

Short Communication

Total *n*-3 fatty acid and SFA intakes in relation to insulin resistance in a Canadian First Nation at risk for the development of type 2 diabetesCatherine Paquet^{1,2}, Sarah L Propsting¹ and Mark Daniel^{1,3,*}¹Social Epidemiology and Evaluation Research Group, Sansom Institute for Health Research, School of Population Health, Division of Health Sciences, University of South Australia, GPO Box 2471, City East Campus, Adelaide, SA 5001, Australia; ²Research Centre of the Douglas Mental Health University Institute, Montreal, Canada; ³Department of Medicine, St Vincent's Hospital, The University of Melbourne, Melbourne, Australia

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Abstract

Objective: The present study sought to investigate the associations of total *n*-3 fatty acid and SFA intakes with insulin resistance in a Canadian First Nation sample at risk for type 2 diabetes.

Design: Fasting values for glucose and insulin were used to estimate insulin resistance by homeostasis model assessment (HOMA-IR). Intakes of *n*-3 fatty acids and SFA were computed from dietary food and drink data obtained using 3 d food records. Associations between HOMA-IR and dietary *n*-3 and SFA consumption were tested using linear regression models accounting for age, sex, community, education, physical activity, waist circumference, fibre, protein and carbohydrate intakes, and HDL-cholesterol and TAG concentrations.

Setting: Rural Okanagan region of British Columbia, Canada.

Subjects: On-reserve First Nation individuals (Interior Salishan) aged 18 years and over, recruited for community-based diabetes screening and determined to be normoglycaemic (*n* 126).

Results: HOMA-IR was negatively associated with dietary *n*-3 fatty acid intake ($\beta = -0.22$; 95% CI $-0.39, -0.04$; $P = 0.016$) and positively associated with dietary SFA intake ($\beta = 0.34$; 95% CI $0.15, 0.53$; $P = 0.001$).

Conclusions: Intake of dietary *n*-3 fatty acids may be protective against whereas SFA intake may promote insulin resistance in this high-risk Canadian First Nation sample. Reduced dietary SFA intake and greater *n*-3 fatty acid intake may assist the prevention of glycaemic disease among First Nations peoples. More rigorous, controlled trials are required to test whether dietary supplementation with *n*-3 fatty acids in natural or supplement-based form might reduce diabetes risk in high-risk aboriginal groups.

Keywords
n-3 Fatty acids
Insulin resistance
Aboriginal peoples

Aboriginal populations worldwide are disproportionately affected by type 2 diabetes mellitus⁽¹⁾. Recent dramatic increases in the prevalence of type 2 diabetes in aboriginal populations have been attributed to rapid 'westernisation'⁽²⁾. In Canada, epidemic rates of diabetes exist among the aboriginal population, with crude prevalence rates being 3.6 to 5.3 times higher than corresponding rates for non-aboriginal Canadians⁽³⁾.

Population-based primary prevention of diabetes through efforts to change the overall nature of dietary behaviour has had limited successes thus far. However the potential remains for prevention through more targeted changes in

the nature of dietary fat consumed. *n*-3 Fatty acids have been proposed to have a protective role against insulin resistance and consequently diabetes in aboriginal and non-aboriginal populations^(4,5). Epidemiological studies have reported a lower prevalence of insulin resistance and type 2 diabetes in Greenland Inuit and sub-Arctic native populations whose diets vary from those typical of mainstream Western European, Australian or North American populations^(5,6). These diets vary not so much in the total quantity of fat, but in its quality, being higher in *n*-3 fatty acids and lower in SFA^(5,7). SFA, on the other hand, have been implicated to have detrimental effects on insulin resistance⁽⁸⁾.

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Little research has investigated the relationship between dietary fats and glycaemic disease for aboriginal populations residing outside the sub-Arctic zone. It is important to investigate such associations in other aboriginal populations similarly at risk for the development of type 2 diabetes, but for which the food supply is not dominated to such a degree by local seafood high in *n*-3 fatty acids. Therefore the present study sought to assess the relationship between total *n*-3 fatty acid and SFA intakes and insulin resistance in a Canadian First Nation sample at high risk for the development of diabetes. Such research has important public health implications for influencing dietary recommendations in First Nations populations suffering an excess burden of insulin resistance and glycaemic disease.

