Relation of insulin resistance with social-demographics, adiposity and behavioral factors in non-diabetic adult Canadians

Sai Yi Pan¹*, Margaret de Groh¹, Alfred Aziz² and Howard Morrison¹

Abstract

Background: Insulin resistance is a pathogenic factor for type II diabetes and has been associated with metabolic abnormalities and adverse clinical outcomes. The purpose of this study was to examine the relationship between insulin resistance and socio-demographics, adiposity and behavioral factors in the general, non-diabetic adult Canadian population.

Methods: Data for 3515 non-diabetic adults aged 18 to 79 years from the Canadian Health Measures Survey (cycles 1 and 2, 2007–2011) were analyzed. Insulin resistance index was measured by the homeostasis model assessment of insulin resistance (HOMA-IR), and insulin resistance (IR) was defined as individuals in the highest quartile of the HOMA-IR index. Logistic regression models were used to examine the effect of demographics, lifestyle factors and adiposity measurements on HOMA-IR.

Results: The risk of IR increased with age, particularly in men. Individuals had adjusted odds ratio (OR) (with corresponding 95% confidence interval) of 5.97 (2.90–8.52) and 25.12 (15.20–41.51) associated with a body-mass-index (BMI) between 25.0 and < 30.0, or ≥30.0, of 9.23 (6.52–13.07) with abdominal obesity (waist circumstance ≥102 cm for men and ≥88 cm for women), of 8.72 (6.13–12.39) with a high waist-to-height ratio (>0.57), and of 6.30 (4.33–9.16) with a high waist-to-hip ratio (>0.90 for men and >0.85 for women). Physically inactive people and non-alcohol consumer also had a significantly higher odd of IR.

Conclusions: This study found that men and older, obese and physically inactive people were at increased risk for IR. Adiposity indices including BMI, waist circumstance, waist-to-height ratio and waist-to-hip ratio were highly associated with IR with similar magnitude of association.

Keywords: Insulin resistance, HOMA-IR index, Waist circumference, Waist-to-height ratio, Waist-to-hip ratio, BMI

Background

Insulin resistance (IR) is defined as decreased sensitivity or responsiveness to the metabolic actions of insulin, such as insulin-mediated glucose disposal and inhibition of hepatic glucose production [1]. Evidence has accumulated showing that insulin resistance is a pathogenic factor for type II diabetes [2–6], with which about 2.5 million Canadians have been diagnosed in 2010, with an estimated economic burden of $12.2 billion including $2.1 billion of direct cost and $10.1 billion of indirect cost) in 2010 [7]. It has also been associated with increased risk of a number of metabolic abnormalities and adverse clinical outcomes, such as essential hypertension, atherogenesis, coronary heart disease, stroke, and systemic inflammation [2, 8–13].

It has been suggested that IR and subsequent compensatory hyperinsulinemia develops earlier than β-cell dysfunction because insulin secretion in insulin-resistant, non-diabetic persons is increased in proportion to the severity of the insulin resistance even though glucose tolerance remains normal. Therefore, IR might exist and progress before diabetes, and pre-diabetes would be detected by impaired fasting glucose or impaired glucose tolerance [6]. Thus, early identification of individuals with IR may be a way to guide earlier intervention strategies (i.e., prior to the

* Correspondence: sai.yi.pan@phac-aspc.gc.ca
¹Science Integration and Social Determinant Directorate, Public Health Agency of Canada, 785 Carling Avenue, AL 6809B, Ottawa, ON K1A 0K9, Canada
Full list of author information is available at the end of the article

© 2016 The Author(s). Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.
emergence of impaired glucose tolerance) to prevent or delay diabetes onset and related chronic diseases.

The gold standard for assessing insulin resistance has been euglycemic-hyperinsulinemic glucose clamp [14, 15]. This method is invasive, complex and expensive; therefore, it has been of limited use in epidemiological studies. Instead, the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) is a simpler and more practical method to measure insulin resistance and has been widely used in large epidemiological studies [16]. The HOMA-IR index has been validated as an acceptable proxy measure of insulin resistance in both normal and diabetic people with a good correlation (correlation coefficient: 0.73–0.88) between estimates of IR derived from HOMA and from the euglycemic clamp, and with a good correlation (correlation coefficient: 0.62–0.90) between estimates of \( \beta \)-cell function using HOMA and estimates using continuous infusion glucose model assessment, hyperinsulinemic clamps, the acute insulin response from the intravenous glucose tolerance test [16–18].

There are no report on HOMA-IR and its association with lifestyle factors in the Canadian population. Therefore, the main purpose of this study was to assess the association of IR with demographic and lifestyle factors using a sample of non-diabetic adult Canadians.

**Methods**

**Data source and study population**
This analysis was based on data from the Canadian Health Measures Survey (CHMS), cycle 1 (2007–2009) and cycle 2 (2009–2011), which was collected by Statistics Canada. The CHMS is an ongoing comprehensive, direct health measures survey, developed to address important data gaps and limitations in existing health information. It provides national estimates at the time of the survey. Ethics approval was obtained from Health Canada’s Research Ethics Board [19]. Cycle 1 covers approximately 96.3 % of the Canadian population aged 6 to 79 living at home and residing in the 10 provinces and 3 territories. Cycle 2 covered the population aged 3 to 79 living at home and residing in the 10 provinces and 3 territories, and represented more than 96 % of the population. Excluded from all cycles of the CHMS are individuals living on reserves or in certain remote areas, institutional residents, and full-time members of the Canadian Forces. Study design, study subjects, and data collection methods have been described elsewhere [20–23]. The overall response rates were 52 % for cycle 1 and 55.5 % for cycle 2 after adjusting for the sampling strategy, and reflecting the proportion of A) households that agreed to participate (70 % for cycle 1 and 75.9 % for cycle 2); B) selected household respondents that participated in the survey (88 % for cycle 1 and 90.5 % for cycle 2); and C) participants who reported to the mobile examination centre (85 % for cycle 1 and 81.7 % for cycle 2).

Measures for fasting insulin and fasting glucose were available for 3734 (1805 for cycle 1 and 1929 for cycle 2) adults aged 18 to 79 years old. Individuals who were diagnosed by a physician as having diabetes or who had fasting glucose levels above 6.9 mmol/L (the level for operationally defining type II diabetes) were excluded from the analysis (n = 219). Therefore, results are based on a sample of 3515 (1716 for cycle 1 and 1799 for cycle 2) adults age 18 to 79 without diabetes.

**Data collection procedure**
During an initial household survey, the CHMS collects self-reported information on socio-demographics, medical history (including current medication use), current health status, and lifestyle behaviours. On an appointed date after the household interview, physical measurements, such as height, weight, waist circumference (WC), blood pressure, and heart rate, were obtained at a mobile examination centre. A sample of blood and urine was also collected from participants for further tests, with approximately one-third of the participants asked to fast for at least 10 h before their clinic visit. A wide range of biometreasures were assessed, such as hemoglobin A1c (HbA1c), high-density lipoprotein (HDL), vitamin D, etc. Fasting participants had additional blood measures available, including triglycerides (TG), insulin, glucose, apolipoprotein A, apolipoprotein B, and low density lipoprotein.

