University of Alberta

The BRAID Study

by

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Dedication

These writings are dedicated to the one who guided me through…

Ek Ongkaar

ABSTRACT

The BRAID study screened 1170 Aboriginal people in Alberta for diabetes, prediabetes, the metabolic syndrome, and other cardiovascular risk factors. 43 unique Aboriginal communities including Metis settlements and First Nations reserves were visited. Portable technology was used for screening and was assessed for diagnostic accuracy. Individuals were screened with one of two strategies; opportunistic or population based. 3.18% of individuals screened had undiagnosed diabetes, 28.3% had prediabetes, 50.4% had the metabolic syndrome, and 51.7% were obese. Age and family history of diabetes were the most significant predictors of diabetes. Regarding diabetes, prediabetes, and the metabolic syndrome, no significant differences in prevalence was found between the opportunistic or population based screening paradigms. Portable technology was shown to be accurate for the determination of diabetes, however it cannot yet be recommended for prediabetes. The BRAID study documented the highest prevalence of prediabetes and the metabolic syndrome in North America.

Acknowledgements

"Great spirits have always encountered violent opposition from mediocre minds."

~ Albert Einstein

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Table of Contents

Chapter 1 – Introduction and Literature Review 1

1.1 – Introduction and purpose 2

1.2 – Type 2 diabetes: the epidemic 4

1.3 – Undiagnosed diabetes and prediabetes 6

1.4 – The metabolic syndrome – a risk factor for diabetes? 9

1.5 – Type 2 diabetes, prediabetes and risk factors in Aboriginal peoples 11

1.5.1 – Diabetes and prediabetes in Aboriginal peoples 11

1.5.2 – Why is diabetes so high in Aboriginal people? 14

1.5.3 – Gestational Diabetes 16

1.6 – Aboriginal perspectives and health determinants 17

1.6.1 – Aboriginal approaches towards health 17

1.6.2 – Health Canada's determinants of health 19

1.7 – Screening for prevention of type 2 diabetes – pros and cons 30

1.7.1 – Disadvantages of screening for diabetes 32

1.7.2 – Benefits of screening for undiagnosed diabetes 35

1.7.3 – Logistics of Screening 38

1.7.4 – Screening for diabetes - summary 40

1.8 – The role of portable technology 41

Chapter 2 – Hypothesis 44

Chapter 3 – Methods 46

3.1 – The projects explained – The SLICK, MDSI, and BRAID projects 47

3.1.1 – The SLICK project 47

3.1.2 – The MDSI project 48

3.1.3 – The BRAID project 49

3.2 – Ethics 52

3.3 – Collection of data 52

3.4 – Quality Assurance 56

3.5 – Biochemical Measurements 61

3.6 – Data collection, counselling, and education 69

3.7 – Statistical Analysis 71

3.8 – Diagnostic Criteria 73

CHAPTER 4 – Results 76

4.1 – Study dataset, demographics and information collected 77

4.2 – Assessment of hypothesis 1: use of portable technology 79

4.2.1 – Performance analysis of portable technology 80

4.3 – Portable testing results in all groups combined 85

4.3.2 –Predictors of glycemia 88

4.4 – Hypothesis 2: Opportunistic vs. Population based screening 90

CHAPTER 5 – Discussion 96

5.1 – Introduction 97

5.2 – Hypothesis testing 97

5.3 – Prevalence of diabetes, prediabetes, and diabetes risk factors 100

5.4 – The metabolic syndrome and cardiovascular risk factors 103

5.5 – Limitations 105

5.6 – Lessons Learned and Future directions 106

5.7 – Conclusion 108

APPENDIX 1A – QUALTIY ASSURANCE - Cholestech LDX® 110

APPENDIX 1B – QUALITY ASSURANCE - DCA 2000® 111

APPENDIX 2 – ETHICS APPROVAL FORM 112

APPENDIX 3A - INFORMATION SHEET AND CONSENT FORM FOR THE SLICK PROJECT 113

APPENDIX 3B – INFORMATION SHEET AND CONSENT FORM FOR THE MDSI PROJECT 118

APPENDIX 3C – INFORMATION SHEET AND CONSENT FORM FOR THE BRAID PROJECT 121

List of Tables

Table 1.3.1 – Undiagnosed diabetes and Impaired Glucose Tolerance 8

Table 1.4.1 – NCEP/ATPIII Criteria for the diagnosis of the metabolic syndrome 10

Table 1.5.1 – Age-standardized prevalence of diabetes in Aboriginal peoples of Canada 1991 13

Table 1.5.2 – Traditional lifestyle vs. Westernization in the Pima Indians 15

Table 1.7.1 – Is screening for undiagnosed diabetes beneficial? 33

Table 1.7.2 – Recommendations for (opportunistic) screening 39

Table 3.1.1 – Exclusion criteria for the SLICK, MDSI and BRAID projects 50

Table 3.4.1 – Performance Characteristics for the Cholestech LDX® Analyzer 60

Table 3.7.1 – Analyses conducted 72

Table 3.8.1 – Diagnostic criteria for glycemia 73

Table 3.8.2 – A1c criteria for the BRAID study 73

Table 3.8.3 – Criteria for the metabolic syndrome 74

Table 3.8.4 – Other risk factors and their criteria 75

Table 4.1.1 – Project, study, and community statistics 77

Table 4.1.2 – Breakdown of gender and age in the three projects 78

Table 4.2.1 – Area under the ROC curve for DCA 2000® and OneTouch® Ultra® 84

Table 4.2.2 – Sensitivity and specificity of portable technology for the diagnosis of probable diabetes and prediabetes using Cholestech LDX® as standard 84

Table 4.3.1 – Comparison of glycemic categories detected by Cholestech LDX® standard vs. portable technology 85

Table 4.3.2 – Total prevalence of probable diabetes, probable prediabetes, the metabolic syndrome, and risk factors tested with portable technology 86

Table 4.3.3 – Age and gender specific prevalence of diabetes and prediabetes in the BRAID study 87

Table 4.3.4 – Familial contribution to increased glucose 88

Table 4.3.5 – Regression analysis on risk factors for diabetes 90

Table 4.4.1 – Demographic comparison of opportunistic and population based screening 91

Table 4.4.2 – Opportunistic and Population based prevalence of diabetes, prediabetes, the metabolic syndrome, and risk factors corrected for age 92

Table 4.4.3 – Gestational and familial history of diabetes between groups 93

Table 5.4.1 – Prevalence of the Metabolic Syndrome in the BRAID study compared with other countries 104

List of Figures

Figure 1.5.1 – Type 2 diabetes incidence in Manitoba First Nation children 14

Figure 1.6.1 – The Medicine Wheel..... 18

Figure 3.1.2 – The SLICK, MDSI, and BRAID projects 51

Figure 3.3.1 – Patient report sheet for the BRAID Project..... 54

Figure 3.4.1 – QA procedure prior to utilization of analyzers 58

Figure 3.4.2 – QA procedures from community to the individual..... 59

Figure 3.5.1 – Capillary holder, and reagent cartridge for the DCA 2000® analyzer 65

Figure 3.5.2 – Capillary tubes and reagent cartridge for the Cholestech LDX® analyzer..... 65

Figure 3.5.3 – OneTouch® Ultra glucometer® and test strip 66

Figure 3.5.4 – DCA 2000® analyzer 66

Figure 3.5.5 – Cholestech LDX® analyzer..... 67

Figure 3.5.6 – Schematic overview of blood collection and analysis..... 68

Figure 3.6.1 – American Diabetes Association Risk Questionnaire and additional BRAID project questions. 70

Figure 4.2.1 – ROC curve for DCA 2000® A1c using Cholestech LDX® standard glucose criteria for diabetes..... 81

Figure 4.2.2 – ROC curve for fasting OneTouch® Ultra® glucose using Cholestech LDX® standard glucose criteria for diabetes 82

Figure 4.2.3 – ROC curve for DCA 2000® A1c using Cholestech LDX® standard glucose criteria for prediabetes (IFG only) 83

Figure 4.2.4 – ROC curve for fasting OneTouch® Ultra® using Cholestech LDX® standard glucose criteria for prediabetes (IFG only) 83

Figure 4.3.1 – Distribution of BMI in the total population screened 87

Figure 4.4.1 – Opportunistic vs. Population – Fasting glucose 94

Figure 4.4.2 – Opportunistic vs. Population – A1c 94

Figure 4.4.3 – Frequency of the Metabolic Syndrome detected by Opportunistic vs. Population based screening strategies 95

List of Equations

Equation 3.5.1 – Measurement of Glucose using the Cholestech LDX 62

Equation 3.5.2 – The Friedewald formula for LDL cholesterol 63

Equation 4.2.1 – Determining diagnostic accuracy 79

Chapter 1

Introduction and Literature Review

1.1 – Introduction and purpose

> The fact that Sandy Lake holds a record, of sorts, as having the third highest prevalence of diabetes in the world is more a tragedy than a source of prestige...it is imperative that we salvage the next generation from the ravages that are plaguing this generation. The preventable nature of this complex combination of physical and social calamity demands action.
>
> ~ Harry Meekis, Sandy Lake First Nation (Elliott, 1997).

The epidemic of diabetes that is facing Aboriginal peoples at present requires further research. This chapter will serve as a literature review of type 2 diabetes, and diabetes in Aboriginal peoples. Included are sections on the epidemic of diabetes, the prevalence of type 2 diabetes, and prediabetes, in various populations, primarily focusing on Aboriginal peoples in Canada and the United States. The metabolic syndrome – which is of interest because of its association with diabetes and cardiovascular risk. – will also be discussed, followed by Aboriginal perspectives of type 2 diabetes, and a chapter on screening for type 2 diabetes with a discussion of the recent literature that has suggested prevention and treatment to prevent type 2 diabetes. Lastly, the use of portable technology and the requirement for it in rural communities will be addressed. Throughout this thesis the terms type 2 diabetes and diabetes will be used interchangeably, since the majority of people (90-95%) who present with the disease have type 2 diabetes (Venkat Narayan et al., 2000). The terms prediabetes and impaired fasting glucose will also be used synonymously.

Purpose

The purpose of this research is to study the prevalence, and the ability to document the prevalence, in Aboriginal people of Alberta. Because many Aboriginal people live in rural and remote locations of Alberta, portable technology is being utilized. The diagnostic

accuracy of the portable technology will be studied in the setting of different strategies for screening.

Definitions:

Type 2 diabetes – Is a metabolic disorder characterized by the presence of hyperglycemia due to defective insulin secretion, insulin action or both (CDA, 2003a).

IFG – impaired fasting glucose, refers to an abnormal glucose value that is below the threshold for diabetes, yet carries significant risk of diabetes and cardiovascular disease, and is associated with substantial health care utilization costs.

IGT – impaired glucose tolerance, refers to abnormal glucose values on a glucose tolerance test, with similar health consequences to IFG.

Prediabetes – is a term that includes – IFG/IGT, indicating a relatively high risk for development of diabetes

Undiagnosed diabetes – refers to the existence of the condition in a relatively asymptomatic state, and as such, it is often found during screening programs.

Metabolic Syndrome – as a surrogate for the Insulin Resistance syndrome, and classified according to the National Cholesterol Education Program, is a constellation of anthropometric, glucose, and lipid values that confer risk of diabetes and cardiovascular disease.

Diagnostic criteria for the above conditions are shown in methods section.

Aboriginal – Refers to the descendants of the original inhabitants of Canada. Aboriginal people are defined in the *Constitution Act, 1982* as all indigenous people including Indians, Metis and Inuit. The Constitution does not define membership in the individual groups (Alberta Aboriginal affairs, 2001).

First Nation – A person who has been registered or is entitled to be registered according to the Indian Act. Most Registered Indians are members of an Indian Band. By virtue of the Indian Act, the Department of Indian Affairs and Northern Development is responsible for providing support and services to all Registered Indians (Alberta Aboriginal affairs, 2001).

Metis – A French word meaning "mixed blood" which usually refers to people of mixed ancestry who merged during the days of the fur trade when Europeans and Indian people had children. The Metis are recognized as Aboriginal people in the *Constitution Act, 1982* (Alberta Aboriginal affairs, 2001).

1.2 – Type 2 diabetes: the epidemic

Type 2 diabetes incidence, prevalence, complications, and costs are increasing worldwide (Rubin et al., 1994; Simpson et al., 2003; Venkat Narayan et al., 2000; Zimmet, 2000). By 2025 it is estimated that 333 million people will have diabetes, most of whom will inhabit China, India, and the United States (King et al., 1998). Unfortunately, individuals within the

lowest socioeconomic status have the highest prevalence of diabetes. In North America, areas that were primarily plagued by infectious diseases in the early 20th century are now plagued by chronic diseases such as diabetes and heart disease. Ethnicity appears to be an important predictor of the disease, as the prevalence rates are higher in virtually all ethnic groups in contrast to the Caucasian population (Kenny et al., 1995). Disease prevalence has been noted to be rising since the early 1960's, however over the past couple of decades there has been an explosion in the incidence of diabetes. Type 2 diabetes was once a disease of the elderly, and has recently become increasingly prevalent in youth. The factors that are thought to predispose people to type 2 diabetes are: heredity, age, ethnicity, socioeconomic status, obesity, and lack of physical activity (Zimmet et al., 2001). Individuals with diabetes are at high risk of cardiovascular disease because the majority have hypertension, dyslipidemia, and are obese (Haffner, 1998).

Over time chronic hyperglycemia can be associated with a variety of complications - the most common being (but not limited to): cardiovascular disease, cerebrovascular disease, peripheral vascular disease, called macrovascular complications; and retinopathy, neuropathy, and nephropathy – termed microvascular complications. Type 2 diabetes is a leading cause of death, end stage renal disease, lower limb amputations, adult blindness, and cardiovascular disease (Venkat Narayan et al., 2000; Klein and Klein, 1995). Diabetes is very expensive to treat, costing Canadians between $4.76 and $5.23 billion United States dollars (USD) in 1998 (Dawson et al., 2002). Cardiovascular disease is the most prevalent complication in individuals with diabetes, and it is estimated that 80% of people with diabetes will die due to a vascular event (Barrett-Connor and Pyorala, 2001). Cardiovascular disease is also the most expensive complication of diabetes to treat in Canada, costing $637

million USD (Dawson et al., 2002). It is estimated that in Americans with diabetes, 50% have a physical disability and 30-60% have diabetic neuropathy. Diabetes is also associated with complications during pregnancy (Harris, 1995; Ryan, 1998).

1.3 – Undiagnosed diabetes and prediabetes

Prediabetes has recently attracted a great deal of attention, as researchers look for predictors of diabetes and methods to prevent the disease and its complications. Prediabetes is a state of elevated blood glucose below the threshold for diabetes (see methods for glucose criteria for diabetes). Individuals diagnosed with prediabetes are not certain, but quite likely to, progress to diabetes (Canadian Diabetes Association Clinical Practice Guidelines Committee, 2003a). Prediabetes is also known as impaired glucose tolerance (IGT) and/or impaired fasting glucose (IFG). These conditions are proposed to be associated with increased cardiovascular risk in addition to increased diabetes risk, through their association with insulin resistance (Reasner and DeFronzo, 2001). World wide, the ratio of prediabetes/diabetes is presently estimated at 314/194 million (IDF, 2003).

Undiagnosed diabetes is also of concern. Undiagnosed diabetes relates to living with diabetes and not knowing it, and can be present for up to 12 years without an individual presenting with signs and symptoms (Harris, 1993). Epidemiologic evidence shows (Kannel and McGee, 1979) that undiagnosed diabetes and undiagnosed impaired glucose tolerance (IGT), have adverse health consequences. At eventual diagnosis these individuals can present with both micro and macrovascular complications associated with diabetes

(Harris, 1993). Retinopathy has been documented to be as high as 21%. Rates of macrovasucalar disease have been found to be approximately the same in undiagnosed patients as compared to patients with diagnosed diabetes, with 61% of people with hypertension, and 49% with hypercholesterolemia (Harris, 1993). Table 1.3.1 illustrates the rates of undiagnosed diabetes and prediabetes in some studies done in North America. Canadian (Young and Mustard, 2001) and US data (Harris, 1993) (not in Aboriginals) and anecdotal data suggest that an important percentage of diabetes, in up to 1/3 to 1/2 of diabetic individuals, is unknown to the patient. When population based sampling is done, the prevalence of undiagnosed diabetes can be quite high, as in the Strong Heart Study which showed rates of undiagnosed diabetes to be 14% (Lee et al., 2000).

Table 1.3.1 – Undiagnosed diabetes and Impaired Glucose Tolerance

Population Study (reference)	Prevalence of diabetes, test utilized, and age group	Prevalence of undiagnosed diabetes	Prevalence of IGT / IFG	% of diabetic individuals undiagnosed
United States NHANES III (Harris and Eastman, 2000)	15.3% OGTT 40-75 yrs	7.4%	14.9% (IGT)	44%
Manitoba MHHS/MSSIP (Young and Mustard, 2001)	Males: 4% Females 5% FPG 18-74 yrs	Males: 2.2% Females: 2.3%	Males: 7.5% Females: 5% (IFG)	Males: 36% Females: 32%
Quebec (Delisle and Ekoe, 1993)	Males: 12% Females: 17% OGTT and A1c >15 yrs	3.7%	Males: 5% Females: 7% (IGT)	25%
Sandy Lake SLS (Harris et al., 1997b)	26% OGTT >10 yrs	10.7%	Males: 7.1% Females:19.8% (IGT)	41%
James Bay Cree DSSP (Dannenbaum, 2001)	15.5% FPG and A1c >10 yrs	2.5%	4.7% (IFG)	10.5%
American Indians SHS (Lee et al., 2000)	50.4% OGTT 45-74 yrs	14.4%	21.2% (IFG)	29%
United States, ARIC (Schmidt et al., 2003)	25% OGTT 53-75 yrs	12%	32% (IFG)	48%
Pima Indians (Knowler et al., 1978)	35.4% OGTT >25 yrs	13.9%	Not collected	39.1%

IGT = Impaired Glucose Tolerance, IFG = Impaired Fasting Glucose,
OGTT = Oral Glucose Tolerance Test, FPG = Fasting Plasma Glucose, A1c = Hemoglobin A1c

It is thought that early detection of type 2 diabetes or prediabetes could lead to effective treatment and cost effective prevention of complications (see screening and prevention of diabetes chapter 1.7).

1.4 – The metabolic syndrome – a risk factor for diabetes?

The metabolic syndrome (MS) is a condition that has been recently identified and is the subject of much attention. The metabolic syndrome has been recognized as a disease by the international classification of diseases (ICD) and is listed as condition 277.7. The metabolic syndrome can be defined as: a clustering of metabolic abnormalities that has been found to be associated with a risk of coronary heart disease, stroke, and cardiovascular mortality greater than that of its individual components (Isomaa et al., 2001). Metabolic syndrome is sometimes used interchangeably with the term insulin resistance. It is possible and quite probable, that individuals with metabolic syndrome have insulin resistance and vice versa, however it is not a definitive relationship. Insulin resistance is described as: inefficient insulin mediated glucose disposal. This results in hyperglycemia prompting hyperinsulinemia to attempt to deal with fluctuations in glucose during the "fed" state or during times of stress. If this hyperinsulinemia is insufficient, or insufficiently effective, hyperglycemia will remain, and present as diabetes. Hyperinsulinemia helps to cope with rising glucose levels and insulin resistance, however over time these high insulin levels lead to high triglycerides, low HDL cholesterol and hypertension (Reaven, 2004b). Reaven proposed that people who were insulin resistant also presented with an increased risk of cardiovascular disease. The cardiovascular community later agreed with this hypothesis after the NCEP/ATP III agreed that the factors listed in Table 1.4.1 significantly increased an individuals risk of a cardiovascular

event. The term "metabolic syndrome" was then used to describe these risk factors. It was also acknowledged that the metabolic syndrome and insulin resistance were closely related. Insulin concentration is not a specific criterion of the metabolic syndrome, but is thought to be the "root of the problem" (Reaven, 2004a). Insulin resistance and hyperinsulinemia have also been recently associated with cancer, polycystic ovarian syndrome (PCOS), and non-alcoholic liver disease (Reaven, 2004c).

The individual components that are referred to in the definition of MS are displayed in Table 1.4.1. There is disagreement about the criteria that should be used to define the metabolic syndrome. The World Health Organization (WHO), the European Group for the Study of Insulin Resistance (EGIR), and the National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATPIII) all have different criteria. The NCEP/ATPIII criterion has recently been the most widely used. The metabolic syndrome has had many different titles. These include: Insulin Resistance syndrome, syndrome X, metabolic syndrome X, dysmetabolic syndrome X, and, and Reaven syndrome (Ford, 2004).

Table 1.4.1 – NCEP/ATPIII Criteria for the diagnosis of the metabolic syndrome

Criteria	Diagnostic values
Waist Circumference	Males: >102cm Females: >88cm
Triglycerides	≥1.70mmol/L
HDL Cholesterol	Males: < 1.0mmol/L Females: <1.3mmol/L
Blood Pressure	≥130/85 mm Hg
Fasting blood glucose	≥6.1mmol/L

The metabolic syndrome is of concern because of its association to cardiovascular events and diabetes. The prevalence of metabolic syndrome in children and adolescents in the US is also increased (Eisenmann, 2003). Poor diet and lack of physical activity, which are rampant in North America, could be the cause of this unfavourable trend of MS in youth.

The metabolic syndrome has been looked at in various populations including Aboriginal peoples. The data is still scarce in Aboriginal populations of Canada, and only a few Aboriginal studies have been conducted in the US with regards to MS.

