University of Alberta

An Investigation of Dietary and Physical Activity Risk Factors for Type 2 Diabetes Among Alberta Youth

by

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Abstract

Due to the increase in type 2 diabetes in the child and adolescent population, examining the lifestyle habits of youth has become important. The purpose of this research was to examine the presence of dietary and physical activity risk factors for type 2 diabetes among youth in Alberta and to evaluate their relationship with insulin sensitivity. Lifestyle habits of Alberta youth with type 2 diabetes (n = 28), and age, sex and BMI matched controls (n = 28) were assessed by a chart review method. Those with diabetes had a higher intake of several nutrients (i.e. protein intake) and were less likely to be physically active. Dietary and physical activity risk factors for diabetes of a large sample of Alberta youth (n = 4981) were also assessed using the Web Survey of Physical Activity and Nutrition (Web-SPAN) and insulin sensitivity was measured in a sub-group (n = 318) using a C-13 glucose breath test. High Glycemic Index (GI) and Glycemic Load (GL) diets were common among Alberta adolescents and dietary patterns associated with dietary GI and GL were assessed. Dietary and physical activity risk factors for type 2 diabetes, including overweight and obesity, high GI, high GL, low fibre, low magnesium, low vegetable and fruit intake, high fat intake and low physical activity levels, were commonly reported among Alberta teens; with some risk factors, such as low fibre intake and high GI being reported by over half of all participants. Youth reported having an average of 3 diabetes risk factors. Boys reported more risk factors than girls, older students reported more risk factors than younger students and students with a higher BMI reported more risk factors than students with a lower BMI. Age, sex, BMI and dietary GI

were associated with Insulin Sensitivity Score as measured by a C-13 glucose breath test. In summary, this research has shown that the dietary and physical activity habits of Alberta adolescents are sub-optimal for type 2 diabetes prevention and the relationship between diabetes risk factors and insulin sensitivity in this group suggests that these behaviours are related to early changes in carbohydrate metabolism.

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Edmonton with me so that I could pursue graduate studies and for all his love, support and encouragement for the last 5 years.

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List of Abbreviations

AN:	Acanthosis Nigricans
ANOVA:	Analysis of Variance
BMI:	Body Mass Index
C-13:	Carbon 13
CCHS:	Canadian Community Health Survey
CDC:	Centre for Disease Control
DKA:	Diabetic Ketoacidosis
FSIVGTT:	Frequently Sampled Intravenous Glucose Tolerance Test
GI:	Glycemic Index
GL:	Glycemic Load
HDL-C:	High Density Lipoprotein Cholesterol
HOMA:	Homeostatic Model Assessment
HOMA-IR:	Homeostasis Model Assessment-Estimated Insulin Resistance
HR:	Hazard Ratio
ICC:	Intra-Class Correlation Coefficients
IFG:	Impaired Fasting Glucose
IGT:	Impaired Glucose Tolerance
IOTF:	International Obesity Task Force
ISS:	Insulin Sensitivity Score
LDL-C:	Low Density Lipoprotein Cholesterol
MANOVA:	Multivariate Analysis of Variance
MET:	Metabolic Equivalent of Task

OGTT:	Oral Glucose Tolerance Test
OR:	Odds Ratio
PAQ-C:	Physical Activity Questionnaire for Children
PCOS:	Polycystic Ovary Syndrome
QUICKI:	Quantitative Insulin Sensitivity Check Index
RR:	Relative Risk
SD:	Standard Deviation
SES:	Socioeconomic Status
TC:	Total Cholesterol
TG:	Triglycerides
TNF-α:	Tumour Necrosis Factor Alpha
VO2 max:	Maximum Volume of Oxygen
WC:	Waist Circumference
Web-SPAN:	Web Survey of Physical Activity and Nutrition
WHO:	World Health Organization

Definitions

C-13 Glucose
Carbon 13 is a stable isotope of carbon containing 6 protons and 7 neutrons. Carbon 13 glucose is a glucose molecule in which all the carbon atoms are carbon 13 atoms.

Child or Youth
In this thesis, a child or youth is defined as a person 18 years of age or younger.

Hazard Ratio
A hazard ratio is similar to a relative risk, but takes into account differing lengths of follow-up. A method frequently used in survival analysis.

Impaired Fasting Glucose
In Canada, Impaired Fasting Glucose is defined as a fasting plasma glucose value between 6.1 and 6.9 mmol/L.

Impaired Glucose Tolerance
In Canada, Impaired Glucose Tolerance is defined as a 75g OGTT 2-hour plasma glucose level between 7.8 mmol/L and 11.0 mmol/L

Insulin Resistance
A decrease in insulin sensitivity that is associated with disease risk.

Insulin Sensitivity
Insulin sensitivity is a measure how efficiently the body uses insulin to control blood glucose levels.

Odds Ratio
An odds ratio compares the odds of being exposed to a risk factor among those who have a disease, to the odds of being exposed among those who do not have the disease. A method commonly used in case control studies.

Physical Activity
Physical activity includes any movement of large skeletal muscles that results in energy expenditure.

Physical Fitness
Physical fitness refers to the body's ability to function, to be healthy and to prevent disease. Components of physical fitness include cardiovascular fitness, flexibility, muscle strength, muscular endurance and body composition.

Pre-Diabetes
Pre-Diabetes may refer to Impaired Fasting Glucose, Impaired Glucose Tolerance or both.

Relative Risk
The relative risk is the probability that a group of people with an exposure to a risk factor will develop a disease compared to those who were not exposed.

Type 2 Diabetes
High blood glucose levels caused by a combination of insulin resistance and beta-cell dysfunction. In Canada, diabetes is defined as: a fasting plasma glucose level $\geq$ 7.0 mmol/L or, following a 75g oral glucose tolerance test, a 2 hour plasma glucose level $\geq$ 11.1 mmol/L

Chapter 1: Introduction

1.1. Rationale

Type 2 diabetes is a disease characterized by the inability of the body to adequately synthesize and/or utilize insulin. This inability results in increased blood glucose levels, which, if untreated, may cause complications such as vision loss, numbness of the extremities, kidney failure and a greatly increased risk for cardiovascular disease (Canadian Diabetes Association Clinical Practice Guidelines Expert Committee 2008). In Canada, the prevalence of type 2 diabetes has been increasing steadily over the last few decades. For example, between 1994 and 2001 there was a 1% increase in the proportion of Canadians with diabetes (Statistics Canada 2006). The estimated cost of diabetes care in Canada is currently over $13 billion per year; and these costs are expected to rise to over $19 billion by the year 2020 due to the increasing prevalence of diabetes in this country (Canadian Diabetes Association 2008).

The increase in diabetes prevalence seen in Canada is not exclusive to the adult population. Although until the 1970's type 2 diabetes was considered to be exclusively an adult disease, cases of childhood onset type 2 diabetes have now been reported and the prevalence of the disease among children has been increasing. Recent studies in the U.S. have estimated the prevalence rate of type 2 diabetes to be 0.42 cases per 1000 children in the general population (Liese et al. 2006) and the prevalence rate may be as high as 5.31% in high risk populations such as the Pima Indians (Dabelea et al. 1998). Although the prevalence of type 2

diabetes in Canadian children is not well documented, a rate of 3.6% has been seen in 10-19 year old Ojibwa-Cree girls in northern Manitoba (Dean et al. 1998) and a medical clinic in Manitoba has seen a 15 fold increase in the number of children treated for type 2 diabetes between 1987 and 2005 (Toth 2005). Earlier onset of type 2 diabetes is of particular concern because of the potential for earlier development of macrovascular and microvascular complications of diabetes. Some patients diagnosed with type 2 diabetes in their youth display serious complications such as nephropathy during young adulthood (Krakoff et al. 2003).

Type 2 diabetes results from an interaction between genetic susceptibility and lifestyle factors and it is therefore a potentially preventable disease. Prevention programs targeting type 2 diabetes in youth are not widely available, likely due to the relative rarity of early onset. However, lifestyle programs targeting diabetes prevention in adults, such as the Diabetes Prevention Program and the Finnish Diabetes Prevention program have demonstrated a substantial decrease in the prevalence of diabetes among high risk individuals (Lindstrom et al. 2006; Ratner 2006). It is suggested that similar programs for youth would help to prevent the early form of the disease.

Lifestyle-related factors of importance for diabetes prevention and diabetes risk in adults include body weight, dietary factors and physical activity. Overweight and obesity, conditions caused by an imbalance between energy intake (diet) and energy output (physical activity), are positively associated with diabetes risk in a dose-response manner (Field et al. 2001). Data from the Nurse's Health Study showed that women with a Body Mass Index (BMI) above 35 kg/m^2

had a relative risk of diabetes of 38.8 compared to women with a BMI under 23kg/m^2 (Hu et al. 2001). Similar results have been reported in men (Chan et al. 1994) and, in addition, nearly all children with type 2 diabetes are obese (Hale and Rupert, G. 2006; McGrath et al. 1999; Perez-Perdomo et al. 2005; Zdravkovic et al. 2004).

Dietary factors and physical activity have been shown to have an effect on diabetes risk, independent of their influence on body weight (Hu et al. 2001). Intake of dietary components such as fibre (particularly from grain products) polyunsaturated fats and low glycemic index (GI) foods have been linked to a lower risk of diabetes; whereas intakes of saturated fat, trans fats, fructose, glucose and high GI foods have been related to increased risk (Colditz et al. 1992; Montonen et al. 2003; Salmeron et al. 2001). Physical activity also has an important role in diabetes prevention. People who spend more than 7 hours per week being active have a relative risk of 0.71 for diabetes compared to those who are active for less than half an hour per week; again this finding is independent of other diabetes risk factors (Hu et al. 2001).

Although the link between unhealthy lifestyles, obesity and type 2 diabetes is well known, lifestyles of Canadian youth do not reflect this knowledge. In fact, obesity among Canadian children and adolescents has increased significantly in the past few decades. Between 1979 and 2004, the prevalence of overweight doubled among Canadian adolescents aged 12-17 increasing from 14 to 29% and rates of obesity tripled, from 3 to 9% (Shields 2006). This increase in overweight and obesity indicates that type 2 diabetes may

be a greater problem in the future and it may develop at an earlier age in future generations. It is therefore important to help young Canadians make dietary and physical activity choices that are conducive to diabetes prevention.

Adolescents provide a unique opportunity for diabetes prevention as they are at a stage of increasing independence and they are starting to make their own lifestyle choices. Encouraging healthy choices at this stage may lead to a continuation of healthy choices into adulthood which may reduce their future risk of developing diabetes. In addition, addressing risk factors during adolescence may help youth at risk for developing early onset type 2 diabetes, prevent or delay the onset of the disease. For these reasons, it is important to examine dietary and physical activity related diabetes risk factors in the adolescent population and to implement diabetes prevention strategies including the promotion of healthy lifestyle habits early in life.

1.2. Purpose

The purpose of the current research was to examine the frequency and distribution (by age, sex, and BMI) of dietary and physical activity risk factors for type 2 diabetes among youth in Alberta and to evaluate their association with insulin sensitivity in this population.

1.3. Research Questions

1. How do the medical and lifestyle profiles of youth with type 2 diabetes differ from the profiles of those who are overweight?

2. What are the Glycemic Index (GI) and the Glycemic Load (GL) of the diets of youth in Alberta?

3. What dietary patterns are associated with less favourable values for GI and GL?

4. How frequently are diet and physical activity related diabetes risk factors reported among Alberta youth?

5. Does the proportion of Alberta youth with diet and physical activity related diabetes risk factors differ with age, sex, and BMI?

6. Are dietary and physical activity risk factors for diabetes associated with insulin sensitivity as measured by a Carbon 13 (C-13) glucose breath test?

1.4. Hypotheses

Hypothesis 1: Youth with type 2 diabetes will differ from those who are overweight in that they will have:

a. a greater frequency of medical history related risk factors for diabetes including:

    i. stronger family history of type 2 diabetes **(Chapter 3)**

    ii. greater frequency of diabetes during gestation **(Chapter 3)**

    iii. greater frequency of high (>4000g) and low (<2500g) birth weights **(Chapter 3)**

b. have greater frequency of features of the metabolic syndrome including:

    i. dyslipidemia, specifically high triglycerides and low High Density Lipoprotein Cholesterol (HDL-C) concentrations **(Chapter 3)**

    ii. higher blood pressure **(Chapter 3)**

c. different dietary and physical activity related behaviours, specifically:

    i. higher dietary fat intakes **(Chapter 3)**

    ii. lower dietary fibre intakes **(Chapter 3)**

    iii. higher rates of inactivity **(Chapter 3)**

Hypothesis 2: The GI and GL of the diets of Alberta adolescents are associated with their macronutrient distribution, food group choices and meal patterns with the following variables being related to:

a. Higher GIs
    i. Macronutrient Distribution
        1. High carbohydrate intakes **(Chapter 4)**
        2. Low fibre intakes **(Chapter 4)**
        3. Low fat intakes **(Chapter 4)**
        4. Low protein intakes **(Chapter 4)**
    ii. Food group choices
        1. High consumption from the "other" categories (particularly the mostly sugar, high salt and fat, high calorie beverage and high sugar and fat categories) **(Chapter 4)**
        2. High consumption from the grain product food group **(Chapter 4)**
    iii. Meal patterns
        1. High frequency of eating away from home **(Chapter 4)**
        2. Low frequency of family meals **(Chapter 4)**
        3. Low meal frequency **(Chapter 4)**
b. Higher GLs
    i. Macronutrient distribution
        1. High carbohydrate intakes **(Chapter 4)**
        2. Low fibre intakes **(Chapter 4)**

3. Low fat intakes **(Chapter 4)**
4. Low protein intakes **(Chapter 4)**

ii. Food group choices

1. High consumption from the "other" categories (particularly the mostly sugar, high salt and fat, high calorie beverage and high sugar and fat categories) **(Chapter 4)**
2. High consumption from the grain product food group **(Chapter 4)**

iii. Meal patterns

1. High frequency of eating away from home **(Chapter 4)**
2. Low frequency of family meals **(Chapter 4)**
3. Low meal frequency **(Chapter 4)**

Hypothesis 3: There will be a greater proportion of participants with diet and physical activity related diabetes risk factors (* see below) observed among youth who:

a. are females compared to males **(Chapter 5)**
b. are older (15-16 year olds) compared to younger (13-14 year olds) adolescents **(Chapter 5)**
c. have BMI percentiles in the overweight (>85th percentile) and obese (>95th percentile) categories compared to those who are non-overweight **(Chapter 5)**

Hypothesis 4: The insulin sensitivity of Alberta adolescents, as measured by a C-13 glucose breath test, is associated with:

a. continuous diet[1] and physical activity[2] related diabetes risk factor variables **(Chapter 6)**.
b. dichotomous diet and physical activity related diabetes risk factor variables **(Chapter 6)**.
c. a composite diet and physical activity diabetes risk score **(Chapter 6)**.

[1] Diet related risk factors for diabetes include: high GI, high GL, low fibre, low magnesium, low vegetable and fruit intake and high fat intake.
[2] Physical activity related diabetes risk factors include: low physical activity score.

1.5. Objectives

Objective 1: To compare diet and physical activity related diabetes risk factors among youth with type 2 diabetes (n = 28) and age, sex and BMI matched control youth (n = 28) as recorded in their medical charts.

Objective 2: To compare family history of diabetes, co-morbidities, blood lipids and blood pressure of youth with type 2 diabetes (n = 28) and age, sex and BMI matched control youth (n = 28) as recorded in their medical charts.

Objective 3: To determine the GI and GL of the diets of a large sample of youth in Alberta (n = 4981) as measured by a web-based 24 hour recall.

Objective 4: To determine what macronutrient distributions and food group and meal patterns are associated with the GI and GL of the diets of a large sample of youth in Alberta (n = 4981).

Objective 5: To determine the proportion of participants reporting dietary and physical activity related diabetes risk factors in a large sample of Alberta youth (n = 4981) as measured by a web-based survey.

Objective 6: To examine the relationship between the presence of diet and physical activity related diabetes risk factors and age, sex and BMI in a large sample of Alberta youth (n = 4981).

Objective 7: To determine what dietary and physical activity diabetes risk factors are associated with insulin sensitivity, as measured by the C-13 glucose breath test, in a sample of healthy Alberta adolescents (n = 318).

1.6. Thesis Organization

Table 0.1.1 Thesis Organization

Chapter 1	Introduction
Chapter 2	Literature Review of Type 2 Diabetes Risk Factors and Risk Assessment in Youth
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Chapter 6	Dietary and Physical Activity Diabetes Risk Factors and Insulin Sensitivity Among Alberta Adolescents
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1.7. References

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Chapter 2: Literature Review of Type 2 Diabetes Risk Factors and Risk Assessment in Youth

2.1. Introduction

Type 2 diabetes is a disease caused by interactions between genetic susceptibility and lifestyle habits. The prevalence of this disease has risen in recent years, parallel to the increasing prevalence of obesity in our society and, in addition, diabetes is now being diagnosed at much younger ages. These trends have raised concern among researchers, health professionals and policy makers, and decreasing the risk of diabetes among young people is considered to be of great importance. Before diabetes risk can be modified, diabetes and diabetes risk factors in youth must be understood. Therefore, the purpose of this literature review is to: (1) define diabetes and pre-diabetes states, such as insulin resistance, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) and to examine the health consequences of these conditions; (2) examine risk factors for type 2 diabetes, focusing particularly on lifestyle related risk factors; (3) examine previously used methods of measuring diabetes risk.

2.2. Type 2 Diabetes in Children

2.2.1. Definition and Prevalence

Type 2 diabetes is a chronic disease caused by a combination of insulin resistance and failure of the beta cells of the pancreas to compensate for increased insulin requirements, which results in hyperglycemia (Rizvi 2004). In Canada, a diagnosis of diabetes is made if a patient has a fasting plasma glucose level ≥ 7.0 mmol/L or, following a 75g oral glucose tolerance test, has a 2 hour plasma

glucose level ≥ 11.1 mmol/L (Canadian Diabetes Association Clinical Practice Guidelines Expert Committee 2008).

Until the 1970s, Type 2 Diabetes was thought to be exclusively an adult disease. However, in 1979, Savage and colleagues (Savage et al. 1979) described the first cases of early onset type 2 diabetes in young Pima Indians aged 15 to 24 in Arizona. The disease was also observed among Canadian aboriginal children as early as 1984 by Dean et al., (Dean et al. 1992) who described a group of Ojibwa-Cree children in Manitoba and Northern Ontario presenting with type 2 diabetes. Since these first reports, type 2 diabetes in children has been reported in clinics around the world and the prevalence of early onset type 2 diabetes has been increasing.

Recent studies in the U.S. have estimated the prevalence of type 2 diabetes to be 0.42 cases per 1000 children in youth aged 10 to 19 years (Liese et al. 2006) and as high as 5.31% in high risk populations such as the Pima Indians (Dabelea et al. 1998). Although the presence of type 2 diabetes in Canadian children is not well documented, a prevalence of 3.6% has been reported in 10 to 19 year old Ojibwa-Cree girls living in northern Manitoba (Dean et al. 1998). Rates of type 2 diabetes among Canadian children have been increasing, with one clinic in Manitoba observing a 15 fold increase in the number of children treated for type 2 diabetes between 1987 and 2005 (Toth 2005) and a clinic in Toronto observing a five fold increase between 1994 and 2002 (Zdravkovic et al. 2004).

2.2.2. Health Consequences of Type 2 Diabetes

Type 2 diabetes in adults results in significant morbidity and mortality as well as increased health care costs. Type 2 diabetes causes macrovascular complications such as atherosclerosis, hyperlipidemia and increased risk of cardiovascular events; as well as microvascular complications such as renal disease, retinopathy and neuropathy. Type 2 diabetes is associated with a 2 to 3-fold increase in cardiovascular disease risk (Kannel and McGee 1979) and it is the leading cause of blindness, kidney failure and amputations in Canada (Canadian Diabetes Association Clinical Practice Guidelines Expert Committee 2008). Type 2 diabetes also shortens life expectancy by 5 to 10 years among adults (Canadian Diabetes Association 2008). The annual cost of diabetes to the Canadian health care system is expected to be 15.6 billion by the year 2010 and is projected to rise to $19.2 billion by 2020 (Canadian Diabetes Association 2008).

As type 2 diabetes among youth is an emerging disease, the consequences have not yet been fully assessed; however, recent studies are showing that due to the longer duration of disease, early onset diabetes may result in greater morbidity than the adult form of the disease.

2.2.2.1. Cardiovascular Health

Although minimal data are available regarding the prevalence of cardiovascular events among those with early onset type 2 diabetes, the prevalence rates of hypertension and hyperlipidemia, important risk factors for cardiovascular disease, have been documented. The prevalence of hypertension among youth with type 2 diabetes is similar to that of obese children, with values

ranging from 10 to 59 % in different populations (Hotu et al. 2004; McMahon et al. 2004; Ohki et al. 2004; Perez-Perdomo et al. 2005; Upchurch et al. 2003; Zdravkovic et al. 2004). The SEARCH for Diabetes Study found that hyperlipidema was very common among youth (aged 10 to 19 years) with type 2 diabetes, with the most common lipid abnormality being high triglycerides at 63%, followed by high LDL-C (Low Density Lipoprotein Cholesterol) levels at 57%, low HDL-C (High Density Lipoprotein Cholesterol) levels at 44% and high total cholesterol was present in 33 % of youth (Kershnar et al. 2006).

