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Adipokines, Ethnicity and Insulin Resistance

**Ethnic variation in adiponectin and leptin levels and their association with adiposity and insulin resistance**

*Short Running Title*: Adipokines, Ethnicity and Insulin Resistance

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**Objective:** To investigate ethnic differences in adiponectin and leptin concentration and to determine whether these adipokines and a high glycemic index diet account for ethnic variation in insulin resistance.

**Research Design and Methods:** In 1,176 South Asian, Chinese, Aboriginal, and European Canadians, fasting blood samples were drawn and clinical history and dietary habits including glycemic index/load were recorded using standardised questionnaires. Insulin resistance was defined using the Homeostatic Model Assessment (HOMA-IR).

**Results:** Adjusted mean (95% CI) adiponectin concentration is significantly higher in Europeans [12.94 (12.27-13.64)] and Aboriginals [11.87 (11.19-12.59)] compared to South Asians [9.35 (8.82-9.92)] and Chinese [8.52 (8.03-9.03)] (overall P<0.001). Serum leptin is significantly higher in South Asians [11.82 (10.72-13.04)] and Aboriginals [11.13 (10.13-12.23)] compared to Europeans [9.21 (8.38-10.12)] and Chinese [8.25 (7.48-9.10)]. BMI and waist circumference are inversely associated with adiponectin in every group except the South Asians (P<0.001 for interaction). Adiponectin is inversely and leptin is positively associated with HOMA-IR (P-values<0.001). The increase in HOMA-IR for each given decrease in adiponectin is larger among South Asians (P=0.01) and Aboriginals (P<0.001) compared to Europeans. A high glycemic index is associated with a larger decrease in adiponectin among South Asians (P=0.03) and Aboriginals (P<0.001), and a larger increase in HOMA-IR among South Asians (P<0.05) relative to other groups.

**Conclusion:** South Asians have the least favourable adipokine profile, and like the Aboriginal people, display a greater increase in insulin resistance with decreasing levels of adiponectin. Differences in adipokines and responses to glycemic foods parallel the ethnic differences in insulin resistance.
Epidemiologic studies have consistently shown that compared to non-white ethnic populations, people of European origin have a relatively low prevalence of insulin resistance and type 2 diabetes despite having comparable or greater body weight (1,2). While there is controversy regarding the definition and use of the term “metabolic syndrome” which is often used to refer to the clustering of risk factors such as abdominal obesity, elevated glucose, abnormal lipids and elevated blood pressure, insights into the pathophysiology of adipose tissue and the presence of these insulin resistance-related factors may be gained from studies of high and low risk populations.

Insulin resistance is closely associated with abdominal adiposity, a surrogate measure of visceral adiposity (3). Adipocytes secrete a variety of bioactive substances known as adipokines, including two proteins, adiponectin and leptin. Adiponectin, a plasma protein secreted from visceral adipose tissue, increases insulin sensitivity and tissue fat oxidation resulting in reduced circulating fatty acid levels (4). Leptin, a protein which circulates in proportion with body fat mass, provides information about nutritional status and subcutaneous fat mass to neural centers which regulate feeding behavior, appetite, and energy expenditure (5). It is therefore plausible that differences in adiponectin and leptin levels correlate with ethnic variations in insulin resistance and metabolic syndrome-related factors.

Dietary factors may also potentially influence adipokine levels and insulin sensitivity. There is a growing body of literature showing that a higher consumption of foods with high glycemic index/load (GI/GL) values is associated with lower adiponectin levels in both healthy and diabetic individuals (6), and higher leptin levels (7). Glycemic foods are known to induce both hyperglycemia and hyperinsulinemia (8,9). Conversely high intake of fiber may attenuate the glycemic effect of a full meal, and cereal fiber intake is positively associated with adiponectin (6). Previous studies have shown that ethnic populations at higher risk for metabolic syndrome-related conditions largely consume a diet consisting of foods with a high glycemic index (10). It is not known whether a higher consumption of glycemic foods influences adipokine levels and insulin resistance in these populations.

Using a multi-ethnic population-based sample in which adiposity, adipokines, and insulin resistance-related factors were measured in a standardized manner, we investigated 1) the ethnic variation in levels of adipokines, 2) if higher intake of glycemic foods differentially affects adipokine levels across ethnic populations, and 3) if levels of adipokines and GI/GL account for ethnic variation in insulin resistance.