1.5 – Type 2 diabetes, prediabetes and risk factors in Aboriginal peoples

1.5.1 – Diabetes and prediabetes in Aboriginal peoples

Canada has three constitutionally recognized Aboriginal groups, the Métis, First Nation, and Inuit. Discussions will be focused on the prevalence of diabetes in the First Nations of Canada and in American Indians of the United States, as available data has been primarily collected in these peoples. Ethnicity appears to be an important predictor of the risk for and development of diabetes, as the prevalence rates are higher in virtually all ethnic groups in contrast to the Caucasian population (Kenny et al., 1995). This impacts Indigenous communities worldwide. Diabetes was unknown in Canadian Aboriginals 50 years ago (West, 1978; Hegele, 2001). At the time Aboriginal peoples were challenged by infectious diseases such as smallpox and tuberculosis, but there has now been an epidemiologic transition towards chronic diseases such as obesity, diabetes, and cardiovascular disease (Harris et al., 1997b; Anand et al., 2001; Omran, 1971). Published studies of prevalence in Aboriginals are as high as 50.4% in the American Indians (Lee et al., 2000), with similar

numbers reported in northern Aboriginal communities in Canada (Delisle and Ekoe, 1993; Fox et al., 1994). Aboriginal peoples of Australia have also been shown to have increased rates of diabetes ranging between 8-28% (O'Dea et al., 1993). The socio-economic disadvantage of these groups is invariably associated with accelerating the appearance of the disease (Young et al., 2000; Zimmet et al., 2001).

Cardiovascular disease is also becoming recognized as a threat in Aboriginal communities in Canada (Anand et al., 2001), and even when this is not associated with overt diabetes, there is often undiagnosed diabetes or prediabetes. The prevalence of type 2 diabetes in First Nations communities in Canada is increased 2- 3 fold over non-First Nations communities (Young et al., 2000). In the Metis population, the prevalence of diabetes has not been well documented. Available Canadian data relies on patient's self reported diabetes in response to various surveys. From the Canadian Aboriginal Peoples Survey (APS) done in 1991, the self reported age standardized rates of diabetes were 5.9% in males, and 10.8% in females (age-standardized) over 15 years of age (Bruce et al., 2003). This correlates to a 3 fold increase in prevalence compared to non-Aboriginal Canadians. Table 1.5.1 illustrates the different age standardized prevalence's in Aboriginal populations of Canada based on the APS.

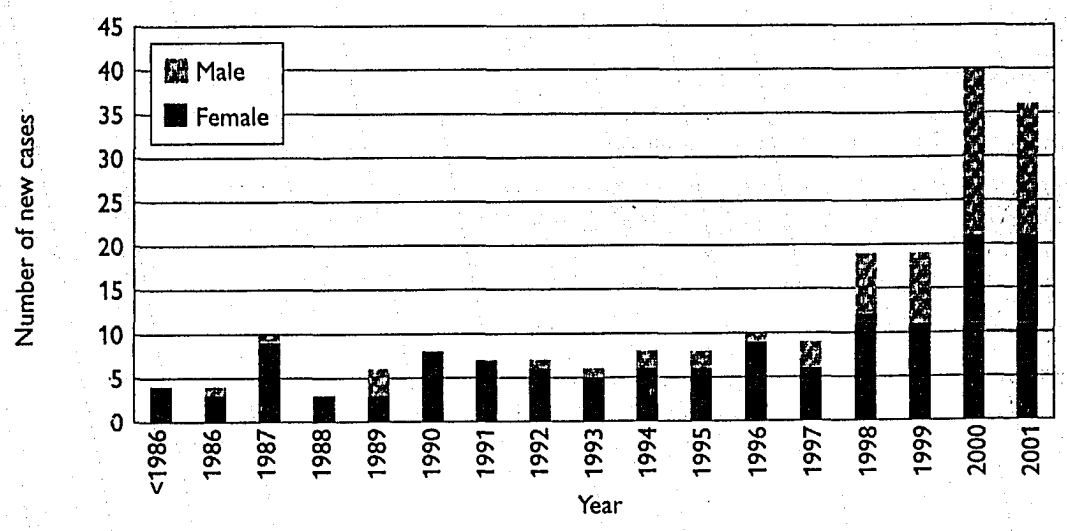
Table 1.5.1 – Age-standardized prevalence of diabetes in Aboriginal peoples of Canada 1991 (self-reported) (Bruce et al., 2003)

Gender	Metis	First Nations	Inuit	Canadians
Data Source	APS	APS	APS	GSS
Male	5.9	8.0	2.4	3.7
Female	10.8	10.5	3.5	3.2

APS = Aboriginal Peoples Survey, GSS = General Social Survey

Aboriginal people have a greater possibility of having a relative who has diabetes due to the increased prevalence in this population, suggesting the need to consider widespread screening for diabetes in Aboriginal communities. Table 1.3.1 (see chapter 1.3) illustrated some of the rates of diabetes and prediabetes in Aboriginals. Diabetes and prediabetes is also occurring at younger ages in Aboriginal peoples. Once unheard of in youth, type 2 diabetes is now a disease that should be screened for in children, as its prevalence in Canadian children (between 5-18 years of age) has been estimate to be as high as 1% (Dean et al., 2003; Dean et al., 1998; Fagot-Campagna, 2000). Figure 1.5.1 shows the increase in type 2 diabetes in children in Manitoba.

Figure 1.5.1 – Type 2 diabetes incidence in Manitoba First Nation children (Dean et al., 2003)



1.5.2 – Why is diabetes so high in Aboriginal people?

The statistics presented previously illustrate the large numbers of Aboriginal people with type 2 diabetes. The logical question is: why do Aboriginal people have such elevated prevalence of type 2 diabetes? One attempt to answer this question involves the "thrifty gene theory". The "thrifty genotype" theory postulates evolutionary adaptation over thousands of years to efficiently store energy. This would enable a population with this adaptation to live with relatively small amounts of food and survive periods of famine (Porte et al., 1997). However, due to the over abundance of high energy foods today, this "thrifty genotype" constitutes a genetic disadvantage.

Genetic contribution (such as the "thrifty genotype") has been suspected to account for a portion of the recent epidemic of obesity, diabetes, and other metabolic disorders (Neel et al., 1998). The foundation for much of the "thrifty genotype" theory originates in from the

Pima Indians of southern Arizona. The Pima in Arizona are closely related to the Pima Indians of Sierra Madre (in the mountains of Northern Mexico. About 700 – 1000 years ago these groups separated and the Arizona Pima lost their land and were forced into the American Indian Reservation system (Neel et al., 1998). It is suspected that this loss of land, forced abandonment of agriculture, accompanying loss of culture, and the government distribution of high-fat, highly refined foods, are a few of the many reasons why the Pima have some of the highest prevalence of diabetes to be documented . The Pima to the south lived a traditional life-style and remained physically active. Some of the differences between the two groups are shown in Table 1.5.2. When studies, the BMI and prevalence of diabetes were significantly less in favour of the Mexican Pima (Ravussin et al., 1994a).

Table 1.5.2 – Traditional lifestyle vs. Westernization in the Pima Indians
(Ravussin et al., 1994b)

Factor Collected	Pima Indians – Arizona (westernized)		Pima Indians – Mexico (Traditional)	
	Females	Males	Females	Males
BMI (kg/m^2)	35.5	30.8	25.1	24.8
Prevalence of diabetes	37%	54%	10.5%	6.3%

To add to this "thrifty gene theory", researchers are also noticing a high rate of diabetes in many immigrant populations in North America. This suggests that this theory is not only specific to Aboriginal people, but perhaps to other cultures as well. Another possible explanation of the high occurrence of diabetes in Aboriginal people is to examine how well, on average, Aboriginal people are living (see the Aboriginal perspectives on diabetes section 1.6).

1.5.3 – Gestational Diabetes

Gestational diabetes (GDM) can be defined as glucose intolerance with first onset or recognition during pregnancy (Metzger and Coustan, 1998). The overall incidence of gestational diabetes is 2 to 4% (Coustan et al., 1989; Engelgau et al., 1995; Forsbach et al., 1988; Remsberg et al., 1999), but this rate is doubled in many ethnic groups, including Aboriginal Canadians (Gerstein and Haynes, 2001). It is suspected that the prevalence of Aboriginal Canadians who have had GDM is between 8 and 18% (Harris et al., 1997a; Dyck et al., 2002). Increasing rates of gestational diabetes and the increasing prevalence of diabetes in Aboriginals helps to support the theory that an epidemic of type 2 diabetes is occurring in North American Aboriginal people (Harris et al., 1997b). Many of these children born to gestational diabetes mothers will become obese in later childhood, and childhood obesity is significantly correlated with adult obesity (Togashi et al., 2002; Maffeis et al., 2002; Deckelbaum and Williams, 2001). Increased prevalence of prediabetes and diabetes in offspring of diabetic mothers is also cause for concern. In addition, adult obesity is significantly associated with diabetes, and other chronic conditions such as heart disease and cancer (Pettitt et al., 1983; Silverman et al., 1995; Hu et al., 2004; Calle et al., 2003). For these reasons alone widespread screening for gestational diabetes is recommended, and is presently implemented in many centres around the world. Fat accumulation tends to be truncal with gestational diabetes, implying that the babies shoulder circumference is larger for a given weight. This leads to an increased risk of cephalopelvic disproportion (head is too large for pelvis) and birth trauma (Langer et al., 1994; Gilbert et al., 1999). Prevalent risk factors for gestational diabetes such as having had a large baby or poor obstetric history, could reflect unnoticed glucose intolerance during a previous pregnancy. Good glucose control (keeping sugars between normal values)

decreases the occurrence of macrosomia, cesarean section, and birth trauma in most pregnancies (Thompson et al., 1994; Naylor et al., 1996; Langer et al., 1994; al Najashi, 1995). Gestational diabetes, if detected, can be controlled, and dangerous side effects can be limited. Presently, nutrition, insulin therapy, and exercise are the accepted methods of treatment (Jovanovic and Pettitt, 2001).

1.6 – Aboriginal perspectives and health determinants

> There are more people with diabetes in the community than there ever were in the past, and it appears that there are more diabetics among Aboriginal people than there are among others in Canada
>
> ~ Ron Bernard, Golden Lake (Ship and Judy, 1998).

The purpose of this chapter is to provide a background of what Aboriginal people think of diabetes. Aspects include how diabetes affects Aboriginal people, and discussions of what can be done to prevent or slow the progression of this disease. This chapter will explore some of the current Aboriginal approaches towards health. Diabetes is affecting the lives of thousands of Aboriginal people across this country; therefore, it is imperative that Aboriginal voices are represented. The sections regarding Aboriginal approaches toward health and possible reasons for such high diabetes rates will include several quotes from Aboriginal people from a variety of communities. Diabetes is a cause for concern in Aboriginal communities today as this disease – which is silently killing many Aboriginal people across Canada - is often negatively affecting their quality of life.

1.6.1 – Aboriginal approaches towards health

Some individuals in today's society believe solely in scientific medicine in which physicians and allied health professionals are the main health care providers. These believers may feel

that Aboriginal forms of medicine and healing, in both the past and present, are less valid or sophisticated. However, "in pre-Columbian times, [Aboriginal] healers used a broad range of techniques, including history taking, physical examination, and treatment modalities that included surgery, massage, fracture setting, wound dressing, and herbal medicines" (Hollow, 1999). This suggests that Aboriginal people were practising similar methods of healing as those used by non-Aboriginal doctors. The suppression of these and other healing practises resulted in the current deficit that Aboriginal people face. One traditional Aboriginal view that is gaining acceptance in the non-Aboriginal community is the importance of attaining balance in each of the four aspects of a person: spiritual, emotional, physical, and intellectual are integral to health. The practices to achieve that balance may vary between Aboriginal groups, but the general principle remains constant. Figure 1.4.1 illustrates the medicine wheel. Each aspect is associated with a direction, north with spirituality, east with physical health, south with mental health, and west with emotional health.

Figure 1.6.1 – The Medicine Wheel

If one of the four aspects of a person is out of balance, that individual could have a greater probability of becoming ill. The view of treating the whole person is shown in the following: "Navajo healers clearly practiced a viable and real medicine that worked with the patients' mind as well as their body" (Alvord and Van Pelt, 1999). Because all four aspects operate synergistically, that individual may not feel physically well until he or she addresses spiritual, emotional, or intellectual problem(s) they are suffering from. If that person chooses to ignore or not deal with these problems, his or her physical ailments may continue to plague them until the issues are properly resolved. In this view, physical illnesses are seen as topical or surface problems. One can choose to ignore the deeply rooted problem by simply trying to "band-aid" their physical ailment, but ultimately, it may not heal until the true cause of the ailment is resolved. Some Aboriginal approaches to health demonstrate that healing begins with the individual. This approach to health gives individuals the power to heal themselves.

1.6.2 – Health Canada's determinants of health

When looking at the determinants of health as defined by Health Canada, the question is raised: do Aboriginal people enjoy the same level of health as non-Aboriginal people? In the next few paragraphs some of the determinants of health will be listed, followed by a brief definition given by Health Canada. Discussion will follow attempting to gage the question if Aboriginal people, on average, are attaining wellness in each particular determinant. Specific details of Canadian laws and policies of the past will be noted, when possible, that have influenced the health and wellbeing of many Aboriginal people.

1. Income and Social Status

Definition[1]: Health status improves at each step up the income and social hierarchy. High income determines living conditions such as safe housing and ability to buy sufficient good food. The healthiest populations are those in societies which are prosperous and have an equitable distribution of wealth.

Aboriginal people have a disproportionately higher poverty rate than other Canadians. In terms of income level, in 1990 54% of the Aboriginal respondents reported an annual income of less than $10,000, only 35% of Canadians as a whole did likewise (Waldram et al., 1995). One Aboriginal person discusses issues of low income with "[we] find no fresh fruits or vegetables available...sometimes the shelves are bare'...when the right foods are available they may be too costly" (Davis, 1999).

One system some Aboriginal peoples had of redistributing wealth within their community was the Potlatch or Give-Away ceremony. Not only did the host family give food, blankets, and other goods to the community members, this ceremony also "enabled individuals... and families to recount their histories and reaffirm their hereditary rights...the Potlatch served as an important institution reaffirming the oral and traditional history of the people" (Waldram et al., 1995). However, the Potlatch was banned in 1884 because the missionaries and government viewed it as "heathen and repugnant, and therefore roadblocks to civilization" (Miller, 1989). It is clear that Aboriginal people have had government laws and polices forced on them that, ultimately, affected their health and wellbeing.

[1] The definitions of all 10 key determinants of health are taken from (Health Canada, 1996).

2. Social Support Networks

Definition: Support from families, friends and communities is associated with better health.

In Canadian history, some Aboriginal peoples were taken away from their family, friends, and communities by legislation. For instance, the government and church operated residential schools which removed young children from their parents and communities. Sometimes, these children would remain at school for years without a single visit home to their family. The trauma, pain, and loss due to residential schools has been, at the very least, devastating for many Aboriginal communities. A loss of language and culture are the most visible today. However, Aboriginal peoples are extremely resilient and many are taking a proactive approach to healing individuals, families, and communities. This is shown with Wilson Bearhead's comment that "For too long we relied on the government to save us. From now on and in the future, we have to work together. We have to insure that those who have diabetes overcome it, and that our young people who don't have it don't get it" (Dansereau, 2001).

Many Aboriginal people believe that in order for health to be achieved, they must work together. The importance of social support networks as a determinant of health ties together with Aboriginal values towards achieving health. This is reflected with: "As First Nations people, we have a responsibility to ourselves, our loved ones and our children now and in future generations, to help each other in our journey to wellness" (Elliott, 1997).

3. Education

Definition: Health Status improves with level of education. Education increases opportunities for income and job security, and equips people with a sense of control over life circumstances – key factors that influence health.

It has been found that Aboriginal peoples, in general, attain a lower level of education when compared the general public. For instance:

> in the fifteen to forty-nine age bracket, only 50 per cent of [Aboriginals] in the survey reported having completed secondary school, with only 3 percent having completed a university degree. Some 17 per cent had not completed grade 9...33 per cent of the Aboriginal people surveyed reported at least some post-secondary education experience, the figure for Canadians nationally was 51 per cent (Waldram et al., 1995).

In more recent surveys, it was discovered that only "8% of the 25-34 age group of Aboriginal peoples had a completed university degree, while 28% of Canadians did" (Canadian Council on Social Development, 2003). These statistics paint an alarming picture, but given the historical trauma of cultural genocide experienced in residential schools these statistics are not surprising. However, Aboriginal people recognize the value of education in its purest form and the need for teachings to be passed down to younger generations. These ideas are reflected with the Akwesanse resident Barbara Barnes' comment:

> We want our Native people in our future generations to be healthy and to be good people...I'm positive about it. I think we can make these changes because we have good young people coming up who are going to be educated, not only in the non-Indian way but also in our way so that when it's combined, we'll have healthy communities (Ship and Judy, 1998).

In terms of type 2 diabetes, many Aboriginal people are optimistic that education will lead to a decrease in the disease. Many Aboriginal people believe western medicine is also proving to be helpful in some ways. For example, Doug Cuthland from Little Pine First Nation states that "we're trying to say, look, this disease is preventable if you don't have it, and if you do have it, it's manageable" (Canadian Diabetes Association (CDA), 2001). In addition, Isabel Benedict of Akwesasne believes that "educating the younger people would be a preventative measure....where you have to start is in the schools, in the elementary level" (Ship and Judy, 1998). Education, both traditional and western, is valued by many Aboriginal people.

4. Employment/Working Conditions

Definition: Unemployment, underemployment and stressful work are associated with poorer health. People who have more control over their work circumstances and fewer stress related demands of the job are healthier and often live longer than those in more stressful or riskier work and activities.

In Canada, the overall unemployment rate is approximately 8%, while the rate for non-Aboriginal Canadians is 25% (Waldram et al., 1995). However, "in some northern Aboriginal communities, the unemployment rate reaches as high as 90 per cent at various times of the year" (Waldram et al., 1995). Another startling statistic is that "in 1995, Aboriginal people in cities were more than twice as likely to live in poverty as non-Aboriginals" (Lee, 2000). In 2001, it was found that Aboriginal youth ages 15-24 were

twice as likely to be unemployed (Canadian Council on Social Development, 2003). The Royal Commission on Aboriginal Peoples stated that:

> Aboriginal people have faced discrimination in hiring and employment. They earn about one-third less in wages. They are less likely to hold down full-time, year-round jobs. They are much more likely to be employed in manual trades such as construction than in white collar jobs as professionals, administrators, managers or clerks (Lee, 2000).

Lower wages would ultimately lead to heightened stress levels and lower levels of control over work circumstances, resulting in poor levels of health.

5. Social Environments

Definition: Social stability, recognition of diversity, safety, good working relationships, and cohesive communities provide a supportive society that reduces or avoids many potential risks to good health. Studies have shown that low availability of emotional support and low social participation have a negative impact on health and wellbeing.

Matthew Penashue of Sheshashit believes that "all of our troubles began since the Government took over the life of the Innu" (Ship and Judy, 1998). This is also reflected with one comment that "ever since everything was forbidden, people have all kinds of sickness" (Garro, 1995). One of the complications that have increased with the increase in diabetes prevalence is heart disease (Laakso, 1999). Other complications mentioned earlier in chapter 1.2 and 1.3 are also evidence of Mr. Penashue's comment.

6. Physical Environments

Definition: Physical factors in the natural environment (eg. air, water quality) are key influences on health. Factors in the human-built environment such as housing, workplace safety, community and road design are also important influences.

When compared with non-Aboriginals, Aboriginal people have poorer housing. It has been stated that "the housing and living conditions of Aboriginal people have consistently been poor and below national standards" (Waldram et al., 1995). Statistics show that "32 per cent of homes nationally require either minor or major repairs, 49 per cent of Aboriginal households were in need of repair. Residents of Indian reserves, in particular, experience poor housing conditions, with 68 per cent of homes requiring minor or major repairs" (Waldram et al., 1995). Even though there is not a direct correlation between housing conditions and diabetes, these conditions do affect the health of the individuals with diabetes living in the home. There is an increased risk of injuries which may go unnoticed to the individual because of neuropathy caused by diabetes. Due to safety concerns of the health professionals, access to emergency services may be delayed or complicated by the condition of the home.

The natural environment of many Aboriginal communities is compromised compared to other Canadian communities. For example, most Canadians take clean tap water for granted, while "20 per cent of [Aboriginal communities'] available water is considered undrinkable" (Waldram et al., 1995). Contaminated water has a definite negative effect on health. Communities that do not have access to clean water are forced to rely on other

fluids for hydration, which are not always appropriate, that usually do more harm than good by increasing glucose levels (ie. Sodas and high sugar juices).

Many Aboriginal people were relocated into different areas by the government. The consequences of this were often disastrous, as they did not have extensive knowledge of the new land. An Innu man from Sheshashit states that "we were all corralled into this community. We didn't know how to live here" (Ship and Judy, 1998). Forced relocation and the destruction of the physical environment have resulted in Aboriginal people becoming less reliant upon the physical environment for sustenance. This creates more barriers to dealing with diabetes. Not only were many Aboriginal people forced to leave their traditional lands, the land, water, and air has now become polluted in many areas. The Nehinaw Cree believe that "pollution and other consequences of white manipulation...and destruction of the environment, such as ...hydroelectric projects... have negatively affected" their way of life (Bruyere and Garro, 2000)).