**Key measures**

**Outcome - Insulin resistance (IR)**
IR was based on the homeostatic model assessment (HOMA) [16]. HOMA index was determined by the fasting insulin concentration and fasting glucose concentration and defined as:

\[
\text{HOMA index} = \frac{[\text{fasting insulin} (\muU/ml) \times \text{fasting glucose (mmol/L)})}{22.5}.\]

Insulin concentration was measured by solid-phase, two-site chemiluminescent immunometric assay. Fasting glucose concentration was measured by the VITROS GLU Slide method (colorimetric). Because there are no universally established cut-offs for classifying IR, as a normal practice, individuals in the highest quartile on the HOMA index (i.e., 25 % of the population) were classified as IR, with the remaining 75 % of the population classified as non-IR [24].

**Adiposity measures**

**Body mass index (BMI) (kg/m²)** BMI was calculated from measured weight and height. Based on BMI, subjects were classified as underweight (<18.5), normal weight (18.5–<25.0), overweight (25.0–<30.0), obese (≥30.0) [25].
**Waist circumference (WC)** A WC ≥102 cm in men and ≥88 cm in women was used to identify those with excess adiposity, i.e. abdominal obesity [25].

**Waist-to-height ratio (WHtR)** WHtR was calculated by dividing waist circumference in centimeter by height in centimeters. A WHtR under 0.570 is generally considered healthy and a WHtR of 0.570 and over (is considered to be risk equivalent to BMI of 30) was used to identify those of excess adiposity [26].

**Waist-to-hip ratio (WHR)** WHR was calculated by dividing waist circumference in centimeter by hip circumference in centimeters. A WHR >0.90 for men and >0.85 for women was used to identify those with excess adiposity [25].

**Socio-demographics**

**Education** Individuals were classified as 4 categories according to their highest level of education: less than secondary school graduation, secondary school graduation without post-secondary education, some post-secondary and post-secondary graduation (including trade certificate, or diploma from a vocational school or apprenticeship training, non-university certificate or diploma from a community college, university certificate below bachelor’s level, bachelor’s degree, university degree or certificate above bachelor’s degree). The 4 categories were defined by Statistics Canada [22, 23].

**Family income adequacy** Individuals were classified as 4 groups based on total household income (Canadian dollars) and the number of people living in the household, which was defined by Statistics Canada: lowest income group, lower middle income group, upper middle income group and highest income group [22, 23]. The definition is as below:

| # of people in the household | Total household income  |
|-----------------------------|------------------------|
| Lowest income group         |                        |
| 1, 2                        | <$15,000               |
| 3, 4                        | <$20,000               |
| >4                          | <$30,000               |
| Lower middle group          |                        |
| 1, 2                        | $15,000–< $30,000      |
| 3, 4                        | $20,000–< $40,000      |
| >4                          | $30,000–< $60,000      |
| Upper middle group          |                        |
| 1, 2                        | $30,000–< $60,000      |
| 3, 4                        | $40,000–< $80,000      |
| >4                          | $60,000–< $80,000      |
| Highest group               |                        |
| 1, 2                        | ≥$60,000               |
| >2                          | ≥$80,000               |

**Behavioural factors**

**Physical activity index** It was based on total daily energy expenditure values calculated from self-reported responses to questions about the frequency and duration of leisure-time physical activity in the past 3 months [22]. These activities include walking, garden/yard work, swimming, bicycling, dance, home exercises, ice hockey, ice skating, rollerblading, jogging/running, golfing, aerobics, ski/snowboard, bowling, baseball/softball, tennis, weight training, fishing, volleyball, basketball, soccer and any other activities. Individuals were classified as being “active”, “moderate” or “inactive” based on total daily energy expenditure values (kcal/kg/day): ≥3, 1.5–<3 or 0–<1.5.

**Alcohol consumption (daily drinks)** Individuals who did not have at least one drink for the last 12 months were classified as non-drinker, and those who had an average of one drink daily as light drinkers, while those who had an average of two drinks daily were classified as moderate drinkers and 3 or more as heavy drinkers.

**Smoking status** Individuals who have never smoked were classified as never smoker, and those who were former daily smokers and former occasional smokers as former smokers, while those who were daily smokers and occasional smokers were classed as current smokers.