2.2.2.2. Nephropathy and Retinopathy

Studies have found nephropathy to be highly prevalent among youth with type 2 diabetes with one study reporting that youth with type 2 diabetes had a significantly higher prevalence of nephropathy than those with type 1 diabetes (Eppens et al. 2006). Similarly, a study that compared the timeline of renal disease development between those diagnosed with type 2 diabetes in their youth and those diagnosed as adults found that those diagnosed early in life developed nephropathy at the same rate as those who were diagnosed when they were older (Krakoff et al. 2003). In contrast to nephropathy, those diagnosed with type 2 diabetes in their youth are slower to develop retinopathy compared to those who are diagnosed as adults (Krakoff et al. 2003). Youth with type 2 diabetes also have a lower prevalence of retinopathy compared to those with type 1 diabetes (Eppens et al. 2006).

2.2.2.3. Neuropathy

The prevalence of neuropathy in type 2 diabetes in youth appears to vary in different populations, but reported prevalence rates range from 12 to 21% (Chuback et al. 2007; Eppens et al. 2006). One study that compared young patients with type 1 and type 2 diabetes found that the prevalence of neuropathy was similar between the groups (Eppens et al. 2006).

2.2.2.4. Mortality

Although few long term prospective studies assessing mortality in those diagnosed with early onset type 2 diabetes have been done, one Swedish study that tracked mortality among people diagnosed with diabetes between the ages of 15 and 35 found a three fold increase in mortality during an average of 8.5 years follow-up among those with type 2 diabetes compared to what would be expected in the healthy population. The greatest number of deaths in this group were due to cardiovascular disease (Waernbaum et al. 2006).

2.3. Insulin Resistance, Impaired Fasting Glucose and Impaired Glucose Tolerance in Children

2.3.1. Definitions and Prevalence

Type 2 diabetes is a disease that develops over time and the onset of disease is generally preceded by milder forms of glucose metabolism dysfunction, including insulin resistance, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT). Insulin resistance is frequently the first abnormality of glucose metabolism observed in the continuum from normal glucose metabolism to diabetes (Lillioja et al. 1993). Insulin resistance is characterized by decreased

responsiveness of cells to the action of insulin. The beta-cells of the pancreas then release more insulin to compensate for decreased sensitivity, resulting in normal blood glucose levels but elevated insulin levels.

The gold standard method of measuring insulin resistance is the hyperinsulinemic euglycemic clamp. For this test, excess insulin is infused into the blood stream and glucose is infused into the blood to maintain a constant, slightly elevated glucose level. The body's ability to absorb glucose from the blood stream is then measured over time (DeFronzo et al. 1979). This method is expensive, complex and invasive; therefore, other methods have been devised. For example, the minimal-model analysis frequently sampled intravenous glucose tolerance test (FSIVGTT) is frequently used as a slightly less invasive, highly accurate measure of insulin resistance. In this test, an intravenous (IV) bolus of glucose is given, followed by an IV bolus of insulin. Blood is collected at multiple time points so that blood glucose and insulin concentrations can be tracked over a time period of 3 to 4 hours (Finegood et al. 1990).

Methods of measuring insulin resistance most commonly used in epidemiological settings include measures derived from fasting glucose and insulin values through calculations such as the HOMA (Homeostatic Model Assessment) index and QUICKI (Quantitative Insulin Sensitivity Check Index). Although these measures are not as accurate as clamp methods or the FSIVGTT, they do correlate with more accurate measures and are much more feasible measures to use in large populations due to their relatively low cost and less invasive nature (Conwell et al. 2004).

Recently, a completely non-invasive method of measuring insulin resistance has been proposed. The Carbon 13 (C-13) glucose breath test has been used for many years to assess carbohydrate oxidation (Moseley et al. 2005). For this method, a stable isotope labelled glucose is ingested and the speed with which the labelled glucose is oxidized can be assessed by measuring the appearance of the C-13 exhaled in the form of carbon dioxide in the breath. Researchers have hypothesized that the speed of oxidation will be reduced among subjects with insulin resistance or diabetes. One study that has assessed this method as a measure of insulin resistance has found that breath test results correlated strongly with insulin resistance as measured by clamp methods and the strength of the relationship was similar to that seen with methods such as HOMA and QUICKI (Lewanczuk et al. 2004).

In youth, there is no widely accepted method of defining insulin resistance, which makes the prevalence difficult to define. Suggested cut-offs using HOMA as a measure of insulin resistance include >2 standard deviations above the mean value for normal weight adolescents (Lee et al. 2006a), the upper quartile of values for all adolescents (Hirschler et al. 2005), a HOMA value above 3.16 (Keskin et al. 2005) or a HOMA value above 3.99 (Wahrenberg et al. 2005). One study that examined insulin resistance in the National Health and Nutrition Examination Survey (NHANES) study population using HOMA values found that the prevalence of insulin resistance was between 3 and 17% in normal weight youth, 15 to 42% for overweight youth and 52 to 75% among obese youth, depending on the cut-off value used (Lee et al. 2006a).

Impaired Fasting Glucose and IGT are conditions characterized by insulin resistance combined with some impairment in beta cell function that is less severe than what is observed in diabetes. In Canada, IFG is defined as having a fasting plasma glucose value from 6.1 to 6.9 mmol/L. The definition of IGT is having a 75g Oral Glucose Tolerance Test (OGTT) 2-hour plasma glucose level between 7.8 mmol/L and 11.0 mmol/L (Canadian Diabetes Association Clinical Practice Guidelines Expert Committee 2008). Using data from the NHANES collected between 1988 and 1994, researchers estimated that the prevalence of IFG (defined as being > 6.1 mmol/L) was 1.76% among 12 to 19 year old Americans between (Fagot-Campagna et al. 2001). Similarly, an estimated prevalence of 1.5% in this age group was calculated using data collected between 1999-2002 (Duncan 2006).

As the diagnosis of IGT requires an OGTT, population-based studies that can determine the prevalence of IGT among youth are rare. However, one population-based Polish study found that the prevalence of IGT among children aged 7 to 19 years was 0.3%. The prevalence of IGT among obese children and adolescents is more frequently studied. In obese children rates of IGT ranging from 1.44% to 36% have been reported, depending on the study population (Atabek et al. 2007; Bhargava et al. 2004; Invitti et al. 2006; Quintos et al. 2006; Sinha et al. 2002; Wabitsch et al. 2004; Wiegand et al. 2004).

2.3.2. Health Consequences

Although Insulin Resistance, IFG and IGT are less severe than type 2 diabetes, these conditions have serious consequences. The probability that a

person will develop type 2 diabetes or cardiovascular disease increases significantly in pre-diabetic states.

2.3.2.1. Risk of Type 2 Diabetes

Insulin resistance has been shown to be related to increased risk of developing type 2 diabetes among both adults and adolescents. An analysis of the Women's Health Initiative Observational Study found that the relative risk (RR) of diabetes over 6 years was 2.03 for every standard deviation (SD) increase in insulin resistance as measured by HOMA-IR (HOMA Insulin Resistance), after correcting for other risk factors (Song et al. 2007). An analysis of the Framingham Offspring Study found that there was an odds ratio (OR) of 2.05 for diabetes for those over the 75^{th} percentile of HOMA-IR scores (Wilson et al. 2007). A recent study that tracked the 10-year risk of developing IFG and diabetes in black and white girls aged 9 to 10 years at baseline found that those with insulin resistance had an OR of 1.25 for developing either type 2 diabetes or IFG compared to those without insulin resistance (Morrison et al. 2008).

Adult studies show that even greater increases in diabetes risk are seen among those diagnosed with IFG or IGT. The ORs for developing type 2 diabetes for those with IGT range from around 3 to 10 (Abdul-Ghani et al. 2006; Bonora et al. 2004; de Vegt et al. 2001; Wilson et al. 2007) and for those with IFG, ORs range from 5 to 11 (Bonora et al. 2004; de Vegt et al. 2001; Wilson et al. 2007). Those with both IFG and IGT have an even greater risk of developing type 2 diabetes, with ORs of 20 to 40 (Bonora et al. 2004; de Vegt et al. 2001).

2.3.2.2. Risk of Cardiovascular Disease

Increased risk of cardiovascular disease has also been seen in pre-diabetic states among adults. Studies that have examined cardiovascular risk in those with insulin resistance have found hazard ratios (HRs) ranging from 1.14 to 1.67 when using HOMA-IR or fasting insulin (Jeppesen et al. 2007; Lawlor et al. 2007; Saely et al. 2005). An increased risk of hypertension has also been seen with insulin resistance, with one study finding an 11% increased risk of hypertension with every unit decrease in insulin sensitivity index as measured by a FSIVGTT (Goff, Jr. et al. 2003). Impaired glucose tolerance and IFG are also related to increases in cardiovascular risk. A meta-analysis that investigated risk of cardiovascular incidents at differing blood glucose levels found that the RR of cardiovascular events with a fasting blood glucose level at the threshold for IFG was 1.33 compared to a value in the normal range and the RR was 1.58 for a 2-hour glucose level at the threshold of IGT (Coutinho et al. 1999).

2.4. Risk Factors for Type 2 Diabetes in Children

One's risk of developing type 2 diabetes depends on many factors, including obesity, dietary factors, physical activity, family history of the disease or genetic predisposition, puberty and prenatal growth environments. In the following section, risk factors for type 2 diabetes among youth will be discussed. The relationship between each risk factor and diabetes will be described and mechanisms for these effects will be examined. Evidence from literature on youth with type 2 diabetes will be used whenever possible, but as type 2 diabetes in youth is a new, relatively rare disease, evidence from adult literature will be used as well as literature focusing on youth and insulin resistance, IGT and IFG.

Specifically, it appears that the following factors may increase the risk of developing type 2 diabetes in youth: increased body weight, high dietary GI/ GL, low fibre/cereal fibre intakes, low magnesium intakes, low vegetable and fruit intakes, high dietary fat intake, and low physical activity/fitness levels. Other factors of importance include a family history of diabetes, puberty and the prenatal environment.

2.4.1. Obesity

2.4.1.1. Relationship with Diabetes in Adults

Obesity is considered by many to be the most important risk factor for diabetes among adults. Large prospective studies have consistently found obesity to be related to substantial increases in diabetes risk. The RR for type 2 diabetes for those who are obese compared to those with a normal weight, ranges from 3.5 to 20 (Hart et al. 2007; Hosseinpanah et al. 2007; Hu et al. 2001; Hui and Nelson

2006; Krishnan et al. 2007; Meisinger et al. 2006; Patja et al. 2005; Rana et al. 2007) depending on the population, length of follow-up and if the values are adjusted to account for other risk factors. In addition, the relationship between weight status and diabetes risk appears to be linear in nature with increases in Body Mass Index (BMI) even within the normal range being associated with increases in diabetes risk (Hu et al. 2001; Rana et al. 2007) and with very obese subjects being at the highest risk. One study reported that women with a BMI over 35kg/m^2 had a RR of developing diabetes of 38.8 compared to those with a BMI of less than 23kg/m^2 (Hu et al. 2001). Overweight and obesity are considered to be responsible for a large number of cases of type 2 diabetes with one study estimating that 65% of the cases of diabetes in a cohort in Tehran could be attributed to excess body weight (Hosseinpanah et al. 2007). Studies in adults have also shown that weight loss is protective against diabetes. The Diabetes Prevention Program found that the HR for diabetes was 0.42 for every 5 kg of weight loss (Hamman et al. 2006).

Although studies have shown that BMI is strongly predictive of diabetes risk, many studies have shown that waist circumference (WC) is as strong a predictor of diabetes risk as BMI, and in some cases, a stronger predictor (Chan et al. 1994; Meisinger et al. 2006; Rana et al. 2007; The Diabetes Prevention Program Research Group 2006; Tulloch-Reid et al. 2003; Wang et al. 2005). Both BMI and WC may be important independent predictors of diabetes and using both variables may yield more information than using either in isolation

(Meisinger et al. 2006). It is hypothesized that the strong relationship between WC and diabetes risk is due to its correlation with visceral adipose tissue.

2.4.1.2. Relationship with Diabetes in Youth

Although early onset type 2 diabetes is rare, one study has investigated longitudinal risk of type 2 diabetes in adolescents. This study found that 1 kg/m^2 increase in BMI was associated with an OR of 1.14 for 10 year risk of type 2 diabetes or IFG among black and white girls aged 9-10 at baseline (Morrison et al. 2008). In spite of the limited longitudinal evidence for obesity as a risk factor for early onset diabetes, it is considered to be the most important risk factor for type 2 diabetes among youth. The increasing incidence of early onset type 2 diabetes, which has been observed in the last three decades, has coincided with an increasing prevalence of childhood obesity. This has lead many to suspect a strong link between the two, particularly in light of the importance obesity plays in the risk of adult type 2 diabetes. In addition, obesity is extremely common among youth with type 2 diabetes, with different clinics reporting the prevalence of obesity to be between 72% and 100% in this population (Ehtisham et al. 2004; Hale and Rupert 2006; Harwell et al. 2001; McGrath et al. 1999; Ohki et al. 2004; Perez-Perdomo et al. 2005; Scott et al. 1997) with mean BMIs ranging from $24kg/m^2$ to $38kg/m^2$ (Ettinger et al. 2005; Glaser and Jones 1998; Grinstein et al. 2003; Hotu et al. 2004; Likitmaskul et al. 2005; Pinhas-Hamiel et al. 1996; Sanders et al. 2006; Scott et al. 1997; Upchurch et al. 2003; Vikram et al. 2005; Wei et al. 2003b; Zdravkovic et al. 2004). In addition, one case-control study of children and young adults with type 2 diabetes in India found that, compared to

age and sex matched controls, the OR of having a high BMI was 7.6 for those with diabetes and the OR for having a high waist circumference was 12.4 (Vikram et al. 2005).

2.4.1.3. Relationship with Insulin Resistance, IGT and IFG in Youth

Obesity has been shown to be strongly related to insulin resistance. Recent studies have shown obesity to be the strongest predictor of insulin resistance among youth (Lee et al. 2006a; Lobstein and Jackson-Leach 2006). A population-based study among American adolescents aged 12 to 18 found that 52% of obese youth were insulin resistant and weight status accounted for 29% of the variation in insulin resistance as measured by HOMA-IR; more than any other risk factor (Lee et al. 2006a).

Glucose Intolerance and IFG also have strong relationships with obesity. One population-based study in Poland found that obese children had significantly higher prevalence rates of IFG and IGT compared to normal weight children. The prevalence rates of IFG and IGT among obese children were 16.7% and 7.1%, compared to 0.67% and 0.3%, respectively, in the whole population (Mazur et al. 2007). In addition, a longitudinal cohort study of African American and Caucasian girls (aged 10 years at baseline) found that baseline BMI predicted both insulin resistance and IFG at 10 years follow-up. Among African American girls there was a 12% increase in the risk of IFG per unit increase in baseline BMI. For Caucasian girls, the rate of weight gain over the 10 year follow-up period was related to IFG risk, with a 7.6–fold increase in IFG risk being seen with every unit per year increase in BMI (Klein et al. 2004).

As observed among adults and children with diabetes, visceral fat content appears to be important in the development of insulin resistance and pre-diabetic states. One study that examined the relationship between fat distribution as measured by magnetic resonance imaging (MRI) and metabolic characteristics among obese adolescents found that 2-hour glucose values increased across increasing tertiles of visceral adipose tissue as did fasting insulin. There were no differences in BMI among the tertiles (Taksali et al. 2008).

2.4.1.4. Mechanisms

Several mechanisms related to body fat and adipose tissue metabolism have been proposed to explain the link between obesity and type 2 diabetes. Adiposity is hypothesized to affect both insulin resistance and beta cell function principally through its effects on circulating free fatty acids and its production and release of inflammatory peptides.

Adipose tissue is the body's main storage depot for fatty acids. Adipose tissue, particularly the more metabolically active visceral adipose tissue, has been shown to release fatty acids into the blood stream at a rate proportional to its volume (Jensen et al. 1989). Larger adipose tissue deposits, as seen in obesity, therefore result in excessive levels of free fatty acids in circulation. These free fatty acids are taken up by non-adipose tissues such as the liver and skeletal muscle. Build-up of triglycerides in these tissues causes a down-regulation of the production of proteins required for insulin action, resulting in insulin resistance (Goodpaster and Wolf 2004; Kabir et al. 2005).

Free fatty acids not only contribute to insulin resistance, but have also been implicated in the deterioration of beta cell function (Dubois et al. 2004). When excess free fatty acids are in circulation, they accumulate in the pancreatic islet cells, which has been shown to reduce glucose stimulated insulin release in cell culture studies, in animal models (Sako and Grill 1990; Zhou et al. 1996) and in humans (Paolisso et al. 1995). The free fatty acid build-up in beta cells also can lead to toxic metabolites of the free fatty acids. These toxins and free radicals can damage beta cells and induce apoptosis further limiting the insulin secreting capacity of the beta cells (Kaneto et al. 1999; Shimabukuro et al. 1998).

Recent research has established that adipose tissue not only stores fat, but also acts as an endocrine organ and part of the immune system, secreting hormones such as adiponectin and cytokines such as Tumor Necrosis Factor Alpha (TNF-α) (Combs et al. 2004; Nishimura et al. 2007; Stephens et al. 1997; Yamauchi et al. 2002). Lower levels of adiponectin are found in obese individuals compared to normal weight individuals (Nishimura et al. 2007). High adiponectin levels increase insulin sensitivity by increasing fatty acid oxidation both in the liver and skeletal muscle (Combs et al. 2004; Yamauchi et al. 2002). Obesity results in greater secretion of TNF-α by the adipose tissue which leads to a decrease in the expression of proteins needed for glucose metabolism, such as the insulin sensitive GLUT 4 transport protein and insulin receptor proteins (Stephens et al. 1997).

As with free fatty acids, inflammatory cytokines and other adipose tissue-derived signalling proteins such as leptin and TNF-α affect beta cell function as

well as insulin sensitivity, with increasing levels of these molecules being associated with decreased insulin production and/or promotion of cell death. Leptin, for example, decreases beta-cell secretion, but it is in fact protective against apoptosis (Finegood et al. 1995; Lupi et al. 1999). Tumour Necrosis Factor-α also inhibits secretion of insulin from the beta cell but is a promoter of apoptosis (Stephens et al. 1999; Zhang and Kim 1995).

2.4.2. Dietary Factors

Dietary factors are significant contributors to diabetes risk. In the following section, dietary diabetes risk factors will be discussed, including several factors related to carbohydrate intake, such as Glycemic Index (GI) and Glycemic Load (GL), fibre and cereal fibre, magnesium intake and vegetable and fruit intake. In addition, a non-carbohydrate risk factor - dietary fat intake, will be discussed. It should be noted that dietary factors discussed in this section are limited to those factors for which we have been able to collect data in the following chapters of this thesis. Data for some dietary risk factors, for example fructose intake, were not available using the dietary collection methods used for this thesis research, therefore these factors are not discussed.

2.4.2.1. High GI, High GL

2.4.2.1.1. Relationship with Diabetes in Adults

The GI, a measure of carbohydrate quality, is calculated based on the glycemic response elicited by a food following consumption, compared to a standard. White bread and glucose, the most commonly used standard foods are given a GI value of 100 and other carbohydrate foods are rated on a scale from 0-

100, with foods having a GI <55 being considered low GI foods, foods with a GI ranging from 56 to 69 being medium GI foods and foods with a GI >70 being considered high GI foods (www.glycemicindex.com). The GL is a measure that takes both the quality and quantity of carbohydrate into account and is calculated by multiplying the GI of a food by the number of grams of carbohydrate in a typical serving of that food.

Several studies have identified a link between high dietary GI, GL and increased risk of type 2 diabetes in adults. A recent meta-analysis of these studies, conducted by Barclay et al, (Barclay et al. 2008) found that the RR of type 2 diabetes among participants in the highest quantile of dietary GI was 1.4 compared to those in the lowest GI quantile group. The RR of diabetes was 1.3 for those in highest GL quantile compared to those in the lowest quantile (Barclay et al. 2008).

2.4.2.1.2. Relationship with Diabetes in Youth

Research on the dietary GI and GL of youth has primarily focused on their impact on weight management. Studies have shown that low GI foods have greater satiety among youth (Ball et al. 2003), which has made these foods potential candidates for weight loss programs. Although the relationship between GI, GL and risk of obesity in children is not clear (Davis et al. 2007; Hui and Nelson 2006; Nielsen et al. 2005), several intervention studies have found low GI and GL diets to be effective in promoting weight loss among youth (Ebbeling et al. 2003; Spieth et al. 2000). In addition, one study has examined GI and GL and

insulin resistance in adolescents but no relationship was found between the variables (Davis et al. 2007).

2.4.2.1.3. Mechanisms

Many potential mechanisms behind the role of the GI and GL in diabetes have been proposed. High GI and GL foods require more insulin and glucagon to be secreted from the beta cells of the pancreas (Brand-Miller et al. 2003; Wolever and Bolognesi 1996). High blood insulin levels have been shown to lead to insulin resistance in humans (Del Prato et al. 1994). In addition, the increased production of insulin may promote beta-cell exhaustion in cells genetically prone to dysfunction (Del Prato et al. 1994). High GI and GL diets also result in higher postprandial blood glucose levels and high blood glucose levels are known to have detrimental effects on beta cell function. Excess glucose increases oxidative stress in the beta cells and triggers apoptosis (Marchetti et al. 2004). Even mild recurring hyperglycemia, as may been seen in individuals with a high GI or GL diet, can be detrimental to beta cell function (Del Guerra et al. 2007). After a high GI meal during the late postprandial period, there is an increase in free fatty concentrations (Kallio et al. 2008) which may result in lipotoxicity in the beta cells, reducing beta cell function. High glycemic index and load diets have also been associated with markers of inflammation such as high C-reactive protein levels, high tumor necrosis factor-R2 levels (Qi et al. 2006b) and reduced levels of adiponectin (Qi et al. 2005; Qi et al. 2006a). As discussed in section 2.4.1.4, inflammatory markers have been shown to affect both insulin sensitivity and beta cell function . In addition, several studies have found GI and GL to be related to

obesity and central adiposity among adults (Hare-Bruun et al. 2006; Sahyoun et al. 2005), both strong risk factors for diabetes. However, this link has not been consistently reported in the literature and the effect of dietary GI and GL on body weight is not conclusively known.