Methods

Data collection

Data analysed in the present observational study were drawn from a diabetes screening initiative conducted among on-reserve First Nation people (Interior Salishan, Plateau Area) in the rural Okanagan region of British Columbia, Canada. The sampling and methodology of the study have been reported previously⁽⁹⁾. The study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the University of British Columbia. Written informed consent was obtained from all participants.

Participants were recruited through community meetings. Individual volunteers for screening were required to be aged 18 years or older and at high risk for diabetes (overweight or obese, and having a family member with type 2 diabetes). Pregnant women and persons with known diabetes were excluded from screening. Fifty-seven per cent of eligible persons (*n* 198) identified from community health records as being overweight (BMI \geq 25 kg/m²) participated in the survey. The main reason for non-participation was lack of interest. Male sex and age less than 30 years were the main correlates of non-participation. All testing was done in meeting halls between 07.30 and 12.00 hours by laboratory technicians and registered nurses from a local hospital. Glycaemic status was determined using a 2-h oral glucose tolerance test with a 75-g carbohydrate load. Participants were classified using WHO criteria as normoglycaemic or having glycaemic disease (2-h glucose \geq 11.1 mmol/l)⁽¹⁰⁾. Only normoglycaemic participants were considered in the present study.

Measures

Insulin resistance was calculated using the homeostasis model assessment (HOMA-IR) algorithm⁽¹¹⁾ from blood glucose and insulin concentrations determined from 12 h fasting venous blood samples. HOMA-IR is used widely in

epidemiological studies and has been validated against 'gold standard' hyper-euglycaemic and hyper-glycaemic clamps respectively^(11,12). Assays were performed on serum specimens obtained on-site and stored at 4°C until analysis on the day of collection. Glucose was assessed via enzymatic assay kits (Kodak Ektachem[®]; Eastman Kodak Co., Rochester, NY, USA); insulin was measured via microparticle immunoassay kits (IMx[®]; Abbott Laboratories, Abbott Park, IL, USA). Intra- and inter-assay coefficients of variation were respectively 1.2% and 1.8% for glucose and 3.8% and 4.2% for insulin.

Dietary food and drink intake was assessed for the week following screening using self-completed records maintained over three consecutive days, including one weekend day. Participants received training by registered nurses and dietitians on how to record their food consumption. Three-dimensional models and illustrations were used to portray serving sizes. All records were rigorously reviewed for completeness and then coded following clarification, verification and/or revision of unusual or likely incorrect responses. Nutrient intakes were computed by a registered dietitian-nutritionist using the Canadian Dietary Information System (CANDI) version 4.0 for food intake analysis, which includes traditional foods consumed by First Nations in Canada⁽¹³⁾. Total grams of *n*-3 fatty acids and SFA consumed over the 3 d period were determined. The reliability and validity of self-report 3 d estimate food records are established⁽¹⁴⁾.

Anthropometric, lipid, sociodemographic and behavioural measures were also obtained. All anthropometric measures were taken three times by the same two registered nurses. Only the median of the three values was retained for analyses. Body mass and height were measured using a beam balance scale and stadiometer. BMI was calculated as body mass (in kilograms) divided by the square of height (in metres). Waist circumference measures were taken where the waist was best defined, halfway between the costal border and the iliac crest. High waist circumference was defined as \geq 88 cm for women and \geq 102 cm for men. Concentrations of TAG and HDL-cholesterol (HDL-C) were determined from 12 h fasting venous blood samples and assessed via enzymatic assay kits (Kodak Ektachem[®]; Eastman Kodak Co.). Sociodemographic measures including age, gender and high school graduation were all obtained in a self-reported demographic questionnaire. Behavioural measures included physical activity, smoking status and alcohol consumption. These were surveyed in a lifestyle questionnaire based on the Canadian National Population Health Survey. Each behavioural measure was self-reported and required a 'yes' or 'no' answer. The following questions were used: 'At least once a week, did you engage in any regular activity similar to brisk walking, jogging, bicycling, etc., long enough to work up a sweat?', 'Do you currently smoke cigarettes daily?' and 'Do you drink alcohol?'