Many Aboriginal people believe the cause of diabetes is due to contamination of food. For example, an Anishnawbe Elder stated that diabetes began when "the white man started to put something into the food" (Garro, 1995). This factor is further analyzed in Garro (1995, p.42) "we eat everything and the cattle get needles, maybe that's where someone gets diabetes from. The grass the cattle eat is also sprayed". Kathleen Nuna from Sheshashit states that "I have never seen people with diabetes when I was in the country because we eat animals and berries ... diabetes...where did it come from?...and I think to myself 'the store'" (Ship and Judy, 1998). Many Aboriginal people believe that diabetes stems from store-bought foods. In the past, "we ate from the land. We were rich in the past; now we

are poor. We were able to have everything from the earth. We didn't take anything to buy" stated one Aboriginal person (Bruyere and Garro, 2000).

7. Personal Health Practices and Coping Skills

Definition: Social environments that enable and support healthy choices and lifestyles, as well as people's knowledge, intentions, behaviours and coping skills for dealing with life in healthy ways, are key influences on health.

Many Aboriginal people are making healthy choices such as exercise and nutrition in order to prevent diabetes. The importance of nutrition is made explicit with Bessie Lazore from Akwesasne's statement that "I know why I'm not diabetic...I don't eat junk food... I don't eat anything that's rich in fat... I do my own cooking and I know what I'm eating is good for me" (Ship and Judy, 1998). Again, the preventative aspect is reflected in: "along with the Elders, I decided we should reintroduce the traditional diet we once had, such as eating wild greens and eating according to the seasons, with ceremonies. We had a good diet; and it's acceptable that we can change back" (Grace, 1998). Anna King from Akwesasne commented on the importance of exercise. She said that "Exercise? Very important...you have to be really determined to change your lifestyle, your eating habits, everything, your energy levels. It has to be changed for you in order to get (control) of the diabetes you have in your system now" (Ship and Judy, 1998). When asked what causes diabetes, "some Elders think diabetes among Aboriginal people is caused by 'a lot of things in the past - - grieving' from a lot of the hurt they have been through since Europeans got here" (Black, 1999). This explanation illustrates how stressful social environments can influence health negatively.

8. Healthy Child Development

Definition: The effect of parental and early childhood experiences on subsequent health, well-being, coping skills and competence is very powerful. Children born in low-income families tend to be more likely than those born to high-income families to have low birth weights, to eat less nutritious food and to have more difficulty in school.

Aboriginal child poverty is at an alarming rate in Canada. According to the Canadian Council on Social Development, "52.1% of all Aboriginal children were poor...[and] Aboriginal children were four times more likely to be hungry" than other children (Canadian Council on Social Development, 2003). The appalling implications of poverty-stricken children are outlined in the definition of healthy child development.

9. Health Services

Definition: Health services, particularly those designed to maintain and promote health, to prevent disease, and to restore health and function contribute to population health.

Many Aboriginal communities do not have the same access to health care or health care professionals as non-Aboriginal Canadians do. First Nation and Inuit have their health care premiums paid for by the Federal Government. The First Nation and Inuit Health Branch (FNIHB) of Health Canada determines the non-insured health benefits that they are entitled to as a matter of policy, stemming from rights negotiated during the Treaties, which nevertheless are open to controversy and interpretation. These benefits are over and above health care premiums and include prominently transportation, strips for diabetes, medications in general, glasses, eye exams, etc. Metis people do not have any Treaty

derived health benefits and they pay for their premiums in the same way as other provincial residents. Geographic location creates disadvantage for many Aboriginal peoples. Many of these people live in rural and remote locations, where access to health services is limited. Cultural barriers to accessing health services, language, beliefs, use of traditional medicine, distrust of non-Aboriginal professionals, and insensitivity by non-Aboriginal professionals all intensify the problem.

10. Culture

Definition: Some persons or groups may face additional health risks due to a socio-economic environment, which is largely determined by dominant culture values that contribute to the perpetuation of conditions such as marginalization, stigmatization, loss or devaluation of language and culture and lack of access to culturally appropriate health care and services.

Rita Cooke form Golden Lake discusses how "an awful lot of people just lost their culture and are just trying to get it back... I know I did...they shipped me up to Spanish, up to a residential school...I know some Indian but not fluently" (Ship and Judy, 1998). Some Nehinaw Cree people "noted that if such [Aboriginal] healing practices had continued, there would undoubtedly exist ininiwimuskiki (medicine) that would be able to 'kill' the sugar [diabetes]" (Bruyere and Garro, 2000). Like Ms. Cooke explains, it is important to many Aboriginal people and others to retain their culture. Culture can create a support network and a feeling of belonging that is important to a healthy lifestyle. Included in cultural awareness and education may be the knowledge of traditional medicines that were used in the past, which could be vital to dealing with diseases such as diabetes.

When looking at the determinants of health, it is evident why Aboriginal peoples do not have the same level of health as other Canadians. These determinants may provide some ideas for research projects to try and reduce the burden on the health of Aboriginal peoples. Perhaps with this, there may be a reduction in the rates of diabetes.

1.6.3 – Chapter summary

In order for the relationship between western health care providers and Aboriginal approaches to health to survive, it is vital for both sides to communicate. A concerted approach would be beneficial to both sides. Aboriginal people are facing an epidemic of diabetes today; however one cannot ignore the other health threats facing many Aboriginal people: AIDS, fetal alcohol syndrome, suicide, drug abuse, addictions, cancer, mental illness, etcetera. Diabetes is only a specific piece of the larger puzzle. This is why it is important to look at the determinants of health as they not only relate to diabetes, but to the other diseases and social problems mentioned above. Limiting the barriers that Aboriginal people face on a daily basis may not eradicate the problems, but it is probable that it will better the status of health.

1.7 – Screening for prevention of type 2 diabetes – pros and cons

Over the past 50 years, there has been an epidemiological shift in terms of the diseases affecting Canadian populations. Within this time frame, there has been an emergence of chronic diseases such as cancer, heart disease, obesity and diabetes, and a reduction of the impact of infectious diseases and starvation (Harris et al., 1997b). The cost of diabetes and its complications and the provision of care in 1998 for Canadians with this chronic

disease (excluding our Aboriginal population) was estimated between $4.76 and $5.23 billion USD (Dawson et al., 2002).

Although the current rates of diabetes are high in the dominant Canadian society, there have been numerous studies that report that minority groups, such as First Nations people (Young et al., 2000; Jacobs et al., 2000) have an elevated prevalence of this disease (Harris and Eastman, 1996). Prevalence of type 2 diabetes ranges from 4.6 to 49.5% in Aboriginal communities worldwide (Harris et al., 1997b).

Undiagnosed diabetes refers to the existence of an elevated glucose levels that would meet criteria established for type 2 diabetes, but has not been diagnosed by a physician (Young and Mustard, 2001). Type 2 diabetes often remains undiagnosed for a number of years because hyperglycemia develops gradually and is often not severe enough for the patient to notice any of the classical symptoms of diabetes (ADA, 2003a). It has been estimated that between 6.3 and 8 million people in the United States have undiagnosed Type 2 diabetes, which translates to 2.7% of the adults over the age of 20 (Harris and Eastman, 1996; Young and Mustard, 2001; Harris, 1993; 2003). In the Diabetes Special Screening Project in the James Bay Cree (Dannenbaum, 2001) and in a study conducted with the Oji-Cree people in the Sandy Lake region of Ontario (Carpentier et al., 2003; Connelly et al., 2003; Harris et al., 1997b; Harris et al., 2002), the incidences of undiagnosed diabetes in 1997 were 2.5% and 10.7% respectively (Dannenbaum, 2001; Harris et al., 1997b). As discussed earlier (section 1.3) it is estimated that, on average, people have had type 2 diabetes for up to 12 years before they are diagnosed (Harris and Eastman, 1996; Harris, 1993). Data also suggests that retinopathy can be present as early as 7 years prior to diagnosis with diabetes and hyperglycemia (Harris, 1993).

So, the question is: Is screening for undiagnosed diabetes a worthwhile venture when considering clinical outcomes, methods of screening, and cost effectiveness? Both sides of this argument will be discussed, beginning with the disadvantages of screening for undiagnosed diabetes, followed by the benefits of such screening and recommendations made by a) diabetes associations/panels and b) those brought forth through studies with Aboriginal communities.

1.7.1 – Disadvantages of screening for diabetes

Although there is no argument that diabetes is a serious health problem that affects too many people, it is debatable whether actively screening for undiagnosed diabetes is practical, feasible, or beneficial. The following table outlines seven principles used to assess the value of screening for any medical condition. Generally, screening in "asymptomatic populations is appropriate when seven conditions are met" (ADA, 2003b).

Table 1.7.1 – Is screening for undiagnosed diabetes beneficial?
(Taken from (ADA, 2003b)

PRINCIPLES/CONDITIONS
1. The disease represents an important health problem that imposes a significant burden on the population.
2. The natural history of the disease is understood.
3. There is a recognizable preclinical (asymptomatic) stage during which the disease can be diagnosed.
4. Tests are available that can detect the preclinical stage of the disease, and the tests are acceptable and reliable.
5. Treatment after early detection yields benefits superior to those obtained when treatment is delayed.
6. The costs of case finding and treatment are reasonable and balanced in relation to health expenditures as a whole, and facilities and resources are available to treat newly diagnosed cases.
7. Screening will be a systematic ongoing process and not merely an isolated one-time effort.

With respect to diabetes, although conditions 1 through 4 are met, it remains unclear for some critics as to how conditions 5 to 7 are met. For example, it has been stated that:

> it is unknown whether the additional years of treatment that might be received by individuals diagnosed through screening would result in clinically important improvements in diabetes-related outcomes...[and] there are no randomized trials demonstrating the benefits of early diagnosis through screening of asymptomatic individuals (ADA, 2003b).

In terms of cost, evidence is not yet available that would suggest that community based screening is cost-effective or could reduce complications associated with the disease in otherwise healthy individuals (ADA, 2003b). Furthermore, no studies have been definitive on the cost-effectiveness of preventing or delaying the complications in newly screened individuals with prediabetes (Sherwin et al., 2003). Some feel that Principle 6 (see Table 1.7.1) regarding "facilities and resources to treat newly diagnosed cases" and Principle 7 (systematic on-going process) will not be adequately met outside of institutions or large managed health care organizations, i.e. the resources are not available in community

settings. This is also accompanied by a reduced likelihood that people who tested positive in the screening process will "follow through" with required repeat testing to ensure test results were accurate and truly positive, or with treatment when recommended by busy practitioners or a health care system already struggling to cope with existing increasing numbers of chronic diseases, including diabetes (ADA, 2003b).

One of the major criticisms regarding screening for previously undiagnosed diabetes is the fact that there is no cure for diabetes, so why screen? It has been stated that screening for diabetes and any other disease is only worthwhile when an effective treatment is available (Hofer et al., 2000). Given the very imperfect success in the treatment of individuals with diagnosed diabetes and its complications, it is suggested that scarce resources be directed primarily at "secondary prevention", given the high levels of evidence that this is effective in preventing or reducing the complications of diabetes (UKPDS, 1998a; DCCT, 1993). Based on the lack of scientific evidence currently available, community based screening for type 2 diabetes, even in high-risk populations such as Aboriginals, is not recommended (ADA, 2003b).

There are further considerations - other than clinical outcomes, cost effectiveness, and method of screening - to take into account. When determining if screening is worthwhile and beneficial, one must not forget to think of the social implications: How will an individual or community react to their diagnosis of type 2 diabetes? Will this cause feelings of stress, loss of hope, and helplessness within Aboriginal individuals or within their communities? Potential harm from the diagnosis of type 2 diabetes should be considered, as follows:

> Individuals can react negatively to whatever label they are given, and some may be discriminated against in the workplace or by insurers. Any intervention can, of course, promote anxiety and be socially disruptive. Finally, hazards resulting from the use of medications are always possible (Sherwin et al., 2003).

1.7.2 – Benefits of screening for undiagnosed diabetes

The documented rates of diagnosed and undiagnosed diabetes are of concern. There is also a distinct correlation between the health problems and diseases associated with the diagnosed and undiagnosed type 2 diabetes. For example, it has been shown that hypertension is as prevalent in individuals with undiagnosed diabetes as it is in those with known diabetes (Harris, 1993). Triglycerides are known to be noticeably elevated in pre-diabetic individuals. Triglycerides have also been shown to be one of the strongest predictors for coronary heart disease and death in individuals with diabetes (Harris, 1993; Young and Mustard, 2001). The total-HDL cholesterol ratio, A1c, body mass index, waist-hip ratio, and systolic and diastolic blood pressure are all elevated in people with undiagnosed diabetes compared with normoglycemic individuals (Young and Mustard, 2001). These risk factors show a striking resemblance to the metabolic syndrome discussed earlier in this chapter. Furthermore, retinopathy is detectable 6.5 to 7 years before diabetes is diagnosed and undiagnosed diabetes may exist for up to 12 years before diagnosis (Harris and Eastman, 1996). It has even been suggested that mortality rates may be higher in undiagnosed compared with diagnosed diabetes (Harris, 1993).

When looking at all of the heightened risks undiagnosed diabetes patients face, it seems evident than these people should be screened. Although there are reports stating that

screening is not economically feasible, supporters of screening conclude in their analysis that early intervention will significantly reduce complications of diabetes and will prove to be cost-effective (Harris and Eastman, 1996). Reductions in complications related to diabetes may prove the interventions to be beneficial in the face of the enormous stress they already placed on the healthcare system (Sherwin et al., 2003). The methods with which to intervene still remain unclear, and methods described in the recent literature do not appear to be feasible in community settings for extended time periods. Section 1.7.3 describes the logistics of screening.

Prevention studies have recently been published that are cause for optimism. Type 2 diabetes onset has been shown to be preventable or delayed by lifestyle or pharmacologic intervention in individuals with IGT, as shown recently by 4 published randomized controlled trials (Pan et al., 1997; Lindstrom et al., 2003; Chiasson et al., 2002; Knowler et al., 2002). The Diabetes Control and Complications Trial (DCCT) showed that near-normal blood glucose levels can be attained and can therefore prevent the development and slow the progression of microvascular complications of insulin-dependent diabetes (Herman et al., 1995). The United Kingdom Prospective Diabetes Study (UKPDS) showed that treatment of complications is more costly than intensive management to reduce or prevent those complications in individuals with diagnosed diabetes (Gray et al., 2002).

Furthermore, trials of other interventions (statins, angiotensin converting enzyme inhibitors, angiotensin receptor blockers...) that may delay or prevent diabetes are presently in progress (Padwal and Laupacis, 2004). Therefore many supporters of screening for undiagnosed diabetes believe that "early detection and treatment can reduce the burden

of the complications of diabetes" (Herman et al., 1995; Harris and Eastman, 1996). This would include the costs associated with complications, which are the most expensive aspect associated with diabetes care, particularly hospitalizations for renal and cardiac complications.

It is tempting to believe there would be benefits to early diagnosis of IGT/IFG and diabetes, such as the possibility of preventing micro-vascular complications that frequently occur in patients with diabetes over time. It is less clear that an early focus on glucose abnormalities would prevent macrovascular disease (UKPDS, 1998b), as the interventions that are beneficial in overt type 2 diabetes are generally multi-factorial. Initiatives such as the Diabetes Prevention Program (DPP) have described the advantages of screening for prediabetes. Diabetes incidence was reduced by 58% using lifestyle intervention and by 31% using pharmacological intervention (metformin). Furthermore, compared to the placebo group, lifestyle intervention can delay the onset of diabetes by 11 years, and metformin by 3 years. The cost per quality adjusted life-years (QALY) for lifestyle intervention was $1100 USD, and $31 300 metformin. These interventions are cost-effective in younger age groups; however metformin was not cost effective in those ≥ 65 years of age. Lifestyle intervention was more cost-effective at $16 000 per case of diabetes prevented, compared to $32 000 for metformin. In this study lifestyle intervention was shown to be "highly cost-effective", and metformin was shown to be "generally cost-effective" (Herman et al., 2005). Herman et al. say that cost-saving interventions should be widely implemented because of their effectiveness and cost benefits as compared to existing therapies. Interventions that cost less than $20 000 per QALY are said to be cost effective, those costing between $20 000 and $100 000 are perhaps appropriate, and

interventions over $100000 are perhaps not the best use of resources or a "Grade of D" (Laupacis et al., 1992).

1.7.3 – Logistics of Screening

Regarding the logistics of screening, some suggest using tools regarding the probability of developing diabetes, such as the American Diabetes Association risk questionnaire, in which a series of questions are asked and a numerical value is produced. However, there have been several publications which criticize this questionnaire because of its low specificity (Rolka et al., 2001). The questionnaire's ability to predict the risk of undiagnosed diabetes has a reported sensitivity of 59-69% and a specificity of 34-46% (Herman et al., 1995). A serious criticism is the fact that questioning regarding the individuals ethnic origin is completely absent, while numerous studies conclude that people of certain minority groups, including First Nations people, have an increased prevalence of type 2 diabetes. One of the questions regarding physical activity (See 3.6.1 for questionnaire) can be confusing to individuals. In addition, two of the seven questions require the individual to have knowledge on their parents' and siblings' medical history in relation to diabetes, when it is possible that the individual does not know if they have any family history of diabetes (Harris, 1993).

Screening with blood tests is more sensitive and specific, although this depends on the exact protocol used and the population prevalence. Official diabetes associations have generally not recommended universal (population based) screening. Opportunistic screening in physician offices in conjunction with periodic health examinations has been recommended by various panels. Table 1.7.2 illustrates these details.

Table 1.7.2 – Recommendations for (opportunistic) screening

	PANEL or ASSOCIATION
Age group	Over 45 years (unless high-risk) – American Diabetes Association (ADA, 2003b). Over 40 years (unless high risk) – Canadian Diabetes Association (CDA, 2003b).
Method of Screening	ADA – FPG or OGTT, community screening not recommended (ADA, 2003b). CDA – FPG or OGTT, community based screening recommended in Aboriginal communities.
Frequency of Screening	ADA – every 3 years (unless high risk) (ADA, 2003b). CDA – every 3 years (unless high risk) (CDA, 2003b)

FPG: Fasting plasma glucose, OGTT: Oral glucose tolerance test.

The Canadian Diabetes Association Clinical Practice Guidelines for the Management of Patients with Diabetes (CDA, 2003b) recommend that:

Recommendation # 1 – "All Individuals should be evaluated annually for type 2 diabetes risk on the basis of demographic and clinical criteria [Grade D, consensus]".

Recommendation #2 - " More frequent and/or earlier testing with either an FPG or 2hPG in a 75-g OGTT should be considered in people with additional risk factors for diabetes, i.e.: a first-degree relative with diabetes, member of a high-risk population (e.g. people of Aboriginal, Hispanic, Asian, South Asian and African descent), history of IGT or IFG, presence of complications associated with diabetes, vascular disease, history of GDM, history of delivery of a macrosomic infant, hypertension, dyslipidemia, overweight,

abdominal obesity, polycystic ovary syndrome, acanthosis nigricans, schizophrenia, [Grade D, consensus]"

In a separate chapter on Aboriginal peoples, the Canadian guidelines recommend (CDA, 2003c):

Recommendation #2 – There must be recognition of, respect for and sensitivity regarding the unique language, culture and geographic issues as they related to diabetes care and education in Aboriginal communities across Canada [Grade D, Consensus]

Recommendation #4 – Community-based diabetes screening programs should be established in Aboriginal communities. Urban people of Aboriginal origin should be screened for diabetes in primary care settings. [Grade D, Consensus].

1.7.4 – Screening for diabetes - summary

Universal population based screening is not yet recommended for diabetes because the cost effectiveness of such a widespread intervention is unknown in the general population. (Metzger and Coustan, 1998; CDA, 2003b). Therefore most experts recommend against systematic screening for undiagnosed diabetes, because of the potential harmful effects of labelling, discrimination, and sense of helplessness in an individual that may be induced in the absence of proof that this would be medical benefit. However communities or groups with a high prevalence, such as ethnic groups or Aboriginals, are encouraged to undertake screening projects for their members if so desired. The method of screening should also be decided by the community members and/or leaders in conjunction with health care professionals, in consideration of costs and practicalities such as availability of labs, transportation, or even more importantly, follow up.

Health practitioners have the knowledge and technology to screen for a disease that is the leading cause of blindness, end-stage renal disease, and lower-extremity amputations. Although there may be individuals who experience more harm than good by learning of their previously undiagnosed diabetes, the decision of whether or not Aboriginal people should learn of their status should not rely exclusively on episodic, incident driven care, such as is common in the present health care system. Systematic screening should be considered. Aboriginal people should be involved in the decision making process.

Resources to undertake this and other important diabetes initiatives are now becoming available in Canada through the Aboriginal Diabetes Initiative (ADI). In view of the interest of many Aboriginal people in understanding and tackling this problem of diabetes it is reasonable to explore the feasibility of strategies for individual or population based screening because of the presumed high prevalence of undiagnosed diabetes and IGT/IFG.

1.8 – The role of portable technology

In Edmonton, the role of portable technology could be considered less important than in Fort Chipewyan, a fly in community in the north of Alberta. Small communities cannot support standard laboratories, so intermittent testing with relatively small and inexpensive portable technology is appealing. Other reasons for portable technology include: funding for staff and resources are limited, and few knowledgeable staff to perform testing are available. For these reasons, portable technology is a feasible alternative for rural screening projects. These projects require equipment that is small enough to be transported in

vehicles such as vans, and they need to be lightweight, durable, withstand temperature changes, and most importantly be effective in the role they are required.

Portable technology has come a long way in the past two decades. Equipment is available that is faster, smaller, and more accurate. However accuracy needs to be comparable to standard laboratory methods and as such quality control programs are required. An in-depth explanation of the portable technology and the quality assurance program used in the BRAID study is presented in the methods section (Chapter 3).