2.4.2.2. Fibre and Cereal Fibre

2.4.2.2.1. Relationship with Diabetes in Adults

Associations have been found between low fibre intake, particularly low cereal fibre intake, and risk of type 2 diabetes. Results of both the Iowa Women's Health Study and the Nurses Health study found that the RR of diabetes was 1.3 for the lowest compared to the highest quintile of total fibre intake after adjustment for various other risk factors including BMI. Fibre intakes in the lowest quintile were less than 14g per day and intakes in the highest quintile were over 22g per day (Meyer et al. 2000; Schulze et al. 2004). An even greater increase in risk of diabetes was seen in the Finnish Mobile Clinic Examination Survey, with a RR of 2.0 between the extreme quintiles of dietary fibre intake (Montonen et al. 2003). The lowest quintile had a mean fibre intake of less than 19g of fibre per day and the highest quintile had an intake of over 33g per day. The difference in findings between the studies may be due to the higher fibre intakes in the highest quintile of the Finnish study.

Recently, low cereal fibre has been found to be strongly related to diabetes risk and several studies have found that cereal fibre may account for most of the effects of total dietary fibre on diabetes risk. When referring to "cereal fibre", this specifically includes fibre found in grain and cereal products (i.e. fibre from

whole grain wheat, rice, rye and other grains). Results of the Nurses Health Study found that cereal fibre remained significantly related to diabetes risk when adjusted for other types of fibre, however, total fibre was not significantly related after adjustment (Schulze et al. 2004). Similarly, several other researchers found a greater protective effect of high cereal fibre compared to total fibre for diabetes risk. For example, the Iowa Women's Health Study demonstrated that cereal fibre had a RR of 1.6 when comparing the lowest and highest quintiles, compared to 1.3 for total fibre (Meyer et al. 2000). In the Finnish Mobile Clinic Examination Survey the RR for cereal fibre was 2.6 vs. 2.0 for total fibre (Montonen et al. 2003). Also, in the Atherosclerosis Risk in Communities (ARIC) study, only cereal fibre and not total fibre was related to diabetes risk (Stevens et al. 2002).

2.4.2.2.2. Relationship with Diabetes and Insulin Resistance in Youth

Few studies have examined fibre and its effects on diabetes or insulin resistance in youth. However, in one study where researchers investigated the diets of youth with type 2 diabetes, they found no differences in fibre intake between those with type 1 and type 2 diabetes (Mayer-Davis et al. 2006). A second study investigating grain intakes and insulin resistance among adolescents showed that increased whole grain intake was inversely related to BMI, waist circumference and insulin sensitivity as measured by euglycemic insulin clamp methods (Steffen et al. 2003).

2.4.2.2.3. Mechanisms

Fibre is known to increase satiety (Nilsson et al. 2008) and decrease the prevalence of obesity (Lindstrom et al. 2006), therefore some of the effects of fibre are likely due to its effects on adiposity. However, as seen in the studies presented above, fibre appears to be related to diabetes risk independent of BMI. High fibre foods frequently also have a lower GI, so it is possible that some of the effects of fibre could be attributed to GI (www.theglycemicindex.com). In addition, foods containing fibre frequently contain other important nutrients such as magnesium and various antioxidants (Zhou et al. 2004). The role of cereal fibre in the pathogenesis of type 2 diabetes is hypothesized to be related to the colonic fermentation of insoluble fibre. During fermentation, colonic bacteria produce short chain fatty acids which stimulate production of glucagon-like peptide 1 which has been shown to stimulate insulin secretion and also promote insulin sensitivity (Freeland et al. 2009; Nilsson et al. 2008).

2.4.2.3. Magnesium

2.4.2.3.1. Relationship with Diabetes in Adults

Prospective studies have demonstrated that low magnesium intakes are associated with increased risk of type 2 diabetes in adults. An analysis of the Nurses Health Study and the Health Professionals Follow-up Study found that those with the lowest magnesium intakes had significantly higher risk of type 2 diabetes compared to those with the highest intakes, with RR values of 1.4 for both women and men, after adjusting for other risk factors (Lopez-Ridaura et al. 2004). Although not all studies have found consistent results in terms of

magnesium and diabetes risk (Schulze et al. 2007b), a recent meta-analysis showed that when all prospective studies were taken into account RR of diabetes was 1.2 per 100mg decrease in magnesium intake per day (Larsson and Wolk 2007).

2.4.2.3.2. Relationship with Diabetes and Isulin Resistance in Youth

The relationship between low magnesium and diabetes risk among youth has not been investigated in longitudinal studies, however, one study that investigated the magnesium intake of youth with type 2 diabetes showed that those with type 2 diabetes consumed significantly less magnesium than youth with type 1 diabetes (Mayer-Davis et al. 2006). In addition, a study that examined magnesium intake and insulin resistance among obese children found that low dietary magnesium intake was related to insulin resistance as measured by QUICKI (Huerta et al. 2005). Other studies investigating diet and insulin resistance in youth have not duplicated this finding (Davis et al. 2007).

2.4.2.3.3. Mechanisms

Magnesium is a required cofactor for many enzymes of carbohydrate metabolism and although the connection between magnesium and diabetes is likely complex, the effect of magnesium on the insulin receptor is one of the most studied pathways. Decreased magnesium concentrations decrease tyrosine kinase activity which in turn decreases the responsiveness of the insulin receptor (Suarez et al. 1995).

2.4.2.4. Vegetables and Fruit

2.4.2.4.1. Relationship with Diabetes in Adults

Low vegetable and fruit intakes may increase the risk of type 2 diabetes among adults. The Cancer-Norfolk Prospective study, found that adults with the lowest vegetable and fruit intake had an OR of 1.3 for diabetes compared to those with the highest intake of vegetables and fruit (Harding et al. 2008). Similarly, an analysis of the National Population Register in Finland found that consuming less than 33 servings of vegetables, fruit and berries per month was associated with an HR of 1.18 for diabetes (Lindstrom and Tuomilehto 2003).

An analysis of the Women's Health Study found greater diabetes risk was associated with low consumption of leafy green (OR = 1.2) and dark yellow vegetables (OR = 1.4), but not other fruit or vegetables (Liu et al. 2004). Similarly, a Chinese study found that low vegetable intake was associated with an increased risk of type 2 diabetes (RR = 1.4), but fruit intake was not (Villegas et al. 2008). These results suggest that some vegetables may be more beneficial for diabetes prevention than others.

2.4.2.4.2. Relationship with Diabetes and Insulin Resistance in Youth

Information on dietary intake in early onset type 2 diabetes is rare; however, one study that examined the diets of youth with type 1 and type 2 diabetes found that mean vegetable and fruit intake was higher among children with type 2 diabetes compared to those with type 1 diabetes; however, both groups had vegetable and fruit intakes well below recommended levels (Mayer-Davis et al. 2006).

Few studies have examined vegetables and fruit as determinants of insulin resistance in youth, however, studies to date have found no relationship between vegetable and fruit consumption and insulin resistance (Davis et al. 2007; Sheikh et al. 2008).

2.4.2.4.3. Mechanisms

Vegetable and fruit consumption could decrease the risk of type 2 diabetes in a variety of ways. Vegetables and fruit are high in fibre, have low calorie density and a low GL, therefore vegetables and fruit may act through pathways discussed above. In addition, vegetables and fruit, particularly green leafy and dark yellow vegetables are high in antioxidants, which may be protective of beta-cell function, countering oxidative stress caused by gluco- and lipo-toxicity (Kaneto et al. 1999). One study that examined the connection between blood antioxidant levels and blood glucose levels found that several antioxidants found in vegetables and fruit were significantly and inversely correlated to blood glucose levels (Ylonen et al. 2003).

2.4.2.5. Dietary Fat

2.4.2.5.1. Relationship with Diabetes in Adults

Several prospective studies have found links between increased dietary fat intake and risk of type 2 diabetes among adults. Results of the Health Professionals Follow-up Study showed a RR for diabetes of 1.27 between extreme quintiles of total fat intake, however this difference disappeared when the data were corrected for BMI (van Dam et al. 2002). Several other studies have failed to show a relationship between total fat and diabetes risk (Harding et al. 2004;

Salmeron et al. 2001). Saturated fat has been linked to increased risk and polyunsaturated fatty acids related to decreased risk of type 2 diabetes. The Cancer-Norfolk Study found an OR of 0.84 per standard deviation increase in the polyunsaturated: saturated fat ratio, however this relationship was no longer significant when corrected for body weight (Harding et al. 2004). Both the Health Professionals and Nurses Health studies observed a protective effect of polyunsaturated fats. The Nurses Health Study saw a RR of 0.63 for every 5% increase in polyunsaturated fat intake (Salmeron et al. 2001) and the Health Professionals Follow-up study showed that linoleic acid was protective against diabetes for younger men and men with a normal BMI with RRs of 0.74 and 0.53, respectively for extreme quintiles (van Dam et al. 2002).

Trans fats have been linked to increased risk of diabetes in the Nurses Health study, with a RR of 1.39 being seen for a 2 % increase in trans fat intake (Salmeron et al. 2001). In summary, there is some evidence that total fat and saturated fat intakes contribute to diabetes risk; however, much of their effects may be due to changes in body weight. Polyunsaturated fatty acids, however, may have a protective effect against diabetes.

2.4.2.5.2. Relationship with Diabetes in Youth

One study that examined dietary intake in youth with type 1 and type 2 diabetes found no differences in total fat, saturated, monounsaturated, polyunsaturated or trans fat content of the diets between groups with different types of diabetes, however, total fat intake and saturated fat intakes were high in both groups (mean fat intakes ranged from 37 % to 38 % of total calories, mean

saturated fat intakes ranged from 13 % to 14 % of total calories) (Mayer-Davis et al. 2006).

2.4.2.5.3. Relationship with Insulin Resistance

Relationships between dietary fat and insulin resistance in youth have been identified by some investigators, but results have not been consistent. One study found that phospholipid saturated fatty acid content (an indicator of dietary fatty acid content) was significantly related to the metabolic syndrome in overweight adolescents, however phospholipid saturated fatty acid content was not linked to insulin resistance as measured by HOMA (Klein-Platat et al. 2005). Similarly several other studies of diet and insulin resistance have found no connection between dietary fat and insulin resistance (Davis et al. 2007; Sheikh et al. 2008). One study where researchers prescribed a low saturated fat diet for children at infancy found increased insulin sensitivity at 9 years of age (Kaitosaari et al. 2006). In addition, a prospective study that examined weight gain in African American and Caucasian girls found that high fat intakes in combination with insulin resistance were strongly predictive of 10 year weight gain (Morrison et al. 2008).

2.4.2.5.4. Mechanisms

The results of several studies have shown that the effects of fat intake on diabetes risk disappears with adjustment for body weight (Harding et al. 2004; van Dam et al. 2002), suggesting that some of the effects of dietary fat may be due to its effect on body mass. It has also been suggested that fatty acid composition of the diet can affect the fatty acid composition of cell membranes

which could, in turn, affect cell function, particularly action of the insulin receptor (Ginsberg et al. 1991). Dietary fat could also influence the quantity and composition of free fatty acids in circulation (Laaksonen et al. 2002). As discussed in section 2.4.1.4 (mechanisms of obesity in type 2 diabetes pathogenesis) free fatty acids are known to induce insulin resistance and harm beta cell function (Dubois et al. 2004; Goodpaster and Wolf 2004; Kabir et al. 2005). Free fatty acids can accumulate in non-adipose tissues causing a down-regulation of the production of proteins required for insulin action (Goodpaster and Wolf 2004; Kabir et al. 2005). In addition, accumulation of fatty acids and their metabolites in the islet cells is toxic and has been shown to reduce glucose stimulated insulin release in cell culture studies, in animal models (Sako and Grill 1990; Zhou et al. 1996) and in humans (Paolisso et al. 1995).

2.4.3. Physical Activity and Physical Fitness

2.4.3.1. Relationship with Diabetes in Adults

Low levels of physical activity and physical fitness may increase diabetes risk. Large prospective studies of the effects of physical activity and diabetes risk from around the world have reported a strong protective effect of physical activity, and physical fitness. Relative risk of diabetes associated with self reported low levels of physical activity compared to high levels range from 1.1 to 1.8 after adjustment for body weight (Hsia et al. 2005; Hu et al. 1999; Manson et al. 1991; Manson et al. 1992; Villegas et al. 2006; Wannamethee et al. 2000; Weinstein et al. 2004). Objectively measured cardio-respiratory fitness has also been related to type 2 diabetes risk with RR of diabetes values ranging from 1.6 to

1.8 for low fitness levels vs. high levels, after adjustments for weight status and other diabetes risk factors (Sawada et al. 2003; Sui et al. 2008). Sedentary activity has also been associated with diabetes risk with one study reporting that watching television, sitting at work or in the car and sitting at home were all associated with increased risk of diabetes with RRs ranging from 1.48 to 1.70 for high frequency of these behaviours compared to lower frequencies (Hu et al. 2003).

Interventions including physical activity have been shown to be effective in preventing diabetes in high risk groups. In both the Diabetes Prevention Program, and the Finnish Diabetes Prevention Study, interventions including dietary changes and physical activity resulted in a decrease in diabetes prevalence of 58% (Knowler et al. 2002; Lindstrom et al. 2003). Although the independent effect of physical activity in these trials is difficult to assess, it is known that physical activity plays a significant role in both the achievement (Jakicic et al. 2003; Slentz et al. 2004) and maintenance (Befort et al. 2008; Jakicic et al. 2008) of weight loss, which was a major goal for participants in both diabetes prevention studies.

2.4.3.2. Relationship with Diabetes in Youth

Very little research has been done on physical activity of youth with type 2 diabetes. One study that investigated physical activity and fitness levels among patients with type 1 and type 2 diabetes found that those with type 2 diabetes had a significantly lower peak volume of oxygen (VO2) score, lower reported levels of physical activity and a lower exercise belief score (Faulkner et al. 2005).

Physical activity is also considered to be a cornerstone of the treatment of type 2 diabetes in youth (Canadian Diabetes Association Clinical Practice Guidelines Expert Committee 2008).

2.4.3.3. Relationship with Insulin Resistance, IGT and IFG in Youth

The relationship between insulin resistance and physical activity has been thoroughly investigated among youth. Studies have consistently shown a strong link between physical activity, physical fitness and insulin resistance. Various methods of assessing physical activity and fitness (ie. VO2 max, accelerometers, physical activity questionnaires) have been shown to be predictive of insulin sensitivity independent of body fat, as measured by various methods including clamps, FSIVGTTs and methods derived from fasting glucose and insulin levels (Allen et al. 2007; Brage et al. 2004; Eisenmann et al. 2007; Imperatore et al. 2006; Ku et al. 2000; Rizzo et al. 2008; Sardinha et al. 2008; Snitker et al. 2007). In terms of the strength of the relationship between physical activity and insulin resistance, inverse correlations between physical activity and insulin resistance range from 0.04 to 0.42 (Allen et al. 2007; Brage et al. 2004; Imperatore et al. 2006; Lee et al. 2006b; Sardinha et al. 2008; Snitker et al. 2007). Correlations are generally attenuated when adjusted for body weight, with significant relationships remaining in some, but not all populations (Imperatore et al. 2006). Many studies using regression models to determine the extent to which physical activity can predict variance in insulin sensitivity have found that physical activity can predict insulin sensitivity independently of body weight (Brage et al. 2004; Imperatore et al. 2006; Ku et al. 2000; Rizzo et al. 2008; Sardinha et al. 2008; Snitker et al.

2007). Two studies demonstrated that physical activity measured by pedometer readings predicted approximately 10% of the variation in insulin resistance after adjustments for body weight (Sardinha et al. 2008; Snitker et al. 2007).

The relationship between IGT and IFG and physical activity has not been thoroughly examined in children, however, one study found that physical activity and physical fitness did not differ between youth with IFG and obese normoglycemic controls. Authors of this study suggested that in their population, the effects of physical activity were mediated through its effect on body weight (Shaibi et al. 2006).

2.4.3.4. Mechanisms

It is believed that the relationship between type 2 diabetes and physical activity is mediated primarily through the effects of physical activity on body weight, body composition and insulin resistance. Physical activity has been consistently linked to better body weight control and leaner body composition in both adults and children (den and Westerterp 2008; Lantz et al. 2008; Photiou et al. 2008; Simon et al. 2008). In addition, physical activity is associated with short term and long term increases in insulin sensitivity in the skeletal muscles. In the first 48 hours after a bout of exercise, both insulin dependent and independent mechanisms of glucose uptake are stimulated, increasing insulin sensitivity and glucose utilization in the skeletal muscle (Nesher et al. 1985). In the long term, physical training results in increased expression of the GLUT 4 glucose transporter protein in skeletal muscle resulting in greater insulin sensitivity (O'Gorman et al. 2006).

2.4.4. Genetics and Family History

2.4.4.1. Relationship with Type 2 Diabetes in Adults

Family history of type 2 diabetes is considered to be an extremely important diabetes risk factor. Adults with a family history of type 2 diabetes are much more likely to develop the disease themselves. For example, results of the Framingham Offspring study showed that having one parent with type 2 diabetes was associated with a RR of diabetes of approximately 3.5 and having 2 parents with diabetes resulted in a RR of 6 (Meigs et al. 2000). Similar results were found in a Norwegian study where maternal and paternal diabetes resulted in RRs of 2.7 and 1.8, respectively and having 2 parents with diabetes resulted in a RR of 6.9 (Bjornholt et al. 2000).

2.4.4.2. Relationship with Type 2 Diabetes in Youth

Although data assessing risk of developing type 2 diabetes for those with a positive family history is not available for children, the prevalence of family history of diabetes is very high among youth with the disease, with studies showing prevalence rates between 50 and 95% (Drake et al. 2002; Glaser and Jones 1998; Harwell et al. 2001; Zdravkovic et al. 2004) and it is considered to be one of the prominent risk factors for early onset type 2 diabetes (Canadian Diabetes Association Clinical Practice Guidelines Expert Committee 2008). In addition, studies in both children and adults have found that those with a family history of type 2 diabetes have poorer insulin sensitivity and beta cell function compared to those with no family history (Arslanian et al. 2005; Vaag et al. 2001). The link between family history and insulin resistance seems to be

explained mostly by family patterns in obesity, whereas susceptibility to impaired beta cell function appears to be primarily genetically determined (Rosenbaum et al. 2004). These data suggest that susceptibility to diabetes is controlled, in part, by one's genotype and that both genetics and environmental or behavioural factors are required for development of the disease. In particular, genes appear to control a person's susceptibility to beta cell failure.

2.4.5. Puberty

Puberty has an important effect on insulin resistance in youth. Studies have shown that there is an increase in insulin resistance during puberty, with insulin resistance peaking at mid puberty (Tanner stage 2-3) and returning to pre-puberty levels in Tanner Stage 5 (Ball et al. 2006). The increase in insulin resistance during puberty appears to be a normal part of development and there is some evidence to suggest that the change may be caused by increases in growth hormone levels that occur during that time. A strong association has been shown between growth hormone levels and insulin sensitivity during puberty (Amiel et al. 1986; Radetti et al. 2004). In addition, growth hormone treatments in youth with growth hormone deficiency are known to result in a significant decrease in insulin sensitivity (Radetti et al. 2004). Type 2 diabetes is most often diagnosed among youth during puberty (Grinstein et al. 2003; Holl R W et al. 2003; Upchurch et al. 2003; Wei et al. 2003b) and it is hypothesized that the onset of disease is triggered in susceptible people by the increase in insulin resistance (Ball et al. 2006). Although insulin sensitivity returns to pre-pubertal levels when

puberty is completed, type 2 diabetes in this age group does not resolve, likely due to glucose toxicity that leads to further deterioration in beta cell function.

2.4.6. Prenatal Growth Environments

Prenatal growth environments have been shown to be important to future diabetes risk. In particular, birth weight and gestational exposure to diabetes have been shown to be strong risk factors for diabetes. In the following section, both of these risk factors will be discussed.

2.4.6.1. Birth Weight

Children born with low, as well as high birth weights have been shown to have an increased risk of diabetes in adulthood (Eriksson et al. 2003; Forsen et al. 2000). Similarly, youth with type 2 diabetes are more likely to be born with either high or low birth weights compared to healthy youth (Dabelea et al. 1998; Dabelea et al. 1999; Wei et al. 2003a), suggesting that gestational environment and early programming is very important to the early onset form of the disease. Studies have also found that youth born with a high or low birth weight are more likely to be insulin resistant and have IFG or IGT compared to those born with a normal weight (Gupta et al. 2007).