**Statistical analysis**

Data were analyzed using SAS Enterprise Guide version 4 (Cary, NC). HOMA-IR index level was estimated in the population by gender and other demographic factors, and weighted to reflect the Canadian population aged 18 to 79 years (using a bootstrap procedure, with 24° of freedom [22, 27]). Associations of socio-demographics, some behavioural factors (physical activity, alcohol consumption and smoking) and adiposity measures such as BMI, abdominal obesity, waist-to-height ratio, waist-to-hip ratio, with IR prevalence were also examined using odds ratios by logistic regression model. Variables included in the regression models as potential confounders were age (continuous), sex, education (less than secondary, secondary graduate and other post-secondary and post-secondary graduate), BMI (continuous), physical activity index (active, moderately active and inactive), alcohol consumption (non, light, moderate and heavy drinkers) and smoking status (never, former and current). The variable being assessed was adjusted to all above variables except for the variable under consideration. For example, when physical activity was assessed, variables included in the regression models as confounders were age, sex, education, BMI, alcohol consumption and smoking status. However, BMI, WC,
| Variable                                      | All          | Men          | Women         |
|----------------------------------------------|--------------|--------------|---------------|
| Age (years) (mean (SD))                      | 45.92 (16.70) | 46.12 (17.02) | 45.74 (16.41) |
| 18–35 years (%)                              | 1058 33.75   | 488 34.78    | 570 32.76     |
| 36–50 years (%)                              | 1108 32.37   | 515 32.42    | 593 32.32     |
| 51–79 years (%)                              | 1349 33.88   | 643 32.79    | 706 34.92     |
| BMI (kg/m²) (mean (SD))                      | 27.48 (7.69) | 27.49 (5.55) | 27.48 (9.18)  |
| Waist circumference (cm) (mean (SD))         | 90.87 (15.42)| 95.63 (14.39)| 86.65 (15.08)|
| Waist-to-height ratio (cm) (mean (SD))       | 0.54 (0.09)  | 0.54 (0.08)  | 0.53 (0.09)   |
| Waist-to-hip ratio (mean (SD))               | 0.95 (0.77)  | 0.95 (0.39)  | 0.94 (0.99)   |
| Fasting glucose (mmol/L) (mean (SD))         | 5.03 (0.75)  | 5.18 (0.79)  | 4.89 (0.68)   |
| Fasting insulin (μIU/ml) (mean (SD))         | 9.24 (7.00)  | 9.77 (7.25)  | 8.77 (6.74)   |
| HOMA-IR index (mean (SD))                    | 2.15 (1.90)  | 2.34 (2.06)  | 1.98 (1.72)   |
| Education level                              |              |              |               |
| Less than secondary                          | 437 12.19    | 222 13.82    | 215 10.62     |
| Secondary graduate                           | 556 16.15    | 243 14.96    | 313 17.28     |
| Other post-secondary                         | 357 9.77     | 178 9.79     | 179 9.74      |
| Post-secondary graduate                      | 2133 60.42   | 984 59.27    | 1149 61.53    |
| Not stated                                   | 32 1.48      | 19 2.16      | 13 0.82       |
| Household income adequacy                    |              |              |               |
| Lowest                                       | 181 3.65     | 65 2.73      | 116 4.54      |
| Lower middle                                 | 512 15.09    | 215 15.14    | 297 15.04     |
| Upper middle                                 | 1089 29.83   | 485 27.62    | 604 31.95     |
| Highest                                      | 1618 48.42   | 833 52.11    | 785 44.88     |
| Not stated                                   | 115 3.01     | 48 2.41      | 67 3.59       |
| BMII (kg/m²)                                 |              |              |               |
| < 18.5                                       | 57 2.11      | 17 1.92      | 40 2.3        |
| 18.5–< 25.0                                  | 1316 39.8    | 511 32.2     | 805 47.16     |
| 25.0–< 30.0                                  | 1288 36.15   | 726 43.85    | 562 28.7      |
| ≥ 30.0                                       | 835 21.93    | 390 22.03    | 445 21.84     |
| Waist circumference (cm)                     |              |              |               |
| < 102 in men or < 88 in women                | 2261 67.77   | 1161 73.84   | 1100 61.97    |
| ≥ 102 in men or ≥ 88 in women                | 1245 32.23   | 481 26.16    | 764 38.03     |
| Waist-height ratio                           |              |              |               |
| ≤ 0.570                                      | 2336 70.37   | 1070 69.07   | 1266 71.64    |
| > 0.570                                      | 1148 29.63   | 570 30.93    | 578 28.36     |
| Waist-hip ratio                              |              |              |               |
| ≤ 0.90 in men or ≤ 0.85 or women             | 1726 50.56   | 597 39.23    | 1129 61.41    |
| > 0.90 in men or > 0.85 in women             | 1764 49.44   | 1046 60.77   | 718 38.59     |
| Alcohol consumption (daily drinks)           |              |              |               |
| None                                         | 1666 55.26   | 652 46.29    | 1014 64.57    |
| Light (1 drink/day)                          | 816 28.09    | 419 29.03    | 397 27.11     |
| Moderate (2 drinks/day)                      | 283 9.17     | 190 11.72    | 93 6.53       |
| Heavy (≥ 3 drinks/day)                       | 207 7.48     | 178 12.96    | 29 1.79       |
WHtR, WHR were not adjusted for each other because their high correlation.

In order to determine the strongest relationship with IR among the four measures of obesity, we standardized the four continuous variables (BMI, WC, WHtR and WHR), such that we could compare the ORs based on one standard deviation change. This standardization was done by the STANDARD PROC of SAS software and the standardized continuous variables were entered into the logistic regression models.

In addition, we also performed the analyses by sex to examine whether there is a difference between women and men on the association of various factors with IR.

**Results**

Table 1 shows the characteristics of the study population. Of the 3515 subjects included in the analysis, there were 1646 men and 1869 women. Men and women were similar in mean age, BMI, waist-to-height ratio and waist-to-hip ratio. However, men were less likely to be defined as abdominally obese (based on WC) but more likely to have a high waist-to-hip ratio and to be overweight (as defined by BMI), compared to women. Obesity rates, based on BMI were similar for men and women (22.03 vs 21.84 %, respectively). More men than women were in the highest household income adequacy category (52.11 vs 44.88 %) and were heavy drinkers (12.96 vs 1.79 %).

Table 2 displays the unadjusted and adjusted odds ratios (OR) of IR associated with demographic and lifestyle factors as well as adiposity measures. People older than 50 years had a significantly higher OR for IR in comparison with younger people. Also, men had a higher OR for IR than women. Compared with normal weight individuals, overweight (BMI: 25.0–< 30.0) and obese (BMI ≥ 30.0) adults had adjusted ORs (95 % CI) of 5.97 (2.90–8.52) and 25.12 (15.20–41.50), respectively. Abdominal obesity (based on WC) was also associated with an increased OR of 9.23 (95 % CI: 6.52–13.07) for IR. Similarly, persons with high waist-to-height ratio (WHtR > 0.570) and waist-to-hip ratio (WHR > 0.90 for men and >0.85 for women) were at increased OR for IR (8.72 and 6.30, respectively). However, these measures of obesity were not adjusted for each other. In addition, compared with physically active people, those who were physically inactive and moderately active were both associated with increased risk for IR (OR = 2.44, 95 % CI: 1.61–3.68 and OR = 2.29, 95 % CI: 1.47–3.55). For alcohol consumption, individuals who were light, moderate and heavy drinkers had decreased ORs for IR compared to those who never drank alcohol. Nevertheless, there were no statistically significant differences for ORs associated with IR for education level, family income adequacy, and smoking status, although there were tendencies of decreasing OR for IR with increasing education level and family income adequacy.

Table 3 shows unadjusted and adjusted ORs of IR associated with demographic factors, lifestyle factors and adiposity measures, stratified by gender. The negative association between IR and alcohol consumption was significant only in men but not in women (but the number of heavy drinkers in women was small). The patterns observed for other factors were similar for men and women. Measures of adiposity and physical activity were significantly associated with IR risk, whereas education, income adequacy and smoking were unrelated to IR risk.

Table 4 presents the unadjusted and adjusted ORs of IR associated with standardized continuous variables, overall and by sex: BMI, WC, WHtR, and WHR. When these four measures were assessed as standardized continuous variables, they were all statistically significantly associated with increased ORs of IR, with their corresponding ORs being 4.20 for BMI, 4.92 for WC, 4.37 for WHtR, and 4.28 for WHR, suggesting that no one measure was superior. However, the ORs for all 4 adiposity measures were slightly higher in men than in women.

