

The impact of diabetes on cardiovascular risk factors and outcomes in a native Canadian population

Stewart B. Harris^b, Bernard Zinman^{a,f,*}, Anthony Hanley^a, Joel Gittelsohn^c,
Robert Hegele^d, Phillip W. Connelly^e, Baiju Shah^f, Janet E. Hux^f

^a Samuel Lunenfeld Research Institute, Mount Sinai Hospital, 600 University Avenue, Suite 782, Toronto, Ont., Canada M5G 1X5

^b Department of Family Medicine, Department of Biostatistics and Epidemiology, The University of Western Ontario, London, Ont., Canada

^c Division of Human Nutrition, Department of International Health, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, MD, USA

^d Robarts Research Institute, The University of Western Ontario, London, Ont., Canada

^e Departments of Medicine, Biochemistry and Clinical Biochemistry, St. Michael's Hospital, University of Toronto, Toronto, Ont., Canada

^f Department of Medicine, University of Toronto, Toronto, Ont., Canada

Received 19 December 2000; received in revised form 7 May 2001; accepted 25 July 2001

Abstract

We measured cardiovascular disease (CVD) risk factors and their relationship to glucose intolerance in a Native Canadian population with very high rates of Type 2 diabetes mellitus. Five hundred and twenty five study-eligible Ojibwa-Cree individuals age 18 and over in the community of Sandy Lake, Canada who had participated in a population-based survey were studied. Diabetes status, plasma concentrations of total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), calculated low density lipoprotein-cholesterol (LDL-C), waist/hip ratio (WHR), BMI, systolic and diastolic BP, and history of smoking were compared to a standard national population. Extremely high rates of obesity (BMI and WHR) were identified in the study population and were associated with increasing glucose intolerance for both males and females. Rates of smoking exceeded 70 and 80% in females and males, respectively. Interestingly, despite obesity individuals who had normal glucose tolerance had significantly lower rates of high risk TC, TG, LDL-C, and HDL-C levels compared to a national Canadian population survey. However, with worsening glucose intolerance, TC, TG, LDL-C and HDL-C dramatically deteriorated in comparison to nationally published levels. These changes in cardiovascular risk factors, as a consequence of diabetes, appear to result in increased clinical outcomes. Admission to hospital for Ischemic Heart Disease (IHD) for Sandy Lake residents increased from a rate of 34.8/10 000 to 109.1/10 000 in 15 years. Although this and similar populations have historically reported low rates of CVD, the impact of diabetes on lipid risk factor is having devastating consequences on cardiovascular outcomes. This trend is expected to continue unless the high rates of diabetes can be modified. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Cardiovascular disease risk factors; Type 2 diabetes; Native Canadians

* Corresponding author. Tel.: +1-416-586-8747; fax: +1-416-586-4740.

E-mail address: zinman@mshri.on.ca (B. Zinman).

1. Introduction

The last two to three decades have witnessed the rising prevalence of diabetes mellitus (DM) in Native American populations [1–4]. This is consistent with the shift in disease burden in these groups from infectious to chronic diseases. It is believed to be due to a dramatic change in lifestyle coupled with a genetic susceptibility resulting in the development of obesity and associated conditions, including DM [5]. A number of studies have examined the relationship of glucose intolerance and associated cardiovascular disease risk factors in these populations [6–9]. Although mortality due to cardiovascular disease (CVD) varies significantly in these studies, there is general consensus that the problem is becoming progressively more serious [6–8]. In Canada, mortality due to CVD in Native Canadians has been reported to be lower than the standardized mortality for the general population [10]. There have been no studies however to describe the relationship of glucose intolerance to CVD risk factors and clinical outcomes in these populations.

The Sandy Lake Health and Diabetes Project (SLHDP) reported in detail the prevalence of diabetes and its associated risk factors in this isolated native population in Northern Ontario [1,11–15]. This community is typical for many remote Native communities in Canada and has undergone major cultural shifts in lifestyle over the last four to five decades. The community was identified as having the third highest published age-adjusted prevalence of Type 2 DM and impaired glucose intolerance (IGT) of 26.1 and 13.6%, respectively [1]. In this paper we will describe the association of CVD risk factors with glucose status and its apparent consequences on ischemic heart disease (IHD) outcomes.