The mechanisms behind this pattern are not yet fully known. It has been suggested that nutrient abundance or shortages in utero lead to metabolic programming that increases susceptibility to insulin resistance and diabetes (Hofman et al. 2004). Maternal diabetes frequently results in high birth weight babies which may explain part of the relationship between high birth weight and diabetes risk (Dabelea et al. 1999). In the case of low birth weight babies, it has

been suggested that the pattern of catch-up growth seen after a pregnancy in which nutrient shortages have occurred promotes insulin resistance (Ong et al. 2004). Animal studies have shown that when nutrient shortages occur during pregnancy, the beta cell mass of the offspring is decreased (Chakravarthy et al. 2008). This has lead to the theory that the development of important organs such as the brain are favoured over development of pancreatic beta cells during nutrient restriction, resulting in underdeveloped beta cells that are more prone to failure.

2.4.6.2. Gestational Diabetes

Being exposed to diabetes (type 2 or gestational diabetes) during pregnancy has also been shown to have profound effects on the risk of type 2 diabetes. Research involving Pima Indians found that 70% of people exposed to diabetes in utero had the disease by 25 to 34 years of age (Dabelea et al. 2000b). One study among the Ojibwa-Cree population of Manitoba found that youth with type 2 diabetes were more likely to have been exposed to diabetes in utero than those who did not have type 2, with an OR of 4.4 (Young et al. 2002). Also, a study that investigated siblings, one of which was exposed to diabetes during pregnancy and one that was not, found that those who were exposed had a greater risk of developing type 2 diabetes with an OR of 3.7 (Dabelea et al. 2000a). The mechanism behind the link between gestational diabetes and future diabetes risk is suspected to be similar to that of babies born with a low or high birth-weight. It has been proposed that exposure to hyperglycaemia in utero causes metabolic changes that increases susceptibility to insulin resistance and type 2 diabetes (Young et al. 2002).

2.5. Diabetes Risk Assessment

Because type 2 diabetes is a preventable disease, identification of individuals at risk for diabetes is important for the development of targeted prevention programs. Although diabetes risk indexes are commonly used for risk assessment in adults, risk scores have not been created and validated for use in children and adolescents. This is likely due to the very recent emergence of type 2 diabetes in younger age groups. The following table outlines scoring methods that have been used around the world to identify adults at higher risk of diabetes. This information shows that although many diabetes risk scores are available, few take into account lifestyle risk factors for diabetes.

Table 2.1 Diabetes Risk Scores for Adults

Name	Population	Variables Assessed	Area under the ROC	Sensitivity	Specificity
Finnish Diabetes Risk Score (Lindstrom and Tuomilehto 2003)	FINRISK study participants	Age, BMI, Waist circumference, antihypertensive use, history of high blood glucose, physical activity, daily consumption of vegetables, fruits or berries	86%	78 – 81%	76 - 77%
Cambridge Risk Score (Griffin et al. 2000)	ELY study, Cambridge, UK	Age, Sex, Family History of Type 2 Diabetes (T2D), Smoking Status, BMI, antihypertensive use, steroid use	76.3%	77%	72%
New Cambridge Risk Score (Simmons et al. 2007)	EPIC Participants	Age, Sex, antihypertensive use, BMI, Family History of T2D, Recreational physical activity, green leafy vegetables, fresh fruit, wholemeal/brown bread	76.2%		
German Diabetes Risk Score (Schulze et al. 2007a)	EPIC-Potsdam Study Participants	Waist, height, age, hypertension, red meat, whole-grain bread, coffee, moderate alcohol, physical activity, former smoker, current heavy smoker.	82 - 84%	80 - 94%	67 – 79%
Diabetes Risk Score for Oman (Al-Lawati and Tuomilehto 2007)	Oman's National Diabetes Survey Participants	Age, waist circumference, BMI, Family history of T2D, Hypertension	83%	63%	78%
Thai Diabetes Risk Score (Keesukphan et al. 2007)	Thailand	Age, BMI, History of hypertension	71%	87%	38%
Indian Diabetes Risk Score (Mohan et al. 2007)	Chennai Urban Rural Epidemiology Study Participants	Age, waist circumference, family history of T2D, physical activity	70%	73%	60%

2.6. Conclusions

Early onset type 2 diabetes is increasing in prevalence in Canada and around the world. This disease has serious consequences in terms of morbidity and mortality as well as increasing health care costs. For the prevention of future cases of early onset type 2 diabetes, risk factors for the disease need to be understood and addressed. As this review has summarized, risk of type 2 diabetes in youth is influenced by many factors including obesity, diet, physical activity, family history, puberty and gestational environment. However, because of the relatively recent emergence of this disease, the influence of many of these risk factors, particularly the effect of dietary factors, has not been fully explored. Although many methods exist to measure diabetes risk among adults, tools to examine risk among youth have not been developed. Future studies are needed to further understand and measure risk factors and diabetes risk in youth; and the development of successful strategies for improving the dietary and physical activity practices of youth are needed to prevent further increases in prevalence in the future.

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Chapter 3: Metabolic and Behavioural Differences of Youth with and without Type 2 Diabetes

3.1. Preface

Type 2 diabetes in youth is a new disease that is increasing in prevalence and has not been thoroughly studied in Canada. In addition, the link between diet and physical activity and type 2 diabetes in youth is not clear, therefore the aims of this analysis were to examine the characteristics of youth diagnosed with type 2 diabetes in Northern Alberta and to examine dietary, physical activity and metabolic differences between those with and without type 2 diabetes. The following chapter is an analysis of data from a chart review that was conducted at the Stollery Children's Hospital Endocrinology Clinic and Paediatric Centre for Weight and Health and it also included the files of a paediatrician specializing in childhood obesity. Charts examined included those of all youth diagnosed with type 2 diabetes at the endocrinology clinic between March 2000 and August 2006 (n = 28) and age, sex and Body Mass Index (BMI) matched controls (n = 28).

3.2. Introduction

Type 2 diabetes, a disease strongly associated with obesity, has increased in prevalence in Canada parallel to increasing obesity rates and has recently been observed with greater frequency in younger age groups. Before the 1970's, type 2 diabetes was considered to be exclusively an adult disease. However, in the past few decades, cases of type 2 diabetes have been identified in children and the prevalence of early onset disease has been rising.

Recent studies in the U.S. have estimated the prevalence of type 2 diabetes to be 0.42 cases per 1000 children in the general population (Liese et al. 2006) and as high as 5.31% in high risk populations such as the Pima Indians (Dabelea et al. 1998). Although the presence of type 2 diabetes in Canadian children is not well documented, a prevalence of 3.6% has been reported in 10 to 19 year old Ojibwa-Cree girls living in Northern Manitoba (Dean et al. 1998). In addition, increasing rates of type 2 diabetes among children have been documented in Canada and around the world (Dabelea et al. 1998; Hale and Rupert 2006; McMahon et al. 2004; Urakami et al. 2005; Zdravkovic et al. 2004).

Type 2 diabetes in youth is of particular concern because the extended duration of disease leads to earlier development of macrovascular and microvascular complications. Some patients diagnosed with type 2 diabetes in their youth display serious complications such as nephropathy in young adulthood (Krakoff et al. 2003). Given the intractable nature of type 2 diabetes, youth with the disease are also at increased risk of cardiovascular disease early in life due to metabolic dysregulation (e.g., hyperglycemia, dyslipidemia).

To date, the characteristics of children with type 2 diabetes in Alberta have not been clearly described. Although sub-optimal diet and physical activity behaviours are linked to the development of type 2 diabetes in adults, very little is known about these lifestyle habits or the metabolic profiles of children with type 2 diabetes. Therefore, the purpose of this cross-sectional study was to characterize children with type 2 diabetes in Northern Alberta and compare their nutrition and physical activity behaviours and metabolic profiles to age-, sex- and BMI-matched children without diabetes.

3.3. Methods

3.3.1. Subjects

This study was a retrospective, case-control chart review of patients with type 2 diabetes. Medical charts were obtained from the Endocrinology Clinic at the Stollery Children's Hospital in Edmonton, Alberta, Canada. The charts of all children (<18 years of age) diagnosed with type 2 diabetes at the clinic between March 2000 and August 2006 were included in the analysis. Diagnosis of type 2 diabetes was based on a combination of clinical indicators (obesity, lengthy duration of symptoms, presence of acanthosis nigricans and having a family history of type 2 diabetes), high c-peptide levels and absent glutamate decarboxylase (GAD) 65 antibody. Charts of age, sex and BMI matched control subjects were collected from the files of a Paediatrician specializing in nutrition, as well as from a subset of youth enrolled at the Paediatric Centre for Weight and Health at the Stollery Children's Hospital. The first 28 charts of potential control subjects pulled that could be matched to diabetes patients were used in this

analysis. When matching for age, the age of each control subject at their first visit had to be within one year of the age of the diabetes patient they were matched to at diagnosis of diabetes. When matching for BMI, control subjects had to be within 10kg/m^2 of their match. This study received ethical approval from the Health Research Ethics Board, University of Alberta (see Appendix A).

3.3.2. Methodology

Information retrieved from medical charts included data from the time of diagnosis for diabetes patients and from the first visit to the paediatrician for control subjects. Information collected from the charts included demographics, anthropometrics, presentation and treatment of diabetes (for diabetes patients only), medical history, family history of diabetes, blood pressure, blood glucose and lipid profile, dietary profile and physical activity patterns.

3.3.2.1. Demographics and Anthropometrics

Demographic information included age, sex, ethnicity and socioeconomic status (SES). Patients were considered to have a low SES if they required financial assistance from social services to purchase medications or pay for transportation expenses for medical appointments.

Anthropometric measures included height, weight, BMI and BMI percentile determined from Centre for Disease Control (CDC) growth charts with a BMI greater than the 85^{th} percentile for age and sex being considered overweight and greater than the 95^{th} percentile being considered obese (Center for Disease Control and Prevention 2000a; Center for Disease Control and Prevention

2000b). Pubertal status was also assessed by clinic physicians using the Tanner Staging method.

3.3.2.2. Symptoms and Treatment of Diabetes

For youth with type 2 diabetes, all symptoms recorded at diagnosis were documented. Information on diabetes treatment included the types of therapy used from diagnosis until the most recent visit before the time of the chart review, and duration of the different treatment regimens.

3.3.2.3. Medical History and Family History

Personal medical history data of interest included birth weight, maternal gestational diabetes and medical problems associated with diabetes and overweight, such as sleep apnea, acanthosis nigricans (AN) and polycystic ovary syndrome (PCOS). For family history of diabetes, the diabetes status of both parents was recorded as well as any occurrence of diabetes within the maternal and paternal sides of the family (grandparents, aunts and uncles).

3.3.2.4. Blood Parameters

Blood pressure was measured (while the patient was sitting) by clinic staff using appropriate cuff sizes after at least 5 minutes of rest. High blood pressure was defined as being above the 95^{th} percentile for age, sex and height as recommended by the National High Blood Pressure Education Program guideline cut-offs (National High Blood Pressure Education Program 2004).

Blood work collected and analysed at the hospital laboratories closest to the time of diagnosis, including fasting glucose or random glucose, haemoglobin A1C, triglycerides (TG), total cholesterol (TC), high density lipoprotein

cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) were recorded. Lipid values were categorized using the National Cholesterol Education Program cut-offs as shown in Table 3.1 (National Cholesterol Education Program et al. 2002). Patients were categorized as having either normal or abnormal blood lipid values as shown in the Table 3.1.

Table 3.1 Lipid Cut-offs from the National Cholesterol Education Program

Blood Lipid Variable	Cut offs* mmol/L	Category**
Triglycerides		
Normal	<1.69	Normal
Borderline High	1.69-2.25	High
High	2.25-5.64	High
Very High	>5.64	High
Total Cholesterol		
Desirable	<5.18	Normal
Borderline High	5.18-6.19	High
High	>6.19	High
LDL		
Optimal	<2.59	Normal
Near Optimal	2.59-3.34	Normal
Borderline High	3.34-4.12	High
High	4.12-4.90	High
Very High	>4.90	High
HDL		
Low	<1.04	Low
Some Risk	1.04-1.55	Normal
Protective	>1.55	Normal

*Cut-offs as defined by the National Cholesterol Education Program (2002)

** Patients were categorized as having normal or abnormal blood lipid levels based on these categories

3.3.2.5. Diet and Physical Activity

Nutrition information from type 2 diabetes patients consisted of diet histories of usual food intake completed by clinic dietitians at the time of diagnosis. Nutrition information available for control subjects varied with 8 charts containing diet histories similar to those of diabetes patients, 9 containing 3-day food records, and 11 containing 4-day food records. Research staff entered diet records into ESHA Food Processor SQL (Version 9.8) (ESHA Research, Salem OR) software and the Canadian Nutrient File (Health Canada 2006) for analysis of macro and micronutrient intakes.

Physical activity information included a general description of activity habits and participants were categorized as being "physically active" or "inactive". They were classified as "physically active" if they regularly engaged in any physical activity outside of school gym class including walking, biking, dancing, going to the gym and sports.

All data were collected independently by two researchers and inter-observer reliability was assessed using kappa statistics for categorical and intra-class correlation coefficients (ICC) for continuous variables. Kappa or ICC values of more than 0.7 were considered to be acceptable (Norusis 2005).

3.3.3. Statistical Analysis

Data were analyzed using SPSS for Windows 14.0 software (SPSS Inc., Chicago IL). Differences between participants with and without type 2 diabetes were assessed using chi squared analysis for categorical data and ANOVA (Analysis of Variance) for continuous demographic variables. MANOVA

(Multivariate Analysis of Variance) models were used to assess differences in blood values (including fasting blood glucose and lipid values) and dietary variables between the groups. Univariate ANOVA follow-up tests were conducted when significant main effects were found, as recommended by Stevens et al. (2002). Many variables, including TG, LDL-C, TC, protein, carbohydrate, total fat, saturated fat, cholesterol, thiamine, niacin, vitamin C, iron and magnesium were not normally distributed. Natural logarithm transformations were performed on these variables prior to analysis. P-values of less that 0.05 were considered to be statistically significant.

3.4. Results

Inter-observer reliability analysis revealed that demographic and anthropometric data were comparable between the two researchers with kappa and ICC values ranging from 0.747 to 1.00. Kappa values for medical history, family history and symptoms of diabetes ranged from 0.639 to 1.00; only the value for the symptom of abdominal pain was below the acceptable cut off of 0.7. ICC values for blood work ranged from 0.835 to 0.998 and ICC values for dietary data ranged from 0.234 to 0.998 with values for carbohydrate, fibre, monounsaturated fatty acids, polyunsaturated fatty acids, trans fats, vitamin B6, riboflavin, vitamin E and sodium being below 0.7. These variables were excluded from further analysis. For physical activity, the kappa value was 0.613.

3.4.1. Subjects

A total of 28 medical charts of patients with type 2 diabetes and 28 control charts were retrieved and analysed. Complete information was not available for

all subjects, therefore, sample sizes differ for the various outcome measures and n values are reported when data is unavailable for more than 2 patients. General characteristics of the study population are shown in Table 3.2. Given that children with and without type 2 diabetes were matched according to age, sex, and BMI, there were no differences between groups in these parameters (all $p>0.05$).

Table 3.2 General Characteristics of Patients with and without Type 2 Diabetes

	Diabetes (n = 28)	Control (n = 28)	P-value
Age at Diagnosis or First Visit	13.17 ± 1.80*	12.82 ± 1.73*	0.464
Weight (kg)	85.29 ± 18.92	85.85 ± 18.22	0.911
Height (cm)	165.12 ± 11.81	160.55 ± 9.00	0.114
BMI (kg/m^2)	31.58 ± 7.00	33.00 ± 5.05	0.391
BMI percentile	97.67 ± 3.97	98.55 ± 1.50	0.279
Gender % (n)			
Male	35.7 (10)	35.7 (10)	1.00
Female	64.3 (18)	64.3 (18)	
Ethnicity (n)			
Caucasian	12	9	n/a**
Aboriginal	11	1	
Asian	5	2	

Data are means ± SD unless otherwise indicated
Differences between groups assessed using ANOVA and Chi-square analysis
* The median age for both the diabetes and control groups was 13yr.
**Data were not available for the majority of control subjects, therefore differences were not analyzed.

3.4.2. Demographics and Anthropometrics

The age of diagnosis for diabetes patients ranged from 9.3 years to 16.3 years with the mean age of diagnosis being 13.3 years. Patients with diabetes were predominantly female (n = 18; 64%), of Caucasian (n = 12; 43%), Aboriginal (n = 11; 39%) or South East Asian descent (n = 5; 18%) and low SES was common (n =10, 36%).

All but one patient with type 2 diabetes met the Canadian Paediatric Society's criteria for obesity (BMI $\geq 95^{th}$ percentile); the individual who did not meet this threshold had a normal BMI percentile at diagnosis, had experienced substantial weight loss prior to diagnosis, and subsequently regained weight upon initiating insulin treatment. Tanner stage analysis showed that pubertal stage ranged from stage 1 to 5, but most diabetes patients (71%) were in mid to late puberty (Tanner stages 3-5) at diagnosis.

3.4.3. Symptoms and Treatment of Diabetes

Symptoms present at diagnosis of type 2 diabetes included polydipsia (n = 22; 79%) and polyuria (n = 21; 75%), fatigue (n = 15; 54%), weight loss (n = 11; 40%), nausea (n = 8; 29%), head aches (n = 6; 21%), and blurry vision (n = 5; 18%) and 14% presented with diabetic ketoacidosis (DKA) (n = 4). In addition, 11% (n = 3) were asymptomatic at diagnosis.

Treatment prescribed by physicians for glucose control included insulin therapy, lifestyle therapy (including dietary and physical activity counselling) and Metformin administration. At diagnosis, insulin was the most commonly

prescribed therapy (n = 19; 68%) followed by lifestyle therapy alone (n = 6; 21%) and metformin (n = 2; 7%). Records showed that only 50% (n=3) of children with type 2 diabetes who started with lifestyle therapy as the sole treatment, achieved glucose control with this method. At each child's most recent appointment relative to the time of the chart review, 54% (n = 15) were taking Metformin, 25% were on insulin (n = 7), 18% were on lifestyle therapy alone (n = 5) and 4% (n = 1) had declined treatment.

3.4.4. Medical History and Family History

Birth weight was known for 16 of the children with type 2 diabetes and 12 controls. Children with type 2 diabetes were more likely to be born with either low (< 2500g) or high (> 4000g) birth weights than control children (p = 0.024). In the diabetes group, 4 patients (14.3%) had low birth weights, 3 patients (10.7%) had high birth weights, and 21 had normal birth weights. All 26 control children with available data had normal birth weights. Although more youth with type 2 diabetes than controls were exposed to diabetes during gestation (n = 7, 25% vs. n = 3, 11%), the difference was not significant (p = 0.125). There were no differences in the presence of sleep apnea or PCOS between youth with and without type 2 diabetes, but those with type 2 diabetes were more likely to present with acanthosis nigricans (n = 21, 75 % vs. n = 13, 46%, p=0.029).

Children with type 2 diabetes were more likely to have a family history of type 2 diabetes than controls (n = 24, 86 % vs. n = 17, 61 %, p = 0.026) with the most significant differences between groups being seen in the frequency of having a mother with type 2 diabetes (n = 9, 32 % vs. n = 1, 4 %, p = 0.04) and having a

history of diabetes on the maternal side of the family (n = 20, 71 % vs. n = 9, 32 %, p = 0.003).

3.4.5. Blood Parameters

High blood pressure was common, with 44% of participants in both the diabetes and control groups being defined as having high blood pressure. As expected, fasting glucose (mean fasting glucose = 13.7 mmol/L) or random glucose (mean random glucose = 32.3 mmol/L) and haemoglobin A1C (mean HbA1C = 11%) were increased among children with type 2 diabetes compared to normative levels. Hemoglobin A1C data were not available for control subjects, however, fasting glucose was normal among controls. When blood parameters were entered into a multivariate model, group differences emerged (Wilks' Lambda = 0.209, F (1, n = 31) = 18.97, $p < 0.001$). Univariate follow-up analysis, presented in Table 3.3, showed that fasting glucose ($p < 0.001$) and TG ($p = 0.048$) were significantly higher in the diabetes versus control group.

When blood lipid values were categorized using the National Cholesterol Education Program standards (National Cholesterol Education Program et al. 2002), results showed that, of those who had blood lipids measured, 61% of diabetes patients and 23% of controls had high TG levels, 48% of diabetes patients and 4% of controls showed elevated TC, 75% of diabetes patients and 50% of controls had low HDL-C levels and 20% of diabetes patients and 11% of controls had high LDL-C levels. Chi square analysis showed significant differences in the presence of high lipid levels between children with type 2 diabetes and controls for TC ($p = 0.001$) and TG levels ($p = 0.039$).

Table 3.3 Blood Glucose and Lipid Concentrations for Patients with and without Diabetes

	Diabetes (n = 10)	Control (n = 21)	P-value
Fasting Glucose (mmol/L)	13.72 ± 6.27	5.00 ± 0.33	<0.001
Triglycerides (mmol/L)	3.39 ± 3.87	1.55 ± 0.75	0.048
Total Cholesterol (mmol/L)	4.90 ± 1.26	4.47 ± 1.10	0.127
HDL-C (mmol/L)	0.91 ± 0.20	1.00 ± 0.21	0.228
LDL-C (mmol/L)	2.70 ± 1.20	2.77 ± 1.12	0.499

Data are means ± SD
MANOVA model: $F(1, n = 31) = 18.97$, $p < 0.001$
P-values from univariate F tests

3.4.6. Diet and Physical Activity

When dietary data were entered into a multivariate model, significant differences between the diabetes and control groups were found (Wilks' Lambda = 0.520, F (1, n = 53) = 2.272, p = 0.021). As presented in Table 3.4, youth with type 2 diabetes consumed foods resulting in higher protein, niacin, and potassium intakes than controls. Total kilocalorie, fat and other micronutrient intakes were similar between the groups. Rates of inactivity appeared to be high with approximately 15% of controls and 46% of diabetes patients not participating in any physical activity outside of school gym classes.

