

TYPE 2 DIABETES AMONG ABORIGINAL PEOPLES IN CANADA; A FOCUS ON DIRECT AND ASSOCIATED RISK FACTORS¹

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ABSTRACT

The need for determining Aboriginal population-specific risk factors of Type 2 Diabetes Mellitus has become increasingly urgent as the incidence and prevalence rates are increasing rapidly and as the need for prevention of diabetes in this population have become a necessity. This is a review of scientific literature that was conducted using PubMed and Medline databases which identified 55 relevant articles. A number of factors including lifestyle, ethnicity, access to health care, and genetic predisposition were identified as putative risk factors of this metabolic disorder. Initial results indicate a number of other risk factors of interest, such as age, Body Mass Index (BMI), Gestational Diabetes Mellitus (GDM), Hypertriglyceridemic Waist (HTGW) and HNF1A a G319S variant and Metabolic Syndrome (MetS). We have categorized these and other risk factors as modifiable, intermediate, and nonmodifiable risk factors; and each of these factors are further subdivided into direct and indirect factors. We will compare these risk factors with those identified by Aboriginal peoples and evaluate for concordance or discordance through focus-group consultations with Aboriginal peoples in our future study. This report describes the role of risk factors acting alone or

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in combination with others and categorized as modifiable, intermediate, or nonmodifiable. We have also identified factors potentially most effective as preventive measures for Type 2 Diabetes Mellitus (T2DM).

Key words: Diabetes Mellitus, Type 2; Aboriginal peoples; risk factors; prevention

INTRODUCTION

The incidence and prevalence of type 2 diabetes mellitus (T2DM) among Aboriginal peoples² in Canada is not only disproportionately higher, but also increasing rapidly. The need to determine population-based risk factors of T2DM is, therefore, urgent and necessary. It is important to remember that diabetes is not a direct outcome of risk factors, but rather a web of interactions of risk factors that play a major role in the higher incidence and prevalence of diabetes in the Aboriginal population.

There is a belief among Aboriginal communities in Canada that diabetes prevention is ineffective in part because it fails to offer Aboriginal population-specific diabetes prevention strategies. Thus there is a need for developing Aboriginal population specific diabetes prevention strategies that consider the diverse realities of all Aboriginal peoples of First Nation, Métis, and Inuit origin, within which the biomedical risk factors of the disease are created and perpetuated. As well, there has been very little recognition of the fact that many of the disease prevention and management solutions lie within the communities themselves. The purpose of this study in the first instance therefore is to identify modifiable, intermediate, and nonmodifiable risk factors of diabetes and use this knowledge in the development of population specific interventions for prevention and control of diabetes. Although a lot of work has been published in the area of Aboriginal diabetes, there is a general lack of published literature that helps to identify and understand the “direct” and “indirect” risk factors of T2DM among the Canadian Aboriginal population.

The classification as modifiable, intermediate, and nonmodifiable is prevention based. The objective primarily is to prevent the disease by targeting the risk factors among high risk-populations. The classification as “direct” or “indirect” is etiology based; it focuses on psychosocial imbalances, hereditary predisposition, physiological disturbances, and viral infec-

2. The Constitution Act, 1982, Section 35.1 states that the Aboriginal peoples of Canada are First Nations, Inuit, and Métis. In this paper, we use different terms to identify Aboriginal peoples of Canada, such as First Nation, Métis, and Inuit as presented in the literature we reviewed. As well, we also used the collective term “Aboriginal” as presented in the literature we reviewed.

tions etc. The specific objective of this study was to review western scientific literature and to collect information on the range of prevention based and etiology based risk factors of diabetes among Aboriginal peoples in the first phase. The secondary objective was to determine a slate of risk factors which could play a practical role in the prevention of T2DM. In most of the studies some risk factors are considered statistically significant and therefore strong evidence. There is speculation about other risk factors which are largely statistically insignificant. Statistically insignificant risk factors still have the potential to play a significant indirect role in diabetes causation.

Having determined the prevention and etiologic risk factors of diabetes among Aboriginal peoples in the first phase, we hope to evaluate these findings in the community by conducting in-depth interviews and focus-group consultations in the second phase of this study. The information collated in both the phases will be used in developing population-specific strategies cognizant of traditional knowledge for the prevention and control of diabetes among Aboriginal peoples. Framing the problem using western scientific knowledge and examining it in the context of traditional Aboriginal knowledge and culture will help integrate the two approaches and identify solutions that transcend the two cultures and knowledge bases. From this, appropriate interventions to prevent new cases and in halt the progression of confirmed cases can be identified.

OVERVIEW OF TECHNICAL MEASURES USED

T₂DM

Type 2 diabetes is caused by the body's ineffective use of insulin (a hormone which controls the amount of sugar in our blood). This leads to an increased concentration of glucose in the blood (hyperglycemia) (World Health Organization [WHO], 2011). Too much sugar in the blood causes problem with making food into energy.

NIDDM

Non-insulin-dependent diabetes is another name for Type 2 Diabetes mellitus caused by body's inability to effectively use insulin, which leads to an increased concentration of glucose in the blood.

GDM

Gestational diabetes mellitus (GDM) is a form of diabetes that can develop during pregnancy. Although GDM usually resolves following birth, both

mother and child are at risk of developing type 2 diabetes in the future. There is strong evidence that treatment of GDM is beneficial and improves health outcomes (Tieu et al., 2010).

BMI

Body mass index is a measure of body fat based on height and weight. People with BMI above the normal range are considered to be at greater risk for developing type 2 diabetes.

IGT

Impaired glucose tolerance is a transition phase; the body starts to have difficulty making enough insulin in the pancreas to keep the blood sugars at an acceptable level. This prediabetic state of abnormal blood sugar level is associated with insulin resistance.

HTGW

Hypertriglyceridemic waist has been used in clinical practice to detect individuals likely to have features of the metabolic syndrome, such as an elevated cholesterol/HDL cholesterol ratio, postprandial hyperlipidemia, hyperinsulinemia, and a dyslipidemic profile typically found in subjects with abdominal obesity. Other studies have also validated the ability of hypertriglyceridemic waist to identify individuals at high risk of CVD. Carriers of the hypertriglyceridemic waist phenotype also have deteriorated plasma glucose-insulin homeostasis compared to individuals without this phenotype.

