, smoking and alcohol consumption were considered as categorical variables (smoking vs. nonsmoking; alcohol drinkers vs. non-alcohol drinkers).

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