Statistical analyses

Of 198 persons screened with an 2-h oral glucose tolerance test, complete data were available for 142 of whom ten had impaired glucose tolerance (2-h glucose ≥ 7.0 and < 11.1 mmol/l) and six had previously unknown diabetes (2-h glucose ≥ 11.1 mmol/l)⁽¹⁰⁾. These sixteen individuals were excluded from statistical analyses. HOMA-IR values were log transformed and modelled against total n-3 fatty acid and SFA intakes. The linear regression model accounted for age, gender, community, education, physical activity, waist circumference, HDL-C and TAG concentrations. Analyses also accounted for additional measures of diet including fibre, protein and carbohydrate intakes expressed as a proportion of total energy intake. Total fat intake, however, was not included in models given its high correlation with total SFA intake already included in models

($r = 0.95$). Accounting for the above covariates, especially additional measures of dietary intake, is important to illustrate that total n-3 fatty acid intake is not merely a marker for low SFA intake, high fibre intake and/or more physical activity⁽¹⁵⁾. Smoking was considered as a covariate but was not found to be statistically significantly related to HOMA-IR and was thus removed to conserve statistical power. Continuous independent variables were standardised prior to analyses. Statistical significance was set at $\alpha = 0.05$. Analyses were conducted using the statistical software package SPSS® version 17.0.

Results and discussion

Characteristics of the participants and results from the regression analysis are reported in Tables 1 and 2,

Table 1 Characteristics of participants: on-reserve First Nation individuals (Interior Salishan) aged 18 years and over (n 126), rural Okanagan region of British Columbia, Canada

Variable	Mean	SD	Percentile	
			25th	75th
Age (years)	40.7	12.7	29.8	47.8
BMI (kg/m ²)	28.5	5.6	24.8	31.9
3 d intake of total n-3 fatty acids (g)	3.9	2.4	2.1	5.0
3 d intake of total SFA (g)	59.2	30.9	39.5	70.5
Fasting glucose (mmol/l)	5.2	0.7	4.9	5.3
Fasting insulin (pmol/l)	96.0	103.6	43.4	97.3
HOMA-IR	23.5	29.1	9.5	23.6
TAG (mmol/l)	2.3	2.6	1.4	2.6
HDL-C (mmol/l)	1.1	0.3	0.9	1.3
2-h glucose (mmol/l)	5.1	1.2	4.2	6.0
	<i>n</i>		<i>%</i>	
Female/male	85/41		67.5/32.5	
Current smokers	68		54.0	
Sweat-producing physical activity ≥ 1 time/week	86		68.3	
Consumes alcohol	58		46.0	
High school graduate	53		42.1	
High waist circumference (≥ 88 cm women, ≥ 102 cm men)	55		43.7	

HOMA-IR, homeostasis model assessment of insulin resistance; HDL-C, HDL-cholesterol.

Table 2 Parameter estimates for multivariable analyses of relationships between HOMA-IR, dietary n-3 fatty acid and SFA intakes* among on-reserve First Nation individuals (Interior Salishan) aged 18 years and over (n 126), rural Okanagan region of British Columbia, Canada

Predictor	Regression coefficient†	95% CI	P
Total n-3 fatty acids	-0.22	-0.39, -0.04	0.016
Total SFA	0.34	0.15, 0.53	0.001
HDL-C	-0.14	-0.33, 0.05	0.15
TAG	0.15	0.00, 0.31	0.05
Protein (% of TEI)	0.26	0.04, 0.48	0.02
Dietary fibre (% of TEI)	-0.05	-0.23, 0.12	0.56
Carbohydrates (% of TEI)	0.15	-0.06, 0.36	0.16
Age	-0.04	-0.21, 0.13	0.64
Gender (male)	-0.18	-0.51, 0.15	0.29
High school graduate (yes)	-0.47	-0.75, -0.20	0.001
Physical activity (yes)	-0.54	-0.84, -0.25	<0.001
High waist circumference (yes)	0.58	0.28, 0.88	<0.001

HOMA-IR, homeostasis model assessment of insulin resistance; HDL-C, HDL-cholesterol; TEI, total energy intake.