Table 3.4 Nutrient Profiles of Patients with and without Diabetes

	Diabetes (n = 28)	Control (n = 28)	P-Value
Total Kcal	2574 ± 1028	2342 ± 915	0.384
Total Fat (g)	85.2 ± 49.9	79.5 ± 42.0	0.631
Saturated Fat (g)	29.0 ± 22.8	28.5 ± 16.5	0.797
Protein (g)	110.4 ± 42.4	89.0 ± 29.9	0.041
Vitamin A (RE)	1025.9 ± 556.6	1183.1 ± 675.1	0.305
Vitamin C (mg)	145.1 ± 96.7	99.9 ± 68.0	0.205
Thiamin (mg)	2.0 ± 1.1	1.8 ± 1.2	0.095
Niacin (mg)	28.2 ± 12.6	19.6 ± 9.4	0.006
Vitamin B12 (µg)	3.9 ± 2.3	3.5 ± 1.7	0.659
Calcium (mg)	1207.8 ± 712.0	1001.9 ± 521.2	0.406
Iron (mg)	15.9 ± 7.6	15.5 ± 8.7	0.908
Magnesium (mg)	316.9 ± 102.5	278.5 ± 114.8	0.130
Phosphorus (mg)	1621.0 ± 803.3	1276.0 ± 432.5	0.089
Potassium (mg)	3513.3 ± 1301.4	2620.9 ± 787.3	0.015

Data are means ± SD
MANOVA model: F (1, n = 53) = 2.272, p = 0.02
P-values from univariate F tests

3.5. Discussion

This case control retrospective chart review has described the characteristics of children with type 2 diabetes in Northern Alberta and has shown differences between children with and without type 2 diabetes with regards to their medical and family histories, their blood lipid profiles and their dietary habits.

3.5.1. Demographics and Anthropometrics

Similar to findings from other clinics in North America and around the world (Likitmaskul et al. 2005; Perez-Perdomo et al. 2005; Pinhas-Hamiel et al. 1996; Scott et al. 1997; Zdravkovic et al. 2004) children with type 2 diabetes in the present study were predominantly female, had a mean age of 13 years and there was overrepresentation from high risk ethnic populations; particularly Aboriginal Canadians. Aboriginal Canadians, who comprise 4% of Edmonton's population represented almost 40% of the diabetes group. There may also have been slight over-representation from the South East Asian Canadians, who comprise 11% of Edmonton's population and represented 18% of boys and girls in the diabetes group (Statistics Canada 2001). Low SES was common among children with type 2 diabetes with approximately one in three requiring financial support for medical travel and medications. Although the variable used to assess SES was unique and therefore difficult to interpret in comparison to standard measures of SES, we feel this is an important issue in this group. Low SES has been shown to be linked both to risk of being overweight and to type 2 diabetes in adults (Loucks et al. 2007) and has been linked to obesity and insulin resistance in

adolescents (Goodman et al. 2005; Goodman et al. 2007). Low SES in this population is an important factor that could affect a patient's ability to make dietary and lifestyle changes. This should be considered when designing interventions for children with type 2 diabetes. Providing opportunities for those with a low SES may be an important priority for improving the effectiveness of treatment.

International studies agree that obesity is a major factor in the early onset of type 2 diabetes (Hale and Rupert 2006; Harwell et al. 2001; Likitmaskul et al. 2005). The present study also supports the importance of obesity in the development of this disease, with severe obesity observed in almost all diabetes patients. Puberty also appears to be associated the onset of type 2 diabetes in children with the disease. The present study found that most children were at mid to late puberty at diagnosis. Decreased insulin sensitivity normally occurs during puberty (Harwell et al. 2001) and it has been suggested that this change in sensitivity may be a trigger for type 2 diabetes in susceptible individuals in this age group (Ball et al. 2006). Preventing obesity, particularly before the onset of puberty may be important to the prevention of early onset type 2 diabetes.

3.5.2. Symptoms and Treatment of Diabetes

The most common symptoms of type 2 diabetes reported in the present study were polydipsia and polyuria. Polydipsia and polyuria are typical symptoms of diabetes that are reported in a high percentage of patients in most studies (Hale 2004; Pinhas-Hamiel et al. 1996). Although DKA is considered a sign of type 1 diabetes and not as typical of adult type 2 diabetes, many studies,

including the present one, have reported that it is not uncommon in children with type 2 diabetes, with the prevalence of DKA ranging from 5 to 15% (Glaser and Jones 1998; Grinstein et al. 2003). This suggests that the aetiology of early onset type 2 diabetes may differ from that of adult type 2 diabetes and optimal treatment and prevention of the disease in youth may also differ.

Insulin therapy was the most common method of treatment upon diagnosis of diabetes. Initial insulin therapy has been recommended for children with type 2 diabetes to manage blood glucose levels and it may also improve insulin secretion (Sellers and Dean 2004). Metformin was the most widely used long-term method of blood glucose control in the present study. Although diet and physical activity therapy alone was initiated in approximately 40% of patients, glucose control was not achieved in half of this group, leading to a change to metformin therapy. Previous studies have shown the limitations of lifestyle therapy in this population with only 8 to 22% achieving glucose control (Grinstein et al. 2003; Zdravkovic et al. 2004). A research group at the University of Manitoba has found that diet and physical activity are adequate to control blood glucose levels of youth with type 2 diabetes in a camp environment (Dean 2007). Interventions that promote adherence to recommendations may increase the effectiveness of dietary and physical activity therapy and decrease the need for pharmacological intervention.

3.5.3. Medical History and Family History

Acanthosis nigricans is known to be related to insulin resistance and it is therefore considered to be a risk factor for type 2 diabetes. The present study

showed that although control subjects were obese and may have had some degree of insulin resistance, children with type 2 diabetes were more likely to present with AN.

The present study as well as previous research have found that both low and high birth weights are associated with increased risk of early onset type 2 diabetes (Wei et al. 2003). This finding suggests that children with a family history of type 2 diabetes born with either a high or low birth weight may be candidates for diabetes prevention initiatives. This observation also highlights the importance of promoting healthy birth weights through maternal weight management and prevention or treatment of gestational diabetes.

Studies have consistently shown that family history of diabetes is a strong risk factor for early onset type 2 diabetes. Studies of type 2 diabetes in centres around the world have found that between 65 and 100% of children presenting with type 2 diabetes have a positive family history of the disease (Glaser and Jones 1998; Harwell et al. 2001; Likitmaskul et al. 2005; Perez-Perdomo et al. 2005; Pinhas-Hamiel et al. 1996; Zdravkovic et al. 2004) with as many as 65% reporting at least one parent with type 2 diabetes (Grinstein et al. 2003). The present study found that maternal family history of type 2 diabetes was more strongly linked to type 2 diabetes, than paternal family history. Similar results have been reported by other studies (Glaser and Jones 1998; Hale 2004) and it has been hypothesized that the maternal inheritance may be attributable to an altered intrauterine environment as well as a greater risk of gestational diabetes or increased blood glucose levels during pregnancy.

3.5.4. Blood Parameters

High blood pressure is common among children with type 2 diabetes (McMahon et al. 2004; Upchurch et al. 2003; Zdravkovic et al. 2004). In the present study, high blood pressure was equally prevalent in the diabetes and control groups, suggesting that high blood pressure may be more strongly related to obesity than diabetes.

Dyslipidemia has been commonly noted among adults with type 2 diabetes, with the most common abnormalities being high TG, a symptom of poorly controlled diabetes, and low HDL-C levels (Tenenbaum et al. 2006). The present study showed high prevalence of blood lipid abnormalities among diabetes patients including higher mean TG levels in the diabetes group and a significantly higher prevalence of high TG and high TC levels compared to controls. However it should be noted that high TG levels, which are indicative of poorly controlled diabetes, were measured prior to the initiation of treatment for diabetes and therefore would be expected to be high. Studies of dyslipidemia in similar populations of youth with type 2 diabetes have also found a high prevalence of blood lipid abnormalities. Similar to results of the present study, the SEARCH for Diabetes study found the prevalence of high TC and TG to be 33% and 63%, respectively among youth with type 2 diabetes. The prevalence of low HDL-C was lower and the prevalence of high LDL-C levels were higher than what was observed in the present study at 44% and 57%, respectively (Kershnar et al. 2006).

3.5.5. Diet and Physical Activity

Diet and physical activity practices have long been known to affect the risk of developing type 2 diabetes in adulthood. The Diabetes Prevention Program, for example, has shown that dietary and physical activity interventions can be more effective than drug therapy to prevent or delay the development of type 2 diabetes among those with impaired glucose tolerance (Ratner 2006). Diet and physical activity counselling are also considered to be the cornerstones of diabetes treatment for both adults and children (Canadian Diabetes Association Clinical Practice Guidelines Expert Committee 2008). However, very little is known about the dietary and physical activity habits of children with type 2 diabetes. One study has previously investigated the dietary intakes of children with type 2 diabetes, comparing the intakes of children with type 2 diabetes to those with type 1 diabetes. This study found that children with type 2 diabetes had lower intakes of magnesium, vitamin C and iron, and higher intakes of vitamin E and simple sugars than those with type 1 diabetes, and that both children with type 1 and type 2 diabetes had high intakes of fat and saturated fat (Mayer-Davis et al. 2006). In the present study, children with type 2 diabetes consumed more protein, niacin, and potassium than controls, nutrients that are commonly found in meat and milk products (protein) grain products (niacin) and vegetables and fruit (potassium). This indicates that no one type of food alone accounts for these differences. In addition, none of these nutrients is commonly indicated in the pathogenesis of diabetes, therefore the significance of these findings is unclear. Although there is not yet an explanation for the results seen,

differences between the diets of children who are obese, and those who are obese and develop diabetes may exist and further investigation of these differences, using more consistent dietary measures could enable us to form more specific dietary guidelines for the prevention and treatment of type 2 diabetes in this age group.

Although the inter-observer reliability for the physical activity variable used in this study was slightly below 0.7 and therefore conclusions about comparative physical activity levels in these groups cannot be made, observers were in agreement that children with type 2 diabetes were more likely to be physically inactive than children without diabetes, suggesting that further research on the physical activity habits of youth with type 2 diabetes is warranted. Physical fitness and physical activity are known to be strongly related to insulin sensitivity in youth at risk for type 2 diabetes (Lee et al. 2006). Further studies investigating the physical activity levels of children with type 2 diabetes using objective measures will be needed to characterize the physical activity and fitness profile of children with type 2 diabetes.

3.5.6. Strengths and Limitations

The present study investigated the dietary and physical activity practices of youth with type 2 diabetes. Strengths of this study include the comprehensive information available from this group of children with type 2 diabetes as well as the availability of similar information from age- sex- and BMI-matched controls. Although the prevalence of type 2 diabetes among youth has been rising in recent years, it is still a rare occurrence in Northern Alberta. The sample size of this

study was not large, however it was sufficient to demonstrate differences between those with and without type 2 diabetes. The main limitation of the study was the consistency of data available from the medical charts. Some variables, such as ethnicity and SES, were not available for all subjects and consistent, validated measures, particularly of physical activity and dietary habits, were not used by clinic staff. It was, unfortunately not possible to control for ethnicity because of a lack of data on the ethnicity of control subjects. Lower ICC values of dietary and physical activity variables indicate that these measures were not as reliable as desired, therefore further investigation of the lifestyle habits of youth with type 2 diabetes using validated measures of diet and physical activity is warranted. Due to the burden that chronic disease during youth puts on patients and their families, integration of validated tools into clinical practice may be one way to obtain additional evidence-based information about this population. In addition, although data were obtained at the time of diagnosis or at the first physician visit for control subjects, it is not known whether prior consultations with physicians or dietitians took place, which could have had some influence on the results.

3.6. Conclusion

This study showed that children with type 2 diabetes in Northern Alberta presented with the disease at approximately 13 years of age. Patients were predominantly female and there was over representation of several ethnic groups including Aboriginal Canadians and South Eastern Asian Canadians. Many children with type 2 diabetes came from low SES backgrounds which may limit their ability for optimal treatment. Children with type 2 diabetes were more likely

to have a family history of diabetes compared to controls; they were more likely to be born with either high or low birth weights; and they were more likely to have blood lipid abnormalities, particularly high TG and TC levels compared to age, sex and BMI matched controls. This study also provides a dietary and physical activity profile of children with and without type 2 diabetes and highlights the need for further characterization of the lifestyle habits of children with type 2 diabetes. Further research may enable us to more effectively prevent and treat this disease in the future.

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Chapter 4: Dietary Patterns Associated with Glycemic Index and Glycemic Load Among Alberta Adolescents[‡]

4.1. Preface

In Chapter 3, we found that our ability to examine the link between dietary and physical activity risk factors and type 2 diabetes in youth was limited by the small sample size available; therefore, we expanded our examination of risk factors to the general population of Alberta youth. Dietary GI and GL are recognized as risk factors for diabetes among adults, but these variables have not been examined among Canadian youth. Modifications were made to the Web-SPAN database so that GI and GL would be automatically calculated during data collection.

The following chapter is based on data collected through a web-based survey, commonly known as the Web Survey of Physical Activity and Nutrition (Web-SPAN). A large sample of students from grades 7 to 10 throughout Alberta participated in this study (n = 4981) between January and December, 2005. Data from this survey were used to examine the dietary Glycemic Index (GI) and Glycemic Load (GL) of Alberta teens. In addition, dietary patterns associated with GI and GL were assessed.

[‡] A version of this chapter has been accepted for publication. Forbes, Storey, Fraser, Spence, Plotnikoff, Raine, Hanning & McCargar, 2009. Applied Physiology, Nutrition and Metabolism.

4.2. Introduction

The prevalence of obesity and type 2 diabetes has increased in most countries in recent years and escalating estimates of future diabetes prevalence have become of great concern to health professionals world wide. Perhaps the most concerning trends are the increase in the prevalence of obesity among youth, which in Canada has increased 3 fold between 1978/1979 and 2004 among 12 to 17 year olds (Shields 2006) and the emergence of early onset type 2 diabetes in children as young as four years of age (Fagot-Campagna 2000). The GI and GL of diets have been proposed as possible targets for the prevention and treatment of both type 2 diabetes (Barclay et al. 2008) and obesity (Ebbeling et al. 2003; Nielsen et al. 2005) and therefore greater exploration of the dietary GI and GL of children and adolescents is warranted.

The GI is a measure of the glycemic response elicited by the ingestion of a carbohydrate-containing food compared to a standard (usually glucose or white bread) and it is considered to be indicative of carbohydrate quality. The GL was then created to take into account both carbohydrate quality and quantity.

Epidemiological studies have demonstrated that both high GI and GL diets are associated with an increased risk of diabetes among adults (Barclay et al. 2008). This is hypothesized to be due to the greater stress that large quantities of low quality carbohydrate place on the beta cells of the pancreas, which could accelerate the deterioration of their function (Du et al. 2008; Ludwig 2002). Although the research is inconsistent, high GI and GL diets have also been associated with obesity among youth (Nielsen et al. 2005); and therefore

suggested as possible targets for weight loss promotion among children and adolescents, in part due to the increased satiety resulting from eating low GI foods (Ball et al. 2003; Ebbeling et al. 2003; Spieth et al. 2000).

Although dietary GI and GL have been examined in a clinical study of obese children in the United States (Davis et al. 2007) these variables have not, to our knowledge, been examined in a population-based sample of North American children or adolescents. Eating patterns related to GI and GL have previously been examined in adults (Du et al. 2008; McCann et al. 2007; Schulz et al. 2005; Wolever et al. 1994) but not in children. Thus, the purpose of this research was to examine the GI and GL of the diets of adolescents in Alberta, Canada based on a web-based 24-hour recall and to explore the associations between specific dietary patterns and GI and GL in this population. We also aimed to examine the relationship between dietary GI and GL and body weight status.

4.3. Methods

The methods for this study have been published previously (Storey et al. 2009) and a full description is included below.

4.3.1. School Recruitment

The Web-Survey of Physical Activity and Nutrition (Web-SPAN) was a self-administered web-based survey of a cross-sectional sample of grade 7 through 10 students (11 to 17 years of age) in Alberta schools. It assessed nutrition, physical activity and meal related behaviours. Data were collected between January and November 2005. Ethics approval was obtained from the Human Research Ethics Board for the Faculty of Agriculture, Forestry and Home

Economics, and the Cooperative Activities Program Faculty of Education, at the University of Alberta; and written consent and assent was obtained from parents and students, respectively. Copies of the school board, school, parent and student information letters, the consent form used and the ethical approval form can be found in Appendix B. Of the 59 Alberta public and separate school boards, 48 agreed to participate in the study and, on average, seven schools within each school board (363 schools) were randomly selected to be invited to participate.

Outlier analysis was conducted and participants were excluded from analysis if dietary intake values or physical activity values were considered to be extreme. Dietary intake was considered to be extreme if total energy intake was >3 standard deviations from the mean and if the intake from at least 2 food groups was >3 standard deviations from the mean. Physical activity outliers were considered extreme if more physical activity was reported per day than the number of hours in a day.

4.3.2. Measures

4.3.2.1. Body Weight, Height and BMI

Students provided self-reported body weight and height. Body mass index (BMI) was then calculated (kg/m^2) and students were categorized as non-overweight, overweight or obese according to International Obesity Task Force (IOTF) cut-offs (Cole et al. 2000) as recommended by a joint report from Dietitians of Canada, the Canadian Paediatric Society, the College of Family Physicians of Canada and Community Health Nurses Association of Canada (Dietitians of Canada 2004).

4.3.2.2. Dietary Intake

The Web-SPAN survey included a 24-hour dietary recall that measured dietary intake using the web-based Food Behaviour Questionnaire originally developed at the University of Waterloo (Hanning et al. 2007). Responding to electronic survey questions, including portion size images and cues regarding beverage intake and other often missed foods, participants reported all foods and beverages consumed the previous day by selecting from approximately 500 foods. Macronutrient intakes were assessed using ESHA Food Processor (version 7.9, ESHA Research, Salem, OR) and the 2001 Canadian Nutrient File (Health Canada 2001) database. When the variable of sugar as a percent of total carbohydrate was calculated, both natural and added sugars were included.

From the 24-hour recall, servings of each of the four food groups were calculated according to Canada's Food Guide to Healthy Eating (CFGHE) (Health Canada 1992), which was the version in use at the time of the survey. Foods not classified according to CFGHE were categorized as Other Foods and divided into the sub-categories; mostly sugar (e.g., candies), high salt/fat foods (e.g., potato chips), high calorie beverages (e.g., regular soft drinks), low calorie beverages (e.g., low calorie soft drinks), or high sugar/fat foods (e.g., pastries) based on Canadian Nutrient File definitions (Health Canada 2001).

For each of the carbohydrate-containing foods in the 24-hour dietary recall database, GI values, determined using a glucose control, were assigned from published values (Foster-Powell et al. 2002; University of Sydney 2005). Glycemic load was calculated using formulas described by (Sahyoun et al. 2005).

Briefly, GL per serving of each carbohydrate containing food was calculated as:

GL/svg = GI x available carbohydrate /100

Where available carbohydrate = total carbohydrate - fibre

The daily GL for each subject was calculated by multiplying the number of servings of each food by the GL/serving value, and the GL values from all the foods eaten were summed.

Daily GL = $\sum$(GL per serving x # servings of each food)

Where GL per serving is the GL of the portion size of each food in the Food Behviour Questionnaire (1 serving was usually equal to 1 serving from Canada's Food Guide to Healthy Eating); and the number of servings equals the number of servings that were reported to be eaten by the student.

Daily GI was calculated as:

Daily GI = (Daily GL/available carbohydrate) x 100

Daily GI values were classified as being low (< 55.9), medium (56-69.9) or high ($\geq$ 70) based on frequently used cut-offs (University of Sydney, 2008).

4.3.2.3. Meal Behaviours

Meal behaviours examined in this study included meal frequency, eating away from home and family meals. Variables used included number of meals eaten the previous day, number of meals eaten away from home the previous day and number of meals eaten with the family the previous day. More comprehensive questions examining meal behaviours were comparable to questions developed for Project EAT (Eating Among Teens), a well-established survey instrument (Neumark-Sztainer et al. 2002; Neumark-Sztainer et al. 2003).

In-depth frequency of meal consumption was assessed by asking “How often do you usually eat?” followed by “breakfast”, “lunch”, “dinner”, “morning snacks”, “afternoon snacks”, or “evening snacks”. Response options of: “Never”, “On weekends only”, “Less than half of the week (≤3 days/week)”, “More than half of the week (≥4 days/week)”, and “Every day” were given a rank from 1 (never) to 5 (every day). In-depth questions on the frequency of consuming meals away from home was assessed by asking “How often do you eat meals or snacks prepared away from home?”, with response options of “rarely or never”, “once a month”, “once a week”, “2-6 times a week”, and “once a day” which were ranked using a 5-point scale. The following locations were assessed: school cafeteria, fast food restaurant or take out, other restaurants, vending machines, snack bars, and convenience stores.