2. Materials and methods

The community of Sandy Lake (Ont., Canada) is located in a remote area of Northern Canada. Approximately 1600 people live in this community which is only accessible by air for most of the

year. Historically the inhabitants of this area lived in small semi-nomadic groups that lead a hunting-gathering subsistence. Diet consisted primarily of protein from wild meats and fish. A dramatic change in lifestyle, characterized by a decrease in physical activity and an alteration in the diet has occurred in the people of this region. This population is consequently undergoing an epidemiological transition with a marked increase in morbidity related to chronic diseases such as obesity and type 2 DM.

The methodology of the SLHDP has been described in detail elsewhere [16]. The analysis for this paper is based on 525 individuals who were 18 years and older at the time of the community-wide survey which took place from July 1993 to March 1995. Signed informed consent was obtained from all participants with ethics review and approval coming from both The University of Toronto Human Subjects Review Committee and the Sandy Lake First Nations Band Council.

Volunteers provided fasting-blood samples for glucose and lipids following an overnight fast. A 75-g oral glucose tolerance test (OGTT) was administered and a second blood sample for glucose was drawn after 120 min. Individuals were excluded from the OGTT if they had physician-diagnosed diabetes (a) were currently receiving treatment with insulin or oral hypoglycemic agents, or (b) if they had a fasting blood glucose exceeding 11.1 mmol/l. DM and IGT were diagnosed according to established criteria [17]. Fasting plasma concentrations of total cholesterol (TC), total triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C) were measured according to standard techniques [18]. Concentration of low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald formula [19].

Anthropometric measurements were performed without shoes and with the volunteer wearing light undergarments. All measurements were performed twice and the mean was used in this analysis which included height and weight. Body mass index (BMI) was then calculated as weight/height² (kg/m²). Waist was measured to the nearest 0.5 cm at the point narrowing between the umbilicus and xiphoid process; the hips were mea-

sure to the nearest 0.5 cm at maximum extension of the buttocks. Waist–hip ratio was then calculated as the ratio between these two circumferences. Percent body fat (% fat) was estimated by bioelectrical impedance analysis (BIA) using the Tanita TBF-201 Body Fat Analyzer (Tanita Corp., Tokyo). This technique was previously validated in patients with Type 2 DM [20].

Blood pressure was measured in the right arm with the volunteer seated. Systolic blood pressure was recorded to nearest 2 mmHg at the appearance of the first Korotkoff sound; diastolic pressure was recorded to the nearest 2 mmHg at the disappearance of the fifth Korotkoff sound. Two measurements were performed and the mean of the two was used in the analysis. Information regarding the new lifetime smoking behaviour was recorded on interviewer-administered questionnaires.

A separate administrative data base evaluating admission rates to hospital for IHD was used to determine IHD outcomes in this community over a 15-year time frame (1993–1997). The International Classification of Diseases of the World Health Organization, 9th revision (ICD-9) codes was used to identify IHD admissions for patients whose home residence was Sandy Lake. These data were obtained from The Canadian Institute for Health Information (CIHI), an administrative database containing abstracts of all hospital discharges. Census population data for Sandy Lake was used as the denominator, with interpolated values using linear regression for the intercensus years. Annual crude rates were then age- and sex-adjusted to the Provincial population using census data from 1991. Individuals from the study population were identified utilizing the mailing location code, which identified the community of the patient's home address.

All statistical analysis was conducted using SAS Version 6.09 in the VMS environment. Data are presented as means, standard deviations and medians, or proportions, where appropriate. Distributions of continuous variables were tested for normality, and natural log transformations of skewed variables were used in subsequent regression analyses.

High risk cut-off points for cardiovascular disease were derived from those employed by the Canadian Heart Health Surveys (CHHS) [21]. This was a national survey carried out at the same time as the SLHDP and was thus used as a comparative standard population. In this context, obesity was defined as body mass index (BMI) of ≥ 27 . Abdominal obesity was defined as a waist–hip ratio (WHR) of ≥ 0.9 for men and ≥ 0.8 for women. High blood pressure was defined as a systolic blood pressure ≥ 140 or a diastolic blood pressure ≥ 90 or current use of medication for hypertension. High-risk lipid levels were defined as follows: TC ≥ 6.2 mmol/l; TG ≥ 2.3 mmol/l; LDL-C ≥ 4.1 mmol/l; HDL-C < 0.9 mmol/l.