METS

Metabolic syndrome is a set of risk factors that includes: abdominal obesity, a decreased ability to process glucose (increased blood glucose and/or insulin resistance), dyslipidemia, and hypertension. Mets was considered an independent predictor for diabetes in many studies, which indicates its important in diabetes screening for the prevention and management of this disease.

CRP

C-reactive protein is found in the blood as a response to inflammation in the body. Some studies suggest that C-reactive protein levels rise as blood sugar levels rise, which could indicate the presence of diabetes. Elevated CRP is also thought to be associated with metabolic syndrome.

IL-6

Interleukin-6 is a protein that can induce or reduce inflammation. This low-grade inflammation is thought to be involved in the pathogenetic processes causing type 2 diabetes.

Prevalence of T2DM

The number of people with diabetes divided by the number of people in the defined population at a particular point of time. Prevalence of a disease gives the probability of having the disease.

Incidence of T2DM

The probability that a person without diabetes will develop the disease during a specified period of time. It is the number of new cases of the disease that occur during the specified time interval divided by the number of people in the population who do not already have the disease.

Leptin

A hormone known mainly for regulating appetite control and energy metabolism. This may play a key role in controlling and potentially reversing diabetes by playing a role in appetite control and subsequently arresting the epidemic of obesity.

HNF1A

The G319S-G319S gene variant is consistent with reduced insulin secretion, likely a consequence of reduced HNF-1A activity, and more likely to play a significant role in diabetes causation.

ACR

Albumin to creatinine ratio is calculated to determine the level of functioning of the kidneys. Albumin is a protein, which is produced in the liver. Creatinine is a break-down product of creatine phosphate that is produced by the body and mostly filtered out of the blood by the kidneys. This is an important test, highly recommended for patients suffering from type 2 diabetes, because it helps to assess if there is any kidney damage due to the high levels of sugar in the blood.

Odds ratio

The ratio of odds of development of disease in one group compared to another group. The odds for the development of T2DM in older Aboriginals

is greater than the odds for development of T2DM in younger Aboriginals. Therefore, the odds ratio for T2DM is higher for older Aboriginals.

Relative risk

The ratio of the probability of disease occurring in one group compared to that in another group. The probability of T2DM occurring in obese Aboriginal women is greater than in nonobese women, therefore, the relative risk of T2DM in obese Aboriginal women is higher.

METHODS

SEARCH STRATEGY

Scientific literature in public databases such as PubMed and Ovid-Medline were searched for studies published between 1996 and 2007. Initial searches were carried out during the period of September 2007 in PubMed and Ovid-Medline databases. Additional searches for relevant articles were also conducted in Health Canada, Public Health Agency of Canada, and World Health Organization (WHO) websites, and Google Scholar. Relevant journals were searched by hand and references cited in identified articles were followed up. We first reviewed the title and the abstracts and then the full text article if it met the selection criteria. The search was restricted to articles published in the English language only. After reviewing the abstracts, 61 articles were selected for inclusion in the review, of which 55 articles were included in the table. Initial results indicate a number of risk factors of interest. These risk factors are characterized in this paper.

DATA EXTRACTION

Information about target population, methods, results including direct and associated risk factors, and the outcome and conclusions were extracted systematically from each original research article.

Inclusion criteria

The inclusion criteria for the studies were:

1. study population: Aboriginal, First Nations, Inuit, Métis, Native American, and American Indians;
2. risk factors for T2DM; we included the studies on gestational diabetes mellitus (GDM) in our review as GDM is considered as one of the risk factors of Type 2 diabetes;
3. language: only English language publications were included in this study;

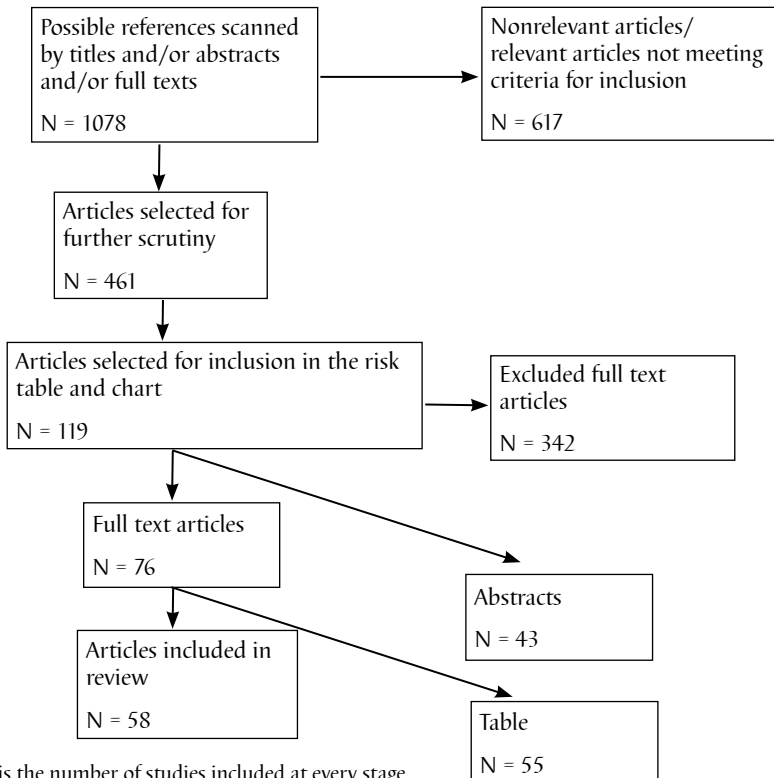
4. geography: in this review, we included studies published in Canada, United States, New Zealand, and Australia because these countries have significant proportion of Aboriginal population.

Categorization of risk factors

Data extraction was carried out on studies selected, and results were analyzed and presented in narrative format. We abstracted information on the risk factors associated with T2DM, including obesity, BMI, age, genetic predisposition (HNF1A G3193), life style factors including physical activity and diet, sociocultural factors, colonialism, and others. The T2DM risk factors identified in the literature were categorized into direct and associated risk factors. From the disease prevention point of view, we further divided these risk factors into modifiable, intermediate, and nonmodifiable risk factors.

A total of 1078 articles were identified as relevant. Subsequent evaluation and inclusion or exclusion of articles for relevance is shown in Fig. 1 below.