**Discussion**

This study assessed the association between IR risk and socio-demographics, behavioral factors and several...
| Variables                      | Unadjusted | Adjusted ** |
|-------------------------------|------------|-------------|
|                              | OR (95% CI) | P for trend | OR (95% CI) | P for trend |
| Age                           |            | 0.0001      |            | 0.0001      |
| 18–35                         | ref        | ref         | ref        | ref         |
| 36–50                         | 1.05 (0.70–1.57) | 0.85 (0.54–1.33) | |
| 51–79                         | 2.16 (1.53–3.03) | 1.91 (1.41–2.58) | |
| Sex                           |            |             |            |             |
| Female                        | ref        | ref         | ref        | ref         |
| Male                          | 1.30 (0.96–1.75) | 1.43 (1.08–1.90) | |
| Education                     |            | 0.1026      |            |             |
| Less than secondary           | ref        | 0.0699      | ref        |             |
| Secondary graduate            | 0.80 (0.50–1.29) | 0.86 (0.52–1.41) | |
| Other post-secondary          | 0.48 (0.28–0.82) | 0.79 (0.44–1.43) | |
| Post-secondary graduate       | 0.52 (0.33–0.83) | 0.66 (0.42–1.04) | |
| Family income adequacy        |            | 0.1305      |            | 0.0773      |
| Lowest                        | ref        | ref         | ref        |             |
| Lower middle                  | 1.57 (0.92–2.68) | 1.15 (0.47–2.35) | |
| Upper middle                  | 0.84 (0.60–1.18) | 0.61 (0.39–0.96) | |
| Highest                       | 0.92 (0.57–1.49) | 0.67 (0.40–1.15) | |
| BMI (kg/m²)                   |            | 0.0000      |            | 0.0000      |
| ≥ 18.5                        | -          | -           | -          | -           |
| 18.5–25.0                     | ref        | ref         | ref        |             |
| 25.0–30.0                     | 5.40 (3.26–8.95) | 5.97 (2.90–8.52) | |
| ≥ 30.0                        | 27.04 (17.08–42.81) | 25.12 (15.20–41.51) | |
| Continuous                    | 1.30 (1.26–1.34) | 1.23 (1.25–1.34) | |
| Waist circumference (cm)      |            |             |            |             |
| < 102 in men or < 88 in women | ref        | ref         | ref        |             |
| ≥ 102 in men or ≥ 88 in women | 8.82 (6.28–12.39) | 9.23 (6.52–13.07) | |
| Waist-to-height ratio         |            |             |            |             |
| ≤ 0.570                       | ref        | ref         | ref        |             |
| > 0.570                       | 9.44 (6.81–13.09) | 8.72 (6.13–12.39) | |
| Waist-to-hip ratio            |            |             |            |             |
| ≤ 0.90 in men or ≤ 0.85 in women | ref        | ref         | ref        |             |
| > 0.90 in men or > 0.85 in women | 6.65 (4.81–9.21) | 6.30 (4.33–9.16) | |
| Alcohol consumption (daily drinks) | 0.0005      | 0.0006      |            |             |
| None                          | ref        | ref         | ref        |             |
| Light (1 drink/day)           | 0.59 (0.44–0.78) | 0.64 (0.44–0.92) | |
| Moderate (2 drinks/day)       | 0.48 (0.34–0.68) | 0.47 (0.30–0.73) | |
| Heavy (> = 3 drinks/day)      | 0.50 (0.31–0.82) | 0.36 (0.19–0.71) | |
| Physical activity             |            | 0.0001      |            | 0.0003      |
| Active                        | ref        | ref         | ref        |             |
| Moderate                      | 2.36 (1.65–3.36) | 2.29 (1.47–3.55) | |
| Inactive                      | 2.60 (1.87–3.60) | 2.44 (1.61–3.68) | |
adiposity measures using a sample of non-diabetic adults. Increasing age, being male, being overweight or obese and being physically inactive were all found to be independently associated with a higher risk of IR, whereas education level, family income, and smoking were not significantly associated with IR.

Our study found a significantly increasing risk of IR with age in the non-diabetic adult Canadian population. This finding is comparable to the results in the US [28] and in Spain [29]. Age has been shown to be the most powerful predictor of IR in some studies, but it could be the residual effect of other factors, because diseases or conditions such as obesity, diabetes and hypertension all increase with age. However, a study of Thai adults over 35 years old showed a correlation between IR and age only in women, not in men [30]. The result from the 2246 non-diabetic adults in a representative Spanish population sample suggested a significant nonlinear association with an increase in HOMA-IR index in those women aged 50 years and older, while no evidence existed in men [29]. The molecular mechanisms for the increase of IR with age are not fully understood. There are several aspects of ageing that contribute to increased insulin resistance, including body fat redistribution (decrease in subcutaneous fat and increase in visceral fat), decrease in muscle tissue, increase in pro-inflammatory cytokines, and decreased mitochondrial function [31]. This redistribution of adipose tissue is associated with leptin resistance. This resistance blunts normal central and peripheral functions of leptin, which leads to a decrease in neuroendocrine function and insulin sensitivity, an imbalance in energy regulation, and disturbances in lipid metabolism [32, 33]. Research has shown improved insulin sensitivity by regulating fat metabolism in white and brown adipose tissues by way of caloric restriction or surgical removal of visceral adipose tissue [33–36].

Our study also found a significant difference in IR risk between men and women, which is similar to other reports [29, 37]. This sex difference may be due to differences in adipose tissue distribution, sex hormones and adipokines [37]. Visceral adipocytes have been shown to be more sensitive to catecholamine-induced lipolysis and less sensitive to insulin’s anti-lipolytic effect than are subcutaneous adipocytes [38]. Therefore, increases in visceral and hepatic adipose tissue contribute to dyslipidemia, enhanced gluconeogenesis and insulin resistance [38, 39]. For a given BMI, men have higher lean mass and more visceral and hepatic adipose tissue, whereas women have more general adiposity. In addition, estrogen has been found to have a favorable effect on insulin sensitivity, glucose homeostasis and adipose tissue distribution [37]. Furthermore, compared with women, men have significantly lower level of adiponectin, an insulin-sensitizing hormone [40, 41]. Therefore, greater amounts of visceral and hepatic adipose tissues, in combination with lack of a possible effect of estrogen and lower adiponectin levels, may contribute to men’s higher IR than women.

Our study showed that adiposity indices including BMI, WC, WHR, WHtR were all associated with IR, regardless of gender, which corroborates with other studies [24, 29, 30, 42]. Our study also showed that these four measures of adiposity had similar magnitudes of association. Obesity, especially central obesity, has been demonstrated to be a risk factor for developing insulin resistance [1, 43, 44]. One mechanism is that the excess visceral adipose tissue releases large amount of free fatty acids, which significantly impairs the insulin-signaling pathways in the main target organs [1]. Another mechanism is that inflammatory events decrease the sensitivity to insulin in obese patients [1, 44], with the focuses on adipose tissue macrophages as the main source of obesity-associated inflammation [45]. Inflammatory processes in liver, muscle and other organs also contribute to obesity-induced IR [1].

The negative association between physical activity and IR observed in our study was consistent with other research [24, 29, 42]. It has been demonstrated that physical activity improves substantially insulin sensitivity [46–50]. In addition, physical activity can reduce body fat and obesity by weight loss, which increase cellular insulin sensitivity and reverses IR caused by obesity [46].