RESEARCH DESIGN AND METHODS

Study population. The study population was comprised of Canadians of South Asian, Chinese, Aboriginal or European origin who participated in the Study of Health Assessment and Risk in Ethnic groups (SHARE), a cross-sectional prevalence study of CVD risk factors conducted between 1996 and 1998 (2). Individuals were randomly selected from three cities (Toronto, Hamilton, Edmonton), and from the Six Nations Reservation (Ohsweken, Ontario) as previously described (1,2). Subjects’ ages were 35-75 years, and had lived in
Canada for ≥5 years. Individuals with treated diabetes mellitus or chronic debilitating illnesses such as terminal cancer and renal failure were excluded. Ethics approval was obtained from the McMaster University Research Ethics Board, and all participating institutions. Informed consent was obtained from each subject. The investigation conforms with the principles outlined in the Declaration of Helsinki.

Assessment of adipokines and insulin resistance-related factors. Participants completed lifestyle questionnaires which recorded information on physical activity, smoking patterns, and dietary intake as previously described (1,2). Physical measurements included height, weight, waist and hip circumference using a standardized protocol. The physical activity index involved summing ordinal categories of intensity of physical exertion estimated from reported type of work, time spent playing sports, and type of leisure time activities. Occupation, sports, and leisure time activities were classified according to exertion as 1 = low, 2 = moderate, and 3 = high based on the published literature (10).

Fasting blood samples were collected in the morning from all participants. Blood samples were collected and processed according to a standard protocol and were shipped to the core laboratory in Hamilton for analysis. All subjects underwent a twelve-hour fast before blood was drawn and non-diabetic participants underwent an oral glucose tolerance test (OGTT) with measurement of glucose, insulin, triglyceride and free fatty acid levels at baseline and at two hours post glucose load. Glucose was measured using enzymatic methods and insulin was determined by manual radioimmunoassay assay (Diagnostic Products Corporation, Los Angeles USA). Analysis of adiponectin and leptin were performed in the laboratory of Dr. Stephan Blankenberg at the University of Mainz, Germany using a commercially available Human adiponectin ELISA assay (RD195023100), and Human Leptin ELISA assay RD191001100), produced by Biovendor Research Products. For adiponectin the intra-assay imprecision is 6.4-7.0% and the interassay imprecision is 7.3-8.2%. For Leptin the intra-assay imprecision is 3.0-7.5% and interassay imprecision is 3.2-9.2%. Basal insulin resistance was calculated using the previously validated HOMA-IR model.

Dietary assessment. On the food frequency questionnaire (FFQ), participants reported how often, on average, they consumed selected foods in the previous year. We calculated nutrient intakes by multiplying the average nutrient content of a particular food portion by the number of times it was consumed. GI and GL were estimated based on the International Table of Glycemic Index for specific foods. Briefly, we assigned GI values to each of the individual FFQ food items by manual review of the GI table. We then computed sex- and serving size-specific GL for each of the food items using the weighted mean methods as described by Subar et al (11). Each unit of GL represents both the quality and the quantity of carbohydrate intake (or the equivalent of 1 g of carbohydrate from white bread). The overall GI for each participant was calculated by dividing the participant’s GL by the total grams of carbohydrate consumed, which represents the overall quality of carbohydrate intake.

Statistical analysis. All analyses were computed using SAS, version 9.1 (Cary, North Carolina). Distributions of adiponectin, leptin, and HOMA-IR were
highly skewed, so geometric means and natural logs are presented, adjusting for age, sex, and adiposity measures where appropriate. Post-hoc pair-wise comparisons were performed using Tukey tests to adjust for multiple comparisons. Pearson correlation coefficients and linear regression were used to assess the association between continuous variables, with age, sex, and markers of adiposity used as covariates where indicated. The independent predictive value of logarithmically transformed adiponectin and leptin on insulin resistance was examined in a linear regression model with log transformed HOMA-IR as the dependent variable along with other known determinants of insulin resistance as independent variables (age, ethnicity, smoking, BMI, waist-to-hip ratio (WHR), glycemic load, energy intake, CRP, and physical activity). Linear regression modelling was also used to assess effects of glycemic index or load on adiponkine concentration and insulin resistance by ethnic origin. Differences with \( p<0.05 \) were considered statistically significant.

**RESULTS**

Complete data were available from 1,258 people from the SHARE population. From this sample, 18 individuals who had implausible levels of adiponectin (> 100 \( \mu \text{g/mL} \)) or leptin (> 180 \( \text{ng/mL} \)) and 64 with treated diabetes mellitus were excluded, leaving a final sample of 1,176 participants.