Figure 1: Flow Chart for Study Selection



N is the number of studies included at every stage.

RESULTS

It is believed that T2DM is not a direct outcome of “a” risk factor, but a web of interlinked risk factors which play a major role in the development of T2DM in Aboriginal populations. Framing the problem in the context of Aboriginal population health in Canada, this preliminary review of literature demonstrates the need for developing a population specific diabetes risk assessment tool for Aboriginal communities. This paper discusses the multiple risk factors of Type 2 diabetes among Aboriginal populations on the basis of review of articles published in PubMed and Medline data bases. This approach, if successful, offers the possibility of population specific risk assessment tool for other populations who are at risk of developing T2DM.

1. DIRECT RISK FACTORS

Direct risk factors have an independent statistically significant relationship with the development of T2DM (Table 1); they may, therefore, unilaterally increase the risk of diabetes among the Aboriginal population. Independent direct relation was found between diabetes and age/maternal age, BMI, family history, Aboriginal ancestry, genetic susceptibility, HNF1A mutation, albuminuria, hypertension, and hypertriglyceridemic waist (HTGW). The nature of the relationship between these direct risk factors and T2DM is discussed in this section.

Age

Several studies have investigated the relationship between age and the development of T2DM and older age. This relationship was found to be associated with an elevated risk of T2DM (Brimblecombe et al., 2006; Hegele et al., 2000a; Bruce, 2000; Liu et al., 2006). A number of studies reported that advancing age also increased the susceptibility to T2DM in both men and women (age-adjusted odds ratio [OR]=24.1, 95% CI 6.0-96.5, $p<0.001$) (Brimblecombe et al., 2006; Godwin et al., 1999). This means that the risk of developing T2DM in older women is 24 times higher than younger women. It was also suggested that a factor predictive of gestational diabetes mellitus (GDM) was age 35 years or more (relative risk [RR] 4.1, 95% CI 1.5-11.7) (Godwin et al., 1999). Therefore older pregnant women have a 4 times higher risk of GDM than younger pregnant women. Diabetic pregnancies play a key role in the initiation, progression, and perpetuation of the T2DM epidemic among Canadian Aboriginal peoples (Dyck et al., 2005). Higher birth weights and mother's older age are both found to be associated with

GDM (Rodrigues et al., 1999a; Rodrigues et al., 1999b). Women with a history of GDM were found to be at future risk of developing T2DM and an increasing number of offspring of diabetic pregnancies were also at risk for becoming overweight and developing T2DM at an early age (Moum et al., 2004; Gahagan and Silverstein, 2003; Mohamed and Dooley, 1998).

Obesity

BMI is found to be strongly associated with T2DM in Aboriginal peoples (Brimblecombe et al., 2006; Wilson et al., 2007; Wang and Hoy 2004; Young et al., 2000; Jørgensen et al., 2002; Daniel et al., 1999a; Daniel et al., 1999b). Brimblecombe et al. (2006) have reported that the risk of developing diabetes is 24 times higher in Aboriginal peoples with higher BMI compared to people with lower BMI with comparable age. This indicates that the probability of diabetes in population increases with the increase in BMI among the Aboriginal population. They also reported that people with the lowest diabetes risk are leaner (BMI < 22 kg/m²) and/or younger (age 15–34 years). Obese children are also at an increased risk of developing diabetes or impaired fasting glucose (odds ratio 5.1, 95% CI 1.51, 17.0). Young et al., 2000 have shown that the rising prevalence of T2DM among children can be explained by higher BMI. Higher proportions of Aboriginal women were found to be insulin resistant compared to white women; and this is believed to be due to trunk fat and not total body fat (Silha et al., 2007). Significant independent relationships between leptin and percent body fat and between leptin and fasting insulin have been reported in Aboriginal communities with high rates of diabetes (Hanley et al., 1997). Leptin, the hormone responsible for controlling appetite in human bodies, plays a role in developing obesity, as well as with fasting insulin among Aboriginal populations at a higher risk of developing diabetes. It has also been observed that the prevalence of obesity among the Aboriginal Canadians is inversely proportional to socioeconomic status (Denny, 2005).

Genetic susceptibility

Several studies (Hegele et al., 2000a; Pollex et al., 2005; Sellers et al., 2002; Hegele et al., 2000b; Hegele et al., 2000c) have reported on the genetic determinants of T2DM specific to Aboriginal populations in Canada. Hegele et al. (2000a) showed that a mutation at G319S specifically (specificity–97%) and positively predicted (95%) development of T2DM by age 50 years. The combined risk from other risk factors, such as hypertriglyceridemic waist

(HTGW) and a mutation at G319S on HNF1A gene increased the risk of T2DM greater than the risk from individual factors (Pollex, 2005). Impaired glucose tolerance (IGT) and T2DM prevalence rates vary widely amongst the Aboriginal population. Despite their cultural and historic variations, the consequences of rapid changes in diet and physical activities appear to have a very similar metabolic consequences on the Aboriginal populations. The level of risk for the different Aboriginal communities differs by their genetic susceptibility and ethnic origins (Yu and Zinman, 2007).

Albuminuria

Data on albuminuria suggest that it precedes and predicts the development of T2DM in Aboriginal peoples (Wang and Hoy, 2006; Rowley, 2000). One nested case control study found that an elevated urine albumin to creatinine ratio (ACR) value — independent of age, sex, BMI, serum cholesterol, C-reactive protein, and fasting plasma glucose — is associated with the development of T2DM in Aboriginal peoples (Wang and Hoy, 2006). Albumin creatinine ratio (ACR) is a very useful measure to gauge the level of functioning of the kidneys in the presence of higher glucose level in blood among Aboriginal people with T2DM. If not treated in time, this could lead to diabetes-related end-stage renal failure. Age, sex, BMI, serum cholesterol, and C-reactive protein predict the development of T2DM; now it appears that ACR, independent of these other factors, can predict disease development. A study (Rowley, 2000) among the Australian Aboriginal people showed that albuminuria is independently associated with T2DM (macroalbuminuria: OR=3.49, 95%CI:1.93-6.28, microalbuminuria: OR=2.10, 95%CI:1.28-3.45). Diabetes, hypertension, and abdominal obesity are major contributors to high rates of albuminuria among Australian Aboriginal peoples (Rowley, 2007).