As far as tests to diagnose diabetes mellitus and IGT/IFG, the oral glucose tolerance test (OGTT) is regarded as the gold standard, although this is not without controversy (Engelgau et al., 2000; Gabir et al., 2000) The fasting plasma glucose has been recommended, however, because of its simplicity as compared to the OGTT (CDA, 2003b). An A1c test, which is also simple and requires no fasting, has also been suggested; however, as of yet the test is not well standardized in its performance (Rohlfing et al., 2000b). The A1c is a well-established biochemical marker of diabetes control over a long time period compared to the fasting glucose. The DCA 2000® by Bayer which measures the A1c is an analyzer that has been used in multiple centres around the world (Shephard and Gill, 2004). This tool, which is small and portable, can be used in rural and remote communities where access to health care services is limited. The Cholestech LDX® has also been utilized around the world for measurement of lipids and glucose (Shephard and Tallis, 2002). Both of the analyzers mentioned here are practical and easy to use. Some of the Aboriginal health care workers involved in the projects have commented on the ease and simplicity of use. Training for the technology is simple and only requires a few hours.

None of these analyzers can be used in the field and be expected to work perfectly the entire time. For this reason we employ an extensive quality assurance procedure which is detailed in the methods section. The OneTouch® Ultra® capillary blood glucose meter was used in one of the projects in addition to the DCA 2000® and Cholestech LDX®. Details and figures of the analyzers are also shown in the methods section.

Chapter 2

Hypothesis

Hypothesis 1

Portable technology will be comparable to standard laboratory methods for determination of diabetes and prediabetes (IFG).

Hypothesis 2

The prevalence of diabetes, prediabetes, diabetes and cardiovascular disease risk factors, and the metabolic syndrome will be higher in an opportunistic screening program (SLICK and MDSI) as compared to a population based screening program (BRAID).

Chapter 3

Methods

3.1 – The projects explained – The SLICK, MDSI, and BRAID projects

Three projects will be utilized for the analysis in this research. All projects are concerned with Aboriginal peoples in Alberta, either with First Nation people on First Nation reserves, or Metis people living on Metis settlements or in remote areas of Alberta. The three projects are named SLICK, MDSI, and BRAID. This section will attempt to briefly describe each of these projects. The three projects have travelled to numerous communities in Alberta.

3.1.1 – The SLICK project– Screening for Limbs, I-eyes, Cardiac, and Kidneys

The SLICK Project is a University of Alberta - Alberta First Nations initiative that aims to reduce the burden of diabetes among First Nations communities in Alberta by providing access to a comprehensive, coordinated, and integrated screening program for limb, retinal, cardiovascular, and renal complications of diabetes. The SLICK project commenced in 2001 and involves the deployment of two mobile vans equipped with screening staff and portable testing equipment to all 44 Alberta First Nations communities. Screening of clients with known diabetes includes retinal photography, and lab testing for glucose, A1c, lipids and microalbumin. Although initially conceived as a program to screen for complications of diabetes, consenting individuals wishing to be screened for diabetes are pre-screened with portable technology and a pre-specified protocol (see Figure 3.1.2). Thus the SLICK project is an opportunistic screening project that screens volunteers wishing to be screened for diabetes. A specialized team travels to First Nation communities transporting portable testing equipment. The exclusion criteria used in this project are shown in Table 3.1.1. The program provides relevant education and counselling in

conjunction with screening activities. The Alberta Aboriginal Diabetes Initiative is being deployed simultaneously, and both programs are coordinated by the Implementation Committee of the Aboriginal Diabetes Initiative (ICADI). The SLICK program is designed to increase awareness of diabetes complications and their management, as well as increase services. Intermediate goals include client empowerment, and increased identification of complications. It is hoped that the achievement of these short-term and intermediate goals will eventually lead to the long-term outcome of decreasing the burden of diabetes among First Nations populations. The SLICK project is currently funded by Health Canada. Dr. Ellen Toth is the principal investigator from the University of Alberta.

3.1.2 – The MDSI project – The Mobile Diabetes Screening Initiative

In May 2003 Health Minister Gary Mar (Alberta) announced the 10 year Alberta Diabetes Strategy, comprising four components of which one was to provide resources for "screening for diabetes and it's complications" in Aboriginal 'off reserve' and remote Alberta communities. The MDSI project is similar to the SLICK project in respect to screening for diabetes. It is also an opportunistic screening program, screening volunteers who are interested in being screened. A specialized team travels to Metis Settlements and other remote communities in a van transporting portable testing equipment. Screening of clients with known diabetes includes retinal photography, and lab testing for glucose, A1c, lipids and microalbumin. Consenting individuals wishing to be screened for diabetes are pre-screened with portable technology and a pre-specified protocol (see Figure 3.1.2). The exclusion criteria used in this project are shown in Table 3.1.1. Individual counselling is provided to all clients by a diabetes educator. The majority (~70%) of individuals who visit

the MDSI van have not been previously diagnosed for diabetes. Dr. Ellen Toth is also the principal investigator of this project.

3.1.3 – The BRAID project - Believing we can Reduce the Aboriginal Incidence of Diabetes

The BRAID project is a unique project that is exclusively carried out in a single First Nation community in northern Alberta. This project's main focus is to screen the entire community over the age of 6 that have not been previously diagnosed with diabetes. This project is different from the SLICK and MDSI project in that it is a population based screening project. This project actively encourages all the members of the community to come and be screened to try and get an accurate representation of the population. The project utilizes health care centre staff (in the community) to recruit individuals to the screening project. The exclusion criteria are similar to the SLICK project and the MDSI project (see Table 3.1.1). The BRAID project screens clients for diabetes using portable technology which will be discussed later in this chapter. Individuals who consent to being screened go through a series of stations, as shown in Figure 3.1.2, where testing of blood glucose, A1c, lipids, and anthropometric measurements are done. All individuals who are screened received counselling on their results. Each individual then has documentation sent to either (and or all): A. themselves, B. their nurse or health centre, and C. their doctor. The BRAID project is one of only a handful of community diabetes screening iniatives in Canada's First Nations. Dr. Ellen Toth is also the principal investigator of this project. This project is partially funded by the Aboriginal Diabetes Initiative (ADI) and the University of Alberta.

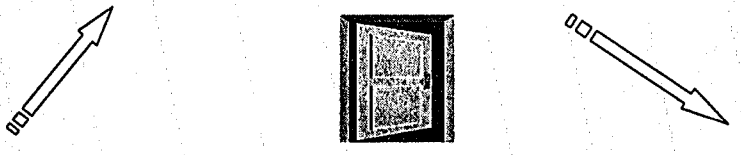
Table 3.1.1 – Exclusion criteria for the SLICK, MDSI and BRAID projects

Exclusion Criteria
Under Age 6
Inability to give consent
Documentation of Diabetes (FPG > 7.0mmol/L or Random >11.1mmol/L)
Prediabetes (IFG > 6.1mmol/L, or Random > 7.8mmol/L)
Medications for Diabetes
Insulin for Diabetes
Pregnancy
< 6 weeks post partum
Foreshortened Life Expectancy (<12 months)
Hospitalization, or any stress (<1 month ago)
Use of Corticosteroids (< two weeks ago)

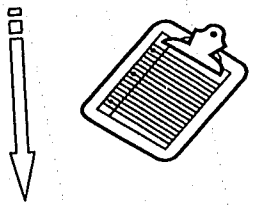
Note: Individuals who were > 6 weeks post partum and had gestational diabetes were screened.

Figure 3.1.2 – The SLICK, MDSI, and BRAID projects

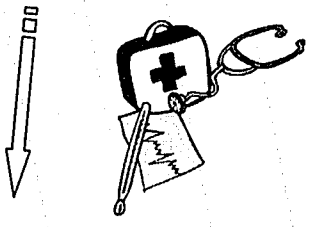
1. Health Centre or Community Reception



2. Exclusion criteria?

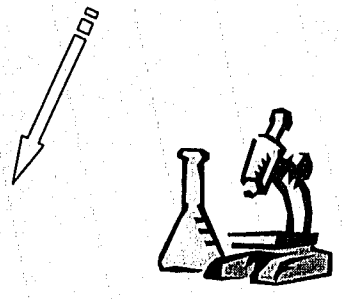


3. Information sheet and consent form

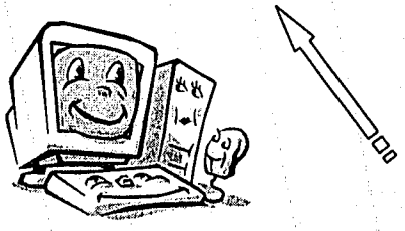


4. Anthropometric parameters – height, weight, waist circumference, blood pressure.

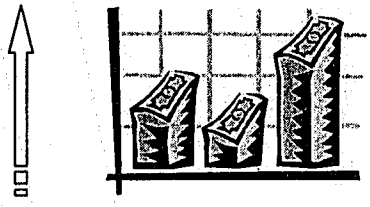
5. Laboratory tests – blood glucose, A1c lipid profile (HDL, LDL, TC, TRG).



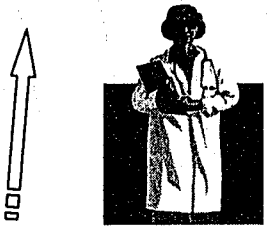
6. Results Output –Data Entered



7. Review of results - Staff



8. Education and Follow-up – Administer risk questionnaire.



3.2 – Ethics

Before obtaining appropriate permission from individuals and organizations the BRAID study underwent an extensive ethics review with the Health Research Ethics Board (HREB) at the University of Alberta. The SLICK, MDSI, and BRAID projects have their own separate ethics approval to work with their respective communities. Ethics approval was obtained simultaneously and in discussion with Health Directors and/or Chief and Council in First Nations Communities, and appropriate persons or committees in Metis settlements who were contacted and asked to verbally and/or in writing provide approval and cooperation with the research. The ethics approval for the BRAID study is attached as Appendix 2. Once the respective community approval was received, and the projects implemented, each individual is asked to read an information sheet and consent to the SLICK, MDSI, or BRAID projects (attached in Appendix 3). The main aspects of the individual consents pertaining to research are the permission to enter the results in a database (computer), and the permission to send relevant clinical results to caregivers (nurses or physicians). Permission for aggregate analysis is also important. Individuals can, upon request, receive "health services" screening for diabetes, and withhold consent for research.

3.3 – Collection of data

After informed consent is discussed, each individual is assessed with respect to whether they meet the exclusion criteria (see Table 3.1.1). In a small number of cases, where exclusion criteria applied, "health services" were carried out if clinically reasonable. These individuals were not included in the analysis of this study. Individuals that were not excluded were then passed on to another station where they had anthropometric

measurements taken. The results were recorded on a report sheet that was created once the individual had consented (see Figure 3.3.1), (the SLICK and MDSI projects had similar report sheets). Height was measured in meters using a standard height scale (Road Rod 214 from Seca); weights were recorded in kilograms by a standard dial weigh scale (Health o meter®) already present in the health centers. Body mass index (BMI) was calculated (automatically by the database) by dividing the weight in kilograms by the height squared (kg/m^2). Waist circumference was measured, in centimeters, using a standard measuring tape (Prym-Dritz Corporation) at the iliac crest. Blood pressure was taken using a standard professional adult sphygmomanometer (A.M.G. Medical) always in a supine position. For children or other individuals with smaller upper arm circumference, a childrens blood pressure cuff was used. Once these measurements were taken individuals were asked to proceed for blood testing. All three projects used the Cholestech LDX® analyzer (Cholestech Corporation) for measurement of blood glucose (fasting or random), high density lipoprotein (HDL cholesterol), low density lipoprotein (LDL cholesterol), total cholesterol (TC), and finally triglycerides (TG). If a random blood test was done (individual being tested had any food or drink within the previous 8 hours) their triglyceride and low density lipoprotein values were disregarded, since these tests are not reliable in a random state. The DCA 2000® analyzer (Bayer diagnostics) was used for measurement of hemoglobin A1c (A1c), which is not affected by the random state.

Figure 3.3.1 – Patient report sheet for the BRAID Project

The BRAID Project

Believing we can Reduce Aboriginal Incidence of Diabetes

Collaboration between *(removed for privacy)* First Nation, Aboriginal Diabetes Initiative, and University of Alberta

Visit #	RESULTS FORMS (1)	Male/ Female

Date:_____

Name (last, first, middle)	
Date of Birth (month/day/year)	

CLINICAL ASSESSEMENT	
Height (cm)	
Weight (kg)	
Waist Circumference (cm)	
Blood pressure	
Time last ate	
BMI (see chart in index)	

American Diabetes Association Risk Assessment Score*

BLOOD WORK	Results		Target
Triglycerides (fat that you eat)			Less than 2.3
Total cholesterol			Less than 5.2
Blood glucose	Meter	Cholestec	Less than 6.1 for fasting Less than 7.0 if after meal
HDL (good cholesterol)			Over 0.9
LDL (bad cholesterol)			Less than 3.4
Hemoglobin A1c (diabetes control)			Less than 6.1 %

RESULTS FORM (2) -- Please refer to the **Results Interpretation Guide** section for guidance

1. Clinical Interpretation:
☐ Obese (BMI over 30) ☐ Overweight (BMI 25-30) ☐ Hypertensive

Notes

2. Lipid Interpretation:
☐ High LDL ☐ High TG + Low HDL
☐ presumed normal ☐ uninterpretable

Notes

3. Glycemia Interpretation:

☐ Presumed diabetes ☐ possible IGT / IFG
☐ presumed normal ☐ uninterpretable

Notes

3.4 – Quality Assurance

Prior to blood collection, a strict quality assurance (QA) procedure is completed on the Cholestech LDX®, and the DCA 2000® analyzers. This QA procedure is completed in cooperation with Canadian External Quality Assurance Laboratories (CEQAL, Vancouver B.C). Figure 3.4.1 and Figure 3.4.2 shows the process for the QA. The analyzers are tested before they are used in the field (by CEQAL) to make sure all instrumentation is functioning. Once the analyzers were initially sent to Edmonton, a workshop was established for all those working with the technology. All staff had two full days of education along with hands on use with the technology. The procedure was explained and all the machines were distributed accordingly. Each project has separate analyzers. The instruments are handled with utmost care because of the delicate instrumentation present in the analyzers. The analyzers do not have an expiry date associated with them, but the reagent cartridges that are used to test the blood expire within three months. Once the reagents are obtained (from a local warehouse that orders and stores the reagents), they are transported on ice (Cholestech LDX® reagents), and at room temperature (DCA 2000® reagents). The Cholestech LDX® reagents must be stored at 2-8°C, until they are ready to use. Once they are removed from refrigeration and placed at room temperature the reagents are only valid for 30 days. The DCA 2000® reagents can be stored at 2-8°C for 1 year, but once placed at room temperature are only valid for 3 months. Both reagents are only used when they have reached room temperature (17-25°C), as recommended by the manufacturers.

In addition CEQAL provides controls. These are samples of blood taken from a venous puncture in the laboratory, and analyzed by CEQAL in Vancouver. CEQAL then

compares their results to an external laboratory in Minnesota, which once completed, establishes the criteria for the QA (shown in Appendix 4). Once CEQAL tests and analyzes the results they establish reference values or a "valid range" for the analyzers. Each analyzer has a "valid range" that the QA must satisfy. QA is performed before screening any individual, and at the end of the day it is repeated. Criteria for the QA have reference values for 5 variables (A1c, glucose, total cholesterol, HDL cholesterol, and triglycerides). For each variable there is an "orange" value referring to the lower scale criteria, and "pink" referring to the higher scale criteria. After the control sample is run and the output has been obtained, the results for the DCA 2000® are recorded in a QA binder. For the Cholestech LDX® a further step is necessary. The Cholestech LDX® needs a correction spreadsheet called the "Cholestech Regression spreadsheet". Each analyzer has its own specific regression spreadsheet (provided by CEQAL). Results that are obtained are corrected by entering in the raw data output from the analyzer into the regression spreadsheet. The spreadsheet automatically corrects the raw data, and labels it "corrected data". This corrected data is then used to assure that the machines are working within the "valid range". If the results for the QA are not valid the first time, they are to be repeated once more. If the results are not valid a second time, a technician is phoned and a problem report and trouble shooting procedure is completed. If the results are in the "valid range", screening commences. This process is then repeated after the last individual is screened for that day. Again if there are any problems they are to be handled in a similar manner as mentioned previously. If the QA results do not fall in the appropriate reference range at the end of the day, the results for that day are to be discarded (however this did not occur in any instances). The Cholestech LDX® correction process is completed for every

individual screened in the three projects using the same regression spreadsheet used in the QA.

Figure 3.4.1 – QA procedure prior to utilization of analyzers

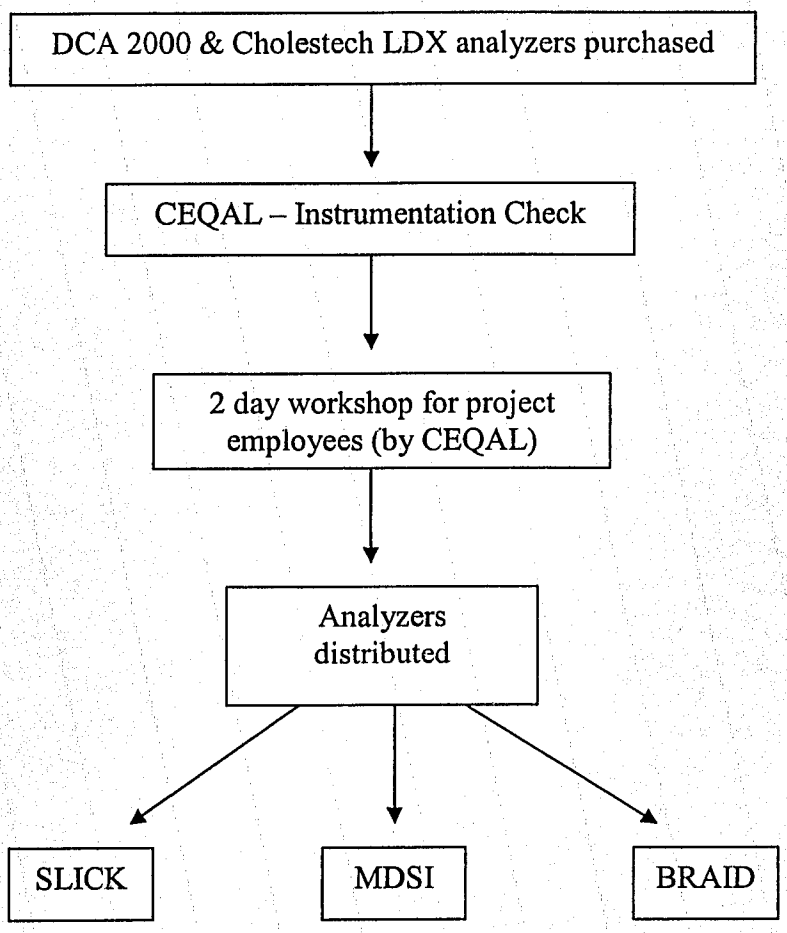
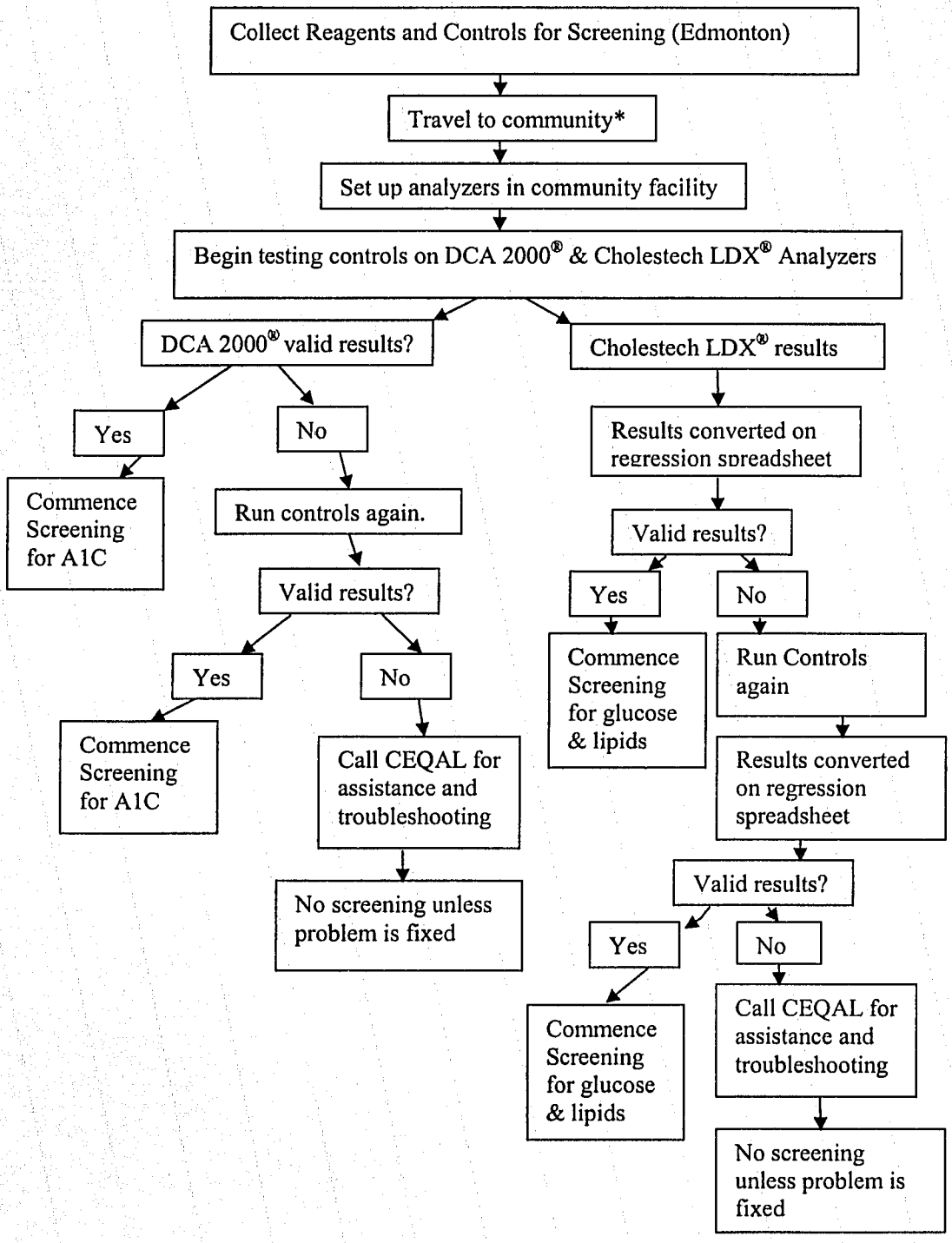


Figure 3.4.2 – QA procedures from community to the individual.