To adjust for age-structure differences, the Sandy Lake admissions rates were standardized to the 1991 census population of Ontario using the direct method, as both surveys were carried out during the same timeframe. Confidence intervals were not constructed given that the objective of the project was to survey the entire population rather than utilize the random sample.

3. Results

The cardiovascular risk factors among adult subjects (age 18–74) from the study community are presented in Table 1. Means, and standard deviation for each risk factor were stratified by sex and diabetes status. As can be noted in the table, the majority of cases of IGT were found in females compared to males (52 vs. 14). Both measures of obesity (BMI and WHR) were associated with increasing glucose intolerance for both sexes. The mean levels were higher in females for BMI but the WHR means were higher in males. TC, TG and LDL-C also increased with deterioration of glucose tolerance for both males and females with the mean levels consistently higher in males. The males had overall lower mean HDL-C values compared to females but the difference is not significant. Blood pressure measurements did not show a significant change with worsening glucose tolerance. Extremely high rates of smoking were noted for both males and females.

Fig. 1 presents the age-standardized prevalence rates of obesity (WHR, BMI) stratified by glucose tolerance status comparing the study population to nationally published rates from the CHSS. As is demonstrated, the burden of obesity is high in the study population, especially in females and increases with worsening glucose tolerance.

Fig. 2 presents the age-standardized prevalence of individuals exceeding high-risk lipid thresholds (TC, LDL-C, HDL-C, and TG) compared to national rates from the CHSS. As can be seen, normal Sandy Lake residents have lower rates of high risk lipids but dyslipidemia (particularly high

risk triglyceride and HDL) worsens as IGT and Type 2 DM develop.

Table 2 presents the multiple linear regression analyses of factors associated with serum lipid abnormalities and blood pressure for those aged 18–79. As can be seen, age was an independent risk factor for TC, LDL-C, HDL-C, SBP and DBP. Sex was identified as a risk factor for only HDL-C, and BP (SBP, DBP). Obesity measurements, especially WHR, were significant predictors of all serum lipids. Glucose intolerance (IGT and DM) was independently predictive of TG, HDL-C, and systolic BP. HT treatment was asso-

Table 1
Cardiovascular risk factors among adult subjects (age 18–74), the Sandy Lake Health and Diabetes Project

Cardiovascular risk factor	Male			Female		
	NGT	IGT	Type 2 DM	NGT	IGT	Type 2 DM
<i>n</i>	168	14	48	172	52	71
Age	32.11 (12.70)	45.98*** (17.82)	45.91**** (13.91)	30.61 (11.32)	41.23**** (15.62)	44.67**** (15.09)
BMI (kg/m ²)	26.07 (4.49)	28.20 (3.79)	29.30**** (4.40)	27.90 (5.70)	30.98*** (5.11)	30.61*** (4.70)
Waist (cm)	94.91 (12.05)	100.94 (8.19)	103.87**** (10.73)	91.65 (11.91)	99.09**** (9.48)	99.96**** (11.05)
WHR (cm/cm)	0.94 (0.07)	0.98* (0.04)	0.99**** (0.06)	0.86 (0.05)	0.89** (0.04)	0.91**** (0.06)
Body fat (%)	26.98 (7.70)	30.79 (5.29)	29.20 (6.56)	43.68 (9.64)	48.18** (5.88)	46.11* (8.16)
Cholesterol (mmol/l)	4.71 (0.99)	5.19 (0.90)	5.27 (0.94)	4.36 (0.70)	4.79**** (0.56)	5.07**** (0.98)
Triglyceride (mmol/l)	1.47 (0.73)	2.05* (1.11)	2.23**** (1.30)	1.28 (0.53)	1.62*** (0.69)	2.00**** (0.90)
LDL-C (mmol/l)	2.84 (0.85)	3.12 (0.61)	3.16** (0.70)	2.49 (0.59)	2.79*** (0.53)	2.87**** (0.75)
HDL-C (mmol/l)	1.22 (0.29)	1.14 (0.32)	1.09** (0.28)	1.30 (0.27)	1.26 (0.28)	1.26 (0.30)
Systolic BP (mmHg)	120.69 (13.66)	132.75** (23.14)	125.83* (13.88)	113.31 (13.25)	123.25**** (15.63)	124.78**** (17.88)
Diastolic BP (mmHg)	69.19 (12.72)	75.07 (16.22)	74.00 (9.41)	65.08 (10.15)	67.99 (11.08)	69.30** (9.17)
Smoking (% current)	80.36	50.00	43.75	73.26	51.92	53.52