Heredity/family history of diabetes

Heredity and family history of diabetes have been identified as important risk factors for diabetes apart from obesity and diet (Jørgensen et al., 2002; Ebbesson et al., 1998). Family history of diabetes is found to be associated with increased odds (4.4) of developing diabetes (Ebbesson et al., 1998).

Ethnicity

Ethnicity is an independent risk factor for both T2DM and GDM (Ben-Haroush et al., 2004; Dyck et al., 2002). In these studies ethnicity as an independent risk factor of T2DM is not correlated with other factors, thus

TABLE 1. STUDIES ON TYPE 2 DIABETES RISK FACTORS AMONG ABORIGINAL PEOPLES

Citation	Population	Risk Factors		Outcome
		Direct	Associated	
1. Dyck R.F. (2005)	Aboriginal Peoples from Saskatchewan	i) genetic ii) Older mother's age iii) GDM iv) high birth-weight baby v) hefty foetal type vi) ethnicity		GDM plays a key role in initiation, progression and perpetuation of T2DM. Ancient survival advantage became risk for pre-pregnancy obesity, GDM and excess foetal nutrition.
2. Ben-Haroush, Yogeve, Y. and Hod M. (2004)	Various population group	i) Ethnicity ii) Obesity	i) Polycystic ovary syndrome ii) Impaired glucose tolerance iii) hypertensive disorder	Association between several high-risk prediabetic states, GDM, and type 2 diabetes. Insulin resistance is suggested as a pathogenic linkage.
3. Dyck R., Klomp H., Tan L.K., Turnell R.W., Boctor M.A. (2002).	Canadian Aboriginal women	i) GDM ii) ethnicity		GDM contributes to an increased risk for type 2 diabetes in Aboriginal women and their offspring. GDM prevention could arrest the diabetes epidemic in this population.
4. Rodrigues S., Robinson E., Gray-Donald K. (1999b).	Cree communities in the eastern James Bay region of northern Quebec.	i) older maternal age ii) Higher body weight before pregnancy. iii) Several pregnancies. iv) Babies with high birth weight.		The prevalence of GDM among these women in northern Quebec is two times higher than North American population and the second highest reported in an Aboriginal group worldwide.
5. Rodrigues, S., Robinson, E.J., Ghezzo, H., Gray-Donald, K. (1999a).	The James Bay Cree of Canada and non-Native women	i) Age ii) pregravid weight iii) overweight women iv) ethnicity		Overweight Cree women are at increased risk of GDM.

Citation	Population	Risk Factors		Outcome
		Direct	Associated	
6. Mohamed, N., Dooley, J. (1998).	Aboriginal women of north western Ontario	i) over weight ii) GDM		The increasing incidence of NIDDM following GDM is very high in Aboriginal women of the Sioux Lookout Zone calls for an urgent need for a structured follow-up program for this group of high-risk women.
7. Moun, K.R., Holzman, G.S., Harwell, T.S., Parsons, S.L. Adams, S.D., Oser, C.S., Spence, M.R., Helgeson, S.D., Gohdes, D. (2004).	American Indians and White mothers			Increasing number of women with a history of GDM are at future risk of type 2 diabetes and an increasing number of diabetic pregnancies
8. Pollex, R.L., Hanley, A.J., Zimman, G., Harris, S.B., Hegele, R.A. (2006).	Oji-Cree community of Sandy Lake	i) hypertension ii) obesity iii) abnormal glucose tolerance iv) hyperttriglyceridemic waist (HTGW) phenotype	ii) hepatic nuclear factor-1 α (HNF1A) iii) MetS	When the HNF1A mutation and HTGW were present in combination, the OR for type 2 diabetes was markedly increased
9. Liu, J., Young, T.K., Zimman, B., Harris, S.B., Connelly, P.W., Hanley, A.J. (2006).	Oji-Cree adults over 18 years of age	i) hypertension ii) dislipidemia iii) obesity iv) abnormal glucose	i) older age ii) higher percentage of body fat iii) lower fitness level iv) MetS	The results showed that older age, higher percentage body fat, and lower fitness levels were associated with increased odds of MetS regardless of MetS definition and subject gender.
10. Kelly, C. and Booth, G. L. (2004).	Aboriginal Peoples	i) gender ii) obesity	ii) Lower socio-economic status iii) Polycystic ovarian syndrome	More Aboriginal women are affected with diabetes than men and the T2DM risk associated with obesity is greater for women. Women with GDM frequently develop DM over the next 10 years

11. Sunday, J. and Eyles J. (2001).	First Nations of Eastern Ontario			<ul style="list-style-type: none"> i) Healthy life-style factors ii) Impact of cultural and societal practices 	<p>The medical construction of diabetes risk has created a population whose health is endangered in a common, though individualized way. There are need for constant surveillance.</p> <p>Higher CRP levels were strongly associated with BMI—an indicator of obesity, which is an important risk factor for the diabetes.</p> <p>Findings suggest that albuminuria can precede and predict the development of diabetes in Aboriginal Peoples.</p> <p>The increases in obesity, diabetes have been linked to move from a country food diet and a less active lifestyle. The social, cultural, spiritual, nutritional and economic benefits of these foods must be considered in concert with the risks of exposure to environmental contaminants through their exposure.</p> <p>Associations between smoking and insulin resistance vary according to glycaemic status. Smoking may have diabetogenic acute and post-cessation effects on b-cell function and insulin resistance.</p>
12. Wang, Z. and Hoy, W.E. (2007).	Aboriginal Australians	ii) obesity		i) C-reactive protein	
13. Wang, Z., Hoy, W.E. (2006).	Aboriginal Australians	i) albuminuria		<ul style="list-style-type: none"> i) C-reactive protein ii) BMI iii) age 	
14. Van Oostrdam, J., Donaldson, S.G., Feeley, M., Arnold, D., Avotire, P., Bondy G., Chan, L., Dewailly E., Furgal, C.M., Kuhlmeier, H., Loring, E., Muckle, G., Myles, E., Receveur, O., Tracy, B., Gill, U., Kalhok, S. (2006).	Dene/Métis and Caucasians of the Northwest territories.	i) genetic predisposition		<ul style="list-style-type: none"> i) dietary choices ii) alcohol consumption iii) socio-economic factors 	
15. Daniel M. and Cargo, M. D. (2004).	Aboriginal Canadians	i) smoker ii) ethnicity		<ul style="list-style-type: none"> i) β-cell function ii) insulin resistance 	
16. Campbell, A. (2002).	Aboriginal Children			<ul style="list-style-type: none">) colonization ii) psychosocial illness-depression iii) social marginalization iv) substance abuse v) poverty 	
17. Booth, G.L., Hux, J.E., Fang, J., Chan, B.T. (2005).	All adults in Ontario	i) access to health care		<ul style="list-style-type: none"> i) residents from rural areas ii) residents from remote areas of province 	<p>Some subgroups of Ontarians experience higher rates of preventable diabetes complications.</p>