*The model also adjusts for community.

†Regression coefficients for continuous measures are for 1 SD increments.

respectively. In this sample of First Nation individuals in rural British Columbia, insulin resistance was inversely associated with *n*-3 fatty acid intake and positively associated with SFA intake (Table 2).

A comprehensive literature review suggests that the current study is the first one published reporting such associations for an aboriginal sample at risk for the development of diabetes, outside the Arctic zone. The results are consistent with observational studies^(16,17) of Greenland Inuit and Alaska Natives that reported an inverse association between dietary *n*-3 fat intake and insulin resistance. However, the results of these studies may to some degree be confounded by overall macronutrient profile, particularly other dietary components that correlate with both *n*-3 fatty acid intake and insulin resistance. The current study does not suffer the same limitation.

Our results are consistent with findings from studies conducted in non-aboriginal populations, which generally support an association between *n*-3 fatty acids consumption and insulin resistance and sensitivity. For instance, Tsitouras and colleagues⁽¹⁸⁾ have reported improvement in insulin sensitivity following an 8-week diet rich in *n*-3 fatty acids. Three randomised controlled trials found that *n*-3 fatty acids had a lowering effect on insulin resistance⁽¹⁹⁾ and improved insulin sensitivity^(20,21). Other randomised controlled trials^(22,23) yielded changes in insulin resistance in the expected direction, although these results were not statistically significant.

Furthermore, it appears that previous dietary studies of aboriginal populations have not yet assessed the relationship between insulin resistance and SFA. The results of the present study are consistent with speculations previously made for aboriginal populations, that a lower dietary intake of SFA might correspond to a lower level of glycaemic disease⁽⁶⁾. Some work has attributed increasing rates of diabetes in Arctic and other aboriginal populations to a change from traditional to westernised diets^(2,6), due in part to the increase in dietary SFA, but any such changes have yet to be investigated longitudinally. The results of randomised controlled trials in non-aboriginal populations both support^(24,25) and contradict^(26,27) a link between insulin resistance and SFA.

The limited detailed dietary research conducted thus far on diet and insulin resistance in aboriginal populations in field settings supports the value of the present study. Research in First Nations settings is challenging, and designs such as randomised controlled trials are widely resisted by aboriginal people⁽²⁸⁾. The associations observed serve to provide a stronger basis for the hypothesised protective role of *n*-3 fatty acids that might subsequently be pursued with stronger, more internally valid, albeit less generalisable, research designs removed from field settings in future research with aboriginal people.

The main limitation of the present study is its cross-sectional design, which precludes knowing the

directionality of the observed relationships and whether the associations are causal. It is, however, an initial step to revealing these relationships. Future research is needed to determine the temporal relationship of change in *n*-3 fatty acids and SFA in relation to change in insulin resistance and β -cell function. A further limitation was the limited sample size of 126 participants. Although small for an epidemiological study, this sample size still provided adequate power to detect statistically significant associations. The focus of the study on normoglycaemic individuals at high risk of diabetes (relatives of persons with diabetes and/or overweight or obese) precludes inference that the results are representative of the overall base population. Finally, gold-standard methods for the assessment of insulin resistance, the hyper-euglycaemic and the hyperglycaemic clamp techniques, could not be used in this research. Both such methods are expensive, labour intensive, invasive and time consuming, and thus impracticable for field-based epidemiological studies. The measurement method used in the present study, HOMA-IR, is appropriate for such studies and has been validated against gold standards.

Conclusions

Our results, which account for a spectrum of confounding influences including macronutrient profile, suggest that total dietary *n*-3 fatty acids may be protective against insulin resistance, and that SFA may promote insulin resistance which may precede the development of diabetes in First Nations individuals. These results, specific to a non-Arctic high-risk aboriginal group, hold a key position for furthering dietary research relevant to the prevention of diabetes in such populations. Our data suggest that the nature or quality of fat consumed is of key importance in relation to insulin resistance and glycaemic risk for aboriginal people.

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