Values are means with S.D. in parentheses. BMI, body mass index; WHR, waist-to-hip ratio; Cholesterol, total cholesterol; Triglyceride, total triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; BP, blood pressure; NGT, normal glucose tolerance; IGT, impaired glucose tolerance; Type 2 DM, diabetes mellitus.

* $P < 0.05$.

** $P < 0.01$.

*** $P < 0.001$.

**** $P < 0.0001$.

Table 2
Multiple linear regression of factors associated with serum lipids and blood pressure (age 18–79), Sandy Lake Health and Diabetes Project

Independent variables	In TC		In TG		In LDL-C		In HDL-C		In SBP		In DBP	
	β	ρ	β	ρ	β	ρ	β	ρ	β	ρ	β	ρ
Ln age	0.1351	0.0001	-0.0305	0.5935	0.1621	0.0001	0.1473	0.0001	0.1042	0.0001	0.0501	0.0248
Sex	0.0107	0.5853	0.0013	0.9774	-0.0060	0.8317	0.0658	0.0075	-0.0647	0.0001	-0.0528	0.0039
BMI	0.0003	0.8625	0.0197	0.0001	0.0019	0.4150	-0.0093	0.0001	0.0060	0.0001	0.0083	0.0001
WHR	0.8689	0.0001	2.1171	0.0001	1.3100	0.0001	-0.6631	0.0003	-0.1172	0.1945	0.2602	0.0575
Glucose intol.	0.0352	0.0460	0.2418	0.0001	0.0051	0.8398	-0.0542	0.0146	0.0145	0.0185	-0.0005	0.9741
HT treatment	0.0526	0.0699	0.1105	0.1132	0.0422	0.3140	0.0187	0.6077	0.1093	0.0001	0.0731	0.0071
Current smoking	0.0199	0.2319	0.0927	0.0208	-0.0153	0.5216	0.0206	0.3251	-0.0108	0.2916	0.0153	0.3256
Model R^2	0.280		0.305		0.260		0.170		0.345		0.190	

TC, total cholesterol; TG, total triglyceride; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; glucose intolerance (0, normal glucose intolerance; 1, impaired glucose intolerance or Type 2 Dm); HT treatment, on hypertension medication (0, no; 1, yes); Smoking, currently smoking (0, no; 1, yes).