Citation	Population	Risk Factors		Outcome
		Direct	Associated	
18. Wang, Z., Hoy, W.E. (2004).	Aboriginal Australians	Women: a) higher waist and hip circumference b) BMI Men: a) higher total body weight and waist to hip ratio.	i) IL-6 ii) diabetes status	Waist circumference, BMI, waist-to-hip ratio, hips circumference and weight are useful predictors of diabetes in the Aboriginal population
19. Connelly, P.W., Hanley, A.J., Harris, S.B., Hegele, R.A. and Zimman, B. (2003).	Sandy Lake Ojji-Cree	i) CRP.		Highly elevated CRP would be most closely associated with IL-6 and diabetes status. There are Ethnic differences in MWS and the traits which constitute the MWS cluster not just linked epidemiologically at the population level but perhaps are also linked genetically at the chromosomal level.
20. Young, T.K., Chateau, D., Zhang, M. (2002).	Cree-Ojibwa, Inuit, non-Aboriginal	i) MWS ii) obesity iii) blood pressure iv) lipid or glucose factor	i) Aboriginal ethnicity	Association between the HNF-1alpha G319S mutation and early-onset type 2 diabetes in this population indicates the need for further investigation of the pathophysiology of this gene in treatment and/or prevention of this disease.
21. Sellers, E.A., Triggs-Raine, B., Rockman-Greenberg, C., Dean, H.J. (2002).	Aboriginal children patient	i) HNF-1alpha G319S mutation ii) Aboriginal ancestry		Association between elevated risk of IGT and diabetes. Reduction in BMI has the potential to prevent a substantial proportion of diabetes cases.
22. Daniel, M., Rowley, K.G., McDermott, R., O'Dea, K. (2002).	Australian Aboriginal populations	i) BMI ii) impaired glucose tolerance		Early detection and intervention directed at obesity are potential strategies to avert the long-term consequences of childhood obesity towards type 2 diabetes.
23. Young, K., Dean, J., Flett, B., Wood-Steiman, P. (2000)	A remote Aboriginal (Ojibwa-Cree) community in northern Manitoba, Canada	i) Childhood obesity ii) BMI		

24. Daniel, M., Marion, S.A., Sheps, S.B., Hertzman, C. Gamble, D. (1999).	Salishan Indians	i) WHR+BMI 25-29	Abdominal adiposity is associated with elevated insulin concentrations and impaired glucose control, suggesting metabolic staging by age on a continuum of insulin resistance to impaired glucose tolerance.
25. Young T.K., Reading, J., Elias, B., O'Neil, J.D. (2000)	Canadian Aboriginal population	i) Ethnicity ii) genetic-environmental interaction iii) homozygous for S319 allele — increased risk of T2DM iv) abdominal obesity-WHR	The current health and social repercussions of the disease are considerable, and the long-term outlook remains guarded. Need for a national Aboriginal diabetes strategy.
26. Dean, H. (1998).	First Nations communities in Manitoba and North Western Ontario	i) genetic ii) super-obese iii) family history of NIDDM	Need for consistent community-based screening programs and RCTs of pharmacologic interventions to test the efficacy of these agents in primary and secondary prevention.
27. Gittelsohn, J., Harris, S.B., Thorne-Lyman, A.L., Hanely, A.J., Barnie, A., Zinman, B.	Cree-Ojibway of northern Ontario	i) Older Cree-Ojibway prefer larger BMI	Knowledge of age and sex-related patterns of body image concepts in communities can assist in the design of obesity-reducing interventions targeting specific at risk groups
28. Hanley, A.J.G., Harris, S.B., Gao, X.J., Kwan, J., Zinman, B. (1997)	Canadian Aboriginal population	Female: i) leptin Male: i) leptin	Significant independent relationships between leptin and percent body fat and between leptin and fasting insulin was found.
29. Bruce, Sharon (2000).	APS self-identified Métis and North American Indians of western Canada	i) age ii) sex iii) obesity iv) level of education	Significant association of age, sex, obesity, and level of education with diabetes.
30. Hanley, A.J.G., Harris, S.B., Mamekesick, M., Goodwin, K., et al. (2005).	Aboriginal population from Sandy Lake	i) higher albumin-to-creatinine ratio	Study found high prevalence rates of both diabetes complications and associated risk factors and highlights urgent need to implement culturally appropriate strategies for diabetes prevention.

Citation	Population	Risk Factors		Outcome
		Direct	Associated	
31. MacMillan, H.L., MacMillan, A.B., Offord, D.R., Dingle, J.L. (1996).	Canada's native people		i) poverty	Poverty as a confounding factor found to have some role on disproportionate burden of disease that Aboriginal people share.
32. Rowley, K.G., Iser, D.M., Best, J.D., O'Dea, K., Leonard, D., McDermott, R. (2000).	Australian Aboriginal Peoples	i) Mets ii) albuminuria iii) obesity iv) insulin resistance		Strong clustering of albuminuria with components of the Mets, diabetes, hypertension and abdominal obesity.
33. Thompson, S.J., Gifford, S.M., Thorpe, L. (2000).	Aborigines in Melbourne, Australia	i) behavioural risk factors — social and cultural understanding of diet and physical activity ii) Sociocultural process — stress and social support		Food and physical activity in this community make the strong connections between individuals to family, community, land, and past. Insiders' categories of food and physical activity derive their meaning from these connections.
34. McCullough, B., McDermott, R., Miller, G., Leonard, D., Elwell, M., Muller, R. (2003).	Australian Aboriginal population		i) lifestyle change including alcohol consumption	Individuals with diabetes living in rural and remote communities are not adopting lifestyle changes required for optimal self-management of the disease, which contributes to the large excess of mortality and morbidity experienced by this population.
35. Daniel, M., Rowley, K.G., McDermott, R., Mylvaganam, A., O'Dea, K. (1999).	Australian Aboriginal population	i) Higher BMI		BMI-specific diabetes incidence rates in Australian Aboriginal Peoples are among the highest in the world.
36. Harris, S.B., Gittelsohn, J., Hanley, A., Barmie, A., Wolever, T.M., Gao, J., Logan, A., Zimman, B. (1997).	Native Canadians	i) female ii) higher prevalence of obesity iii) IGT iv) younger ages		High prevalence rates of IGT and NIDDM among young women indicates urgent need to develop culturally appropriate community-based public health intervention programs