* Analysers are transported with the SLICK and MDSI projects (in vans), whereas they are kept in the Community in the BRAID project.

The controls that were used in the three projects were shipped (frozen, and on ice) to a warehouse in Edmonton. Controls were obtained by staff from the projects before every trip, or screening visit was planned. These controls were kept frozen (<-10°C) while transported to communities, and while stored in community health centres. Once the controls were thawed, they could not be frozen again, and they were to be used within 3 days of thawing.

Once screening is completed in a community, the QA results are entered into various spreadsheets (created by CEQAL) and emailed to CEQAL. CEQAL provides detailed feedback on the function of the analyzers. If any problems are occurring CEQAL provides feedback as to what actions need to be taken. The DCA 2000® analyzer operates with a CV of 2.5% and an average bias of 6.19% for a total error of 12.1%. Total cholesterol, HDL cholesterol, triglycerides, calculated LDL and glucose are all measured using a single testing cassette on the Cholestech LDX® analyzer. The performance characteristics for these tests on this analyzer are shown in Table 3.4.1:

Table 3.4.1 – Performance Characteristics for the Cholestech LDX® Analyzer

Analyte	CV (%)	Average Bias (%)	Total Error (%)
Total cholesterol	2.68	0.86	6.1
HDL cholesterol	1.95	- 0.06	3.9
Triglycerides	2.38	- 0.66	5.3
Glucose	1.97	- 2.75	6.6

These performance characteristics are similar to those that are currently being achieved at major testing centers in urban communities, as assessed by the CEQAL. Thus, in our analysis we plan to use the Cholestech LDX® determined fasting glucose as the "standard"

3.5 – Biochemical Measurements

When blood collection is to begin, the individual is asked if they have washed their hands; additionally a health care professional sanitizes the finger that will be utilized for the puncture with a Webcol® isopropyl alcohol sterile swab (Kendall). Only one capillary puncture is done for the testing (in some instances where more volume of blood is required another puncture is done). We utilize the Accu-Chek Safe-T-Pro (Roche Diagnostics) lancet for all blood testing. The depth of the puncture can be adjusted on these pen-shaped tools for the various skin thickness of the individual being tested. Once the puncture has been administered the first blood droplet is discarded using a sterile cotton swab. The subsequent blood is collected for the DCA 2000®. This is done by using the capillary holder (Figure 3.5.1). This holder uses capillary action to collect 1uL of blood. Then the Cholestech LDX® analyzer sterile capillary tubes (see Figure 3.5.2) are used to collect blood for this test. These capillary tubes collect between 45-60uL of capillary whole blood (although venous whole blood could be used).

A1C

The DCA 2000® Analyzer utilizes an immunochemical technique for measuring HbA_{1C}. The blood is loaded onto the reagent cartridge shown in Figure 3.5.2. A monoclonal antibody reacts specifically with an amino acid sequence on the A_{1C} molecule. A_{1C} is formed by the non-enzymatic glycation of the N-terminus of the beta-chain of $H\text{-}A_0$. The concentration of HbA_{1C} and total Hb are measured and the ratio is reported as percent HbA_{1C}.

Glucose

For measurement of glucose the Cholestech LDX® utilizes the glucose oxidase method. Glucose oxidase catalyzes the oxidation of (beta)-D-glucose to D-gluconic acid and hydrogen peroxide. The quantity of hydrogen peroxide is measured by a colour change when reacted with a chromogenic oxygen receptor. The glucose concentration in the blood is derived from this colour change. This reaction is shown in Equation 3.5.1.

Equation 3.5.1 – Measurement of Glucose using the Cholestech LDX

$$b-D-Glucose+O_2 \xrightarrow[oxidase]{glucose} O-D-Glucolactone+H_2O_2$$

$$2H_2O_2+4AAP+\underset{no\ colour}{TOOS} \xrightarrow{peroxidase} \underset{purple\ colour}{Quinoneimime\ dye}+H_2O$$

Total Cholesterol and Triglyceride

These two predictors of cardiovascular disease are measured enzymatically using a Trinders indicator system with N-ethyl-N-sulfohydroxylpropyl-m-toluidine sodium salt (Trinder, 1969).

HDL Cholesterol

HDL needs to be separated from other lipoproteins prior to analysis. The cholesterol is isolated using dextran sulphate/magnesium acetate (Warnick *et al.*, 1982). The remaining filtrate, which contains the HDL cholesterol, is moved to the HDL cholesterol reaction pad where it is measured enzymatically as above.

LDL Cholesterol

LDL Cholesterol is calculated using the formula shown in Equations 3.5.2. This is known as the Friedewald formula, and it provides an adequate estimate of the LDL cholesterol (Friedewald *et al.*, 1972). It is important to note that triglyceride concentrations must be under 4.5 mmol/L. This is one of the reasons why fasting measurements are preferred during lipid screening.

Equation 3.5.2 – The Friedewald formula for LDL cholesterol

$$LDL\ Cholesterol = Total\ Cholesterol - HDL\ Cholesterol - \frac{Triglyceride}{2.2}$$

The Cholestech can analyze concentrations within the following ranges: total cholesterol 2.6 to 12.9 mmol/L, triglyceride 0.5 to 7.3mmol/L, and HDL cholesterol 0.4 to 2.6 mmol/L.

For the SLICK and MDSI projects, the blood collection phase is now completed. Every individual is then asked to proceed to the next station to wait for their results to be printed, interpreted, and then finally discussed.

In the BRAID project we have a unique addition to the assortment of tools that have been mentioned previously. We utilize the OneTouch® Ultra® (LifeScan) blood glucometer (Figure 3.5.3) as an additional measure of glycemia. Each glucometer is coded to the correct test strip lot number, and is then verified to be working properly using the quality

assurance method that is provided with each machine. New lots of test strips are opened every 3 months. All strips are stored at room temperature, and are never left exposed to light or surrounding environment. Once this step is done, health care staff in the BRAID project collect blood for the glucometer using a OneTouch® Ultra® test strip (see Figure 3.5.3). The blood for the glucometer is directly collected onto the strip which has been loaded into the glucometer before any sample has been absorbed. The test strip utilizes 1uL of blood. Following this, the blood was collected for the DCA 2000® and the Cholestech LDX® analyzers. A sterile cotton swab is then administered to the finger where the puncture had taken place. The individual being tested is then asked to place pressure on this finger until the bleeding has ended.

Now that the blood is collected, the next phase is to administer the blood into the reagent cartridges for the Cholestech LDX® and the DCA 2000® analyzers. For the DCA 2000® the capillary holder (shown in Figure 3.5.1) is then placed into the reagent cartridge (Figure 3.5.1). This reagent cartridge is then placed into the DCA 2000® analyzer (Figure 3.5.4), where the results will be analyzed and displayed. Once the reagent cartridge is loaded for the DCA 2000®, the reagent cartridge for the Cholestech LDX® is loaded into the analyzer (Figure 3.5.5). The DCA 2000® takes 6 minutes to complete, whereas the Cholestech LDX® takes approximately 4 minutes to complete. The DCA 2000® A1c determines both the concentrations of the HbA1c molecule and the total haemoglobin. The ratio of these two quantities is expressed as a percentage HbA1c (A1c). Figure 3.5.6 gives an overview of the collection procedure.

Figure 3.5.1 – Capillary holder, and reagent cartridge for the DCA 2000® analyzer (Bayer diagnostics)

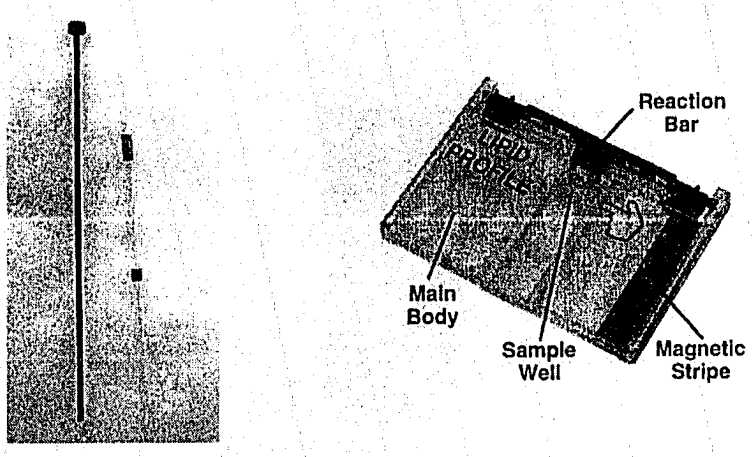
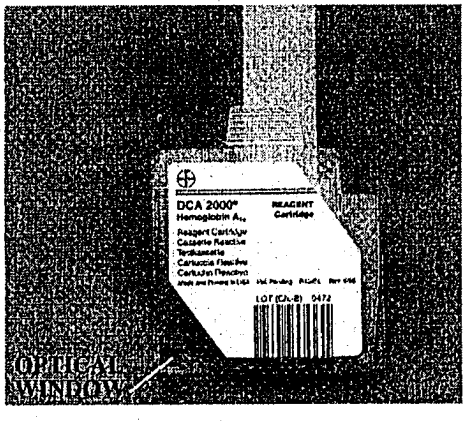


Figure 3.5.2 – Capillary tubes and reagent cartridge for the Cholestech LDX® analyzer (Cholestech Corporation)



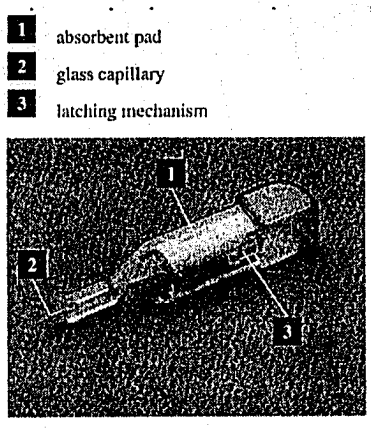


Figure 3.5.3 – OneTouch® Ultra glucometer® (LifeScan) and test strip

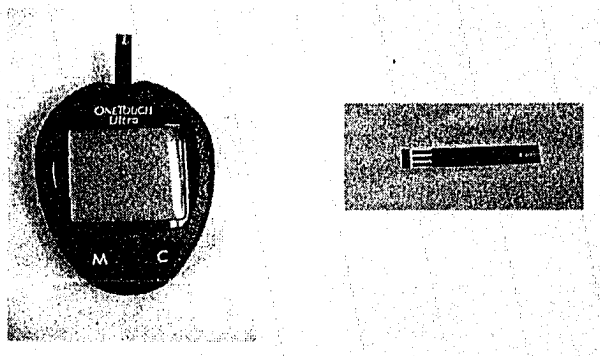


Figure 3.5.4 – DCA 2000® analyzer (Bayer technologies)

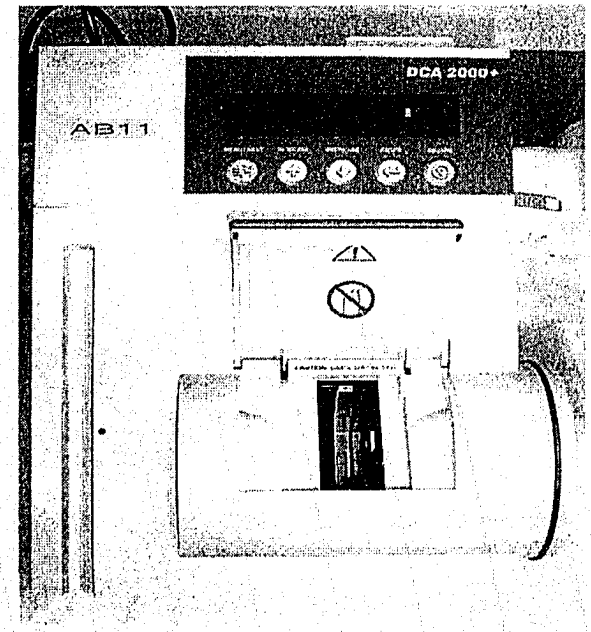


Figure 3.5.5 – Cholestech LDX® analyzer (Cholestech Corporation)

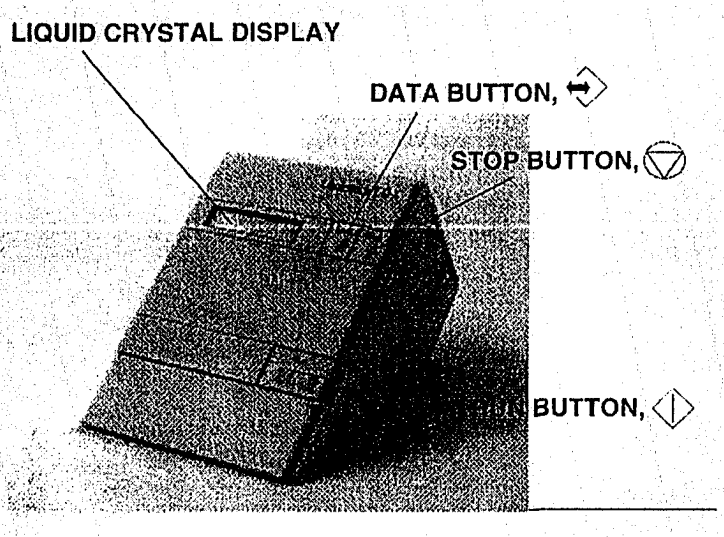
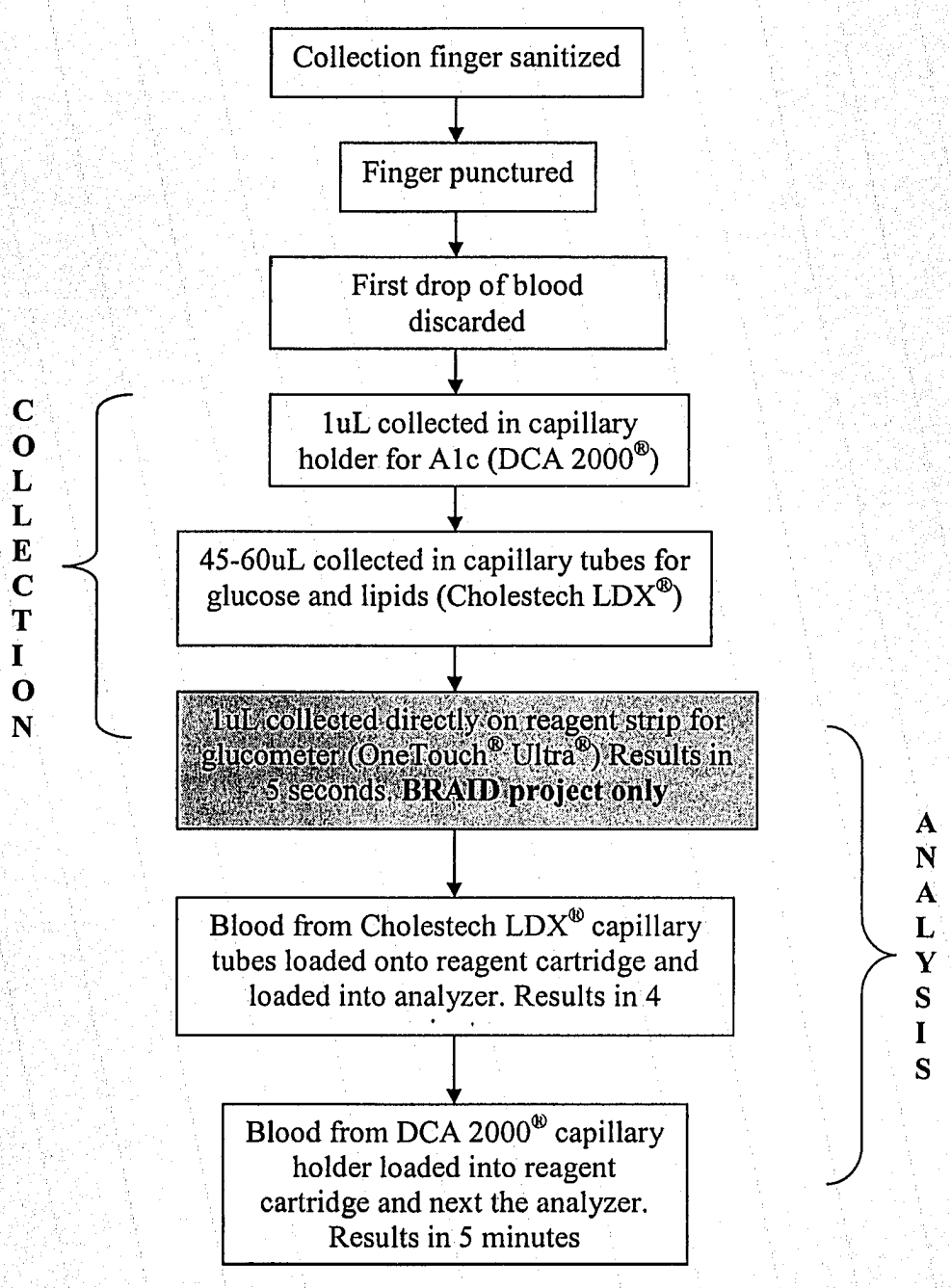


Figure 3.5.6 – Schematic overview of blood collection and analysis



3.6 – Data collection, counselling, and education

Once the results have been printed and displayed, the data is collected and entered into a computer. The data for the DCA 2000® does not have to be corrected and is therefore directly entered onto each individuals chart immediately. However the data for the Cholestech LDX® must be corrected, using the same procedure use for the quality control discussed previously. Data for each patient is entered into the "Cholestech LDX® regression sheet" and is converted. Finally, this data is then entered onto each individual's chart. Now that the blood collection and results have been completed, a health care professional reviews the data and then discusses these results with the individual who is being tested. During this discussion a brief educational session on nutrition and lifestyle is completed. Also administered at the time (BRAID and MDSI projects only) is the seven question "American Diabetes Association Risk Questionnaire" (ADA Score) as shown in Figure 3.6.1. The questions asked relate to the individuals BMI, age, physical activity, mothers with high birth weight offspring, and genetic precursors to diabetes. Each question is given a score, and then once the questionnaire has been administered the scores are summed. A score of 10 or greater places an individual at higher risk for having undiagnosed diabetes (Table 3.8.3) Three additional questions are being asked (see questionnaire Figure 3.6.1), to determine any influence of heredity, medications, or history of gestational diabetes in women on the frequency of diabetes. These values were not scored, rather answered as yes or no. Individuals have the option to receive a copy of their results immediately, or have them sent to them by mail. Individuals can also have results sent to a family doctor, and/or the local health care centre. All individuals with significant abnormal findings were referred and encouraged to see their doctors.

Figure 3.6.1 – American Diabetes Association Risk Questionnaire and additional BRAID project questions.

The BRAID project

Name:

If the client answers **YES** to any of these questions, they receive the appropriate point(s).

ADA Risk Questionnaire

Question	Points
1. (For women) have you delivered a baby weighing more than 9 pounds (4 kg)?	1
2. Do you have one or more siblings (brother or sister) with diabetes?	1
3. Do you have one or more parents with diabetes?	1
4. Body Mass Index of more than 27 (as previously calculated)	5
5. Less than 65 years old and little or no physical activity in most weeks?	5
6. Between the ages of 45 and 64?	5
7. Over 65 years old?	9
Total	

Questionnaire	Yes/No	Additional Info
Medications (lipids, Hg, other)		Please list:
Grandparents with Diabetes?		
Gestational Diabetes		Date:

3.7 – Statistical Analysis

All analyses were carried out using SPSS 13.0 statistical software, unless otherwise mentioned. Data was collected until June 30 2004 (with the exception of SLICK which was collected until July 2003) into three separate databases. These databases were then amalgamated into one single database called the "BRAID database". This dataset was eventually imported into SPSS and analyzed. Simple frequency distributions were completed on all of the data collected. Linear and logistic regression modelling was carried out on certain risk factors to determine their relationship to diabetes and prediabetes. Categorical variables such as those relating to familial contribution and gestation diabetes were analyzed using a chi-square and logistic regression analysis. Multiple regression analysis was conducted to illustrate the contribution of each continuous variable to glucose. ROC (receiver operating characteristic) analysis was carried out on the DCA 2000® A1c comparing it to the standard (fasting Cholestech LDX® blood glucose) used in this thesis, which was used for the diagnosis of diabetes and prediabetes. A further ROC analysis was done in the BRAID project with the glucometer and comparing it to the standard Cholestech LDX® glucose. An independent t-test was performed to compare the means of the continuous variables between two groups. The SLICK and MDSI projects were grouped in to an "opportunistic" group, and the BRAID project is referred to as the "population" group. This analysis describes any significant differences between opportunistic screening and population based screening in this study. The prevalence of the metabolic syndrome was computed only on individuals who had the five risk factors (see Table 3.8.3) collected and were $\geq$ 18 years of age. The prevalence of the condition was compared between the two groups. Summary of the analysis conducted is displayed in Table 3.7.1 below.