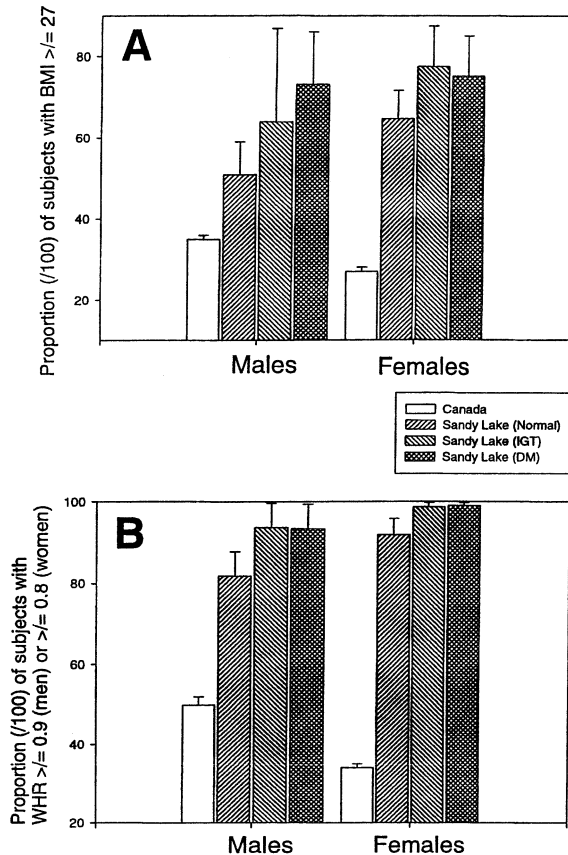


Fig. 1. Prevalence (%; 95% confidence intervals (CI)) of obesity in Sandy Lake compared to the general population of Canada, by gender and glucose tolerance status. Data are age-standardized to the 1991 national population of Canada using the direct method. (A) Obesity defined as BMI ≥ 27 (males: NGT vs. Canada, $P < 0.0001$, IGT vs. Canada, $P < 0.05$, DM vs. Canada, $P < 0.0001$; females: NGT, IGT, and DM vs. Canada, all $P < 0.0001$). (B) Abdominal obesity defined as WHR ≥ 0.9 (men) or ≥ 0.8 (women) (males: NGT vs. Canada, $P < 0.0001$, IGT vs. Canada, $P < 0.05$, DM vs. Canada, $P < 0.0001$; females: NGT, IGT, and DM vs. Canada, all $P < 0.0001$).

ciated with SBP and DBP and smoking was only predictive for TG.

Fig. 3 shows rates of IHD admissions per 5-year intervals from 1983 to 1997 for individuals from the study community. Clearly IHD rates have increased dramatically over this timeframe rising from a rate of 34.8 per 10000 to 109.1/10000 in contrast to the declining rates in the population of the province of Ontario [22].

4. Discussion

Although high prevalence rates of diabetes have been described for many Native populations, the full impact of this metabolic abnormality on microvascular and macrovascular complications appears to be evolving. In the Sandy Lake population, we documented a high prevalence of obesity as evidenced by a high mean BMI and WHR in the study population (Table 1). However, obesity itself, which is endemic in this community, was not sufficient to adversely affect lipid levels compared to national norms. Nonetheless, obesity is a major risk factor for Type 2 Diabetes. This has been demonstrated in other studies, which documented worsening glucose tolerance associated with an increase in obesity for both males and females [2,8]. WHR was also shown to be a significant predictor for diabetes (Table 2), consistent with the important pathophysiological role of visceral obesity in mediating insulin resistance. Of interest, in the Sandy Lake population increased TNF α levels appear to be associated with the insulin resistance state as well as hypertension [15]. These risk factors for diabetes, coupled with the extremely high rates of smoking in the community, all contribute to a CVD potential. Interestingly, smoking was identified as an independent risk for elevated TG (Table 2). This is consistent with other reports on the effects of smoking on lipids [23,24].

Our findings of excellent lipid levels in normal subjects compared to the Canadian standard is consistent with previous studies reporting lower serum lipid levels in American Indians compared to the general population [8,25,26]. The Strong Heart Study, reported mean TC concentrations consistently lower for both males and females than the general US population [8]. In studies of Pima Indians, men and women were found to have lower serum concentrations of total and LDL cholesterol compared to Caucasians [26]. HDL levels were also lower for both sexes. Of note in the Sandy Lake population, despite obesity normal glucose tolerance was associated with a low risk lipid profile compared to the Canadian population. However, with worsening glucose tolerance, the lipid profile, particularly the TG and

HDL-C levels dramatically deteriorate. Fig. 2 show stepwise worsening of lipids with increasing glucose intolerance for both males and females. However, the magnitude of this deterioration was greater in males.

Thus, it would appear that IGT and DM have a major impact in mediating the lipid abnormalities in this community. These changes translate into clinical endpoints as demonstrated by a tripling of IHD admission rates over a 15-year period (Fig. 3). Our data, if anything, underestimate the true burden of IHD due to the known

limitations of hospital data recording and missed pre-hospitalization IHD morbidity. Our study supports the concept that the development of DM and IGT is the primary pathophysiologic event responsible for IHD in aboriginal Canadian communities. This observation highlights the imperative of dealing effectively with the global epidemic of diabetes in indigenous people.