The characteristics of participants are displayed in Table 1. The mean age of the overall population is 50.3 years, and men and women are equally represented. Significant differences in age, lifestyle factors including current smoking, physical activity, measures of adiposity, plasma lipids, diastolic blood pressure, and insulin resistance are present among ethnic groups (Table 1). For example, Aboriginal people have substantially higher BMI and abdominal obesity relative to other ethnic groups. Conversely people of Chinese origin have the lowest BMI and abdominal adiposity. Europeans have a higher BMI, yet less abdominal obesity compared to South Asians. Despite these differences, South Asians and Aboriginal people are more insulin resistant compared to the Europeans (all \( P<0.05 \)).

**Adipokines and ethnicity.** Adiponectin levels are significantly higher in Europeans and Aboriginals compared to the other ethnic groups [age- and waist-adjusted mean (95% CI) in Europeans: 12.96 (12.27-13.64) and Aboriginals: 11.87 (11.19-12.59) versus South Asians: 9.35 (8.82-9.92); Chinese: 8.52 (8.03-9.03) \( \mu \text{g/mL} \), overall \( P<0.001 \)] (Table 1). Serum leptin is significantly higher in South Asians [11.82 (10.72-13.04)] and Aboriginal people [11.13 (10.13-12.23)] compared to Europeans [9.21 (8.38-10.12)] and Chinese [8.25 (7.48-9.10)] (Table 1).

South Asian women and men have significantly higher leptin concentrations compared to all other groups (Table 1). A significant sex by ethnic origin interaction with serum leptin is present (\( P=0.01 \)), as Aboriginal women have significantly higher leptin concentrations compared to European women for the same BMI, whereas no significant differences are observed among men. No significant sex by ethnic origin interaction is observed for adiponectin.

**Adipokines and ethnicity by adiposity.** Adiponectin is strongly and inversely associated with all adiposity measures, whereas leptin is positively associated with the adiposity measures (all p-values
<0.001). As shown in Online Appendix Table 1 (which is available at [http://care.diabetesjournals.org](http://care.diabetesjournals.org)), adiponectin is negatively associated with BMI, waist circumference, waist adjusted for hip circumference, and WHR in Europeans, Chinese, and Aboriginal people, but not in South Asians. Leptin is significantly associated with BMI and central adiposity measures across all ethnic groups.

**Adipokines and insulin resistance.** To determine if adiponectin and leptin are independently associated with insulin resistance over and above factors known to be associated with insulin resistance (i.e., adiposity, glycemic diet, smoking, physical activity), a multivariate linear regression analysis was performed. As shown in Appendix Table 2, factors which are positively associated with insulin resistance include South Asian ($P<0.001$), Chinese ($p<0.001$), and Aboriginal ($P<0.001$) ancestry, serum leptin ($P<0.001$), age ($p=0.01$), BMI ($P<0.001$) and WHR ($P<0.001$). Factors which are negatively associated with insulin resistance include serum adiponectin ($P<0.001$), female sex ($P=0.02$), and physical activity ($P=0.003$). C-reactive protein, glycemic index/load, current smoking, and energy intake are not independently associated with insulin resistance after accounting for the above factors (Appendix Table 2). These factors account for 0.3% ($P=0.11$) of the variance in HOMA-IR scores beyond the contribution of other factors. The individual factor contributions to the model are shown in Appendix Table 3.

In a linear regression analysis of HOMA-IR scores as a function of log adiponectin by ethnic categories, the association between adiponectin and insulin resistance varies significantly across ethnic groups ($P=0.009$ for interaction), as the increase in HOMA-IR for each given decrease in adiponectin is larger among South Asians ($P=0.024$) and Aboriginals ($P=0.010$) compared to Europeans. No significant effect modification by ethnicity is found for leptin. There is no significant 3-way effect modification between ethnicity, adiponectin/leptin, and BMI/WHR.

**Adipokines, insulin resistance and glycemic index/load.** No significant association of glycemic index or glycemic load with adipokine concentration is observed overall. In an assessment of effect modification by BMI and ethnicity, there is significant 3-way effect modification between ethnicity, glycemic index, and BMI in predicting adiponectin ($P=0.006$). Among study participants with BMI $\geq 30$, there is a larger decrease in adiponectin levels for each given increase in glycemic index in South Asians ($P=0.03$) and Aboriginals ($P<0.001$) compared to Europeans. However, among non-obese participants, the degree of change in adiponectin with greater glycemic index is similar across ethnic groups. No significant 2-way or 3-way effect modification between ethnicity, glycemic index/load, and BMI is found for leptin.