Table 3.7.1 – Analyses conducted

Hypothesis	Data Fields Required	Data Source	Analyses
Diagnostic Accuracy	1. Fasting Cholestech LDX® Glucose 2. Fasting OneTouch® Ultra® Glucometer Glucose 3. A1c (DCA 2000)	1. BRAID, MDSI, SLICK 2. BRAID 3. BRAID, MDSI, SLICK	1. A1c ROC 2. Glucometer ROC
Prevalence of: Undiagnosed DM IFG Metabolic Syndrome Risk Factors	1. Fasting Cholestech LDX® Glucose 2. Blood Pressure 3. Lipid Panel 4. Waist Circumference 5. BMI 6. Age 7. Gender 8. Gestational Diabetes 9. Parental Diabetes 10. Siblings with Diabetes 11. Grandparents with Diabetes	1. BRAID, MDSI, SLICK 2. BRAID, MDSI, SLICK 3. BRAID, MDSI, SLICK 4. BRAID, MDSI, SLICK 5. BRAID, MDSI, SLICK 6. BRAID, MDSI, SLICK 7. BRAID, MDSI, SLICK 8. BRAID, MDSI 9. BRAID, MDSI 10. BRAID, MDSI 11. BRAID, MDSI	1 – 11: Frequency distribution on data 1-6: Linear regression analysis for the continuous variables and logistic regression for the categorical variables. 1-6: Analysis of Covariance - for test comparison between groups (opportunistic vs. population based). 8-11: Chi-Square comparisons for determination of association.

3.8 – Diagnostic Criteria

Diagnostic criteria for classifying individuals based on glycemia was taken from the Canadian Clinical Practice Guidelines (Canadian Diabetes Association Clinical Practice Guidelines Committee, 2003b). The criteria are shown in Table 3.8.1.

Table 3.8.1 – Diagnostic criteria for glycemia (Canadian Diabetes Association Clinical Practice Guidelines Committee, 2003c)

Criteria	Defining level
Normal	Fasting < 5.7mmol/L
Prediabetes (IFG)	Fasting: ≥ 5.7 < 7.0mmol/L
Diabetes	Fasting: ≥ 7.0mmol/L Random: ≥ 11.1mmol/L

An A1c standard for the diagnosis of diabetes has not been clearly established. For the purpose of this study we are using the following criteria for A1c suggested by Rohlfing et al. (Table 3.8.2) (Rohlfing et al., 2000a).

Table 3.8.2 – A1c criteria for the BRAID study

Criteria	Defining level
Normal	< 5.5%
Upper limit of normal (1SD)	≥ 5.5% < 6.1%
High risk (2SD)	≥ 6.1%

SD: Standard deviation

The metabolic syndrome has gathered recent interest in the literature (discussed in Chapter 1.5). The risk factors associated with the condition are shown in Table 3.8.3. If an individual has three or more of the risk factors mentioned, they have the metabolic

syndrome as defined by the National Cholesterol Education Program (2001). The risk factors were collected in all three projects; however only individuals who were tested for at least 4 of the 5 criteria were included in the analysis. A simple frequency distribution for the criteria was done using SPSS to calculate who had the risk factors, and how many were positive for the syndrome. Logistic regression modelling was then done (using SPSS) on each of the risk factor of the metabolic syndrome to determine the specific relationship to diabetes and prediabetes.

Table 3.8.3 – Criteria for the metabolic syndrome (≥ 18years)

Risk factor	Defining level- NCEP –ATP III
Glucose	Fasting: ≥ 6.1 < 7.0mmol/L
High Density Lipoprotein	Men: < 1.0mmol/L Women: <1.3mmol/L
Triglycerides	≥ 1.7mmol/L
Blood Pressure	≥ 130/85mm Hg
Waist circumference	Men: > 102cm Women: > 88cm

Other risk factors that were measured in the three projects were height and weight, which was calculated as BMI (kg/m^2), LDL cholesterol, and total cholesterol. The MDSI and BRAID projects also used the American Diabetes Association risk questionnaire (Figure 3.6.1) as an extra screening tool to test its validity in Aboriginal communities of Alberta. Analysis was done using a simple frequency distribution to determine how many individuals had risk factors for diabetes. Linear regression modelling was then done (using SPSS) on each of the risk factors to determine the specific relationship to diabetes and prediabetes.

Table 3.8.4 – Other risk factors and their criteria

Risk factor	Defining level: At risk	Defining level: High risk
Obesity – (BMI)	$\geq 25 < 30$ kg/m^2	≥ 30 kg/m^2
ADA Risk Score (BRAID & MDSI project only)	≥ 10	
Low Density Lipoprotein	> 3.4mmol/L	

CHAPTER 4

RESULTS

4.1 – Study dataset, demographics and information collected

1170 unique individuals were screened in the BRAID study. All individuals had no prior knowledge of having diabetes, were not on medications for diabetes, and had no exclusions to screening (a complete list of exclusion criteria is provided in chapter 3). All 1170 individuals were of Aboriginal ancestry. Of the 1170 unique individuals, 251 were screened in the BRAID project, 562 in the MDSI project, and 357 in the SLICK project. A total of 43 communities were visited by the three projects from January 2002 to July 2004. MDSI visited 8 unique communities from November 2003 to July 2004, SLICK visited 34 unique communities from January 2002 to July 2004, and the BRAID project was only involved with one single First Nation community[2]. Table 4.1.1 summarizes this data.

Table 4.1.1 – Project, study, and community statistics

	STUDY			
Project	BRAID	MDSI	SLICK	Total
Number Screened (unique)	251	562	357	1170
Communities Visited (unique)	1	8	34	43
Potential Population Available for Screening	450	3694	43144	47288
Percent Screened	55.8%	15.2%	0.8%	2.5%

Out of 1170 clients, 728 (62.2%) were female, and 442 (37.8%) were male. The breakdown of gender in the three projects is shown in Table 4.1.2. BRAID has the most balanced gender ratio of the three projects, followed by MDSI, and then SLICK. Recruitment was not knowingly directed at women in any of the three projects. It is presumed women were

[2] The specific communities involved in this study are not mentioned throughout this document for privacy of the communities and the individuals screened.

more interested in being screened, or were more available. The fact that Aboriginal women are known to have a higher prevalence of diabetes than men is also a presumable factor.

Table 4.1.2 – Breakdown of gender and age in the three projects

	STUDY		
	BRAID	**MDSI**	**SLICK**
Gender			
Female Total	57.0%	62.6%	65.3%
Female 6-17 years	47.1%	52.9%	46.2%
Female ≥18 years	62.4%	64.9%	66.0%
Male Total	43.0%	37.4%	34.7%
Male 6-17 years	52.9%	47.1%	53.8%
Male ≥ 18 years	37.6%	35.1%	34.0%
Age (Mean years)	29.8	38.4	41.9
5-19	37.2%	19%	5.3%
20-39	30.8%	31.9%	42%
40-59	26%	35.8%	39.2%
60-79	6%	12.3%	12.4%
≥80	0%	1%	1.1%

The BRAID project screened many more individuals in the 5-19 age category as compared to the MDSI or SLICK project; conversely, SLICK and MDSI screened more individuals in the >60 years age categories.

The projects also collected a variety of other information such as: history of gestational diabetes (GDM) or baby over 9 lbs, any siblings with diabetes, any parents with diabetes, and any grandparents with diabetes at the time of screening. The question regarding "Grandparents with diabetes" was not administered to the SLICK participants. The American Diabetes Association Risk Assessment Questionnaire (ADA Score) was administered in the MDSI and BRAID projects.

4.2 – Assessment of hypothesis 1: use of portable technology

Hypothesis 1 states that "portable technology is comparable to standard laboratory methods for the determination of diabetes and prediabetes". Regression and ROC (Receiver Operating Characteristic) analysis were done on the portable technology to assess its performance. ROC analysis is a useful tool to help decide a threshold at which a new diagnostic tool will be comparable to a standard tool that is already in use. The area under the curve (AUC) provides an idea of the accuracy of the test, the higher the AUC the better the accuracy. Two other important determinants of the ROC analysis are the sensitivity and specificity. Sensitivity refers to the ability of a diagnostic tool to predict "true positive" cases, whereas specificity refers to predict "true negative" cases. A diagnostic tool that has a high sensitivity and high specificity is the most useful. Sensitivity is also used interchangeably with the term true positive fraction (TPF), and specificity with true negative fraction (TNF). From the sensitivity and specificity one calculates diagnostic accuracy. Diagnostic accuracy is measured by the formula provided in Equation 4.2.1. P(D+) refers to the prevalence of the disease in the population using the standard diagnostic tool (Cholestech LDX® in this study), and P(D-) is the simply 1 – P(D+), signifying absence of disease

Equation 4.2.1 – Determining diagnostic accuracy (Metz, 1978)

Accuracy = [Sensitivity x P(D+)] + [Specificity x P(D-)]

For each decision point that a user defines (e.g. the cut-off point for the diagnostic gold standard) a sensitivity and specificity are produced. These values are used to calculate the diagnostic accuracy of the new test using Equation 4.2.1.

In this study the terms "probable" diabetes and prediabetes are used, throughout, because in the absence of symptoms measurements should be repeated once; however single measurements are acceptable for epidemiological investigations. In addition there are no guidelines to date that approve the use of portable technology in these determinations.

4.2.1 – Performance analysis of portable technology: (DCA 2000® A1c, and fasting OneTouch® Ultra® glucometer)

DCA 2000® A1c was compared to fasting Cholestech LDX® glucose in the project to assess its probability of predicting states of glucose tolerance. Firstly, regression analysis was completed on the A1c to determine its "fit". The A1c performed well in the regression analysis having a correlation coefficient of 0.734 (R^2 = 0.539). The fasting OneTouch® Ultra® also performed very well compared to the fasting Cholestech LDX® glucose (R =0.817, R^2=0.667). A further analysis on sensitivity and specificity was performed (ROC). Figure 4.3.1 and Figure 4.3.2 display the ROC curves for both the DCA 2000® A1c, and the OneTouch® Ultra® capillary glucose respectively. The area under the curve for the A1c is 0.862 (S.E. = 0.052) and 0.939 (S.E. = 0.029) for the capillary glucose. The glucose criteria utilized was a fasting glucose ≥7.0mmol/L representing diabetes. The sensitivity and specificity for the fasting OneTouch® Ultra® glucometer using 7.0mmol/L as the cutoff was 0.600 and 0.995 respectively, which has a diagnostic accuracy of 0.982 (scale 0-1). The glucometer had the best diagnostic accuracy for diagnosing diabetes at a glucometer

value of 7.10mmol/L. The DCA 2000® A1c has a sensitivity and specificity of 0.65 and 0.95 respectively using 6.1% as a diagnostic point, and a diagnostic accuracy of 0.938. The optimum point for diagnosing diabetes using the A1c in this study for was 7.05%, which produced a diagnostic accuracy of 0.981.

Figure 4.2.1 – ROC curve for DCA 2000® A1c using Cholestech LDX® standard glucose criteria for diabetes

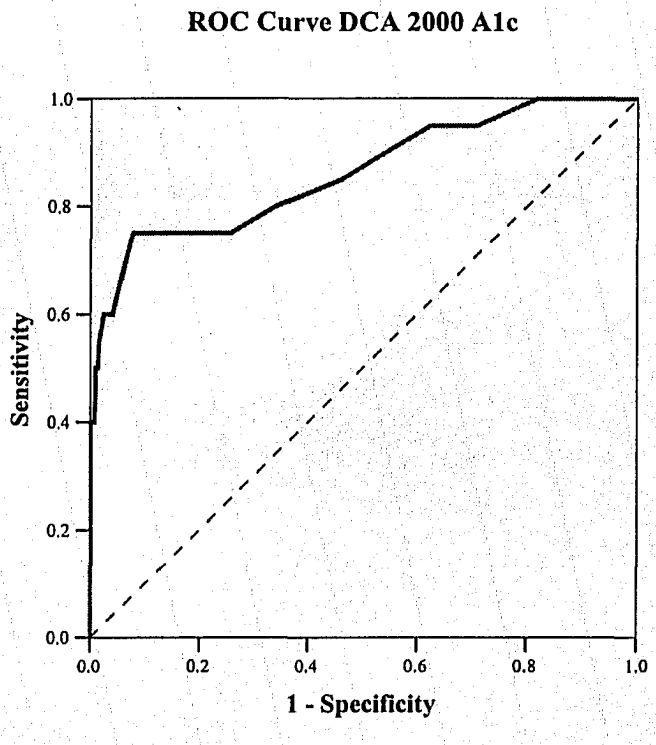
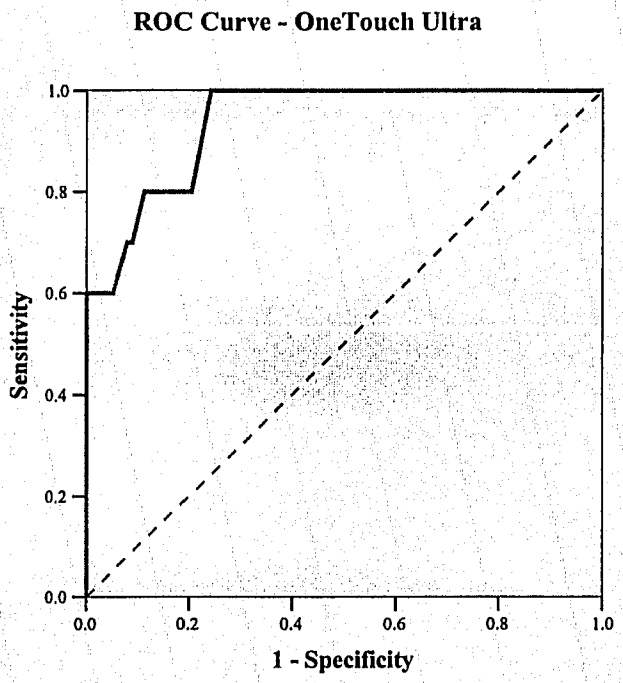


Figure 4.2.2 – ROC curve for fasting OneTouch® Ultra® glucose using Cholestech LDX® standard glucose criteria for diabetes



When using glucose criteria for "prediabetes" the ROC curves for both the A1c and the capillary glucose drift downwards, displaying a smaller area under the curve as shown by Figure 4.3.3 and 4.3.4 below. The glucose criteria used for prediabetes was a fasting glucose between 5.7 and 7.0mmol/L.

Figure 4.2.3 – ROC curve for DCA 2000® A1c using Cholestech LDX® standard glucose criteria for prediabetes (IFG only)

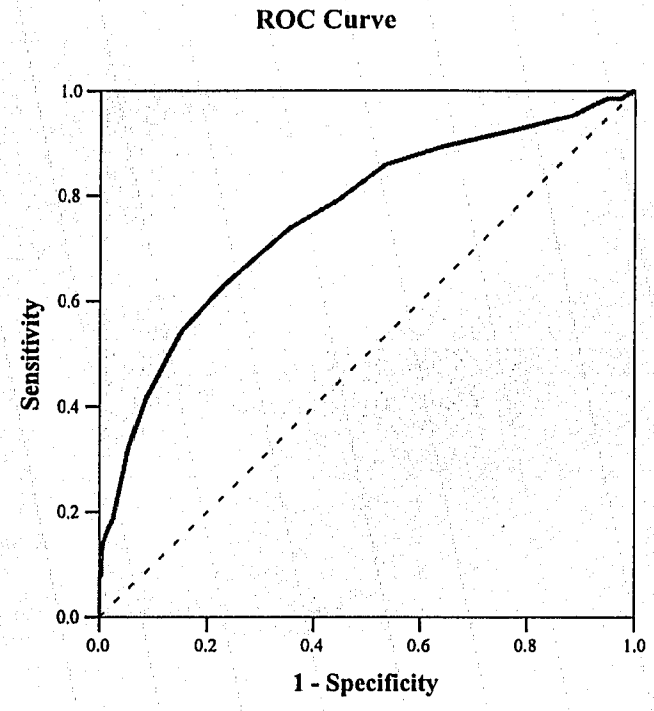


Figure 4.2.4 – ROC curve for fasting OneTouch® Ultra® using Cholestech LDX® standard glucose criteria for prediabetes (IFG only)

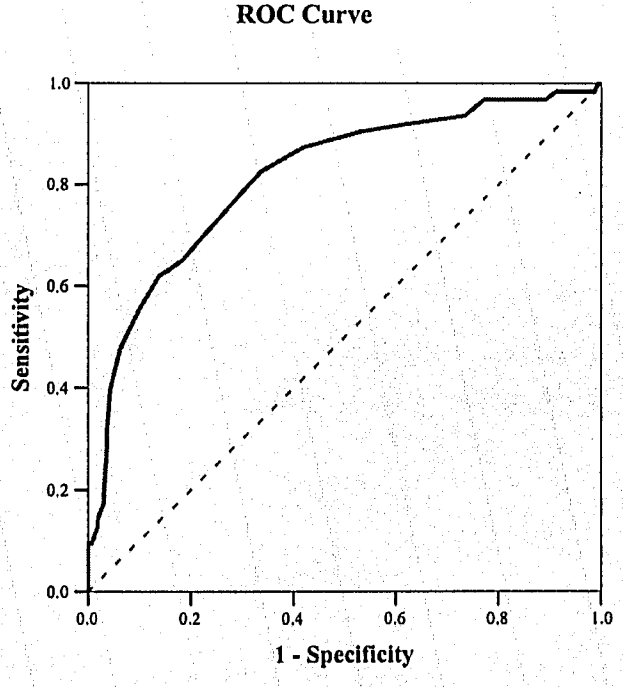


Table 4.2.1 shows the area under the curve for the two instruments with respect to diagnosing diabetes and prediabetes. Table 4.2.2 describes the sensitivity and specificity for both instruments using two different cut points, one for diabetes, and one for prediabetes.

Table 4.2.1 – Area under the ROC curve for DCA 2000® and OneTouch® Ultra®

	AUC A1c (S.E)	AUC Fasting Capillary Glucose (S.E)
Probable Prediabetes – 2003 criteria (CDA, 2003a) (≥5.7 <7.0mmol/L)	0.760 (0.025)	0.814 (0.033)
Probable Diabetes (≥7.0mmol/L)	0.862 (0.052)	0.939 (0.029)

Table 4.2.2 – Sensitivity and specificity of portable technology for the diagnosis of probable diabetes and prediabetes using Cholestech LDX® as standard

Diagnostic Reading	Sensitivity	Specificity	Diagnostic Accuracy
A1c ≥6.1%	0.65	0.94	0.938
A1c ≥5.5%	0.74	0.65	0.663
A1c DM optimal – 7.05%	0.40	1.00	0.981
Fasting Glucometer ≥7.0mmol/L (Probable Diabetes)	0.60	0.995	0.982
Fasting Glucometer ≥5.7<7.0mmol/L (Probable Prediabetes)	0.556	0.899	0.840
Fasting Glucometer DM optimal – 7.10mmol/L	0.60	1.00	0.987

DM: Diabetes Mellitus

In summary the DCA 2000® and the fasting OneTouch® Ultra® perform well in the field for the detection for diabetes. The optimal cut point for prediabetes as measured by a glucometer was not possible to determine because prediabetes is a range having an upper and lower cut point.

4.3 – Portable testing results in all groups combined

The following tables and figures describe the results of portable testing in the combined dataset. Opportunistic and population based screening groups were combined and analyzed to look at the distribution of the data in 1170 unique Aboriginal individuals in Alberta.