This study documents the finding that the recent rise in prevalence of diabetes in Aboriginal Canadians is associated with a worsening of their lipid CVD risk factors. Furthermore, the impact

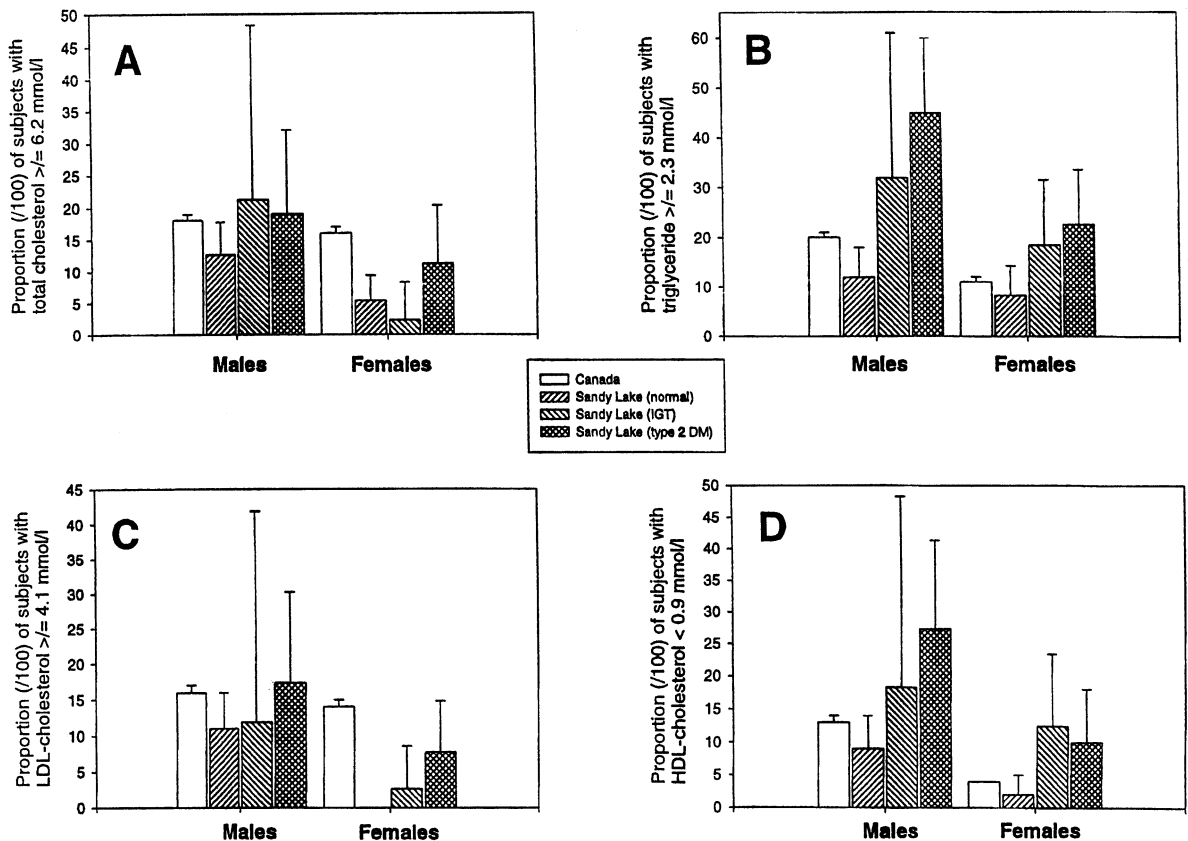


Fig. 2. Prevalence (%; 95% CI) of dyslipidemia in Sandy Lake compared to the general population of Canada, by gender and glucose tolerance status. Data are age-standardized to the 1991 national population of Canada using the direct method. (A) Hypercholesterolaemia defined as cholesterol ≥ 6.2 mmol/l (males: NGT, IGT, and DM vs. Canada, all $P > 0.05$; females: NGT vs. Canada, $P < 0.0001$, IGT vs. Canada, $P < 0.05$, Canada vs. DM, $P > 0.05$). (B) Hypertriglyceridemia defined as triglyceride ≥ 2.3 mmol/l (males: NGT vs. Canada, $P < 0.05$, IGT vs. Canada, $P > 0.05$, DM vs. Canada, $P < 0.0001$; females: NGT and IGT vs. Canada, both $P > 0.05$, DM vs. Canada, $P < 0.0001$). (C) High-risk LDL-cholesterol defined as LDL-C ≥ 4.1 mmol/l (males: NGT, IGT and DM vs. Canada, all $P > 0.05$; females: NGT vs. Canada, $P < 0.01$, IGT vs. Canada, $P < 0.05$, DM vs. Canada, $P > 0.05$). (D) High risk HDL-cholesterol defined as HDL-C < 0.9 mmol/l (males: NGT and IGT vs. Canada, both $P > 0.05$, DM vs. Canada, $P < 0.01$; females: NGT vs. Canada, $P > 0.05$, IGT and DM vs. Canada, both $P < 0.05$).