Our study also observed a negative correlation between alcohol consumption and IR. This is confirmed in several studies, which reported strong positive associations between alcohol and increased insulin sensitivity [51–53]. Regular low-to-moderate alcohol consumption

| Smoking status | Odds ratio (95% CI) | OR (95% CI) |
|---------------|-------------------|-------------|
| Never         | ref               | ref         |
| Former        | 1.52 (1.12–2.05)  | 1.02 (0.75–1.39) |
| Current       | 1.11 (0.70–1.75)  | 1.11 (0.63–1.94) |

HOMA homeostasis model assessment, BMI body mass index, CHMS Canadian Health Measures Survey, OR odds ratio

** ORs were adjusted for age, sex, BMI, education, physical activity and alcohol consumption, except for the variable under consideration
** ORs were not adjusted for each other among BMI, waist circumference, waist-to-height ratio and waist-to-hip ratio
**Table 3** Odds ratios of insulin resistance associated with demographics, adiposity and behavioral factors, by sex, CHMS, Cycle 1 & 2, 2007–2011

| Variable                                      | Unadjusted OR (95% CI) | Adjusted OR (95% CI) ** | p for trend | Unadjusted OR (95% CI) | Adjusted OR (95% CI) ** | p for trend |
|-----------------------------------------------|------------------------|-------------------------|-------------|------------------------|-------------------------|-------------|
| Age (years)                                   |                         |                         | 0.0031      |                         |                         | 0.0194      |
| 18–35                                         | ref                    | ref                     | ref         | ref                    | ref                     |             |
| 36–50                                         | 1.06 (0.60–1.88)        | 0.85 (0.51–1.42)        | 0.04 (0.56–1.93) | 0.87 (0.41–1.84)        |                         |             |
| 51–79                                         | 2.36 (1.51–3.68)        | 1.98 (1.28–3.05)        | 2.00 (1.18–3.38) | 1.79 (1.04–3.09)        |                         |             |
| Education                                     |                         |                         | 0.0959      |                         |                         | 0.5085      |
| Less than secondary                           | ref                    | ref                     | ref         | ref                    | ref                     |             |
| Secondary graduate                            | 0.92 (0.46–1.84)        | 1.09 (0.45–2.62)        | 0.72 (0.40–1.29) | 0.74 (0.40–1.37)        |                         |             |
| Other post-secondary                          | 0.44 (0.19–1.01)        | 0.88 (0.34–2.31)        | 0.53 (0.20–1.41) | 0.77 (0.26–2.29)        |                         |             |
| Post-secondary graduate                       | 0.58 (0.28–1.19)        | 0.60 (0.28–1.29)        | 0.47 (0.28–0.79) | 0.75 (0.44–1.27)        |                         |             |
| Family income adequacy                        |                         |                         | 0.0399      |                         |                         | 0.792       |
| Lowest                                        | ref                    | ref                     | ref         | ref                    | ref                     |             |
| Lower middle                                  | 1.74 (0.65–4.65)        | 1.07 (0.35–3.29)        | 1.35 (0.67–2.70) | 1.10 (0.49–2.46)        |                         |             |
| Upper middle                                  | 0.80 (0.38–1.70)        | 0.46 (0.19–1.08)        | 0.85 (0.57–1.26) | 0.73 (0.41–1.32)        |                         |             |
| Highest                                       | 0.89 (0.44–1.82)        | 0.50 (0.20–1.25)        | 0.88 (0.45–1.72) | 0.84 (0.40–1.77)        |                         |             |
| BMI (kg/m²)                                   |                         |                         | 0.0000      |                         |                         | 0.0000      |
| 18.5–<25.0                                    | ref                    | ref                     | ref         | ref                    | ref                     |             |
| 25.0–<30.0                                    | 4.92 (2.18–11.09)       | 4.47 (2.01–9.94)        | 5.75 (2.87–11.51) | 5.76 (2.62–12.68)       |                         |             |
| ≥ 30.0                                        | 27.69 (12.81–59.85)     | 25.93 (11.51–58.39)     | 25.78 (14.63–45.41) | 24.85 (13.12–47.06)     |                         |             |
| Continuous                                    | 1.38 (1.31–1.46)        | 1.38 (1.30–1.48)        | 1.25 (1.21–1.30) | 1.25 (1.20–1.29)        |                         |             |
| Waist circumference (cm)                      |                         |                         |             |                         |                         |             |
| < 102 in men or < 88 in women                 | ref                    | ref                     | ref         | ref                    | ref                     |             |
| ≥ 102 in men or ≥ 88 in women                 | 9.97 (6.60–15.04)       | 8.93 (5.65–14.12)       | 10.45 (6.91–15.80) | 10.42 (6.42–16.92)       |                         |             |
| Waist-to-height ratio                         |                         |                         |             |                         |                         |             |
| ≤ 0.570                                       | ref                    | ref                     | ref         | ref                    | ref                     |             |
| > 0.570                                       | 8.83 (5.86–13.29)       | 7.99 (5.02–12.71)       | 10.16 (6.74–15.33) | 9.82 (6.13–15.73)        |                         |             |
| Waist-to-hip ratio                            |                         |                         |             |                         |                         |             |
| ≤ 0.90 in men or ≤ 0.85 in women              | ref                    | ref                     | ref         | ref                    | ref                     |             |
| > 0.90 in men or > 0.85 in women               | 8.79 (5.83–13.27)       | 8.21 (4.72–14.28)       | 5.88 (4.05–8.54)  | 5.67 (3.60–8.93)        |                         |             |
| Alcohol consumption (daily drinks)            |                         |                         | 0.0038      |                         |                         | 0.0585      |
| None                                          | ref                    | ref                     | ref         | ref                    | ref                     |             |
| Light (1 drink/day)                           | 0.57 (0.38–0.85)        | 0.64 (0.38–1.07)        | 0.55 (0.36–0.83) | 0.65 (0.38–1.10)        |                         |             |
| Moderate (2 drinks/day)                       | 0.43 (0.28–0.66)        | 0.42 (0.22–0.83)        | 0.45 (0.24–0.83) | 0.54 (0.23–1.27)        |                         |             |
| Heavy (≥3 drinks/day)                         | 0.43 (0.25–0.75)        | 0.33 (0.15–0.76)        | 0.27 (0.003–23.2) | 0.36 (0.004–34.5)       |                         |             |
| Physical activity                             |                         |                         | 0.0572      |                         |                         | 0.0019      |
| Active                                        | ref                    | ref                     | ref         | ref                    | ref                     |             |
| Moderate                                      | 2.32 (1.40–3.85)        | 2.21 (1.14–4.28)        | 2.81 (1.21–6.53) | 2.65 (1.01–7.00)        |                         |             |
| Inactive                                      | 2.11 (1.31–3.41)        | 1.74 (1.05–2.87)        | 3.94 (2.09–7.42) | 3.82 (1.54–9.53)        |                         |             |
has been shown to improve insulin sensitivity [51], but chronic heavy alcohol intake may promote insulin resistance [54]. However, there were very few women in the category of heavy drinkers in this study and the negative association between alcohol consumption and IR in women should be interpreted with caution given the wide range of 95% confidence interval. For this study, because information on separate numbers of drinks of beer, wine and liquor had not been collected, quantity of alcohol intake (grams/day) could not be calculated.