4.3.3. Intra-individual Variability and Relative Validity of Survey Tool

A subset of students (n = 459) who participated in the Web-SPAN survey completed the survey on two days at least a week apart, completed a 3-day food record and had measured height and weight measurements taken as part of a validation study. Intra-class correlation coefficients (ICC) of nutrients between the web-based 24-hour dietary recall and the 3-day food record were within the ranges reported elsewhere in the adolescent population (Rockett and Colditz 1997), and mean differences between the two measures on nutrient intakes were small (Calengor 2007). In addition, a validation of the survey tool conducted in Ontario (Vance et al. 2008) found that results using the online 24-hour recall were similar to results obtained with a dietitian administered 24-hour recall (ICCs for

all nutrients > 0.5). Intra-class correlation coefficients between self-reported and measured height and weight were 0.88 and 0.93, respectively (n=459) (Calengor 2007).

To determine of reliability of the GI and GL values calculated by the web survey, intra-individual variability was measured among all students who had completed the Web-SPAN survey twice (n = 561) by comparing survey results at times 1 and 2. This analysis showed that, similar to patterns observed with other nutrients (Bingham et al. 1997), day to day variation in GI and GL were high with ICCs of 0.28 ($p < 0.001$) and 0.45 ($p < 0.001$) for daily GI and GL, respectively. Mean daily GI and GL, however, were similar between the days with mean differences being -0.49 ($p = 0.159$) and 6.60 ($p = 0.06$) for daily GI and GL, respectively. These data show that although day to day variation in GI and GL is high, mean values provide valid information at the population level.

Of the 459 students who had completed the validation study, a random sample of 40 students was chosen to be included in an analysis that aimed to examine of the relative validity of the daily GI and GL measures calculated by the Web-SPAN survey. The entire validation study group was not included in this analysis due to the time intensive process required to calculate GI and GL for a 3 day food record. In this sample of 40 students, the mean daily GI and GL from the 3-day food records were calculated using the same list of foods and GI values used in the web survey. Relative validity of daily GI and GL values was assessed by comparing values from Web-SPAN at time 1 to mean values from the 3-day

food record. This analysis revealed ICCs for daily GI and GL of 0.5 ($p < 0.01$) and 0.3 ($p < 0.05$), respectively, showing similar comparability between these methods as observed with other nutrients (Bingham et al. 1997).

4.3.4. Statistical Analysis

Characteristics of study participants were examined using descriptive statistics. Early analyses revealed differences in results between boys and girls; therefore results are separated by gender. Differences between girls and boys were assessed using independent t-tests for continuous data and chi squared tests for categorical data.

Relationships between macronutrient intakes and GI and GL were assessed using Pearson correlation coefficients. Multiple regression models were used to assess the associations between food group choices and food behaviours and GI and GL using separate models for food groups and meal behaviours. For the food group analysis, in addition to simple multiple regression models, hierarchical models were used to assess the collective association between the "other" food categories and GI and GL. The initial meal behaviour model included the variables: number of meals eaten yesterday, number of family meals and number of meals away from home. To obtain a more detailed look at meal behaviours, separate models were constructed for meal frequency and eating away from home using the more detailed variables described above in the section entitled 4.3.2.3 Meal Behaviours. For each of the above models, analysis for males and females were conducted separately and all of these analyses were performed using both raw data and values adjusted for total energy intake using

the Willett method (Willett and Stampfer 1986). Variables entered into regression models were chosen by purposeful selection methods. For purposeful selection, logic, as well as examples from previous studies (Du et al. 2008; McCann et al. 2007; Schulz et al. 2005; Wolever et al. 1994) were used to determine what variables to include in the different models. The linear relationship between the dependent variable and the independent variables were assessed using scatterplots. The assumption that residuals are normally distributed was also tested by plotting the standardized residual against the standardized predicted value. Multicollinearity between the independent variables was assessed by examining correlation matrixes (Pearson's correlations > 0.5 were considered a potential problem) and because of multicollinearity, the relationship between macronutrients and GI and GL could not be assessed using regression models. Multicollinearity was not a problem in food group or food behaviour models. All variables were entered into the regression models simultaneously.

The relationships between weight status and daily GI and GL were assessed by Pearson correlation coefficients. In addition, one-way ANOVAs (Analysis of Variance) were performed to assess mean differences in daily GI and GL among those with non-overweight, overweight and obese weight classifications. These analyses were performed using both absolute and energy adjusted GI and GL values.

4.4. Results

In total, 4981 students from 136 schools participated in the study. Those who did not complete the nutrition section of the survey were excluded from

participation (n=79), as were those with extreme dietary intake or physical activity levels (n=36) based on outlier analysis. A final sample of 4866 adolescents was included in the analyses.

General characteristics of the study participants are presented in Table 4.1. Age and sex characteristics of this study population were similar to that seen in the Alberta school system (Plotnikoff et al. 2009). Participants ranged in age from 9 to 17 with a mean age of 13.6 years. More girls than boys participated in this study with girls representing 54% of the study population. Boys were significantly taller, heavier, had a greater BMI and had significantly higher energy intakes, macronutrient intakes and daily GIs and GLs compared to girls. Mean daily GI and GL values were 56 and 168 for boys (medians 56 and 155), and 55 and 128 for girls (medians 55 and 119).

Table 4.1 Characteristics of Study Participants

	Boys n = 2252	Girls n = 2614	Mean Difference	P-Value
Age	13.6 ± 1.2	13.6 ± 1.2	0.01	0.852
Grade	8.3 ± 1.0	8.3 ± 1.0	-0.04	0.157
Height (cm)	167.5 ± 14.3	161.6 ± 10.7	5.90	<0.001
Weight (kg)	59.5 ± 16.5	53.0 ± 11.6	6.59	<0.001
BMI (kg/m^2)	21.5 ± 7.8	20.5 ± 4.6	1.01	<0.001
Weight Status % (n)				
Non-Overweight	73.4 (1464)	84.1 (1797)	N/A	<0.001
Overweight	18.8 (375)	11.4 (243)		
Obese	7.8 (155)	4.5 (97)		
Energy Intake (kcal)	2398 ± 1204	1801 ± 913	598	<0.001
Carbohydrate (g)	313±158	245 ± 123	69	<0.001
Fat (g)	90 ± 57	65 ± 42	25	<0.001
Protein (g)	93 ± 50	66 ± 38	26	<0.001
Glycemic Index	56 ± 7	55 ± 7	1.17	<0.001
GI Category % (n)				
Low	48.5 (1092)	55.0 (1439)	N/A	<0.001
Medium	49.5 (1114)	43.7 (1142)		
High	2.0 (45)	1.3 (33)		
Glycemic Load	168 ± 89	128 ± 68	40.02	<0.001

Values are presented as mean ± SD unless otherwise specified.
Differences between boys and girls assessed using chi square tests for categorical and student's t-tests for continuous variables.

4.4.1. Diet and GI and GL

4.4.1.1. Macronutrients

Table 4.2 shows the correlations between macronutrients and daily GI and GL for both boys and girls. For boys, energy, carbohydrate, fat and sugar intakes were positively correlated with GI, with carbohydrate (r = 0.13) and energy (r = 0.10) having the strongest relationships. A similar pattern was seen with girls; however, sugar intake did not correlate with GI (r = 0.01). When values were adjusted for total energy intake, protein intake became the strongest correlate of GI for both boys and girls, with an inverse relationship between the variables (boys: r = -0.21; girls: r = -0.22). Carbohydrate was positively related (boys: r = 0.11; girls: r = 0.07) and fibre was negatively correlated (boys: r = -0.08; girls: r = -0.07) with GI for both boys and girls after energy adjustment. In addition, sugar was negatively related to GI for girls (r = -0.08).

For GL, all nutrients were positively correlated prior to energy adjustment, with carbohydrate (boys: r = 0.97; girls: r = 0.97) and energy (boys: r = 0.89; girls: r =0.90) having the strongest correlations for both boys and girls. After adjusting for energy intake, carbohydrate remained the strongest correlate (boys: r = 0.38; girls: r = 0.42), with a positive relationship with GL. Fat and protein were both negatively related to GL and sugar and fibre were both positively correlated with GL for girls, but fibre was not correlated for boys.

Table 4.2 Correlation of Absolute and Energy Adjusted Macronutrient Intakes with GI and GL

	Glycemic Index							
	Boys				Girls			
Nutrient	r	p-value	r (adj)	p-value	r	p-value	r (adj)	p-value
Energy (kcal)	0.097	<0.001	-	-	0.109	<0.001	-	-
Carbohydrate (g)	0.133	<0.001	0.110	<0.001	0.123	<0.001	0.068	0.001
Fat (g)	0.078	<0.001	-0.027	0.207	0.114	<0.001	0.031	0.114
Protein (g)	-0.039	0.066	-0.213	<0.001	-0.032	0.104	-0.224	<0.001
Sugar (g)	0.042	0.042	-0.024	0.247	0.012	0.543	-0.075	<0.001
Fibre (g)	0.010	0.645	-0.079	<0.001	0.019	0.337	-0.069	<0.001
	Glycemic Load							
	Boys				Girls			
Nutrient	r	p-value	r (adj)	p-value	r	p-value	r (adj)	p-value
Energy (kcal)	0.891	<0.001	-	-	0.902	<0.001	-	-
Carbohydrate (g)	0.974	<0.001	0.377	<0.001	0.972	<0.001	0.424	<0.001
Fat (g)	0.697	<0.001	-0.286	<0.001	0.715	<0.001	-0.324	<0.001
Protein (g)	0.586	<0.001	-0.285	<0.001	0.616	<0.001	-0.278	<0.001
Sugar (g)	0.741	<0.001	0.235	<0.001	0.720	<0.001	0.235	<0.001
Fibre (g)	0.641	<0.001	0.031	0.147	0.680	<0.001	0.120	<0.001

r , Pearson correlation coefficients raw data

r (adj), Pearson correlation coefficients adjusted for total energy intake

4.4.1.2. Food Groups

Results of the regression analysis for food groups and daily GI are presented in Table 4.3 and results for GL are presented in Table 4.4. Before adjusting for energy intake, food groups accounted for 24% and 28% of the variation in daily GI for boys and girls, respectively (boys: $F[11,2240] = 60.24$ $p<0.001$; girls: $F[11,2603] = 87.43$, $p<0.001$). Strongest associations for boys were observed for milk products ($\beta = -0.34$), grain products ($\beta = 0.32$) and vegetables and fruit ($\beta = -0.14$). Strongest associations with daily GI for girls were seen with milk products ($\beta = -0.39$), grain products ($\beta = 0.36$) and the mostly sugar category ($\beta = 0.13$). Also of interest, hierarchical analysis showed that, after the four food groups were entered into a regression model, the "other" categories explained an additional 3.5% of the variance in daily GI.

After adjusting for total energy, the food group model accounted for 27% and 29% of the variation in GI for boys and girls, respectively (boys: $F[11,2240] = 87.43$, $p<0.001$; girls: $F[11,2603] = 95.892$, $p<0.001$). Strongest associations with GI were seen with milk (boys: $\beta = -0.45$; girls $\beta = -0.46$), vegetables and fruit (boys: $\beta = -0.27$; girls: $\beta = -0.19$) and grain products (boys: $\beta = 0.11$; girls: $\beta = 0.17$) for both girls and boys. The meat and alternatives group (boys: $\beta = -0.17$; girls: $\beta = -0.13$) and the high sugar and fat ($\beta = -0.07$ both boys and girls) foods, which were not significantly related to GI prior to energy adjustment, but they became significantly related after adjustment. The high calorie beverages and mostly fat groups were no longer related to GI after adjustment. Hierarchical analysis (data not shown in Table 4.3) showed that, after energy adjustment, the

other food categories collectively accounted for 1.6% of the variation in GI for boys and 1.3% of the variation for girls.

Table 4.3 Multiple Regression Models for GI and Food Group Choices

	Daily Glycemic Index (Unadjusted)						Daily Glycemic Index (Energy Adjusted)					
	Boys			Girls			Boys			Girls		
Variable	β (SE)	Partial R^2	p-value	β (SE)	Partial R^2	P-value	β (SE)	Partial R^2	p-value	β (SE)	Partial R^2	P-value
Grain products	0.317 (0.031)	0.100	<0.001	0.355 (0.037)	0.126	<0.001	0.111 (0.042)	0.011	<0.001	0.167 (0.051)	0.024	<0.001
Vegetables & fruit	-0.144 (0.032)	0.023	<0.001	-0.081 (0.032)	0.008	<0.001	-0.273 (0.043)	0.061	<0.001	-0.189 (0.045)	0.029	<0.001
Milk & milk products	-0.343 (0.059)	0.123	<0.001	-0.388 (0.061)	0.160	<0.001	-0.454 (0.081)	0.147	<0.001	-0.459 (0.088)	0.147	<0.001
Meats & alternatives	-0.025 (0.051)	0.001	0.207	-0.024 (0.067)	0.001	0.194	-0.171 (0.071)	0.025	<0.001	-0.134 (0.086)	0.018	<0.001
Mostly fat	0.096 (0.099)	0.010	<0.001	0.070 (0.113)	0.006	<0.001	0.013 (0.107)	0.000	0.506	0.019 (0.119)	0.000	0.259
Mostly sugar	0.107 (0.078)	0.014	<0.001	0.128 (0.091)	0.020	<0.001	0.041 (0.081)	0.002	0.032	0.071 (0.096)	0.006	<0.001
High salt & fat	0.081 (0.099)	0.008	<0.001	0.073 (0.112)	0.007	<0.001	-0.089 (0.137)	0.006	<0.001	-0.058 (0.156)	0.003	0.008
High calorie beverages	0.054 (0.088)	0.003	0.005	0.067 (0.106)	0.006	<0.001	-0.070 (0.106)	0.004	0.002	-0.020 (0.121)	0.000	0.291
Low calorie beverages	0.028 (0.073)	0.001	0.141	0.006 (.063)	0.000	0.727	0.023 (0.072)	0.001	0.205	0.010 (0.063)	0.000	0.554
High sugar & fat	0.008 (0.120)	0.002	0.042	-0.005 (0.135)	0.000	0.788	-0.070 (0.130)	0.006	<0.001	-0.071 (0.151)	0.006	<0.001
Other misc.	-0.038 (0.845)	0.000	0.676	-0.010 (1.120)	0.000	0.535	-0.046 (0.834)	0.003	0.012	-0.024 (1.121)	0.001	0.142

β = Standardized Coefficient, SE = Standard Error. Each food group presented as total # of servings

Unadjusted data boys: $F[11,2240] = 60.24$ $p<0.001$; girls: $F[11,2603] = 87.43$, $p<0.001$. Energy adjusted data boys: $F[11,2240] = 87.43$, $p<0.001$; girls: $F[11,2603] = 95.892$, $p<0.001$

Food group choices, prior to adjustments for energy intake, explained 84% of the variation of daily GL for boys and 85% of the variation for girls (boys: $F[11,2240] = 959.68$, $p<0.001$; girls: F[11,2603] 1207.14, $p<0.001$). Most important contributors to the models included vegetables and fruit (boys: $\beta = 0.35$; girls: $\beta = 0.43$), grains (boys: $\beta = 0.38$; girls: $\beta = 0.41$), high calorie beverages (boys: $\beta = 0.34$; girls: $\beta = 0.28$), high salt and fat (boys and girls: $\beta = 0.23$) and mostly sugar groups (boys and girls: $\beta = 0.21$) for both boys and girls. Hierarchical analysis showed that the "other" categories contributed an extra 24% to the variance in daily GL for girls and 30% to the variance for boys after the regular food groups were entered into the model.

After adjusting for energy intake, the food group model accounted for only 12% of the variability in GL for boys and 14% for girls (boys: $F[11,2240] = 28.174$, $p<0.001$; girls: F[11,2603] 38.694, $p<0.001$). In this model, meats and alternatives most strongly related to GL in both boys and girls (boys: $\beta = -0.20$; girls: $\beta = -0.27$). Other important variables in this model included milk and milk products (boys: $\beta = -0.14$; girls: $\beta = -0.11$) and mostly sugar groups (both boys and girls: $\beta = 0.10$) for both boys and girls and high calorie beverages for boys ($\beta = 0.16$) and vegetables and fruits for girls ($\beta = 0.17$). Categories that were no longer associated with GL after adjusting for energy intake included the high salt and fat group and the high sugar and fat group. Hierarchical analysis showed that even after energy adjustment the "other" categories collectively accounted for 3.2% of the variation in GL for boys and 1.9% of the variation for girls (this data is not presented in Table 4.3).

Table 4.4 Multiple Regression Models for GL and Food Group Choices

	Daily Glycemic Load (Unadjusted)						Daily Glycemic Load (Energy Adjusted)					
	Boys			Girls			Boys			Girls		
Variable	β (SE)	Partial R^2	p-value	β (SE)	Partial R^2	p-value	β (SE)	Partial R^2	p-value	β (SE)	Partial R^2	P-value
Grain products	0.383 (0.181)	0.429	<0.001	0.410 (0.164)	0.473	<0.001	0.066 (0.576)	0.003	0.007	0.094 (0.546)	0.007	<0.001
Vegetables and fruit	0.349 (0.186)	0.393	<0.001	0.427 (0.142)	0.513	<0.001	0.070 (0.583)	0.003	0.005	0.172 (0.478)	0.020	<0.001
Milk and milk products	0.128 (0.341)	0.083	<0.001	0.145 (0.274)	0.110	<0.001	-0.142 (1.108)	0.014	<0.001	-0.105 (0.940)	0.007	<0.001
Meats and meat alternatives	0.032 (0.298)	0.005	0.001	0.025 (0.301)	0.003	0.004	-0.200 (0.966)	0.029	<0.001	-0.269 (0.917)	0.058	<0.001
Mostly fat	0.050 (0.573)	0.012	<0.001	0.026 (0.505)	0.004	0.002	-0.043 (1.454)	0.002	0.043	-0.066 (1.261)	0.005	<0.001
Mostly sugar	0.210 (0.450)	0.197	<0.001	0.207 (0.405)	0.203	<0.001	0.098 (1.106)	0.010	<0.001	0.100 (1.024)	0.010	<0.001
High salt and fat	0.232 (0.571)	0.238	<0.001	0.232 (0.502)	0.256	<0.001	-0.027 (1.870)	0.000	0.316	-0.039 (1.656)	0.001	0.100
High calorie beverages	0.342 (0.508)	0.394	<0.001	0.281 (0.474)	0.323	<0.001	0.164 (1.450)	0.020	<0.001	0.065 (1.289)	0.004	0.002
Low calorie beverages	0.011 (0.421)	0.001	0.199	-0.012 (0.283)	0.001	0.118	0.023 (0.977)	0.001	0.248	0.005 (0.672)	0.000	0.800
High sugar and fat	0.136 (0.693)	0.097	<0.001	0.155 (0.603)	0.131	<0.001	0.017 (1.771)	0.000	0.434	0.015 (1.602)	0.000	0.444
Other miscellaneous	0.011 (4.888)	0.001	0.205	0.027 (5.006)	0.005	<0.001	0.009 (11.368)	0.000	0.645	-0.021 (11.914)	0.000	0.258

β = Standardized Coefficient, SE = Standard Error. Each food group presented as total # of servings

Unadjusted data boys: $F[11,2240] = 959.68$, $p<0.001$; girls: $F[11,2603]$ 1207.14, $p<0.001$. Energy adjusted data boys: $F[11,2240] = 28.174$, $p<0.001$; girls: $F[11,2603]$ 38.694, $p<0.001$

4.4.1.3. Meal Behaviours

Meal behaviours of interest included meal frequency, family meals and restaurant eating. Meal behaviours were not related to daily GI for either boys or girls. Table 4.5 shows the results of regression models assessing associations between daily GL and meal behaviour variables. Meal behaviours accounted for 5% of the variation in daily GL for boys ($F[3,1207] = 24.08$, $p<0.001$) and 6% of the variation in daily GL for girls ($F[3,1248] = 27.83$, $p<0.001$). Meal frequency was most strongly related to daily GL (boys: $\beta = 0.23$; girls: $\beta = 0.23$). In addition, restaurant meals were associated with daily GL for girls ($\beta = 0.11$) but not for boys. Family meals were not associated with daily GL for boys or girls.

The association between meal frequency and restaurant eating and daily GL were assessed using separate models to examine these meal behaviours in more detail. Variables included in the meal frequency model included the frequency of eating each meal and snack of the day. The results, presented in Table 4.5, showed that this model explained 8 % of the variation in daily GL males ($F[6,1450] = 23.08$, $p<0.001$) and 12 % of the variation for females ($F[6,1685] = 39.50$, $p<0.001$). Afternoon snack, breakfast and evening snack were most strongly related to GL for both boys and girls. Only frequency of dinner consumption was not associated with daily GL.

The model for eating out included variables for the frequency of eating at different locations, including cafeterias, fast food outlets, restaurants, vending machines, snack bars and convenience stores. This model (see Table 4.5) explained 5% and 3% of the variation in daily GL for boys and girls, respectively (boys: $F[6,1904] = 12.85$, $p<0.001$; girls: $F[6,2289] = 10.58$, $p<0.001$). Contributors to the

model were vending machines (β = 0.08), convenience stores (β = 0.08) and snack bars (β = 0.07) for boys and snack bars (β =0.09) and fast food outlets (β = 0.05) for girls. After adjusting for energy intake, neither the meal frequency or the eating away from home models were associated with GL.