In a linear regression analysis for HOMA-IR scores as a function of glycemic index by ethnic categories, the association between glycemic index and insulin resistance varies significantly across ethnic groups ($P=0.01$ for interaction), as a positive association is found only among South Asians ($P<0.001$). The increase in HOMA-IR for each given increase in glycemic index is significantly larger among South Asians compared to Europeans ($P=0.03$), Chinese ($P=0.008$), and Aboriginals ($P=0.006$). No significant effect modification by ethnicity is found for
glycemic load (P=0.31). There is no significant 3-way effect modification between ethnicity, glycemic index/load, and adiponectin/leptin.

CONCLUSIONS
To our knowledge, this investigation is the first to compare adiponectin, leptin and other insulin resistance-related factors in a large randomly assembled multi-ethnic population. Our study demonstrates that South Asians have an unfavourable adipokine profile which is characterized by lower adiponectin and higher leptin for the same degree of adiposity as Europeans. Furthermore, we have shown that a greater consumption of foods with a high glycemic index is associated with a significantly larger decrease in adiponectin among South Asians and Aboriginals compared to Chinese and Europeans. In addition, these groups display a greater increase in insulin resistance with decreasing levels of adiponectin, and a high glycemic diet predicts higher insulin resistance predominantly in South Asians. To date, few studies have assessed dietary effects on adipokine concentrations, and we know of no previous study to assess dietary glycemic index in relation to adipokine profile and insulin resistance in multiple ethnic groups including populations at high-risk. Our findings suggest that modifying intake of glycemic foods could especially improve adipokine concentrations and insulin sensitivity in South Asians and Aboriginals, two populations at increased risk for insulin resistance.

The large size and ethnic variation of our cohort allowed us to examine adiponectin and leptin over a wide range of body weights and abdominal fat distribution. Overall, adiponectin decreased and leptin increased with higher adiposity, which is consistent with recent evidence showing that the amount of intra-abdominal fat modulates serum adipokine levels (12). Cultured adipocytes derived from visceral fat are known to secrete an increased amount of adiponectin in response to insulin or rosiglitazone treatment, whereas adipocytes derived from subcutaneous fat are unaffected (13). In subgroup analyses, we found that there is no association between adiponectin and BMI, waist circumference, waist adjusted for hip circumference, or WHR in South Asians. Similar results have been observed in a recent study of healthy South Asians (14), yet another investigation showed an inverse association between adiponectin and BMI in South Asian women with gestational diabetes (15). Our findings may reflect the lack of specificity of measuring adiposity using BMI and waist circumference, or may reflect different pathogenic pathways including the type, amount and distribution of adipose tissue accumulation as well as dietary and genetic influences that may exist among South Asians.

Few previous studies have assessed adipokine levels in South Asians compared to those of European origin. Several reports showed that adiponectin is significantly lower in South Asians than in Europeans (16,17). These studies, however, were generally small and often did not include a comparison group (15,18). In our study, South Asians displayed the least favourable adipokine profile (lower adiponectin and higher leptin) of all ethnic groups, despite having comparable BMI to Europeans. The metabolic disturbance behind these differences is not known, but might be related to differences in adipocyte properties (eg, hypertrophic versus hyperplastic adipocytes) or distribution of...
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adipose tissue between the groups (19). We also found strikingly high levels of leptin among South Asian women compared to European women, a finding that was noted previously in young adults (20). Higher leptin in women compared to men is attributed to their greater subcutaneous fat mass. However, prior studies did not assess whether these relationships vary by ethnic origin. Our subgroup analysis showed a significantly stronger correlation between serum insulin and leptin among European women than South Asian women, while waist-to-hip ratio and leptin levels showed similar correlation values across groups. Therefore distribution of fat (i.e. truncal obesity) and hyperinsulinism do not appear to explain the higher leptin levels among South Asian women. There is, however, evidence that hypertrophic adipocytes secret more leptin than do hyperplastic adipocytes (21), and subcutaneous adipocyte hypertrophy could account for the higher leptin in South Asians (19).

Our study showed that Aboriginal people have higher leptin compared to Europeans, but similar adiponectin. The findings of previous studies comparing adiponectin in Aboriginal people to Europeans have been inconclusive, with some studies reporting lower levels in Aboriginals (22) and other recent studies showing no significant differences (12). These discrepant findings may also be attributable to the smaller sample of participants and different sample selection. Our finding that Chinese have lower adiponectin levels compared to Europeans is consistent with previous results in East Asian populations (23), and with our past observations showing that despite having relatively low BMIs the Chinese are at increased risk of developing impaired fasting glucose, impaired glucose tolerance, and type 2 diabetes with central fat accumulation (2).