Because IR exists and progresses before pre-diabetes and diabetes could be detected, IR might be the earliest detectable abnormality to predict the development of diabetes and is of clinical relevance. IR could be used a screening tool for early detection of high risk people for diabetes, such as those with high BMI and with abdominal obesity. In addition, IR could be used as a target of therapeutic approach.

Strengths and limitations
There are several strengths of this study. First, a large national sample of the non-diabetic adult population in Canada was available for this study. This allowed for sufficient power to consider the relationship of a number of variables simultaneously. Second, a number of key variables were measured, not self-reported, thus reducing the possibility of bias. However, there are also some limitations to our study that should be considered when interpreting results. For example, this is a cross-sectional study; therefore, we cannot draw causality from the observed associations among IR and socio-demographics, adiposity and behavioral factors.

In the absence of a universally accepted cut-off point for HOMA-IR, we used an arbitrary cut-off point of the 75% percentile to define IR, corresponding to a threshold value of 2.61. Previous studies have used the 66th [55], 75th [56, 57], 80th [58] and 90th [30, 59, 60] percentile. Three studies used receiver operator characteristic (ROC) curves to establish their cut-off points [61–63]; while this is preferable, it requires information on sensitivity and specificity which can only be obtained when data from insulin clamp testing is also available. HOMA-IR threshold values from these studies ranged from 1.55 in a south-east Asian population [30] to 3 in a Spanish population aged 7–16 years [62]. A large multinational study involving 17 European and 2 American sites noted a 23% prevalence of insulin resistance based on insulin clamp, similar to our classification of the top 25% of our population as insulin resistant [64]. A major limitation of this study is that the cut-off point used has not been validated with the gold standard for the Canadian population.

Furthermore, because this study combined data from two consecutive cycles, study methods and assay procedures may have introduced small non-differential variation across the two cycles. In addition, the two cycles of the CHMS have only a modest response rate, which could affect the representation of the Canadian population, although this level of response rate is common in other surveys in current time.

Table 3 Odds ratios of insulin resistance associated with demographics, adiposity and behavioral factors, by sex, CHMS, Cycle 1 & 2, 2007–2011 (Continued)

| Smoking status | Unadjusted | Adjusted * |
|----------------|------------|------------|
| Never          | ref        | ref        | 0.6536     | 0.282      |
| Former         | 1.47 (1.00–2.17) | 0.94 (0.59–1.49) | 1.49 (0.95–2.35) | 1.07 (0.76–1.51) |
| Current        | 0.78 (0.39–1.55) | 0.91 (0.47–1.77) | 1.56 (1.01–2.41) | 1.38 (0.75–2.54) |

HOMA homeostasis model assessment; BMI body mass index; CHMS Canadian Health Measures Survey; OR odds ratio
** ORs were adjusted for age, BMI, education, physical activity and alcohol consumption, except for the variable under consideration
** ORs were not adjusted for each other among BMI, waist circumference, waist-to-height ratio and waist-to-hip ratio

Table 4 Association of standardized continuous variables with insulin resistance, overall and by sex, CHMS, Cycle 1 & 2, 2007–2011

| Variable                  | Both men and women | Men | Women |
|---------------------------|--------------------|-----|-------|
|                           | Unadjusted         | Adjusted * | Unadjusted | Adjusted * | Unadjusted | Adjusted * |
|                           | OR (95% CI)        | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| Standardized continuous   |                    |     |       |     |     |     |
| BMI (kg/m2)               | 4.30 (3.57–5.17)   | 0.28 (3.48–5.08) | 6.01 (4.36–8.29) | 6.07 (4.23–8.72) | 3.52 (2.88–4.29) | 3.41 (2.77–4.19) |
| Waist circumference (cm)  | 4.73 (3.91–5.72)   | 0.37 (4.38–9.08) | 6.31 (4.13–9.23) | 4.34 (3.46–5.43) | 4.25 (3.40–5.31) |
| Waist-to-height ratio     | 4.80 (3.92–5.88)   | 0.37 (4.38–9.08) | 6.52 (4.64–10.23) | 6.88 (4.63–10.23) | 3.96 (3.19–4.91) | 3.97 (3.18–4.96) |
| Waist-to-hip ratio        | 2.95 (2.44–3.58)   | 0.28 (3.08–5.95) | 4.36 (3.30–7.54) | 5.14 (3.33–7.94) | 3.89 (2.91–5.20) | 3.98 (2.81–5.66) |

HOMA homeostasis model assessment; BMI body mass index, CHMS Canadian Health Measures Survey; OR odds ratio
* ORs were adjusted for age, BMI, education, physical activity and alcohol consumption, except for the variable under consideration
* ORs were not adjusted for each other among BMI, waist circumference, waist-to-height ratio and waist-to-hip ratio
Conclusion
In summary, the current study demonstrated a positive association for obesity and a negative association for physical activity with IR. The current study results, particularly the elevated risk of IR observed in obese people suggest that early interventions such as weight loss and physical activity may be important in preventing diabetes. With the high prevalence of overweight and obesity in the Canadian population, the study of IR could be considered an important research and public health topic.

Abbreviations
BMI, body mass index; CHMS, the Canadian Health Measures Survey; HOMA, homeostasis model assessment of insulin resistance; IR, insulin resistance; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio

Acknowledgements
We thank all participants of the Canadian Health Measures Survey, and Statistics Canada for data collection, and the Data Coordination and Access Program at the Public Health Agency of Canada for database management.

Funding
No external funding was provided.

Availability of data and supporting materials
All data underlying the findings are available from the corresponding author on request.

Authors’ contributions
SYP conceived the study, performed the analyses, wrote the manuscript and incorporated input from all other authors on the manuscript. MDG and AA conceived methods instrumental to the study, and provided critical comments on the results and on the manuscript. HM provided critical input and revision to the manuscript. All authors read and approved the final manuscript.

Competing interests
All the authors declare that they have no competing interests.

Ethics approval and consent to participate
Ethics approval was obtained from Health Canada’s Research Ethics Board. The consent to participate was obtained by Statistics Canada when the data was collected.

Author details
1Science Integration and Social Determinant Directorate, Public Health Agency of Canada, 785 Carling Avenue, AL 6809B, Ottawa, ON K1A 0K9, Canada. 2Food Directorate, Health Products and Food Branch, Health Canada, Ottawa, ON, Canada.