Table 4.5 Regression Models for GL and Meal Behaviours

	Daily Glycemic Load (Unadjusted)					
	Boys			Girls		
Variable	β (SE)	Partial R^2	P-Value	β (SE)	Partial R^2	P-Value
Meal Behaviour Model						
Number of meals	0.230 (1.937)	0.053	<0.001	0.232 (1.482)	0.054	<0.001
Family Meals	-0.042 (3.118)	0.002	0.131	0.012 (2.486)	0.000	0.660
Meals at restaurants	0.043 (5.595)	0.002	0.127	0.106 (4.099)	0.012	<0.001
Meal Frequency Model						
Breakfast	0.129 (2.012)	0.016	<0.001	0.138 (1.201)	0.019	<0.001
Lunch	0.062 (3.560)	0.003	0.029	0.093 (1.971)	0.008	<0.001
Dinner	0.010 (5.862)	0.000	0.707	0.005 (3.078)	0.000	0.833
Morning snack	0.062 (1.688)	0.003	0.035	0.077 (1.053)	0.006	0.002
Afternoon snack	0.085 (2.031)	0.006	0.004	0.144 (1.274)	0.019	<0.001
Evening snack	0.133 (1.989)	0.015	<0.001	0.135 (1.193)	0.018	<0.001
Eating outside the Home Model						
Cafeteria	-0.022 (1.413)	0.000	0.367	0.016 (0.989)	0.000	0.438
Fast food	0.043 (2.734)	0.001	0.132	0.050 (1.970)	0.002	0.049
Restaurants	-0.015 (2.798)	0.000	0.598	0.014 (2.138)	0.000	0.578
Vending machines	0.079 (2.096)	0.004	0.006	0.014 (1.429)	0.000	0.553
Snack bars	0.068 (2.138)	0.003	0.020	0.089 (1.507)	0.005	<0.001
Convenience stores	0.078 (2.178)	0.004	0.007	0.048 (1.537)	0.002	0.052

β = Standardized Coefficient, SE = Standard Error

Meal behaviour model boys: $F[3,1207] = 24.08$, $p<0.001$, girls: $F[3,1248] = 27.83$, $p<0.001$. Meal frequency model boys: $F[6,1450] = 23.08$, $p<0.001$, girls: $F[6,1685] = 39.50$, $p<0.001$. Eating outside the home model boys: $F[6,1904] = 12.85$, $p<0.001$; girls: $F[6,2289] = 10.58$, $p<0.001$

4.4.2. GI, GL and Weight Status

Pearson correlations showed no significant relationship between absolute GI and BMI among boys ($p = 0.31$), however, daily GI was positively correlated with BMI in girls with a coefficient of 0.05 ($p = 0.02$). Correlation results for energy adjusted GI were similar to absolute values. There was no correlation between either absolute or energy adjusted GL and BMI in either boys or girls.

When students were classified by IOTF cut-offs for weight status and daily GI and GL was compared between the groups, no significant differences in dietary GI were observed between the groups for either boys or girls. However, a significant difference existed among weight status groups with daily unadjusted GL for boys. Specifically, non-overweight boys had a significantly higher GL than overweight boys (mean GL 177 vs. 153; effect size [d] = 0.27; $p < 0.001$). The mean energy adjusted GL for obese boys (mean = 163) was not significantly different than that of either overweight or non-overweight boys. When energy adjusted GL values were used, the difference between weight categories was no longer significant ($p = 0.08$). No significant difference existed for GL across weight categories for girls.

4.5. Discussion

To our knowledge, this study is the first to assess GI and GL in a large group of Canadian adolescents and to examine dietary patterns related to GI and GL in this age group. Results provide evidence of the quality of carbohydrates consumed by Canadian adolescents, and also identify dietary patterns that could be targeted in future interventions to determine if promoting these patterns would lead to improvements in GI and GL in this population.

Mean daily GI was similar among boys and girls at 55 to 56 and daily GL was higher among boys than girls with mean values of 168 and 128 for boys and girls respectively. Other studies from the United States and Europe have found similar mean GI values, ranging from 56 to 60 and GL values ranging from 115 to 310 (Buyken et al. 2006; Davis et al. 2007; Ebbeling et al. 2003; Nielsen et al. 2005; Scaglioni et al. 2005; Verduci et al. 2007).

The levels of dietary daily GI and GL that confer a benefit to health have not been well defined. Individual foods are considered to have a low GI if the value is <55 and a high GI with a value of >70 (University of Sydney, 2008). However, these definitions do not appear to translate well to the whole diet where the mean daily GI generally falls in the low to medium GI range from ~50-60 (Barclay et al. 2008; Buyken et al. 2006; Davis et al. 2007; Ebbeling et al. 2003; Scaglioni et al. 2005; Verduci et al. 2007). A meta-analysis that investigated the effect of GI and GL on chronic disease risk in adults found a relative risk of 1.4 for diabetes in the highest quantile of GI compared to the lowest. The mean GI in the lowest quantile was 49 and the mean GI in the highest quantile was 58 (Barclay et al. 2008). This suggests that small differences in daily GI can make a difference in health risk at a population level and although the mean daily GI value in the current study (at 55) was not as high as 58, improvements could be made and could be beneficial for the disease risk of this population. In terms of a healthy GL level, Barclay and colleagues (Barclay et al. 2008) found that a quantile with a median daily GL of 142 was associated with a relative risk of diabetes of 1.27 compared to a quantile with a median GL of 92. Thus, the mean daily GL value of 137 found in our study suggests that many of our

participants could be at increased risk for diabetes. However, it should be noted that it is possible that values obtained from adult studies are not appropriate to be used as guidelines for younger age groups.

4.5.1. Diet and GI and GL

4.5.1.1. Macronutrients

As would be expected due to the nature of GI and GL, this study showed that macronutrient content was strongly related to dietary GI and GL. Carbohydrate, total energy and fat were the strongest correlates of GI before adjusting for energy intake and protein (negative) and carbohydrate (positive) intakes were most strongly correlated after energy correction. In addition, sugar intake and fibre intake were inversely correlated with GI. Previous studies have reported similar results (Du et al. 2008; Wolever et al. 1994). Collectively, this data suggests that diets low in protein and high in carbohydrate are more likely to contain more poor quality, high GI foods and could be related to increased risk of diabetes.

Consistent with previous studies (Du et al. 2008; Schulz et al. 2005) we found daily GL to be strongly correlated with total carbohydrate and energy intake ($r = 0.97$ for both boys and girls for carbohydrate; $r = 0.89$ for boys and 0.90 for girls for total energy). This suggests that low GL diets frequently are also low carbohydrate and/or low energy diets; and the specific health effects of each of these dietary traits is unclear.

4.5.1.2. Food Groups

In the current study, food groups were strongly associated with daily GI. The most important variables in food group models were milk products and vegetables and

fruit, which were negatively associated with daily GI and grain products which were positively related to daily GI. This pattern was largely similar both before and after energy adjustment and other studies that have investigated relationships between food types and daily GI in adults have found similar results (Du et al. 2008; McCann et al. 2007; Schulz et al. 2005).

Prior to energy adjustment, food groups accounted for 85% of the variation in GL and similar to previous studies (Du et al. 2008; McCann et al. 2007; Schulz et al. 2005), all food groups showed positive associations with GL. After energy adjustment, food groups accounted for only 12 to 14% of the variation in GL highlighting the strong relationship between daily GL and the total energy intake. The most important contributors to daily GL models after energy adjustment included milk and milk products, vegetables and fruit and meat and alternatives, all of which were negatively related to GL and grains which were positively associated with daily GL.

Our results also show that foods in the other categories played a significant role in determining daily GI and GL. However, the decrease in their relationship with GI and GL after energy adjustment, suggests that although foods in the other categories influence GI and GL, a large part of their effect, on GL in particular, is related to the total amount of energy they supply.

Several of the relationships observed in the food group analysis initially appeared contradictory and warrant further discussion. One example is the emergence of the meat and alternatives group as being significantly related to low GI, after energy adjustment. Meat alternatives such as legumes are low GI foods, however, it is likely that meats, which do not contribute to GI due to the lack of carbohydrate, make up the

majority of servings in this group. It is possible that legumes contribute to this trend, but it is also possible that meats are either eaten in conjunction with low GI carbohydrate foods or replace or decrease the consumption of high GI foods. Another relationship requiring further explanation is the result that high sugar intake (from the macronutrient analysis) was associated with low GI, but high intake of "mostly sugar foods" (from the food group analysis) was related to high GI, which initially seems contradictory. Total sugar intake may have a different effect than "mostly sugar foods" because sugars are found in a variety of foods with a wide range of GI values including fruits, vegetables, breads, and cakes, whereas mostly sugar foods include only candies (i.e. hard candies or chewy candies) or table sugar (i.e. white or brown) which have fairly consistent moderately high GI values of ~65 (Foster-Powell et al. 2002). Alternatively, this pattern may have resulted from associations between variables. For example, people who consume more "mostly sugar foods" may be more likely to eat more high GI foods.

The results of this study suggests that those who choose more milk, meats and alternatives, fruits and vegetables and fewer, grain products, soft drinks, and mostly sugar foods are more likely to have a lower dietary GI. Those choosing fewer carbohydrate-containing foods are more likely to have a lower GL.

4.5.1.3. Meal Behaviours

Meal behaviours such as frequency of eating and eating meals outside the home were only weakly associated with daily GL and were not related to daily GI. In addition, these behaviours were not related to GL after adjusting for total energy intake. This indicates that the number of meals eaten and eating away from the home

may be indicative of the amount of food eaten rather than the quality of the carbohydrates. It should also be noted that the relationships observed with eating behaviours may be underestimated due to the great day to day variability seen in daily GI and GL values and it may be beneficial to examine these relationships using an average of several days' GI and GL values.

4.5.2. GI, GL and Weight Status

The small associations observed between daily GI and GL and weight status, along with the inconsistent findings between girls and boys, bring into question the practical significance of these results. Daily GL was seen to be higher among non-overweight boys compared to overweight boys, which initially seems counterintuitive as we would expect a higher GL with a higher BMI. However, research has shown that leaner adolescents frequently have higher food intakes due to higher levels of physical activity, so it is likely that total energy intakes explain much of this difference (Stallmann-Jorgensen et al. 2007). The attenuation of this effect when energy adjusted GL values were used, supports the notion that total energy intake is at least partially responsible for this pattern. Previous studies examining the link between weight status and GI and GL have shown inconsistent results (Davis et al. 2007; Hui and Nelson 2006; Nielsen et al. 2005; Scaglioni et al. 2005). Although this study does not disprove the possibility that GI and GL have an effect on body weight, it is also possible that daily GI and GL have very little effect on weight status and they may affect diabetes risk independently from weight status. In this case, daily GI and GL could still be important targets for improving the health and future disease risk of

adolescents, however the evaluation of the effects of GI and GL on markers of diabetes risk was outside the scope of the present analysis.

4.5.3. Strengths and Limitations

Strengths of the current study include the large sample size and the wide geographical area covered. Detailed dietary data were also collected in a completely anonymous way, which may have improved compliance and truthfulness in participants. One limitation of this study was that only one day of dietary data was collected for the majority of subjects. Our study found that daily GI in particular has high day to day variance and having 2 or 3 days of dietary data would have been beneficial. Repeating the survey would have taken up more class time and may have lead to reduced participation rates, which was a major consideration for this research. The use of self-reported dietary intake and height and weight information can be inaccurate (Guenther et al. 1997). However, a validation study of the on-line 24-hour recall tool found that dietary results were similar to dietitian administered 24-hour recalls performed on the same day with ICC values for all nutrients being > 0.5 (Vance et al. 2008). A validation study of the self reported methods used in the present study found that measured heights and weights were very similar to self reported values (ICCs of 0.88 for height and 0.93 for weight) (Calengor 2007). Another possible limitation of the present study was that many of the GI values used to calculate daily GI and GL came from data from other countries when Canadian data were not available; and it has been shown that the GIs of similar foods can vary between countries (Foster-Powell et al. 2002). Values for GI and GL also vary depending on the methods used in the laboratories where the GI and GL of foods are tested (Wolever

et al. 2003). In addition, although 500 foods were available to choose from in the 24-hour recall section of the survey, a greater number of foods may have provided greater detail and may have resulted in more accurate estimates of daily GI and GL.

4.6. Conclusion

This study assessed the dietary GI and GL of a large sample of adolescents in Alberta, examined associations between dietary patterns and daily GI and GL and examined the relationship between daily GI, GL and weight status. Macronutrient intake patterns related to high GI diets included high carbohydrate and low protein, sugar and fibre intakes. In terms of food groups, high intakes of grains, mostly sugar foods, high salt and fat foods and mostly fat foods and low intakes of vegetables and fruit, milk and milk products and meats and alternatives were related to high GI diets. Meal behaviours were not related to GI in this population. For GL, in terms of macronutrients, carbohydrate and energy intakes showed the strongest correlations. All food groups were positively related to GL values prior to energy adjustment; however, after adjustment, meats and alternatives and milk and milk products were negatively associated with GL. Meal frequency and eating meals away from home were related to GL, but this relationship disappeared with energy adjustment. This study also found weight status to be weakly related to GI and GL but results were inconsistent between boys and girls. This study identified specific dietary patterns and food behaviours related to GI and GL. Future studies could determine if targeting these behaviours would be useful for diabetes risk reduction among Alberta adolescents.

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Chapter 5: Frequency and Distribution of Dietary and Physical Activity Risk Factors for Type 2 Diabetes in a Large Sample of Alberta Youth

5.1. Preface

After examining the risk factors of GI and GL in detail in Chapter 4, we aimed to expand our exploration of dietary and physical activity risk factors in Alberta youth to include a wide range of factors. Data examining lifestyle risk factors for diabetes among Canadian adolescents are currently rare.

The following is the second chapter in this thesis to be based on data from the Web Survey of Physical Activity and Nutrition (Web-SPAN), which was a survey of grade 7 to 10 students in Alberta (n = 4981). Data for this study were collected between January and December 2005. In this chapter, data from the Web-SPAN survey were used to examine the proportion of students reporting dietary and physical activity risk factors for type 2 diabetes.

5.2. Introduction

Type 2 diabetes is a disease characterized by insulin resistance and impaired beta-cell function, resulting in increased blood glucose levels (Rizvi 2004). Both genetic predisposition and lifestyle factors play important roles in the development of this disease. Although type 2 diabetes is traditionally considered to be an adult disease, type 2 diabetes in children was first reported in the late 1970s (Savage et al. 1979) and since that time, the prevalence of early onset disease has been rising (Dabelea et al. 1998; Hale and Rupert 2006; Urakami et al. 2005; Zdravkovic et al. 2004).

Lifestyle factors contribute significantly to the development of type 2 diabetes. Lifestyle risk factors for type 2 diabetes, according to the adult literature include obesity (Hu et al. 2001; Krishnan et al. 2007), dietary factors, such as high dietary glycemic index (GI), high dietary glycemic load (GL) (Barclay et al. 2008), low fibre (Schulze et al. 2004), low magnesium intake (Lopez-Ridaura et al. 2004), low vegetable and fruit consumption (Liu et al. 2004) and high fat intake (van Dam et al. 2002), as well as lack of physical activity (Hsia et al. 2005). In adults, it has been shown that small lifestyle changes including dietary changes and increasing physical activity can prevent and/or delay type 2 diabetes (Lindstrom et al. 2003; Ratner 2006). Delaying or preventing early onset type 2 diabetes is especially important, as early development of the disease leads to longer disease duration, earlier development of macro- and microvascular complications (Krakoff et al. 2003) and greater health care costs.

Due to the increase in type 2 diabetes in children and adolescents, examining the lifestyle habits of youth has become important. However, few Canadian studies have specifically examined the prevalence and distribution of lifestyle risk factors for type 2 diabetes in this age group. In addition, previous studies have observed differences in lifestyle practices and diabetes risk between boys and girls and among different age and Body Mass Index (BMI) groups Specifically, girls are more likely to be diagnosed with type 2 diabetes (Likitmaskul et al. 2005; Perez-Perdomo et al. 2005; Pinhas-Hamiel et al. 1996) and are more likely to be physically inactive (Koezuka et al. 2006; Shields 2006; Springer et al. 2009), whereas boys are more likely to have low diet quality (Hurley et al. 2009). Older youth are more likely to be physically inactive than younger youth (Koezuka et al. 2006; Springer et al. 2009). Those with a higher BMI are more likely to be inactive (Shields 2006), to have low diet quality (Hurley et al. 2009) and to be diagnosed with type 2 diabetes (Likitmaskul et al. 2005; Perez-Perdomo et al. 2005; Pinhas-Hamiel et al. 1996). Therefore, the purpose of this study was to examine the presence of lifestyle risk factors for type 2 diabetes in a large sample of Alberta adolescents and to examine differences in risk factor presence across sex, age and BMI groups.

5.3. Methods

The methods for this study has been published previously (Storey et al. 2009) and a full description is included below.

5.3.1. Participants

Briefly, between January and November 2005, grade 7 to 10 (11 to 17 years of age) students in Alberta were recruited to participate in the Web Survey of Physical

Activity and Nutrition (Web-SPAN). This survey was a self administered, web-based questionnaire which aimed to assess dietary and physical activity patterns as well as social and environmental determinants of these behaviours. All 59 Alberta School Boards were invited to participate in the study and of these, 48 agreed to participate. On average, 7 schools per school board (total: 363) were randomly selected for the study. Before participating in this survey, parental consent and assent of the students was obtained. This research was approved by the Human Ethics Research Board, Faculty of Agricultural, Life and Environmental Sciences and the Cooperative Activities Program, Faculty of Education, University of Alberta. Where required by certain school boards, additional ethical approval was received. Copies of the school board, school, parent and student information letters, the consent form used and the ethical approval form can be found in Appendix B.

5.3.2. Measures

The Web-SPAN survey was completed during school time and took approximately 45 minutes for students to complete; it was frequently completed during a single class period. Teachers were given unique logins and passwords which were randomly distributed among all students who had parental consent to participate in the Web-SPAN survey. Teachers were provided with an information package to instruct them on how to administer and assist students in completing the survey. A research assistant was also on call when surveys were being done in case the teacher had any questions or if technical problems arose.

5.3.2.1. Height, Weight and BMI

The students reported their own height and weight in the first section of the Web-SPAN and BMI (kg/m^2) was calculated.

5.3.2.2. Dietary Intake

Dietary intake of participants was measured by a web-based 24-hour recall tool; the *Food Behaviour Questionnaire,* originally developed by Dr. Rhona Hanning at the University of Waterloo (Hanning et al. 2003). Using this tool, students recorded all foods and beverages consumed in the previous day, choosing from a list of over 500 foods. The survey tool provided cues for portion sizes and prompted students to record foods often missed such as spreads, toppings and beverages. Dietary intake data were analyzed and macronutrient (i.e. fat, carbohydrate) and micronutrient (i.e. magnesium) intakes were calculated using the ESHA Food Processor (version 7.9, ESHA Research, Salem, OR) and the 2001 Canadian Nutrient File (Health Canada 2001) database. In addition, food group intake according to Canada's Food Guide to Healthy Eating (Health Canada 1992) (i.e. vegetables and fruit) was calculated. This version of the food guide was used, as it was the guide in use in the school curricula at the time of the survey. A new food guide was released in 2007 (Health Canada 2007).

To calculate dietary GI and GL, each carbohydrate containing food in the Web-SPAN database was assigned a GI based on published values (Foster-Powell et al. 2002; University of Sydney 2005). Daily dietary GI and GL were calculated by the method described by (Sahyoun et al. 2005) and briefly outlined below:

GL/svg = GI x available carbohydrate /100

Where available carbohydrate = total carbohydrate - fibre

The daily GL for each subject was calculated by multiplying the number of servings of each food by the GL/serving value, and the GL values from all the foods eaten were summed.

Daily GL = ∑(GL per serving x # servings of each food)

Where GL per serving is the GL of the portion size of each food in the Food Behviour Questionnaire (1 serving was usually equal to 1 serving from Canada's Food Guide to Healthy Eating); and the number of servings equals the number of servings that were reported to be eaten by the student.

Daily GI was calculated as:

Daily GI = (Daily GL/available carbohydrate) x 100

(More detail is provided in Chapter 4).

5.3.2.3. Physical Activity

Physical activity was assessed using an online version of the Physical Activity Questionnaire for Older Children (PAQ-C) (Kowalski et al. 2004). Physical activity levels were determined based on self-reported activities performed in the last 7 days. Sub-categories of activities included organized sports and activities, active transport, and activity at recess, lunch, after school, in the evenings and on weekends. The PAQ-C scores range from 1 to 5 with 1 being least active and 5 being most active (Kowalski et al. 2004).

5.3.3. Defining Risk Factors

Literature searches were conducted to identify major dietary and physical activity risk factors for type 2 diabetes for adults and to determine cut-offs for identifying those at risk. Wherever possible, studies relevant to children and youth were also evaluated, but these were limited in number. Risk factors identified included obesity, GI, GL, fibre, magnesium, vegetable and fruit intake, fat intake and physical activity. All large, longitudinal cohort studies examining the relationship between these variables and type 2 diabetes risk were compiled and summarized. A table containing these summaries for each risk factor can be found in Appendix C. In addition, a panel of experts was consulted including experts in the areas of GI and GL, childhood obesity, physical activity measurement and statistical analysis. Table 5.1 outlines the risk factor cut-offs used and the rationale related to each cut-off. More detailed explanations of the rationale can be found in Appendix D. For each risk factor, dichotomous variables were constructed, designating participants as either at risk or not at risk, depending on their survey results relative to cut-off values.