37. Brimblecombe, J., Mackerras, D., Garrngulkpuy, J., Mayplama, E., Bundhala, L., Dhurrkay, R., Fitz, J., Maple-Brown, L., Shemesh, T., Rowley, K.G., O'Dea, K. (2006).	Australian Aboriginal population	i) BMI ii) age	Strategies to prevent or delay the onset of diabetes should focus on the maintenance of leanness from adolescence and throughout adult life.
38. Hegee, R.A., Cao, H., Harris, S.B., Hanley, A.J.G., Zinman, B. (1999a)	Canadian Oji-Cree	i) HNF1 α G319S variant ii) ethnicity iii) age	The presence of the private HNF1 α G319S with a distinct form of type 2 diabetes, characterized by onset at an earlier age, lower body mass, and a higher postchallenge plasma glucose.
39. Pollex, R.L., Hanley, A.J.G., Zinman, B., Harris, S.B., Khan, H.M.R., Hegele, R.A. (2005)	Oji-Cree Nation	i) Combination of modified metabolic syndrome and the private HNF1 α G319S mutation ii) Independent risk factor – MetS or HNF1 α G319S mutation	The risk of type 2 diabetes was similar (approximately five-fold increased) for subjects with either the presence of the modified metabolic syndrome or the private HNF1 α G319S mutation.
40. Silha, J.V., Nyoma, B.L.G., Leslie, W.D., Murphy, L.J. (2007).	First Nations	i) Trunk fat	First Nations women are more insulin resistant than white women and this is explained by trunk fat not total body fat.
41. Hegele, R.A., Cao, H., Hanley, A.J., Zinman, B., Harris, S.B., Anderson, C.M. (2000a).	Oji Cree	i) HNF1 α S319 ii) Older age	Presence of HNF1 α S319 increases the risk of having diabetes or IGT by 50 years of age.
42. Pollex, R.L., Hanley, A.J., Zinman, B., Harris, S.B., Khan, H.M., Hegele, R.A. (2006b).	Oji Cree of Ontario, Canada	i) MetS ii) Increased waist girth	The high MetS prevalence in adults, especially among women, is consistent with their high risk of T2DM suggesting that genesis of MetS begins in youth, especially among Aboriginal females.
43. Hegele, R.A., Hanley, A.J., Zinman, B., Harris, S.B., Anderson, C.M. (2000b).	Oji-Cree Type 2 Diabetes	i) HNF1 α G319S	G319S has a very important pathogenic role in Oji-Cree diabetes, based upon the highly suggestive association studies.
44. Hegele, R.A., Cao, H., Harris, S.B., Hanley, A.J., Zinman, B. (1999).	Canadian Oji-Cree Type 2 diabetes	i) genetic predisposition ii) recent life-style change iii) G319S mutation — HNF1 α	Population either heterozygous or homozygous for HNF1 α -G319S indicate that a population specific marker could target for life-style intervention for this population at risk.

Citation	Population	Risk Factors		Outcome
		Direct	Associated	
45. Yeates, K., Tonelli, M. (2006).	Australia, New Zealand, the USA and Canada Diabetes	i) genetic predisposition ii) obesity	i) loss of traditional land ii) increased westernization of the indigenous diet iii) disparity in access to healthcare	There is a recognized need and role for improved collaboration between indigenous health researchers among USA, Canada, Australia and New Zealand.
46. Yu, C.H., Zinman, B. (2007).	Aboriginal population worldwide	i) IGT ii) Past history of prediabetic stage		Type 2 diabetes and IGT prevalence rates vary widely amongst the world's Aboriginal populations; the magnitude of which may be determined by genetic susceptibility.
47. Carter, E.A., MacCluer, J.W., Dyke, B., Howard, B.V., Devereux, R.B., Ebbesson, S.O., Resnick, H.E. (2006).	Eskimos in Norton Sound, Alaska	i) abdominal obesity ii) higher IFG (Fasting glucose)		The high prevalence of IFG and specifically high Abdominal obesity in women indicate general increase in diabetes incidence and sex-related diabetes prevalence in this population.
49. Denny, C.H., Holtzman, D., Goins, R.T., Croft, J.B. (2005).	Alaska Natives Diabetes	i) obesity		Prevalence estimates of smoking, lack physical activity, obesity, all risk factors for chronic disease were higher among American Indians and Alaska Native than White elders.
50. Gahagan, D., Silverstein, J. (2003).	Alaska Native Children	i) obesity ii) GDM		This chronic disease requires preventive efforts, early diagnosis, and collaborative care of the patient and family within the context of a medical home.
51. Jørgensen, M.E., Bjeregård, P., Borch-Johnsen, K. (2002).	Inuit	i) age ii) BMI iii) family history of diabetes	i) sedentary lifestyle, and place of residence were significant	Heredity, obesity and diet were identified as an important factors for high diabetes incidence in this population. The high proportion of unknown cases suggests a need for increased diabetes awareness in Greenland.