Received: 6 April 2016 Accepted: 4 August 2016
Published online: 11 August 2016

References
1. Mercurio V, Carlonagno G, Fazio V, Fazio S. Insulin resistance: is it time for primary prevention? World J Cardiol. 2012;4(1):1–7.
2. Bogardus C. Insulin resistance in the pathogenesis of NIDDM in Pima Indians. Diabetes Care. 1993;16(1):228–31.
3. Bunt JC, Krakoff J, Ortega E, Knowler WC, Bogardus C. Acute insulin response is an independent predictor of type 2 diabetes mellitus in individuals with both normal fasting and 2-h plasma glucose concentrations. Diabetes Metab Res Rev. 2007;23(4):304–10.
4. Weyer C, Tataranni PA, Bogardus C, Pratley RE. Insulin resistance and insulin secretory dysfunction are independent predictors of worsening of glucose tolerance during each stage of type 2 diabetes development. Diabetes Care. 2001;24(1):89–94.
5. Lillioja S, Mott DM, Spraul M, Ferraro R, Foley JE, Ravussin E, et al. Insulin resistance and insulin secretory dysfunction as precursors of non-insulin-dependent diabetes mellitus. Prospective studies of Pima Indians. N Engl J Med. 1993;329(27):1988–92.
6. DeFronzo RA. Pathogenesis of type 2 diabetes mellitus. Med Clin North Am. 2004;88(4):87–835. ix.
7. Canadian Diabetes Association. An economic tsunami: the cost of diabetes in Canada. 2009.
8. Ginsberg H, Kimmerling G, Olefsky JM, Reaven GM. Demonstration of insulin resistance in untreated adult onset diabetic subjects with fasting hyperglycemia. J Clin Invest. 1975;55(3):454–61.
9. Bonora E, Formentini G, Calcaterra F, Lombardi S, Marini F, Zerani L, et al. HOMA-estimated insulin resistance is an independent predictor of cardiovascular disease in type 2 diabetic subjects: prospective data from the Verona Diabetes Complications Study. Diabetes Care. 2002;25(7):1135–41.
10. Sakurai T, Iimuro S, Araki A, Umegaki H, Ohashi Y, Yokono K, et al. Age-associated increase in abdominal obesity and insulin resistance, and usefulness of AHA/NHLBI definition of metabolic syndrome for predicting cardiovascular disease in Japanese elderly with type 2 diabetes mellitus. Gerontology. 2010;56(2):141–9.
11. Despres JP, Lamarche B, Mauriege P, Cantin B, Dagenaïs GR, Moorjani S, et al. Hyperinsulinaemia as an independent risk factor for ischemic heart disease. N Engl J Med. 1996;334(15):952–7.
12. Sandeep S, Gokulrakshhan K, Deepa M, Mohan V. Insulin resistance is associated with increased cardiovascular risk in Asian Indians with normal glucose tolerance—the Chennai Urban Rural Epidemiology Study (CURES-66). J Assoc Physicians India. 2011;59:480–4.
13. Reaven GM. Insulin resistance: from bit player to centre stage. CMAJ. 2011;183(5):536–7.
14. DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol. 1979;237(3):E214–23.
15. Muniyappa R, Lee S, Chen H, Quon MJ. Current approaches for assessing insulin sensitivity and resistance in vivo: advantages, limitations, and appropriate usage. Am J Physiol Endocrinol Metab. 2008;294(1):E15–26.
16. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes Care. 2004;27(6):1487–95.
17. Bonora E, Targher G, Albereiche M, Bonadonna RC, Saggiani F, Zenere MB, et al. Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity: studies in subjects with various degrees of glucose tolerance and insulin sensitivity. Diabetes Care. 2000;23(1):57–63.
18. Gungor N, Saad R, Janosky J, Ardalanian S. Validation of surrogate estimates of insulin sensitivity and insulin secretion in children and adolescents. J Pediatr. 2004;144(1):47–55.
19. Day B, Langlois R, Tremblay M, Knoppers BM. Canadian Health Measures Survey: ethical, legal and social issues. Health Rep. 2007;18(Suppl):37–51.
20. Tremblay M, Wolfson M, Gorber SC. Canadian Health Measures Survey: rationale, background and overview. Health Rep. 2007;18(Suppl):7–20.
21. Tremblay M, Langlois R, Bryan S, Essler D, Patterson J. Canadian Health Measures Survey pre-test: design, methods, results. Health Rep. 2007;18(Suppl):21–30.
22. Statistics Canada. Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 1. 2010.
23. Statistics Canada. Canadian Health Measures Survey (CHMS) Data User Guide: Cycle 2. 2012.
24. Kelishadi R, Cook SR, Amna B, Adibi A. Factors associated with insulin resistance and non-alcoholic fatty liver disease among youths. Atherosclerosis. 2009;204(2):538–43.
25. World Health Organization. Obesity: preventing and managing the global epidemic. WHO technical report series no. 894. Geneva: WHO; 2000.
26. Lee CM, Huley RR, Wildman RP, Woodward M. Indices of abdominal obesity are better discriminators of cardiovascular risk factors than BMI in a meta-analysis. J Clin Epidemiol. 2008;61(7):646–53.
27. Statistics Canada. Boothbr User Guide (Bootb 3.2 - SAS Version). 2010.
28. Ioannou GN, Byson CL, Boyko EJ. Prevalence and trends of insulin resistance, impaired fasting glucose, and diabetes. J Diabetes Complications. 2007;21(6):363–70.
29. Gayoso-Diaz P, Otero-Gonzalez A, Rodriguez-Alvarez MX, Gude F, Cadarso-Suarez C, Garcia F, et al. Insulin resistance index (HOMA-IR) levels in a general adult population: curves percentile by gender and age. The EPICRE study. Diabetes Res Clin Pract. 2011;94(1):146–55.
30. Do HD, Lohsoonthorn V, Jamjarasangsri W, Lertmaharit S, Williams MA. Prevalence of insulin resistance and its relationship with cardiovascular
7. Hes AO. Alcohol consumption and its role in the development of obesity in older patients. Clin Interv Aging. 2013;8:309–44.

8. Rogers NH, Smith RG. Brown-to-white transition in subcutaneous fat: linking aging and disease. Aging (Albany NY). 2012;4(11):728–9.

9. Lin L, Saha PK, Ma X, Henshaw IO, Shao L, Chang BH, et al. Abation of ghrelin receptor reduces adiposity and improves insulin sensitivity during aging by regulating fat metabolism in white and brown adipose tissues. Aging Cell. 2011;10(8):1095–10.

10. Gabriei L, Barzilai N. Surgical removal of visceral adipose tissue effects on insulin action. Curr Diab Rep. 2003;3(3):201–6.