Table 4.3.1 – Comparison of glycemic categories detected by Cholestech LDX® standard vs. portable technology

	Cholestech LDX®	OneTouch® Ultra® glucose
Probable Diabetes	3.18%	2.17%
Probable Prediabetes (fasting only)	28.3% **	20.1%

** $p<0.01$

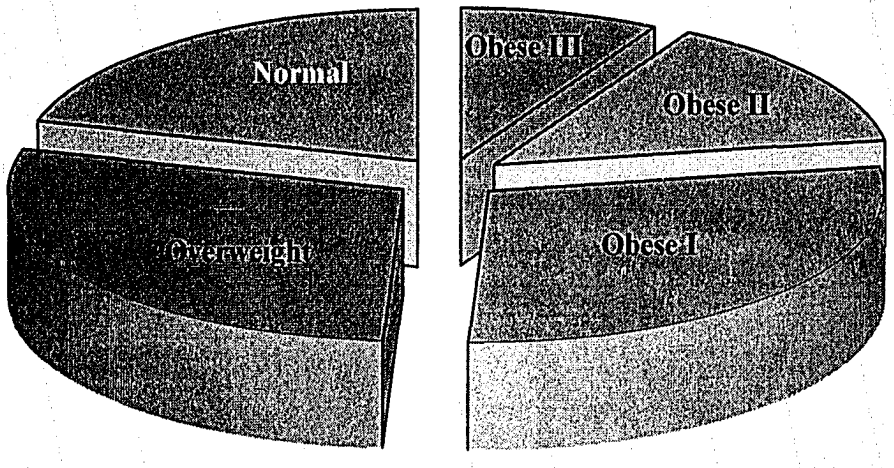
Table 4.3.2 – Total prevalence of probable diabetes, probable prediabetes, the metabolic syndrome, and risk factors tested with portable technology

	The BRAID study N = 1170	
	Positive or High Risk: N (%)	**Total N**
Probable Diabetes	3.18%	1132
Probable Prediabetes (fasting only)	28.3%	473
Hemoglobin A1c (≥6.1%)	8.92%	1143
Hemoglobin A1c (≥5.5%)	40.2%	1144
Metabolic Syndrome (≥18years)	50.4%	357
Body Mass Index (Obese)	51.7%	1160
Increased waist circumference (≥18years)	71.1%	957
Blood pressure (≥ 18 years)	35.9%	950
HDL cholesterol (≥18 years)	61.1%	640
LDL cholesterol (≥18 years)	23.1%	632
Triglycerides (≥18 years)	54.1%	637
ADA Score (≥10)	38.7%	788

Table 4.3.3 – Age and gender specific prevalence of diabetes and prediabetes in the BRAID study

	Diabetes		Prediabetes (IFG only)	
Age Category	Female	Male	Female	Male
6-19	0%	0.9%	15.3%	24.5%
20-39	2.6%	2.5%	17.7%	38.0%
40-59	4.0%	3.6%	32.7%	35.8%
60-79	8.7%	7.5%	37.5%	40.0%
>80	0%	0%	0%	0%

Figure 4.3.1 – Distribution of BMI in the total population screened



BMI Categories: Normal 18.5 – 24.9, Overweight 25.0 – 29.9,
Obese I 30.0-34.9, Obese II 35.0 – 39.9, Obese III >40.0

Apart from risk assessment, four questions related to familial and gestational contribution to diabetes were asked. All females were asked if they had either a baby over 9 lbs or gestational diabetes. The 2nd question referred to parental genetic contribution to diabetes. The third question asked, "do you have grandparents with diabetes" and the last question

asked if the individual had any siblings with diabetes. Table 4.3.4 shows that individuals with increased glucose had a significant familial contribution as compared to those with normal glucose. Females with gestational diabetes or a baby over 9lbs were not more likely to have increased glucose, however individuals who had parents or grandparents with diabetes were 1.48 and 1.45 times more likely to have prediabetes or diabetes ($p<0.05$) as compared to those with normal glucose. Individuals who had siblings with diabetes were 1.62 times more likely to have prediabetes or diabetes ($p<0.01$).

Table 4.3.4 – Familial contribution to increased glucose

GROUP:	Total prevalence:	Normal %	Glucose PDM or DM	Odds Ratio
GDM or baby over 9lbs (N = 715)	16.5%	15.7%	20.9%	1.42
Siblings with DM (N =797)	28.2%	25.8%	36.1%	1.62**
Parent with DM (N =793)	37.9%	35.3%	44.7%	1.48*
Grandparent with DM (N =557)	37.1%	35.4%	44.4%	1.45*

PDM: prediabetes DM: diabetes mellitus, * $p<0.05$, ** $p<0.01$

4.3.2 –Predictors of glycemia

Logistic regression analysis was performed for the total population to asses the relationship of each risk factor to diabetes. This analysis explores what significantly predicts diabetes in this study, and expresses it as the odds of the disease occurring. An odds value >1 signifies that as the units of the predictor increase so too does the diabetes risk. If odds values are <1, the diabetes risk decreases as the units of the predictor increase. The following risk

factors were assessed: Age (in categories), blood pressure (systolic and diastolic separately, ≥18 years), BMI, waist circumference (≥18), lipids (≥18), and ADA risk score.

Table 4.3.5 below describes the odds estimate for each risk factor collected. Age was significantly correlated with probable diabetes and being over the age of 44 placed an individual at 3.44 times higher risk of having diabetes. Waist and BMI were significantly associated with risk of diabetes. Total cholesterol, HDL cholesterol, and triglycerides were significantly associated with probable diabetes. As compared to people with low triglycerides, individuals with high triglycerides were approximately 1.7 times more likely to have diabetes. HDL cholesterol had an odds ratio <1 due to its negative correlation to diabetes risk, therefore an increase in HDL cholesterol was associated with a significant decrease in diabetes risk. Individuals who had a sibling or parent with diabetes had a significant increase in diabetes risk. An ADA score ≥10 was also associated with increased odds of having diabetes.

Table 4.3.5 – Regression analysis on risk factors for diabetes

	Regression Coefficients	
	Odds	**Significance**
Age	1.04	0.001
≥45 years	3.44	0.001
Waist Circumference	1.03	0.004
BMI	1.09	<0.001
Systolic BP	1.02	0.074
Diastolic BP	1.03	0.136
TC	1.43	0.009
LDL	1.37	0.103
HDL	0.089	<0.001
Triglycerides	1.70	<0.001
GDM or baby > 9lbs (females only)	1.05	0.927
Sibling with DM	3.03	0.002
Parent with DM	2.48	0.010
Grandparent with DM	1.05	0.922
ADA score	1.19	<0.001

BP: blood pressure, LDL: Low density Lipoprotein, HDL: High Density Lipoprotein, TC: total cholesterol, DM: Diabetes Mellitus, GDM: Gestational Diabetes

4.4 – Hypothesis 2: Opportunistic vs. Population based screening

The objective of hypothesis 2 is to compare the opportunistic group to the population based group and determine if there is any significant difference between the two regarding diabetes, prediabetes, and risk factors. Throughout, the terms "probable" diabetes and "probable" prediabetes are used as explained above. To recap, the opportunistic group was a sample of people from various Aboriginal communities who were screened because they presented and were presumably worried about their risk for diabetes. The population

group was a representation of a single community where a majority of the population was screened. The two groups are compared with respect to age and gender in Table 4.4.1. Independent t-tests were completed to asses the possibility of a significant difference between group means. Levene's statistic was calculated to determine if variance between the groups was normal (Levene's $p>0.05$) and only then was normal the t-statistic was calculated.

Table 4.4.1 – Demographic comparison of opportunistic and population based screening

Criteria	Opportunistic		Population	
	N	X1: Mean (C.I) X2: Percent	N	X1: Mean (C.I) X2: Percent
1. Age (years)	919	40** (38.63, 0.87)	250	30(27.59, 31.91)
2. Sex	M: 334 F: 585	M: 36 % F: 64%	M: 107 F: 143	M: 43% F: 57%

** P<0.001, M: Males, F: Females

There is a significant difference in age between the two groups ($p<0.001$) and it will therefore be controlled for in the analysis of all variables. There was no significant difference in the gender ratio between the two groups. Table 4.4.2 below describes the similarities and difference between the two populations with respect to diabetes, prediabetes, the metabolic syndrome, and risk factors, corrected for age.

Table 4.4.2 – Opportunistic and Population based prevalence of diabetes, prediabetes, the metabolic syndrome, and risk factors corrected for age

	The BRAID study	
	Positive or High Risk	
	Opportunistic	Population
Probable Diabetes	2.93%	4.12%
Probable Prediabetes (fasting only)	32.3%	23.9%
Hemoglobin A1c (≥6.1%)	9.60%	6.48%
Hemoglobin A1c (≥5.5%)	40%	41.3%
Metabolic Syndrome (>18years)	50%	51%
Body Mass Index (Obese)	53.1%	46.8%**
Increased waist circumference (≥18years)	70.2%	77.6%**
High Blood pressure (≥18years)	33.8%	24.8%**
Low HDL cholesterol (≥18years)	54.9%	69.1%**
High LDL cholesterol (≥18years)	30.5%	22.5%**
High Triglycerides (≥18years)	46.5%	39.2%*
ADA Score	45.2%	34.6%

M:Males F:Females NA: Not Applicable. Difference between means (t) * $p<0.05$, ** $p<0.01$

Age correction was completed using analysis of covariance controlling for age. After correcting for age, there was no significant difference between opportunistic screening and population based screening for individuals diagnosed with "probable diabetes" and "probable prediabetes". A1c ≥5.5% and A1c ≥6.1% was not significantly different

between the two groups. A significant difference in obese individuals, LDL and HDL cholesterol, and triglycerides was seen between the two groups. Systolic and Diastolic blood pressure were also shown to be significantly different between the two groups after correcting for age. Comparison of inter-group (opportunistic vs. population) differences in regards to familial and gestational contribution to diabetes was not possible due to the low numbers of individuals found with undiagnosed diabetes. Table 4.4.3 compares the prevalence of gestational diabetes, siblings with diabetes, parents with diabetes, and grandparents with diabetes between the two groups. The groups were not significantly different in any of the categories.

Table 4.4.3 – Gestational and familial history of diabetes between groups

	Opportunistic	Population
	%	%
GDM or baby over 9lbs (females only)	15.9%	17.5%
Siblings with DM	29%	25.4%
Parents with DM	37.8%	38.2%
Grandparents with DM	37.5%	36%

Figure 4.4.1 shows the distributions of glucose between the two groups and figure 4.4.2 shows the distribution of A1c.

Figure 4.4.1 – Opportunistic vs. Population – Fasting glucose

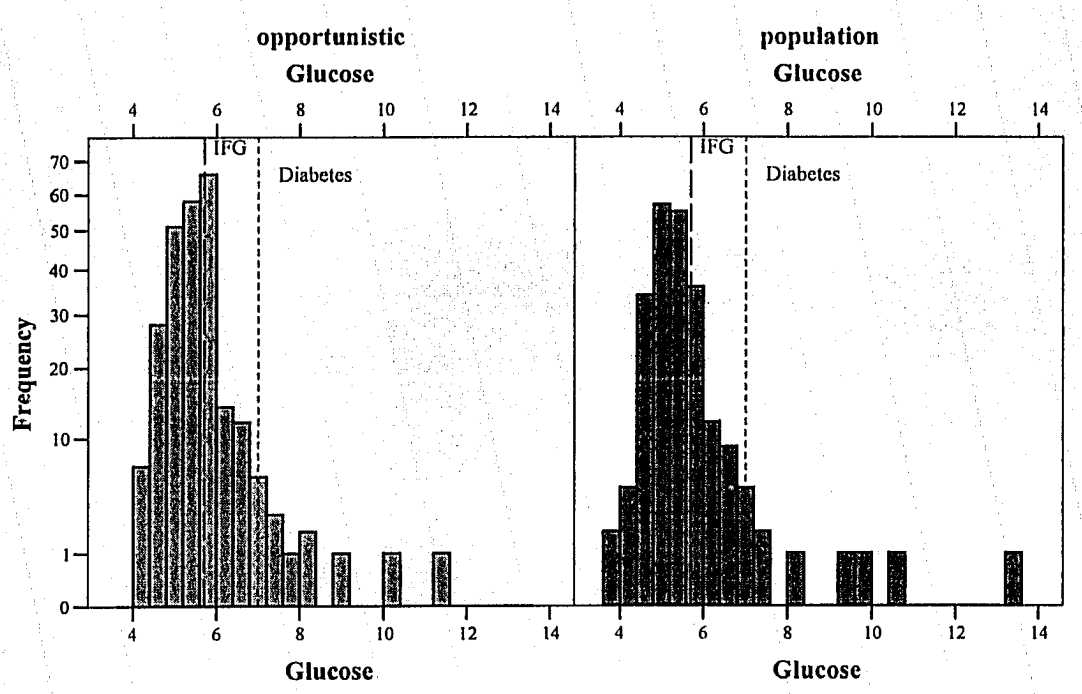
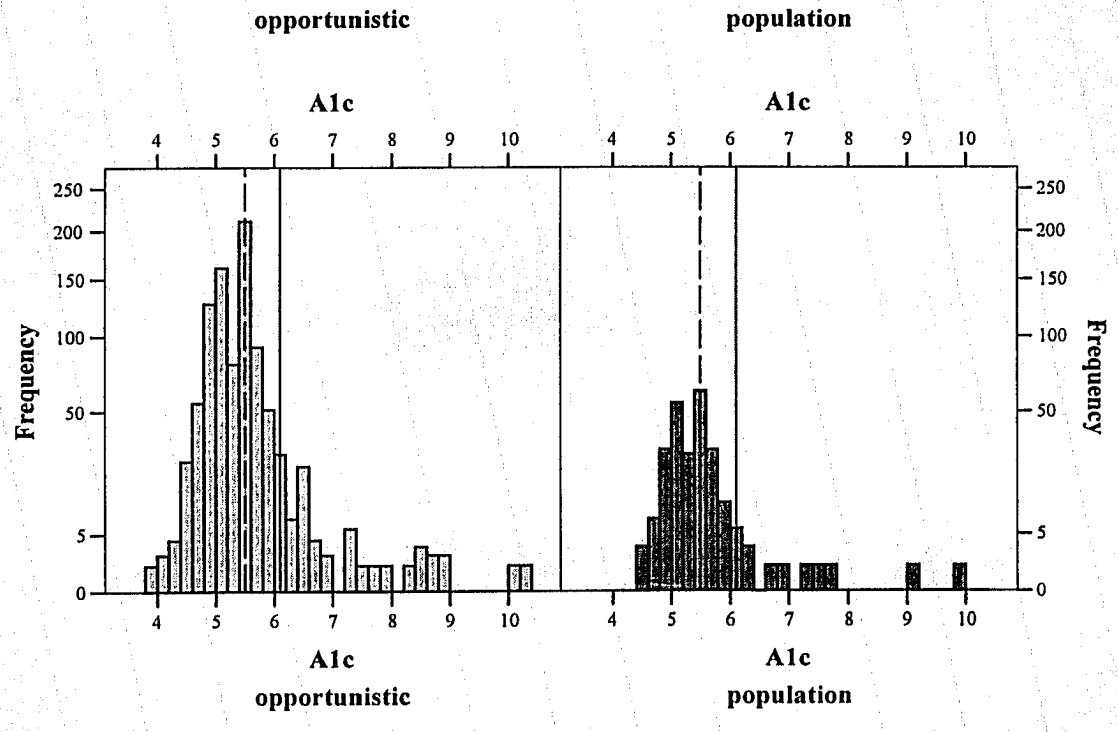
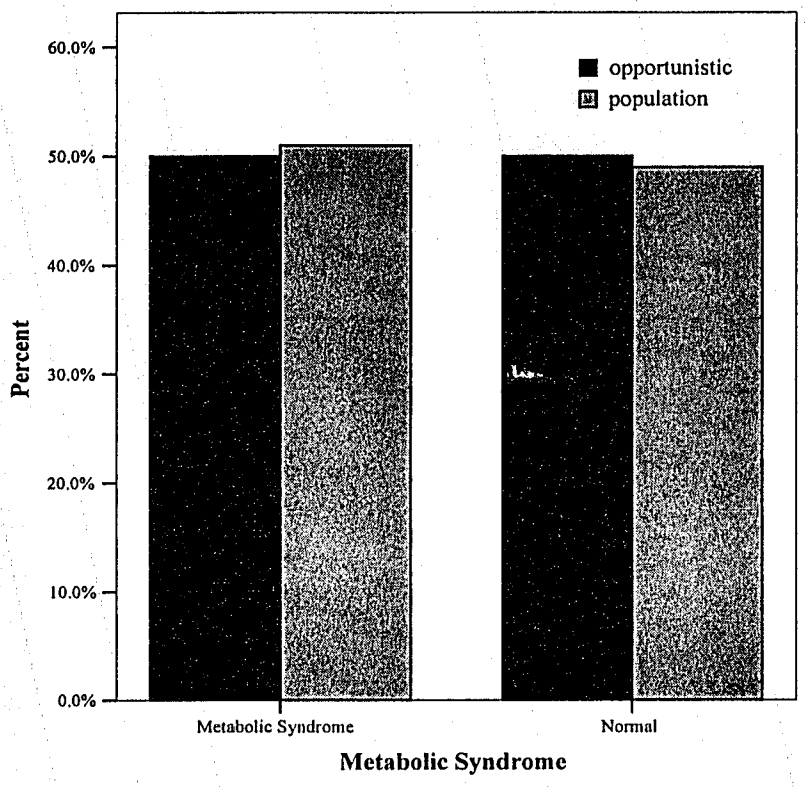


Figure 4.4.2 – Opportunistic vs. Population – A1c



The metabolic syndrome prevalence was not significantly different between the two groups, despite some significant differences in the individual metabolic syndrome components. Waist circumference, high triglycerides, and low HDL cholesterol were the most frequent contributors to the metabolic syndrome (Table 4.3.2 and 4.4.2). Figure 4.4.3 illustrates the prevalence in both the opportunistic group and the population based group.

Figure 4.4.3 – Frequency of the Metabolic Syndrome detected by Opportunistic vs. Population based screening strategies



The mean ADA score for the opportunistic group was 7.19 (6.78, 7.60) and 6.40 (5.76, 7.05) for the population group. A significant difference did not occur between the two groups when corrected for age.

CHAPTER 5

DISCUSSION

5.1 – Introduction

Although the SLICK, BRAID and MDSI projects are different with respect to their target population, research question and methods, there are similarities. The three projects have as a main objective: to reduce the burden of diabetes on Aboriginal people. The projects are also connected by one principal investigator, and lessons learned from one project could quickly and simply be transferred to another. Weekly and at least monthly meetings allow discussion of issues and challenges that are occurring in the field. From data collection and quality assurance, to community feedback and translation, the three projects are intertwined. The BRAID study looked at an aspect of pooled data that the three projects have collected.

5.2 – Hypothesis testing

In the BRAID study 1170 Aboriginal people in Alberta were screened for diabetes and its risk factors. Over 60% were women. Recruitment was not knowingly directed at women in any of the three projects. It is presumed women were more interested in being screened, or were more available, the 1991 Aboriginal peoples survey (APS 1991) also reported a predominance of women with diabetes (Health Canada, 1997).

Testing of hypothesis 1 illustrated that portable technology was a useful tool for detecting diabetes as compared to the "standard". The OneTouch® Ultra® glucometer used in fasting individuals was an accurate tool for detecting undiagnosed diabetes. The diagnostic accuracy using standard glucose criteria for diabetes (7.0mmol/L) was 0.982. Therefore, in this study 98.2% of the time the glucometer accurately detected diabetes as compared to

the standard. Receiver operating characteristics (ROC) analysis showed that this accuracy could be further improved to 98.7% by using a cut-off point of 7.10mmol/L, however the clinical benefit to be gained from this improvement is minimal.

The DCA 2000® A1c also performed well for detecting diabetes with a diagnostic accuracy of 0.938 using 6.1% (2SD from the mean) as a cut point. 93.8% of the time the A1c was accurate at detecting diabetes, however at an optimal cut point of 7.05%, the A1c was accurate at detecting diabetes in 98.1% of cases. This suggests that if this technology were to be used in the field, a cut point of 7.05% should be used. The sensitivity and specificity for the A1c ≥6.1% using the DCA 2000® in the BRAID study was 0.65 and 0.94 respectively. These results are very similar to the United States third National Nutrition and Health Examination Survey (NHANES III) looked at 6559 individuals, and found a sensitivity and specificity of 0.63 and 0.97 using venous blood. This study concluded that A1c is a highly specific and convenient alternative to diabetes screening when using a cut off of 2 standard deviations above the mean. Furthermore, a recent study conducted in 1253 veterans in the United Stated showed that in those that did not have diabetes at recruitment the A1c value was highly predictive of the development of diabetes within 3 years (Edelman et al., 2004b). Individuals with an A1c in the "high normal range" (5.6 to 6.0%) had an incident rate of 2.5% per year, and those with an "elevated" A1c (6.1-6.9%) progressed at a rate of 7.8% per year.

Prediabetes refers to a condition where glucose is elevated, but does not reach diagnostic criteria for diabetes. However it is increasingly recognized as a risk factor not only for diabetes, but also for cardiovascular disease which accounts for the largest burden of

dysglycemia related morbidity and mortality. The diagnostic criteria and strategies for testing for prediabetes are not as well established as compared to diabetes. For instance there is much confusion about the relative importance of impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) in their contribution to prediabetes. IFG is diagnosed by a fasting glucose measurement; IGT requires a 2hr glucose tolerance test. Therefore a simple test for diagnosing prediabetes would be desirable. ROC analysis showed that the OneTouch® Ultra® glucometer and the DCA 2000® were not very accurate in detecting prediabetes. Diagnostic accuracy was considerably lower for both instruments as compared to accuracy for diagnosing diabetes. The area under the curve (AUC) was significantly lower for detecting prediabetes as compared to diabetes. The glucometer was accurate 84% of the time using the accepted range between ≥5.7 and <7.0mmol/L. The A1c was only accurate 66.3% of the time using a cut point of 5.5% (1 SD from the mean). From the AUC and the diagnostic accuracy, screening for prediabetes using this portable technology can not be recommended at this time.

Regarding hypothesis 2, comparison of opportunistic and population groups was conducted with respect to diabetes, prediabetes, diabetes and cardiovascular risk factors, and the metabolic syndrome. It was expected that individuals who were screened in an opportunistic paradigm would have some prior inclination to be tested, i.e. were previously told by a health care professional or family member about some health risk. It was thought that the population based screening group would be a more complete representation of an Aboriginal population and would therefore have significantly lower prevalence. For diabetes, prediabetes, A1c ≥6.1%, A1c ≥5.5%, ADA risk score, and the metabolic syndrome there was no significant difference between the two groups, failing to confirm

hypothesis. Confirming hypothesis 2, however, the opportunistic group had significantly increased levels of obesity, blood pressure, triglycerides, and LDL cholesterol. This suggests that the differences in favour of the hypothesis were more pronounced with respect to cardiovascular risk factors than to diabetes risk factors. The fact that increased waist circumference and increased low HDL cholesterol, however, were more frequent in the population based group, probably explains why we were not able to show a difference with respect to the metabolic syndrome.