Our finding that lower adiponectin and elevated leptin are independent determinants of increased insulin resistance over and above lifestyle factors, anthropometric indices, and inflammatory markers is consistent with previous cohort studies (24). In addition, when we assessed the effect of serum adipokines on insulin resistance by ethnic group, South Asians and Aboriginals showed a significantly greater increase in insulin resistance per unit decrease in adiponectin compared to Chinese and Europeans. Several smaller studies (18) but not all (16,17) have also related low adiponectin to HOMA-IR values in young healthy South Asians. In Alaskan and Canadian Native populations, adiponectin was also inversely associated with HOMA-IR scores (12,25). Our findings suggest that pharmacologic agents which work by altering adiponectin levels may be more effective in these groups. Adiponectin levels increase with reduction in fat mass, PPAR gamma agonists such as the thiazolidinediones administration and renin-angiotensin system blockade and individuals with the lowest baseline levels may benefit the most from these therapeutic strategies (4).

Our finding that glycemic index predicts greater increases in insulin resistance in South Asians compared to other ethnic groups has not been reported previously. There is some evidence that carbohydrate intake is associated with poorer glycemic control in South Asians (8) and Aboriginals (9), but total glycemic index/load or long-term intake were not evaluated. In this study, we did not find evidence that glycemic index is associated with insulin resistance. Nevertheless, our findings show that South Asians and Aboriginals display a
greater decrease in adiponectin with increasing glycemic index, particularly at higher BMI. We are not aware of any previous study that assessed dietary effects on adipokine concentrations in ethnic populations. Our findings suggest that modifying intake of glycemic foods could improve adipokine concentrations and insulin sensitivity most profoundly in South Asians and Aboriginals.

While the underlying mechanism linking glycemic index to adipokine levels is not clear, the findings are compatible with the overall poor adipokine profile observed in these groups. Glycemic foods are known to induce both hyperglycemia and hyperinsulinemia. There is evidence that adipose tissue expression of adiponectin is inversely correlated with fasting glucose concentration and that a glucose-rich diet reduces adiponectin expression in adipose tissue (26). South Asian and Aboriginal populations largely consume a diet consisting of foods with a high glycemic index (10). It has been recognized that glycemic foods influence body fat (27), which suggests that the effects could be at least partly mediated by adipose-related pathways. Conversely, fiber intake is positively associated with adiponectin (6), and may promote the clearance of lipids and thus reduce free fatty acids available for storage in adipose tissue (28).

Our study has some limitations. We used surrogate measures of adiposity (eg, BMI and waist circumference), which are merely proxy indicators of visceral fat, a stronger predictor of insulin resistance. Although these measures show considerable variation among different ethnic groups (1,2), the findings relating central fat with adiponectin in our study should be viewed with caution. Our study used total adiponectin as opposed to the active high molecular weight (HMW) multimer which may be the critical determinant of insulin sensitivity. Nevertheless, total adiponectin was significantly associated with insulin resistance, and ethnic comparisons in our study likely reflect similar relative differences in HMW adiponectin. Drug treatment for diabetes can alter adipokine concentration, and thus, we excluded these patients from our analyses. In a sensitivity analysis that further excluded patients with new clinically diagnosed diabetes (N=76), the ethnic differences in adipokine levels and accompanying associations between adipokines and insulin resistance were unaltered. Exclusion of individuals with impaired fasting glucose (N=27), impaired glucose tolerance (N=167), and new diagnosed diabetes preserved the trends that we observed although the significance was diminished due to a loss of statistical power.

Conclusion: South Asians have an unfavourable adipokine profile compared to other ethnic groups, and like the Aboriginal people, display a greater increase in insulin resistance with decreasing levels of adiponectin. Differences in adipokines and responses to glycemic foods parallel the increased propensity of certain ethnic groups to develop insulin resistance.