11. Einstein FH, Fishman S, Bauman J, Thompson RF, Huffman DM, Atzmon G, et al. Enhanced activation of a nutrient-sensing pathway with age contributes to insulin resistance. FASEB J. 2008;22(10):3450–7.

12. Geer EB, Shen W. Gender differences in insulin resistance, body composition, and energy balance. Gend Med. 2006;3 Suppl 1:160–75.

13. Wajchenberg BL. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. Endocr Rev. 2000;21(6):697–738.

14. Ritchie SA, Connell JM. The link between abdominal obesity, metabolic syndrome and cardiovascular disease. Nutr Metab Cardiovasc Dis. 2007;17(4):219–26.

15. Choo M, Havel PJ, Utschneider KM, Carr DB, Sinha MK, Boyko EJ, et al. Relationship of adipostatin to body fat distribution, insulin sensitivity and plasma lipoproteins: evidence for independent roles of age and sex. Diabetologia. 2003;46(4):459–69.

16. Yamautchi T, Karon J, Waki H, Terauchi Y, Kubota N, Hara K, et al. The fat-derived hormone adiponectin reverses insulin resistance associated with both lipopathy and obesity. Nat Med. 2001;7(8):941–6.

17. Jimenez-Pavon D, Castillo MJ, Moreno LA, Kafatos A, Manios Y, Kondaki K, et al. Fitness and fatness are independently associated with markers of insulin resistance in European adolescents; the HELENA study. Int J Pediatr Obes. 2011;6(3–4):253–60.

18. Kim SH, Abbasi F, Reaven GM. Impact of degree of obesity on surrogate estimates of insulin resistance. Diabetes Care. 2004;27(8):1996–2002.

19. Zeyda M, Stulnig TM. Obesity, inflammation, and insulin resistance–a mini-review. Gerontology. 2009;55(4):379–86.

20. Fain JN. Release of interleukins and other inflammatory cytokines by human adipose tissue is enhanced in obesity and primarily due to the nonfat cells. Vitam Horm. 2006;74:443–77.

21. Venkataramy VV, Pericherla S, Manthuriirthi S, Mishra S, Hanno R. Effect of physical activity on Insulin Resistance, Inflammation and Oxidative Stress in NIDDM patients. J Nutr Sci Vitaminol. 2013;59(1):176–4.

22. Goodyear LJ, Kahn BB. Exercise, glucose transport, and insulin sensitivity. Annu Rev Med. 1998;49:235–61.

23. DeFronzo RA, Sherwin RS, Kraemer N. Effect of physical training on insulin action in obesity. Diabetes. 1987;36(12):1379–85.

24. Fedewa MV, Gist NH, Evans EM, Dishman RK. Exercise and insulin resistance in youth: a meta-analysis. Pediatrics. 2014;133(1):e163–74.

25. Roberts CK, Hevener AL, Barnard RJ. Metabolic syndrome and insulin resistance: underlying causes and modification by exercise training. Compr Physiol. 2013;3(3):1–58.

26. Kiechl S, Willeit J, Poewe W, Egger G, Oberhollenzer F, Muggeo M, et al. Insulin sensitivity and regular alcohol consumption: large, prospective, cross-sectional population study (Bruneck study). BMJ. 1996;313(7064):1040–4.

27. Mayer EJ, Newman B, Quenzenbery Jr CR, Friedman GD, Selby JV. Alcohol consumption and insulin concentrations. Role of insulin in association of alcohol intake with high-density lipoprotein cholesterol and triglycerides. Circulation. 1993;88(8 Pt 1):2190–7.

28. Razay G, Heaton KW, Bolton CH, Hughes AO. Alcohol consumption and its relation to cardiovascular risk factors in British women. BMJ. 1992;304(6819):80–3.

29. de la Monte S, Derdač Z, Wands JR. Alcohol, insulin resistance and the liver-brain axis. J Gastroenterol Hepatol. 2012;27 Suppl 2:33–41.

30. Summer AE, Cosi CC. Ethnic differences in the ability of triglyceride levels to identify insulin resistance. Atherosclerosis. 2008;196:696–703.

31. Hedinblad B, Nilsson P, Janson L, Berglund G. Relation between insulin resistance and carotid intima-media thickness and stiffness in non-diabetic subjects. Results from a cross-sectional study in Malmo, Sweden. Diabet Med. 2000;17:299–307.

57. Marques-Vidal P, Mazoyer E, Bongard V, Gourdy P, Ruidavets JB, Drouet L, Ferrieres J. Prevalence of insulin resistance syndrome in Southwestern France and its relationship with inflammatory and haemostatic markers. Diabetes Care. 2002;25:1371–7.

58. Miccoli R, Bianchi C, Odgaard-L. Prevalence of the metabolic syndrome among Italian adults according to ATP III definition. Nutr Metab Cardiovasc Dis. 2005;15:250–4.

59. Nakai Y, Fukushima M, Nakashi S, Kishimoto H, Seino Y, Nagasaka S, Sakai M, Taniguchi A. The threshold value for insulin resistance on homeostasis model assessment of insulin sensitivity. Diabet Med. 2002;19:346–7.

60. Geloneze B, Repetto EM, Geloneze SR, Tambascia MA, Ermitone MN. The threshold value for insulin resistance (HOMA-IR) in an admixture population. J in the Brazilian metabolic syndrome study. Diabetes Res Clin Pract. 2006;72:19–20.

61. Esteghamati A, Ashraf H, Esteghamati AR, Meyesamie A, Khalizadeh O, Nakhjavani M, Abbasi M. Optimal threshold of homeostasis model assessment for insulin resistance in an Iranian population: the implications of metabolic syndrome to detect insulin resistance. Diabetes Res Clin Pract. 2009;84:276–87.

62. Aascos JF, Romero P, Real JT, Prieo A, Valdecabres C, Carmena R. Insulin resistance quantification by fasting insulin plasma values and HOMA index in a non-diabetic population. Med Clin (Barc). 2001;117:530–3.

63. Tomé MA, Botana MA, Cadarso-Suarez C, Rego-Ireta A, Fernandez-Marino A, Mata JO, Solache I, Perez-Fernandez R. Prevalence of metabolic syndrome in Galicia (NW Spain) on four alternative definitions and association with insulin resistance. J Endocrinol Invest. 2009;32:505–11.

64. Stern SE, Williams K, Ferrannini E, DeFronzo RA, Bogardus C, Stern MP. Identification of individuals with insulin resistance using routine clinical measurements. Diabetes. 2005;54(2):333–9.

Submit your next manuscript to BioMed Central and we will help you at every step:
• We accept pre-submission inquiries
• Our selector tool helps you to find the most relevant journal
• We provide round the clock customer support
• Convenient online submission
• Thorough peer review
• Inclusion in PubMed and all major indexing services
• Maximum visibility for your research

Submit your manuscript at www.biomedcentral.com/submit