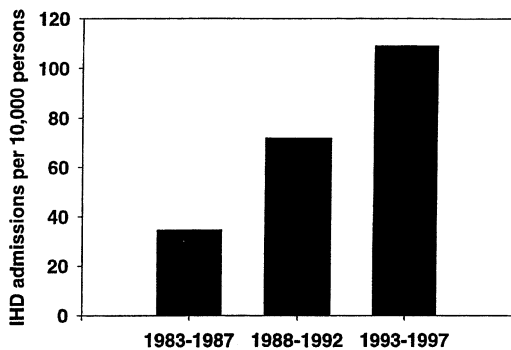


Fig. 3. Rates of admissions to hospital for ischemic heart disease (IHD) events in 5-year intervals from 1983 to 1997 for Sandy Lake community using ICD-9 codes adjusted for age and sex using Provincial Census data from 1991.

of these changes is now being experienced at the community level and highlight the urgent need for primary and secondary prevention strategies targeting diabetes and its associated CVD risk factors [27].

Acknowledgements

The invaluable partnership and support of the Chief and Council of the First Nations people of Sandy Lake, Ontario is gratefully acknowledged. We also wish to acknowledge the community surveyors including Louisa Kakegamic, Tina Noon, Madeline Kakegamic, Annette Rae, Elda Anishinawbe, Areta Bekintis and Tracy Mamokeesic.