52. Wilson, C., Gilliland, S., Moore, K., Acton, K. (2007).	American Indian and Alaska Native	i) obesity ii) BMI	Extreme degrees of obesity are a common and increasing problem among AI/AN adults with diabetes. Effective and culturally appropriate weight management interventions are needed.
53. Retnakaran, R., Hanley, A.J., Connelly, P.W., Harris, S.B., Zinman, B. (2006).	Native Canadian Children	i) childhood obesity	Subclinical inflammation is an early complication of childhood obesity in Native children and may foreshadow an increased burden of CVD and type 2 diabetes in the future.
54. Gittelsohn, J., Wolever, T.M., Harris, S.B., Harris-Giraldo, R., Hanley, A.J., Zinman, B. (1998).	Native Canadian	i) fatty foods	More fatty methods of food preparation are also associated with increased risk for diabetes in this population (OR = 2.58, CI = 1.11–6.02).
55. Zimmet, P.Z., McCarthy, D.J., de Courten, M.P. (1997)	Mexican- and African-Americans and Australian Aborigines and Torres Strait Islanders	i) lifestyle	Enormous variation in NIDDM prevalence between populations, and exceptionally high rates have been documented in populations who have changed from a traditional to a modern lifestyle.

exerts independent effects on the outcome of diabetes. The probability of diabetes in a population at a given point of time has been found to increase among certain ethnic populations. It has also been reported that a majority of First Nations youths diagnosed with non insulin-dependent diabetes mellitus (NIDDM) or T2DM had a family history of diabetes (Ben-Haroush et al., 2004). Multivariate analysis by Dyck et al. (2002) demonstrates that Aboriginal ethnicity, most notably when combined with obesity, was an independent predictor for GDM in the Aboriginal population.

2. ASSOCIATED RISK FACTORS

Associated risk factors are those that do not have an independent statistical relation with the onset of T2DM. Associated risk factors alone do not necessarily play a causal role in development of diabetes. These risk factors — Mets³ (metabolic syndrome), CRP⁴ (C-reactive protein), poverty, SES, food, alcoholism, smoking, physical activity, or access to a health care system — are secondary to the development of the disease, working in combination with other direct or associated risk factors. However, when combined with other direct risk factors they can act synergistically to create increased risk for T2DM.

MetS

A higher prevalence of MetS was found to be closely associated with higher percentage of body fat and lower physical activities among Aboriginal populations (Liu et al., 2006; Ebbesson et al., 1998; Pollex et al., 2006a; Pollex et al., 2006b). Multiple Metabolic Syndrome (MMS), when certain conditions act in unison to increase the risk of MetS, is disproportionately higher in certain ethnic groups. This demonstrates that the ethnic differences in MMS are linked genetically at the chromosomal level and not only at the population level (Young et al., 2002). The risk of T2DM was observed to be increased approximately five-fold for subjects with the presence of either the modified metabolic syndrome or G319S mutation in HNF1A gene (Pollex et al., 2006b). This study also found that these two independent risk factors if present in combination appeared to act synergistically to create an even greater increased risk of T2DM. An association has been reported between the development of Mets and Aboriginal youth, specifically young

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3. Metabolic syndrome (MetS) is a common phenotype that is clinically defined by threshold values applied to measures of central obesity, dysglycemia, dyslipidemia, and/or elevated blood pressure, which must be present concurrently in any one of a variety of combinations (Hegele et al., 2005).
 4. C-reactive protein (CRP) is an inflammatory marker produced and released by the liver under the stimulation of cytokines such as tumor necrosis factor- α and interleukins 1 and 6 (Wang et al., 2007).

females (Pollex et al., 2006b). Prevalence of MetS in Oji-Cree adults, especially women, is consistent with their high risk of T2DM.

Lifestyle

Sedentary lifestyle along with age, BMI, family history of diabetes, and place of residence is a significant predictor of T2DM and impaired glucose tolerance (Liu et al., 2006; Jørgensen et al., 2002; Zimmet et al., 1997; Van Oostdam et al., 2005). Changes in lifestyle from traditional to modern including a shift away from country food diet and a less active lifestyle are linked to obesity and T2DM (Zimmet et al., 1997; Van Oostdam et al., 2005). Moreover, lower physical activity and fitness together with higher percentage body fat were associated with a higher prevalence of MetS in Aboriginal communities, which is in turn associated with an elevated risk of cardiovascular disease and T2DM (Jørgensen et al., 2002). Association between smoking and insulin resistance varies according to glycemic status, with serious implications for diabetes incidence in this population group. Smoking may have acute and post-cessation effects on beta cell function and insulin resistance (Daniel and Cargo, 2004). Lifestyle changes for diet, physical activities, substance abuse including alcoholism and smoking, when combined with other direct and associated risk factors can act collectively to confer increased risk for T2DM (McCulloch, 2003; Van Oostdam et al., 2006).

C-reactive protein (CRP)

This protein, found in the blood and synthesized by the liver, rises in level in response to inflammation and is believed to be associated with an increased risk of T2DM. The C-reactive protein (CRP) values vary significantly among race/ethnic groups; among the Aboriginal peoples the CRP levels are much higher compared with other ethnic populations (Wang and Hoy, 2007). Scientific literature suggests that elevated levels of CRP are associated with an increased risk of developing T2DM among Aboriginal populations (Wang and Hoy, 2007; Connelly, 2003). High elevated CRP levels have been reported among the Sandy Lake Oji-Cree nation; this population also has a high prevalence of obesity and diabetes (Connelly, 2003). These authors have also confirmed that elevated levels of C-reactive protein are most closely associated with higher levels of Interleukin-6 and higher prevalence of diabetes among both men and women (Retnakaran et al., 2006). The levels of CRP are on the rise among the Aboriginal children and so is the increased burden of T2DM in this population. Multivariate analyses on waist circumference and interleukin-6 (IL-6) levels have shown these as independent de-

terminants of CRP levels for Aboriginal children. Some of the risks may be mediated through obesity and factors related to insulin resistance.

Sociocultural factors

Sociocultural factors including diet, physical activity, and behavioural patterns play an important role in T2DM incidence among Aboriginal communities (Retnakaran et al., 2006). Poverty and social marginalization, gravely exacerbated by colonization, bring serious challenges for contemporary Aboriginal populations, creating a negative health outcome with an increased risk of T2DM (Campbell, 2002; Sunday and Eyles, 2001). Altered methods from the traditional methods of food preparation, and increased fat consumption are also associated with increased risk for diabetes in some Aboriginal population communities (OR=2.58, CI=1.11-6.02) (Gittelsohn et al., 1998). These sociocultural factors, in the greater context of Aboriginal living, could affect Aboriginal peoples over the generations among different age groups and across genders.