5.3 – Prevalence of diabetes, prediabetes, and diabetes risk factors

Consistent with other studies, the strongest predictors of diabetes were age, family history, BMI and waist circumference, and abnormal lipids. The ADA score was also a significant predictor of diabetes. Many studies have shown the impact of family history on diabetes risk (Mitchell et al., 2004; Meigs et al., 2000). The presence of familial history of diabetes in the BRAID study was similar in both groups. When looking at total prevalence of family history of diabetes with respect to elevated glucose; those with a sibling with diabetes, parent with diabetes, or grandparent with diabetes were at significantly higher risk of increased glucose (≥5.7mmol/L). Having a sibling with diabetes was shown to be the most important contributor to increased glucose with an odds ratio of 1.62. Gestational diabetes or having a baby over 9lbs did not significantly increase the likelihood of having an elevated glucose. This is contrary to many other studies. We did not collect information regarding the interval transpired since presence of gestational diabetes or having a baby over 9lbs. Since the mean age of the females in this study was 37, it is possible that type 2 diabetes had not yet had time to develop.

Total prevalence of undiagnosed diabetes in the study was 3.18%, and was not significantly different between the two groups. This finding is similar to the prevalence found in Quebec Aboriginals by Deslile and Ekoe in 1993, and to Dannenbaum in the James Bay Cree (3.7% and 2.5% respectively) (Dannenbaum, 2001; Delisle and Ekoe, 1993). This is lower however than the prevalence found by Harris in Sandy Lake prior to 1997 (10.7%) and to Knowler in the Pima Indians in 1978 (13.9%) (Knowler et al., 1978; Harris et al., 1997b). These differences may be due to the discrepancies in age of the populations studied. The Sandy Lake and the James Bay Cree studies were conducted in subjects over 10 years of age. The study in Quebec was performed in those over 15 years of age, and the Pima Indians were studied after 25 years of age. There were also differences in the testing strategies (fasting glucose, OGTT, A1c) and cut-offs utilized. Additionally in this regard Young found differences in the prevalence of undiagnosed diabetes in Manitoba according to the use of older and newer diagnostic criteria for diabetes e.g. 7.8mmol/L prior to 1998 (Young and Mustard, 2001). Furthermore, differences in undiagnosed diabetes maybe accounted for by the dates in which a study was done, for instance the report in the Pima Indians was published in 1978. At this time, there would have been less awareness of the existence of undiagnosed diabetes or of the epidemic of type 2 diabetes in Aboriginals. The high prevalence in the Sandy Lake study maybe due to the presence of the "Oji-Cree gene" (Hegele, 2001). More recent studies, including ours, tend to show lower prevalences of undiagnosed of diabetes.

The highest rate of undiagnosed diabetes reported in Aboriginals was in the Strong Heart Study, where the prevalence was 50.4% in those aged 45-74 years. By contrast Leiter reported a prevalence of only 2.2% in those over 40 in the general population (Leiter et al.,

2001). The BRAID study showed a prevalence of 4.9% in those over 40. The youngest individuals diagnosed in the study were 18 and 21 years of age and were detected in the population based screening project (BRAID). This is consistent with the fact that type 2 diabetes has been reported in Aboriginal youth in other studies (Dean et al., 2003; Dean et al., 1998). Dean has found a prevalence of approximately 1% in her studies of children aged 4-19, and the prevalence in the BRAID study aged 6-19 is 0.5%.

The prevalence of prediabetes was high in this study. The total overall prevalence of prediabetes (IFG only) in all the projects was 28.3%. Due to lack of recent studies with new criteria for prediabetes it is difficult to compare to other studies. All the studies in Table 1.3.1 used criteria prior to 2003 (IFG $\geq$6.1 <7.0mmol/L), whereas our study used "new" criteria (IFG $\geq$5.7 <7.0mmol/L). A recent analysis of the NHANES III compared IFG by old and new criteria in those 40-74 years of age in the U.S population. By old criteria there were 13 million persons with IFG, by new criteria the figure was 35 million. Using old criteria our prevalence of IFG was 10.8%. With a cut off of 6.1mmol/L the Manitoba Heart Health study showed a prevalence of 5% in females and 7.5% in males, the James Bay Cree study found 4.7% in both sexes, the Strong Heart Study found 21.2%, and the ARIC study found 32%. The last two studies were done in older age groups. With the old criterion the prevalence of prediabetes in the BRAID study is twice as high as that in the James Bay Cree which was recently done in a population with a similar age distribution (Dannenbaum, 2001). In comparison to the Sandy Lake study, we did not find a pronounced male/female difference. Our prevalence for females was 9.5% vs. 12.9% for males whereas Harris et al found 19.8% vs. 7.1% respectively (Harris et al., 1997b). Our calculated prevalence of 28% with the new criteria was found in those aged 6-91, and the

age specific prevalence shown in Table 4.3.3 shows a worrisome rate of 19.8% in the youngest age group (5-19 years). Therefore in spite of differences in measurement strategies it appears there is cause for concern in regards to rates of prediabetes in our study.

5.4 – The metabolic syndrome and cardiovascular risk factors

The overall prevalence of the metabolic syndrome in the BRAID study was 50.4% using NCEP/ATPIII criteria. Table 5.4.1 shows the results from the BRAID study compared to other studies from around the world.

Table 5.4.1 – Prevalence of the Metabolic Syndrome in the BRAID study compared with other countries Adapted from: (Cameron et al., 2004)

Country	Age Group	Men %	Women %
BRAID study	≥18	43.7	54
BRAID study	≥40	41.2	68.1
India	20-75	36.4	46.5
Mexico	20-69	26.6	
Oman	>20	19.5	23
Ireland	50-69	21.8	21.5
Turkey	>31	27	38.6
Mauritius	>24	10.6	14.7
France	30-64	10	7
USA Natives	45-49	43.6	56.7
USA Filipina	50-69	—	34.3
USA	30-79	26.9	21.4
USA (Non-Hispanic White)	30-79	24.7	21.3
USA (Mexican American)	30-79	29	32.8

Subjects in the BRAID study had the highest prevalence of all groups indicating their high diabetes and cardiovascular risk. Very little information is available about North American Aboriginals. In addition to the US Natives shown in Table 5.4.1 above, a study performed in the Inuit of Northern Canada has shown a low prevalence of 13.1% (Pollex et al., 2004).

Other risks associated with the metabolic syndrome are: polycystic ovarian syndrome (PCOS), non-alcoholic fatty liver disease (NAFLD), and cancer. NAFLD can be a cause of cirrhosis through its association with non-alcoholic steatohepatitis (NASH) (Matteoni et al., 1999). Indeed, pediatric NASH is becoming a cause of great concern and appears to affect ethnic minorities disproportionately (Schwimmer et al., 2003). Cancers thought to be associated with the metabolic syndrome and obesity in increasing order of relative risk are: prostate and colon (1.35-1.99), breast, uterus and kidney (2.0-4.9), and esophagus (>5.0) (Blackburn, 2003).

5.5 – Limitations

The three projects involved in this study had slightly different methodologies, notably the collection of two questions: gestational diabetes history, and grandparents with diabetes. These two items were not collected in the SLICK project. The questions were included in the MDSI and BRAID projects which were initiated at a later time. Another limitation was that in SLICK and MDSI the majority of samples were collected in the random state, as it was difficult to recruit all patients to come fasting. In the BRAID project a greater effort was taken to request individuals to fast for ≥8 hours before being screened. Therefore in the BRAID study the results reported for prediabetes (IFG), and hyperlipidemia rely more on the patients from the BRAID study. In the BRAID project 91.6% of subjects were fasting (n=229), whereas only 27% were fasting in the SLICK and MDSI projects combined (n=252).

The portable technology that was utilized in this study had potential limitations. The instruments utilized were not standard and the use of capillary blood is not standard,

however a rigorous quality assurance process was in place that yielded performance characteristics acceptable in any standard lab (See methods section 3.4). In particular, the use of the fasting Cholestech LDX® as the standard for the calculations regarding diabetes and prediabetes could be challenged. The ideal gold standard would be a 2 hour oral glucose tolerance test performed on venous blood. This was not logistically possible in the BRAID study, but is presently underway in the MDSI project. Glycemic categories were assigned on the basis of a single measurement, in order to keep things simple, thereby not discouraging recruitment. This was also not ideal.

In our population based sample, a recruitment of only 56% was achieved. Although the BRAID project is ongoing, complete ascertainment will likely never succeed because of the reluctance of some individuals to be screened. The causes for this possible reluctance have been described in section 1.7 and include but are not limited to, fear of diagnosis of diabetes and its implications. In addition, unfortunately, in any Aboriginal community there is a small but significant portion of the population that is unavailable for screening because of multiple stressors.

5.6 – Lessons Learned and Future directions

Portable testing utilized in this study proved to be accurate for screening for type 2 diabetes in Aboriginal populations. Therefore fasting glucometer or random A1c testing can be used for community based screening programs, which are recommended by the Canadian Diabetes Association (see chapter 1.7). The cost of a single test strip used in the OneTouch® Ultra® is $1.00, as compared to $18 dollars (includes lipids) for the Cholestech LDX®, and approximately $8 for the A1c.

Of particular benefit, the A1c is not affected by the fasting or random state, which allows individuals to be screened with a larger window of opportunity to access screening services. However the A1c requires a rigorous quality control process that limits its use in screening for small numbers of individuals, and makes infrequent use impractical. Unfortunately a random glucometer reading was not assessed in this study, but this is being looked at in MDSI. MDSI is also performing Oral Glucose Tolerance tests to give more information than can be provided in this thesis. Further research is required to learn the most practical way to detect prediabetes.

In all individuals screened, high A1c was more prevalent than undiagnosed diabetes. This might suggest that individuals who had a high A1c should be administered an oral glucose tolerance test to confirm the absence or presence of the disease, or be followed for the development of diabetes. A prospective study looking at these individuals with high A1c and normal glucose might prove beneficial, as A1c may perform well as a predictor of diabetes in longitudinal studies (Edelman et al., 2004a). Fortunately all individuals screened in the BRAID study will be followed, as all projects, BRAID, SLICK and MDSI are on-going. It will be attempted to assess changes in lifestyle, anthropometric measurements, laboratory measurements and disease states, and health care utilization, amongst some or all of these individuals. Future research linking this data with determinants of health such as social support networks, culture, physical and social environments, employment, and education are required. This may help researchers and communities to better understand the reasons for the explosion in diabetes, prediabetes, and other chronic conditions in these communities.

Recruitment for this study proved to be difficult. Merely travelling to a rural Aboriginal community was not enough. Intensive recruitment strategies and collaborations with community health workers are vital to the success of any future screening programs. Translation of the data collected and analyzed in the community through reports, discussion and, meetings are also integral to a successful relationship. In summary community partnership should be placed high on the priority list, and community involvement in the research is crucial.

5.7 – Conclusion

Based on this data it could be argued that population based screening for undiagnosed diabetes and prediabetes should be recommended for Aboriginal people age 6 and over. This is in contrast to the recommendations of the American Diabetes Association that favours testing only in the medical setting. The Canadian Diabetes Association favours "community based screening" (Grade D, consensus) although it does not recommend the tests that should be utilized. This thesis provides a contribution towards understanding which tests are feasible.

The prevalence of prediabetes in the BRAID study is the highest recorded in an Aboriginal population based screening initiative in Canada. These individuals are almost certain to progress to diabetes in due time if interventions are not implemented. Fortunately the resources are in place to tackle the burden. Community based screening programs should not be implemented otherwise.

From the information presented, it is evident that diabetes is a major health concern facing Aboriginal people today, with indications that the situation may worsen in the coming years if changes are not made. Although diabetes has, is, and will affect the lives of many Aboriginal people, one must hope that through education, research, and advocacy, the number of people affected by this silent killer will be greatly reduced in upcoming years.

Acceptance Limits for Lipid/Glucose Internal Quality Control (IQC)
Lipid/Glucose IQC Lot # 2003024

Limits Applicable AFTER Cholestech Raw Data Corrected by Spreadsheet *Specific for Reagent Lot #*

ANALYTE		IQC ORANGE			IQC PINK		
		TARGET	Acceptable Limit	Warning Limit	TARGET	Acceptable Limit	Warning Limit
Triglyceride	mmol/L	1.36	1.16 – 1.56	1.09 – 1.63	3.23	2.75 – 3.71	2.59 – 3.87
Cholesterol	mmol/L	4.84	4.40 – 5.28	4.27 – 5.41	6.87	6.25 – 7.49	6.06 – 7.68
HDL Cholesterol	mmol/L	1.64	1.46 – 1.82	1.40 – 1.88	1.13	1.01 – 1.25	0.97 – 1.29
Glucose	mmol/L	4.64	3.94 – 5.34	3.73 – 5.55	11.81	10.04 – 13.58	9.48 – 14.14

discussed with you. Your answers to the survey will be sent anonymously to evaluators who will assess the success of the SLICK program.

Benefits: Having these tests will be helpful to you to know if your diabetes is causing you problems now or if there are early signs of trouble that can be treated now to prevent future problems. These are the kind of tests you would get in a city if you went for a check on your diabetes.

- Keeping your tests and answers in a computer will help us develop or improve diabetes services in your community, and hopefully in other First Nations' communities.

- **Privacy and Confidentiality**: You will be given all your results. We will also send them to whichever doctor/s you wish. If you allow us, we will enter your results in the computer. When we look at the results and answers in the computer, your name and any identifying information will be hidden. We will share the anonymous summarized results with you, with your leaders, and with Health Canada. We may present the anonymous results to others such as doctors, students, or administrators. When we communicate with others, we will never talk about individual people, and we will never identify communities by name.

Freedom to withdraw: You do not have to have these tests done. You do not have to allow us to enter your results in the computer in order to receive the SLICK services. If you do not want to participate in the SLICK project we will offer you other available options.

Risks: You may find the blood tests pokes hurt slightly. You may feel upset, anxious or discouraged because your diabetes is not well controlled or you are developing problems from it. Please talk about this with the team. You may feel your community has too much diabetes. This is one of the reasons why we are here! We want to help your community deal with diabetes.

The eye drops may sting a little and the bright lights may be uncomfortable. Your eyes will be dilated and your vision blurred for about two hours after the examination. You will not be able to drive till this resolves. You may experience some uncomfortable side effects due to these drops including:

1. Irritable and stinging eyes.
2. Blurry vision or glare.
3. Irregular shaped pupils.
4. Minor eye redness or pain and some tears.

These are normal effects that most people will experience when given eye drops of this type. Most of these symptoms will go away when the effects of the eye drops have worn off fully in 6 hours.

If you experience the following symptoms 4 to 24 hours after being given eye drops:

1. **Extreme pain in the eye with sudden loss of vision.**
2. **Nausea and vomiting.**
3. **Extremely watery eyes.**

PLEASE INFORM THE SLICK NURSES. IF THE SLICK STAFF ARE NOT AVAILABLE OR YOUR SYMPTOMS OCCUR AT NIGHT, PROCEED TO YOUR NEAREST PHYSICIAN OR EMERGENCY ROOM IMMEDIATELY. PRESENT THIS INFORMATION SHEET TO YOUR DOCTOR WHEN YOU ARE BEING EXAMINED.

Information for Physicians

This patient has volunteered in the SLICK project. As a part of the assessment, the patient was given the mydriatic agent Diophenyl-T (Tropicamide 1%, and Phenylephrine 2.5%) for the purposes of taking retinal images. If the person presents with the above symptoms as well as the following signs:

1. Mid-dilated, non reactive pupil.
2. Hazy, edematous cornea with conjunctival injection and copious tearing.
3. Narrow anterior chamber on slit lamp exam, or oblique penlight examination.
4. Elevated intraocular pressures via tonometry if possible, or direct palpation.

the patient may be suffering from an acute attack of angle-closure glaucoma.

Please call The Royal Alexandra Hospital switchboard in Edmonton at (780) 477-4111 and ask to speak with the Ophthalmology resident on-call. The residents are familiar with the project and will assist you with this patient.

Additional contacts: If you have any questions or concerns about any part of this study, please contact Dr Toth or the other the study staff listed at the top of this document. If you have any complaints about SLICK you may contact the Patient Concerns Office at 780- 407-1040. There is an independent person there to deal with complaints. If you have any questions about the SLICK evaluation survey (questionnaire being used to assess the impact of SLICK), please contact Ms Neera Data or Dr Penny Jennettt at the Health Telematics Unit in Calgary: (403) 220-2881

I agree to have blood and urine tests for this project. Yes No

I agree to have eye drops and photographs of my eyes. Yes No

I agree for my results to go into a computer. Yes No

_____ _____ _____

Signature of Participant and/or Parent /Guardian Date Witness

_____ _____

Printed Name/s Printed Name

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

_____ _____

Signature of SLICK team member Date

THE INFORMATION SHEET MUST BE ATTACHED TO THIS CONSENT FORM AND A COPY GIVEN TO THE PARTICIPANT

APPENDIX 3B – INFORMATION SHEET AND CONSENT FORM FOR THE MDSI PROJECT

PROJECT TITLE: Mobile Screening Initiative for Diabetes and its Complications in Off-Reserve Aboriginal Communities - (Mobile Diabetes Screening Initiative – MDSI)

CONTACTS:

Dr. Ellen Toth — **Diabetes Doctor, University of Alberta**

Phone:

Donna Prokopczak — **Study Coordinator, University of Alberta**

Phone:

Local contact:

INTRODUCTION: Aboriginal people have a lot of diabetes. Diabetes is causing people to be very concerned in some communities. This is causing a lot of problems.

People with diabetes suffer from having to look after it with diet, exercise, pills and sometimes needles (insulin). They can also suffer problems with harm to eyes, kidneys, heart, nerves and feet.

It would be easier to prevent diabetes than its problems. However, to find risk of diabetes, fasting blood tests or glucose tolerance tests are needed. These are usually done in a town or city. We want to find out if we can screen you for diabetes here in your community. We will do this by using portable machines.

PROCEDURES: If you want to volunteer we will ask you some questions. We will weigh you and measure you and check your blood pressure. Then we will take some blood from your fingertip for tests. These tests will tell us whether you are at risk of diabetes or have diabetes.

From the blood test results we will be able to tell you right away whether you are at a high or low chance of having diabetes. You may have to see your family doctor to confirm this. We may also ask you to have blood drawn from a vein if you are over 18 years of age. This will help us to find out how accurate our other tests are.

We are hoping to follow as many people as possible, regardless of the initial results, over time. This will be done in further studies. If you allow us to contact you in a year or 2, we may have a new information sheet and consent process.

STUDY TITLE: **Mobile Screening Initiative for Diabetes and its Complications in Off-Reserve Aboriginal Communities - (Mobile Diabetes Screening Initiative – MDSI)**

CONTACTS:

Dr. Ellen Toth Diabetes Doctor, University of Alberta
Phone:

Dr. Mark Greve Eye doctor, Royal Alexandra Hospital
Phone:

Donna Prokopczak Study Assistant Manager, University of Alberta Phone:

Local contact:

I understand that I am participating in a research study. An MDSI team member has explained the benefits and risks involved in taking part in this study. I have received and read a copy of the attached information sheet.

I understand who has access to my records and that my results will be remain confidential.

I also understand that I am free to refuse to participate or withdraw from this study at any time. I do not have to give a reason to withdraw and it will not affect my care.

This study was explained to me by: _____.

If at anytime I have further questions I may ask an MDSI team member.

I agree to have blood and urine tests for this study Yes No

I agree to have eye drops and photographs of my eyes Yes No

_____

Signature of Participant and/or Parent/Guardian Date Witness

_____ _____

Printed name/s Printed Name

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

_____ _____

Signature of Study Team Member Date

THE INFORMATION SHEET MUST BE ATTACHED TO THIS FORM AND A COPY GIVEN TO THE PARTICIPANT

APPENDIX 3C – INFORMATION SHEET AND CONSENT FORM FOR THE BRAID PROJECT

INFORMATION SHEET

The BRAID project
Believing we can Reduce the Aboriginal Incidence of Diabetes

Contacts: **Ellen L. Toth MD, diabetes doctor -**
Norry Kaler -

Local contact:

INTRODUCTION: First Nations' people have a lot of diabetes. Diabetes is reaching epidemic proportions in some communities, and is causing a lot of problems.

People with diabetes suffer from having to look after it with diet, exercise, pills, and sometimes needles (insulin), and can also suffer complications with damage to eyes, kidneys, heart, nerves and feet.

It would be easier to prevent diabetes than its complications. However to identify risk of diabetes fasting blood tests or glucose tolerance tests are needed.

PROCEDURES: We would like to blood tests to assess risk of diabetes.

If you want to volunteer we will ask you some questions, weigh you and measure you, check your blood pressure, and then do some finger tip blood tests.

From the blood test results we will be able to tell you immediately whether you are at a high or low chance of having diabetes. The results will take a week to come back, and we will make sure you get those results as well with an explanation of what they mean.

BENEFITS: You may benefit from knowing whether you do or do not have diabetes, or if you are at risk for getting it.

RISKS: You may not like finding out if you have diabetes or are at risk of getting it. You may experience minor pain and bruising from having blood tests.

IS THIS RESEARCH? : Yes. Dr Toth is a specialist and researcher at the University of Alberta and is interested in finding better ways to diagnose and help people with diabetes. She works with other researchers at the University and with companies. In the past and even today there are many examples of researchers abusing the trust of First Nations' people and taking away data and information. You can decide whether you want to trust this research team.

CONFIDENTIALITY: You will be given all your results with an explanation of what they mean. We will also send them to your doctor if you wish. All your information will be kept

Reference List

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