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Table 1. Distribution of risk factors among Europeans, Chinese, South Asians, and Aboriginal People living in Canada [mean (SE)].

| Risk Factor                          | European (n=312) | Chinese (n=303) | South Asian (n=317) | Aboriginal (n=244) | Overall P |
|--------------------------------------|------------------|-----------------|---------------------|---------------------|-----------|
| Age, years                           | 51.3 (0.6)       | 47.8 (0.6)      | 49.4 (0.6)          | 52.9 (0.6)          | <0.001    |
| Female, N (%)                         | 160 (51.3)       | 150 (49.5)      | 142 (44.8)          | 141 (57.8)          | 0.169     |
| Current smoker, N (%)                 | 52 (16.7)        | 17 (5.6)        | 32 (10.1)           | 97 (39.8)           | <0.05     |
| Body mass index, kg/m² †              | 27.5 (0.3)       | 23.8 (0.3)      | 26.1 (0.3)          | 31.9 (0.3)          | <0.001    |
| Waist-to-hip ratio †                  | 0.87 (0.004)     | 0.86 (0.004)    | 0.88 (0.004)        | 0.93 (0.004)        | <0.001    |
| LDL cholesterol, mmol/L †             | 3.17 (0.05)      | 3.14 (0.05)     | 3.29 (0.04)         | 3.16 (0.05)         | 0.085     |
| HDL cholesterol, mmol/L †             | 1.19 (0.02)      | 1.19 (0.02)     | 1.05 (0.02)         | 1.07 (0.02)         | <0.001    |
| Triglycerides, mmol/L †               | 1.39 (0.07)      | 1.46 (0.08)     | 1.79 (0.20)         | 3.32 (0.28)         | <0.001    |
| C-reactive protein, mg/L †            | 1.25 (0.17)      | 0.70 (0.14)     | 1.79 (0.20)         | 3.32 (0.28)         | <0.001    |
| Free fatty acids, mEq/mL †            | 512 (13)         | 523 (13)        | 535 (13)            | 544 (14)            | 0.35      |
| HDL cholesterol, mmol/L               | 6.08 (0.17)      | 6.79 (0.17)     | 7.14 (0.16)         | 6.41 (0.19)         | <0.001    |
| Fasting glucose, mmol/L               | 3.18 (0.05)      | 3.14 (0.05)     | 3.29 (0.04)         | 3.16 (0.05)         | 0.085     |
| HbA1c, %                              | 5.32 (0.04)      | 5.59 (0.04)     | 5.76 (0.04)         | 5.95 (0.05)         | <0.001    |
| Impaired fasting glucose, N (%)        | 8 (2.6)          | 1 (0.3)         | 7 (2.2)             | 11 (4.5)            | 0.16      |
| Impaired glucose tolerance, N (%)     | 35 (11.2)        | 46 (15.2)       | 56 (17.7)           | 30 (12.3)           | 0.11      |
| Newly diagnosed type 2 diabetes, N (%)¶ | 16 (5.1)        | 12 (4.0)        | 27 (8.5)            | 21 (8.7)            | 0.02      |
| Systolic blood pressure, mm Hg †      | 119 (0.9)        | 119 (0.9)       | 120 (0.9)           | 118 (1.0)           | 0.625     |
| Diastolic blood pressure, mm Hg †     | 73 (0.6)         | 75 (0.6)        | 76 (0.6)            | 67 (0.6)            | <0.001    |
| Energy intake, kcals †                | 1994 (41)        | 1850 (44)       | 1754 (42)           | 2218 (49)           | <0.001    |
| High physical activity, N (%)         | 90 (31.6)        | 44 (16.7)       | 43 (15.5)           | 41 (22.9)           | <0.001    |
| Physical activity, hrs/wk †           | 8.05 (0.09)      | 7.11 (0.09)     | 7.25 (0.09)         | 7.74 (0.10)         | <0.001    |
| Adiponectin, µg/mL ‡                  | 10.89 (0.86)     | 7.53 (0.88)     | 8.26 (0.45)         | 9.63 (0.39)         | <0.0001   |
| Leptin, ng/mL §                       | 5.93 (0.86)      | 5.37 (0.88)     | 7.24 (0.60)         | 5.37 (1.39)         | <0.0001   |

† Means are adjusted for age and sex.
‡ Geometric means for adiponectin are adjusted for age and waist circumference (since adiponectin is highly correlated with waist girth).
¶ New clinically-diagnosed type 2 diabetes as determined by 2-hour oral glucose tolerance test.
§ Geometric means for leptin are adjusted for age and body mass index (since leptin is highly correlated with body mass index).
1 P<0.05, European versus Chinese.
2 P<0.05, European versus South Asian.
3 P<0.05, European versus Aboriginal People.
4 P<0.05, Chinese versus South Asian.
5 P<0.05, Chinese versus Aboriginal People.
6 P<0.05, South Asian versus Aboriginal People.