References

- [1] S.B. Harris, J. Gittelsohn, A. Hanley, et al., The prevalence of NIDDM and associated risk factors in Native Canadians, *Diabetes Care* 20 (1) (1997) 185–187.
- [2] H.F. Deslisle, J.M. Ekoe, Prevalence of non-insulin dependent diabetes mellitus and impaired glucose intolerance in two Algonquin communities in Quebec, *Can. Med. Assoc. J.* 148 (1993) 41–47.
- [3] C. Fox, S. Harris, E. Brough, Diabetes among Native Canadians in northwestern Ontario: 10 years later, *Chron. Dis. Can.* 15 (1994) 92–96.
- [4] E. Lee, B. Howard, P.J. Savage, et al., Diabetes and impaired glucose tolerance in three American Indian populations age 45–74 years: The Strong Heart Study, *Diabetes Care* 18 (1995) 599–610.
- [5] T.K. Young, Are subarctic Indians undergoing the epidemiologic transition?, *Soc. Sci. Med.* 26 (1988) 659–671.
- [6] B.V. Howard, E.T. Lee, L.D. Cowan, et al., Coronary health disease prevalence and its relation to risk factors in American Indians. The Strong Heart Study, *Am. J. Epidemiol.* 142 (3) (1995) 254–268.
- [7] J.L. Ellis, D. Campos-Outcalt, Cardiovascular disease risk factors in Native Americans: a literature review, *Am. J. Prev. Med.* 10 (5) (1994) 295–307.
- [8] T.K. Welty, E.T. Lee, J. Yeh, et al., Cardiovascular disease risk factors among American Indians: The Strong Heart Study, *Am. J. Epidemiol.* 142 (3) (1995) 269–287.
- [9] A. Gault, K. O’Dea, A.G. Rowley, et al., Abnormal glucose intolerance and other coronary heart disease risk factors in an isolated aboriginal community in Central Australia, *Diabetes Care* 19 (11) (1996) 1269–1273.
- [10] T.K. Young, *The Health of Native Americans: Towards a Biocultural Diversity*, Oxford University Press, New York, 1994.
- [11] T.M. Wolever, S. Hamad, J. Gittelsohn, et al., Nutrient intake and food use in an Ojibwa-Cree community in northern Ontario assessed by 24h dietary recall, *Nutr. Res.* 17 (4) (1997) 603–618.
- [12] J. Gittelsohn, T.M. Wolever, S.B. Harris, R. Harris-Geraldo, A.J.G. Hanley, B. Zinman, Specific patterns of food consumption and preparation are associated with diabetes and obesity in a native Canadian population with high rates of NIDDM, *J. Nutr.* 128 (1998) 541–546.
- [13] A.J.G. Hanley, S.B. Harris, J. Gao, J. Kwan, B. Zinman, Serum immunoreactive leptin concentrations in a Canadian aboriginal population with high rates of NIDDM, *Diabetes Care* 20 (9) (1997) 1408–1415.
- [14] R. Hegele, H. Cao, S.B. Harris, A.J.G. Hanley, B. Zinman, Hepatocyte Nuclear Factor α G319S. A private mutation in Oji-Cree associated with type 2 diabetes. Letter to the Editor, *Diabetes Care* 22 (3) (1999) 524.
- [15] B. Zinman, A.J.G. Hanley, S.B. Harris, J. Kwan, I.G. Fantus, Circulating tumor necrosis factor- α concentrations in a Native Canadian population with high rates of type 2 diabetes mellitus, *J. Clin. Endocrinol. Metab.* 84 (1) (1999) 272–278.
- [16] A.J.G. Hanley, S.B. Harris, A. Barnie, et al., The Sandy Lake health and diabetes project: design, methods and lessons learned, *Chron. Dis. Can.* 16 (1995) 149–156.
- [17] World Health Organization. Diabetes mellitus: report of a WHO study group. World Health Organization. Tech. Rep. Ser. No. 727, 1985.
- [18] Lipid Research Clinics Program: manual of laboratory operation. Government Printing Office, Bethesda, MD, 1984, pp. 1–81. NIH publication No. 75282.
- [19] P.H. Winocour, M. Ishola, P.N. Durrington, Validation of the Friedewald formula for the measurement of low density lipoprotein cholesterol in insulin-dependent diabetes mellitus, *Clin. Chim. Acta* 179 (1) (1989) 79–83.

- [20] E.Y.L. Tsui, X.J. Gao, B. Zinman, Bioelectrical impedance analysis (BIA) using bipolar foot electrodes in the assessment of body composition in type 2 diabetes mellitus, *Diabetic Med.* 15 (2000) (1998) 125–128.
- [21] P.W. Connelly, D.R. MacLean, L. Horlick, B. O'Conner, A. Pestravovits, J.A. Little, Canadian health research group. Plasma lipids and lipoproteins and the prevalence of risk for coronary heart disease in Canadian adults, *Can. Med. Assoc. J.* 146 (11) (1992) 1977–1987.
- [22] B.R. Shah, J.E. Hux, B. Zinman, Increasing rates of ischemic heart disease in the native population of Ontario, Canada, *Arch. Intern. Med.* 160 (2000) 1862–1866.
- [23] T.P. Whitehead, D. Robinson, S.L. Allaway, The effects of cigarette smoking and alcohol consumption on blood lipids: a dose-related study on men, *Ann. Clin. Biochem.* 33 (1996) 99–106.
- [24] B. Eliasson, N. Mero, M.R. Taskinen, U. Smith, The insulin resistance syndrome and postprandial lipid intolerance in smoking, *Atherosclerosis* 129 (1) (1997) 79–88.
- [25] R.F. Gillum, B.S. Gillum, P.J. Smith, Cardiovascular risk factors among urban American Indians: blood pressure, serum lipids, smoking, diabetes, health knowledge and behavior, *Am. Heart J.* 107 (1984) 765–776.
- [26] B.V. Howard, M.P. Davis, D.J. Pettitt, W.C. Knowler, P.H. Bennett, Plasma and lipoprotein cholesterol and triglyceride concentrations in the Pima Indians: distribution differing from those of Caucasians, *Circulation* 68 (1983) 712–724.
- [27] S.B. Harris, B. Zinman, The primary prevention of type 2 diabetes in high risk populations, *Diabetes Care* 23 (7) (2000) 879–881.