Gender

Approximately two-thirds of diabetic individuals are women among Aboriginal Canadians. Although obesity is more prevalent among men than women (35% vs. 27%), the T2DM risk factors associated with obesity are greater among women. Socioeconomic status for these women is inversely related to T2DM. Women with gestational diabetes frequently develop T2DM later in their lives (Gahagan et al., 2003; Kelly and Booth, 2001).

Access to health care

Access to health care appears to play a significant role for Aboriginal people with diabetes in rural and remote communities. These individuals experience increased T2DM complications (Booth et al., 2005). They have lost interest in the lifestyle changes required for optimal self-management of this disease which may contribute to the high rates of mortality and morbidity experienced by this population (McCulloch et al., 2003). Early intervention is the key to efficient management of T2DM; compromised access to health care delays intervention, leading to higher prevalence of uncontrolled disease.

MODIFIABLE, INTERMEDIATE, AND NONMODIFIABLE RISK FACTORS

The direct and associated risk factors of diabetes, from a prevention point of view, have been recategorized as modifiable, intermediate, and nonmodi-

fiable. The modifiable, intermediate, and nonmodifiable risk factors for Aboriginal populations are shown in Fig. 2. The modifiable risk factors of T2DM and the conditions created by intermediate risk factors can be modified or controlled to affect the outcome of disease development. We also observed that some intermediate risk factors may pass from one generation to the next and are modifiable to some extent, such as effects of colonization in present days, poverty, sociopolitical condition, access to health care, and GDM. Although nonmodifiable risk factors affect the disease outcome,

Figure 2: Modifiable, Intermediate, and Nonmodifiable Risk Factors of Diabetes among Aboriginal Peoples



they are beyond the control of Aboriginal individual, communities, and governments.

DISCUSSION

T2DM, a relatively new disease in Aboriginal communities, is influenced by host of complex factors and predominately linked to the move away from traditional hunter-gatherer to a more western lifestyle (Zimmet et al., 1997; Wang and Hoy, 2007). The conventional scientific view is that adoption of a western lifestyle has led to decreased physical activity, increased prevalence of obesity, and major shifts in diet. These factors, combined with genetic susceptibility, have resulted in the observed increases in diabetes incidence among Aboriginal populations (Rowley et al., 2000; Ben-Haroush et al., 2004; Young et al., 2000; McDermott et al., 2000). The significant risk factors for higher incidences of T2DM among Aboriginal populations were inconsistent across the different studies, although several of the studies, indicated that multiple risk factors may be responsible for T2DM incidence. The likelihood of T2DM appearance may vary within and between Aboriginal population groups based on relative exposure to various risk factors identified in the studies. Health care providers and policy makers must continue to recognize the sociocultural factors, within which individual modifiable risk factors of T2DM are created and perpetuated.

Modifiable risk factors are believed to be primarily under control of the individual and can influence the disease development. The majority of the associated modifiable or intermediate risk factors for T2DM are more likely preventable with alterations in diet and lifestyle. Intermediate risk factors are not directly under the control of the individual or the community, and these factors create conditions or situations which initiate or promote disease development. It may not be possible to alter these factors in a generation but it is certainly possible to alter the outcomes produced by these factors. These outcomes are modifiable and preventable and these factors, therefore, can alter the disease outcome. Nonmodifiable factors are beyond the control of the individual and the community, and are also associated with the disease development.

Modifiable risk factors (such as obesity, physical activities, diet, SES, stress) are consequences of intermediate risk factors (such as effects of colonization, poverty, sociopolitical condition, access to health care) and often remain beyond the individual control. These intermediate risk factors must be addressed in developing prevention strategies. Improved connection to culturally appropriate health and social services, patient advocacy organizations, and medical assistance may help achieve these goals. In addition to these issues, research on Type 2 diabetes risk factors are often generalized to all Aboriginal peoples, without acknowledging the diversities that exist within and between Aboriginal People. Initiatives that acknowledge and incorporate these understandings should encourage the Aboriginal peoples to make use of comprehensive health care services that are culturally appropriate and preventative in nature. T2DM in Aboriginal women and children is cyclical, which carries the potential for being passed on from one generation to the next through GDM. The increasing incidence of Type 2 diabetes observed in Aboriginal population groups, coupled with increased risk of complications, indicate that prevention is the best method of reducing the burden of diabetes among Aboriginal people.

IMPLICATIONS FOR PREVENTION STRATEGIES

Diabetes, particularly Type 2 diabetes, is a serious public health and population health concern for the Canadian Aboriginal people since they bear a disproportionate burden of this disease compared to non-Aboriginal people. Diabetes prevention strategies for Aboriginal people must address the upstream factors or broader determinants of health within which individualized risk factors of diabetes are generated and propagated. The majority of

these broader determinants are outside the control of the individual and require policies or actions by others. It is important to have effective and culturally appropriate prevention strategies based on knowledge of broader and individualized risk factors identified in collaboration within Aboriginal communities (Brimblecombe et al., 2006; Hanley et al., 2005). A complex web of linkages connects the Aboriginal peoples to their family and community. An understanding of these linkages as well as the potential resilience of these individuals and communities in coping with this disease must be taken into account to develop culturally appropriate effective interventions with long-term success (Retnakaran et al., 2006). Early detection and culturally and age appropriate intervention directed at obesity and IGT (impaired glucose tolerance) are potential strategies that could reduce childhood and early onset of T2DM, eventually averting the long-term consequences of T2DM (Young et al., 2000; Daniel et al., 2002; Harris et al., 1997; Gittelsohn et al., 1997). Incorporating waist to hip (WHR) ratio into health examinations could enhance the evaluation of co-morbidity factors for diabetes and CVDs (Wang et al., 2007). There is also a need for consistent community-based screening programs and pharmacologic interventions through randomized controlled trials to test the safety and efficacy of these agents in primary and secondary prevention of complications in various age groups (Dean, 1998). Regional variations in disease prevalence among Aboriginal peoples in Canada according to language, family, geographic location, and degree of isolation (Smylie, 2001) indicate that for Aboriginal populations specific prevention strategies are important. There is a recognized need and role for improved collaboration between indigenous health researchers among Canada, USA, Australia, and New Zealand (Yeates and Tonelli, 2006). The lessons from interventions and approaches to diabetes prevention and from successes and failures among these international researchers could serve to further improve health outcomes for Canadian Aboriginal peoples.

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