Table 5.1 Summary and Rationale of Cut-offs Used for Assessing Diabetes Risk Factors

Variable	Cut-off = ↑ risk	Reference	Rationale
Overweight and Obesity	International Obesity Task Force (IOTF) cut-offs for Overweight and Obesity	(Hart et al. 2007; Hosseinpanah et al. 2007; Hu et al. 2003; Krishnan et al. 2007; Meisinger et al. 2006; Rana et al. 2007)	Appropriate for children. Reference values come from an international sample. Youth are considered overweight or obese if their BMI is on or above the point on the centile growth curve for their age and sex that passes through either the adult overweight or obesity cut off at age 18. Studies have shown that there is increasing diabetes risk with increasing BMI category, however, for children, only overweight and obese classifications exist (no class I, II, III obesity).
Glycemic Index	>58	(Barclay et al. 2008)	This study was the best available source of information. As a meta-analysis, it included information from many studies.
Glycemic Load	>142	(Barclay et al. 2008)	This study was the best available source of information. As a meta-analysis, it included information from many studies.
Fibre	<14.75g	(Meyer et al. 2000; Schulze et al. 2004)	Both of these studies are North American and had similar results therefore the mean value between the two studies was taken.
Magnesium	<222mg/day females <280mg/d males	(Lopez-Ridaura et al. 2004)	This study was the largest study available that measured magnesium in units comparable to the Web-SPAN survey (mg/d). (One meta-analysis was considered but the units of change in risk per 100mg increase in magnesium intake were not applicable to Web-SPAN results)
Vegetables and Fruit	<2 servings/day (>1.99 servings = not at risk)	(Liu et al. 2004)	This study used portion sizes similar to sizes from Canada's food guide.

Fat Intake	>39% of calories	(van Dam et al. 2002)	Due to the characteristics of our dataset, only total fat could be used. This study was the best study that showed the risk that could be attributed to total fat intake.
Physical Activity	<3 score from the PAQ-C	(Plotnikoff et al. 2009)	This value has been used in a previous study assessing overall chronic disease risk in the same sample (Plotnikoff et al. 2009). A MET (Metabolic Equivalent of Task) value was not available from the PAQ-C (however, a relative MET score could be calculated, see Chapter 6 and Appendices D and F). Also, this cut off results in a inactivity rate similar rates in the Canadian Community Health Survey (CCHS) (Koezuka et al. 2006).

5.3.4. Statistical Analysis

Characteristics of participants were assessed using descriptive statistics and differences between boys and girls were determined using independent sample t-tests. The reported frequency of each diabetes risk factor was assessed using descriptive statistics. Differences in the proportion of participants reporting risk factors between sex, age and BMI groups were determined through chi-square tests. The total number of risk factors was calculated for each participant. For the risk factors of overweight and obesity, overweight individuals were considered to have one risk factor as a result of their weight. Those who were obese were considered to have 2 risk factors due to their weight status (i.e. they were considered both overweight and obese). Differences in the mean number of risk factors between sex and age groups were determined by independent sample t-tests and differences among BMI categories were assessed by one-way Analysis of Variance (ANOVA). Post hoc analysis for the ANOVA was conducted with a Scheffe test. When assessing diabetes risk factors by BMI category, BMI was not included as a risk factor. All statistical analyses were performed using the SPSS statistical software program (Version 16.0; SPSS Inc, Chicago).

5.4. Results

In total, 4981 students from 136 schools participated in the study. Students who did not report their sex (n = 58) were excluded from analysis as were those with extreme dietary intake or physical activity levels (n = 36) based on outlier analysis. A total of 4887 students were included in this analysis, however, sample sizes vary as some students did not answer all survey questions.

Age was reported by 4883 students, BMI values were available for 4131, dietary data were available for 4867 students and physical activity data were completed by 4371 students. A total of 3671 students had complete information for all risk factors.

Characteristics of participants, detailed in Table 5.2, show that boys and girls did not differ in age (mean age 13.6 years), but boys had significantly higher mean BMIs, physical activity scores and dietary intakes for all reported variables, with the exception of % of energy from carbohydrates, which was significantly higher among girls.

Table 5.2 Characteristics, Dietary Intake and Physical Activity Scores of Study Participants

Variable	Total n = 4887	Boys n = 2264	Girls n = 2623	P-Value
Age (years)	13.6 ± 1.2	13.6 ± 1.2	13.6 ± 1.2	0.852
BMI (kg/m^2)	20.8 ± 4.9	21.2 ± 5.2	20.5 ± 4.6	<0.001
Total Energy Intake (kcal)	2077 ± 1101	2398 ± 1204	1801 ± 913	<0.001
Carbohydrate (% kcal)	54.7 ± 11.4	53.4 ± 11.4	55.8 ± 11.2	<0.001
Fat (%kcal)	31.6 ± 9.2	32.2 ± 9.1	31.0 ± 9.2	<0.001
Protein (%kcal)	15.3 ± 5.3	15.8 ± 5.4	14.9 ± 5.2	<0.001
Glycemic Index	55.4 ± 7.3	56.1 ± 7.4	54.9 ± 7.1	<0.001
Glycemic Load	147 ± 81	168 ± 90	128 ± 68	<0.001
Fibre (g)	14.5 ± 9.8	16.0 ± 10.8	13.2 ± 8.6	<0.001
Magnesium (mg)	277 ± 158	313 ± 172	247 ± 138	<0.001
Vegetables and Fruit (svg/d)	5.1 ± 4.1	5.3 ± 4.4	4.8 ± 3.9	<0.001
PAQ-C Physical Activity Score	2.9 ± 0.7	3.0 ± 0.7	2.8 ± 0.6	<0.001

Data are Means ± SD

Differences between boys and girls were determined by student's t-tests

5.4.1. Diabetes Risk Factors: Boys Versus Girls

Results of the analysis of risk factors by sex (see Table 5.3) showed that the most frequently reported diabetes risk factors (highest average frequency to lower) included low fibre intake (53% for boys, 64% for girls), low physical activity score (50% for boys, 63% for girls), low magnesium intake (48% for boys, 50% for girls), high GL (56% for boys, 35% for girls) and high GI (39% for boys and 33% for girls). Low vegetable and fruit intake (30% for both boys and girls), high fat intake (22% for boys, 18% for girls) and overweight and obesity were less commonly seen risk factors.

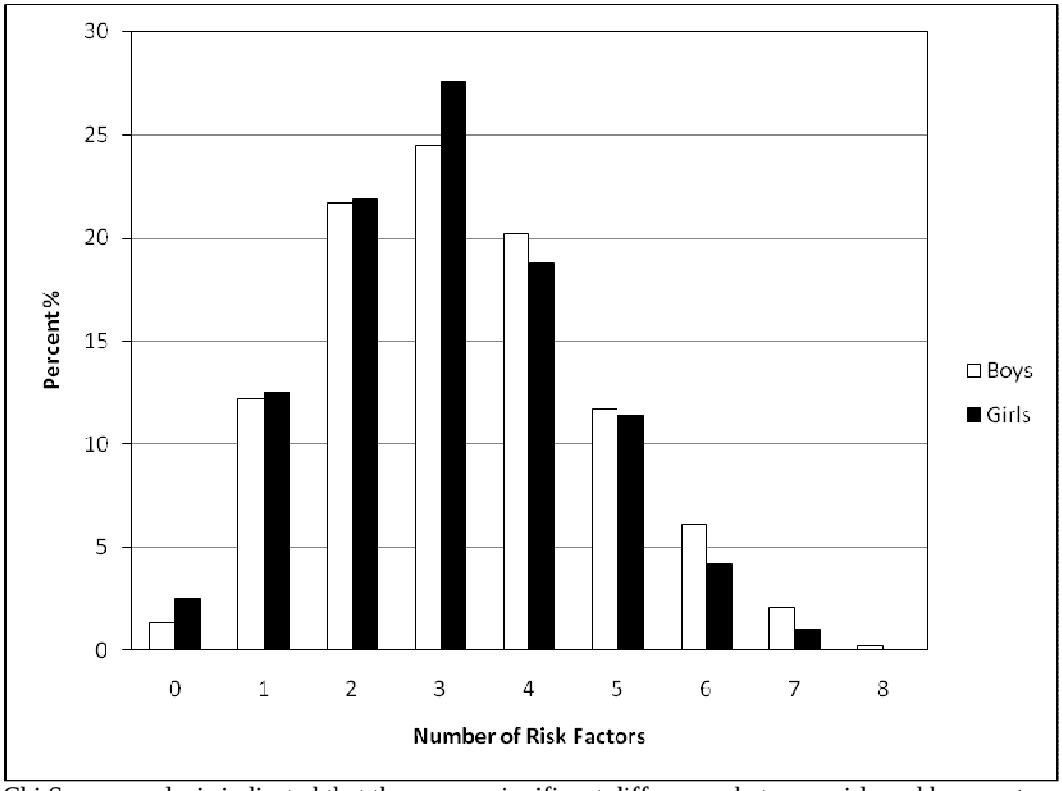
The proportion of students who were classified as overweight and obese was higher among boys (18.8% overweight, 7.8% obese) than girls (11.4% overweight, 4.5% obese) ($p < 0.001$). Boys were more likely than girls to have high dietary GI, GL, and fat intakes ($p < 0.001$ for all variables). Girls were more likely to have low fibre intakes and low physical activity scores ($p < 0.001$ for both variables). The proportion of students reporting low vegetable and fruit intake and low magnesium intake was similar between boys and girls. On average, boys had a greater total number of risk factors than girls (mean number of risk factors for boys was 3.2 vs. 3.0 for girls, $p < 0.001$). The distribution of risk factors by sex can be seen in Figure 5.1.

Table 5.3 Proportion of Participants with Diabetes Risk Factors: Boys Versus Girls

Risk Factor	Boys n = 2264 % Yes (n)	Girls n = 2623 % Yes (n)	P-Value
Weight Status IOTF Non-overweight Overweight Obese	 73.4 (1464) 18.8 (375) 7.8 (155)	 84.4 (1797) 11.4 (243) 4.5 (97)	 <0.001
High GI	39.1 (882)	33.0 (864)	<0.001
High GL	56.3 (1269)	35.1 (918)	<0.001
Low Fibre	52.9 (1191)	64.2 (1680)	<0.001
Low Magnesium	48.0 (1080)	49.5 (1294)	0.151
Low Vegetable and Fruit	30.3 (525)	30.4 (610)	0.509
High Fat	21.8 (492)	17.6 (460)	<0.001
Low physical activity	50.3 (1003)	63.4 (1500)	<0.001

Differences between boys and girls assessed by chi-square tests

Figure 5.1 Distribution of the Total Number of Risk Factors: Boys Versus Girls



Chi Square analysis indicated that there were significant differences between girls and boys $p < 0.05$.
Mean number of risk factors per group: 3.2 ± 1.5 (boys) vs. 3.0 ± 1.5 (girls) ($p < 0.001$)

5.4.2. Diabetes Risk Factors by Age Group

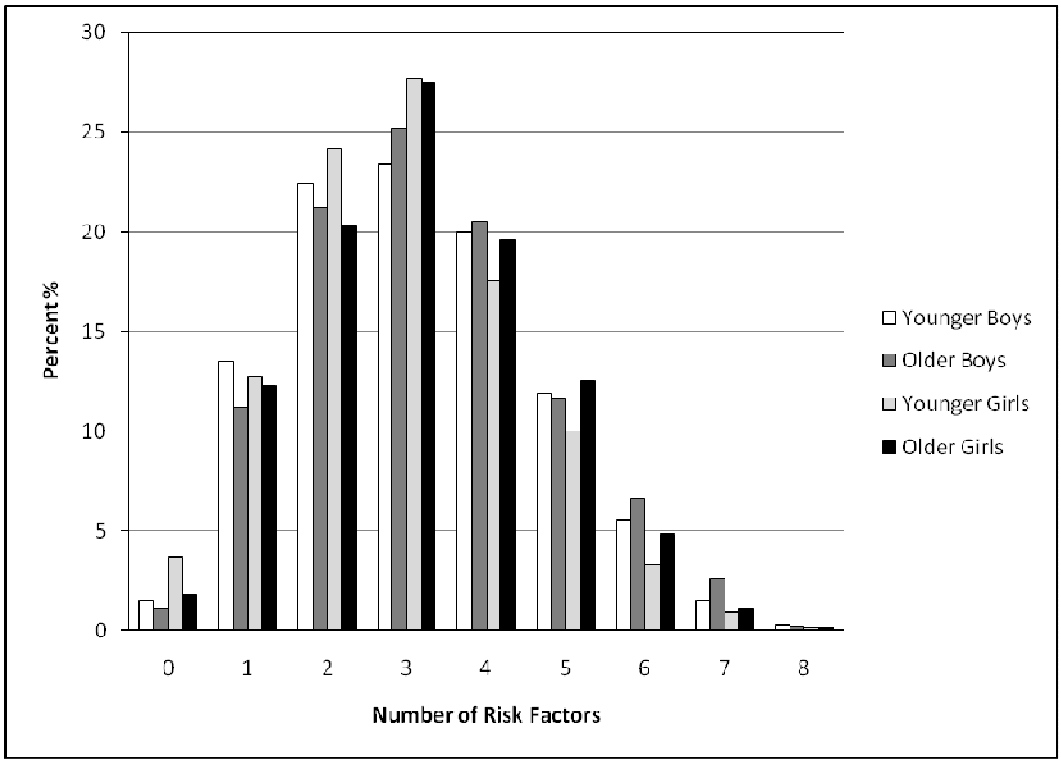
A comparison of the presence of diabetes risk factors between younger (9 to 13 yr) and older (14 to 17 yr) age groups is shown in Table 5.4. Compared to younger boys, older boys were more likely to have a high GL ($p < 0.001$), high fat intake ($p = 0.023$) and low physical activity score ($p < 0.001$), whereas younger boys were more likely to have low magnesium intakes ($p = 0.005$). Older girls were more likely to have a high GI ($p = 0.03$), low intake of vegetables and fruits ($p = 0.03$) and a low physical activity score ($p < 0.001$) compared to younger girls. Older boys showed a trend toward a higher total number of risk factors compared to younger boys (mean 3.3 vs. 3.1) ($p = 0.059$). Older girls had a significantly higher number of risk factors compared to younger girls (mean 3.1 vs. 2.9, $p = 0.001$). Figure 5.2 shows the distribution of the total number of risk factors by age and sex.

Table 5.4 Proportion of Participants with Diabetes Risk Factors by Age for Boys and Girls

	Boys			Girls		
Risk Factor	Younger (9-13yrs) n = 731 % Yes (n)	Older (14-17yrs) n = 1015 % Yes (n)	P-Value	Younger (9-13yrs) n = 1155 % Yes (n)	Older (14-17yrs) n = 1459 % Yes (n)	P-Value
Weight Status						
Non-overweight	65.0 (562)	71.9 (812)	0.166	84.2 (740)	84.0 (1057)	0.425
Overweight	17.7 (153)	19.6 (222)		10.7 (94)	11.8 (149)	
Obese	6.8 (59)	8.5 (96)		5.1 (45)	4.1 (52)	
High GI	37.4 (380)	40.6 (502)	0.065	31.0 (358)	34.5 (504)	0.031
High GL	51.0 (518)	60.7 (750)	<0.001	34.7 (397)	35.7 (521)	0.252
Low Fibre	54.8 (556)	51.3 (634)	0.056	63.3 (731)	65.0 (947)	0.201
Low Magnesium	51.0 (518)	45.4 (561)	0.005	48.4 (559)	50.3 (733)	0.181
Low Vegetable and Fruit	32.5 (249)	28.6 (275)	0.112	27.3 (248)	32.8 (360)	0.029
High Fat	19.9 (202)	23.5 (290)	0.023	18.0 (208)	17.3 (252)	0.329
Low physical activity	45.6 (394)	53.9 (608)	<0.001	57.0 (595)	68.3 (903)	<0.001

Differences between younger and older age groups were assessed by chi square analysis

Figure 5.2 Distribution of the Total Number of Risk Factors by Age and Sex



Chi Square analysis indicated that there were significant differences between older and younger age groups $p < 0.05$.
Mean number of risk factors per group: 3.3 ± 1.6 (older boys) vs. 3.1 ± 1.5 (younger boys) ($p = 0.059$); 3.1 ± 1.5 (older girls) vs. 2.9 ± 1.4 (younger girls) ($p = 0.001$).

5.4.3. Diabetes Risk Factors by BMI Categories

When the presence of diabetes risk factors was assessed by weight status categories (excluding BMI as a risk factor), it was found that the proportion of participants with low fibre intakes was highest among overweight participants (64%) compared to obese (59%) and non-overweight (56%) students ($p = 0.004$). The proportion of students reporting high total fat intakes and low physical activity levels increased across weight categories ($p = 0.007$ and $p = 0.014$ for fat and physical activity, respectively).

When results were separated by sex, a higher proportion of overweight boys reported low fibre and low magnesium intakes compared to non-overweight and obese boys ($p = 0.005$ for fibre, $p = 0.031$ for magnesium) (see Table 5.5). A greater proportion of non-overweight boys reported having a high glycemic load (61%) compared to overweight and obese boys (50% for both overweight and obese boys). The proportion of boys reporting low physical activity scores increased with weight status ($p < 0.001$). As seen with boys, overweight girls were more likely to report low fibre intakes compared to non-overweight or obese girls ($p = 0.012$), but no other differences between BMI categories were observed among girls.

The mean number of risk factors increased across BMI categories with non-overweight youth having an average of 2.8 risk factors, overweight youth having 3.0 risk factors and obese youth reporting 3.1 ($p <0.001$). Post hoc analysis showed that differences in mean scores were statistically significant between non-overweight and overweight ($p = 0.021$) and non-overweight and

obese subjects ($p = 0.006$), but not between overweight and obese subjects ($p = 0.482$). The distribution of the number of risk factors by BMI category can be seen in Figure 3.

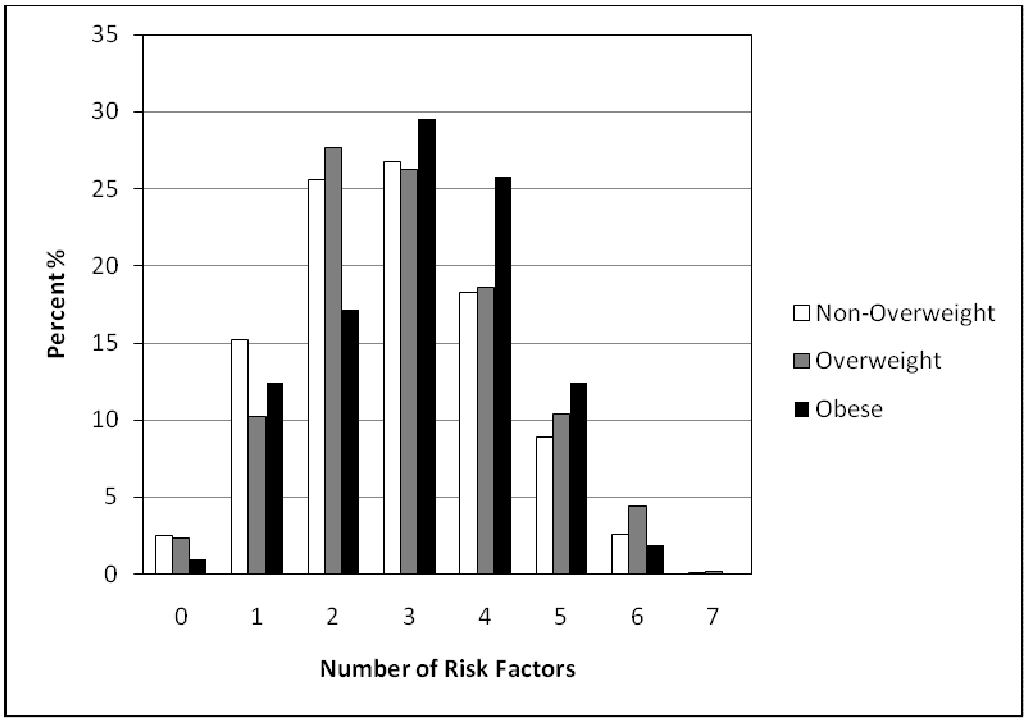
Table 5.5 Proportion of Participants with Diabetes Risk Factors by BMI Category*

	Boys				Girls			
Risk Factor	Non-Overweight n = 1456 % Yes (n)	Overweight n = 374 % Yes (n)	Obese n = 153 % Yes (n)	P-value	Non-Overweight n = 1791 % Yes (n)	Overweight n = 243 % Yes (n)	Obese n = 97 % Yes (n)	P-value
High GI	38.7 (564)	42.5 (159)	37.9 (58)	0.367	32.6 (583)	32.9 (80)	43.3 (42)	0.091
High GL	60.9 (887)	50.0 (187)	50.3 (77)	<0.001	36.1 (647)	32.5 (79)	40.2 (39)	0.363
Low Fibre	49.2 (717)	58.6 (219)	52.9 (81)	0.005	62.2 (1114)	71.2 (173)	69.1 (67)	0.012
Low Magnesium	45.0 (655)	52.4 (196)	49.0 (75)	0.031	47.9 (858)	49.8 (121)	51.5 (50)	0.692
Low Vegetable and Fruit	21.6 (314)	24.3 (91)	27.5 (42)	0.166	23.0 (412)	22.6 (55)	21.6 (21)	0.948
High fat	21.1 (307)	23.5 (88)	28.1 (43)	0.104	16.9 (302)	15.6 (38)	24.7 (24)	0.109
Low Physical Activity	46.7 (600)	52.2 (177)	65.2 (86)	< 0.001	62.9 (1021)	65.8 (146)	66.7 (58)	0.576

Differences between BMI categories were assessed using chi square analysis

* BMI categories defined according to IOTF guidelines

Figure 5.3 Distribution of the Total Number of Risk Factors by BMI Category



Chi Square analysis indicated that there were significant differences among BMI categories $p < 0.05$.
Mean number of risk factors per group: 2.8 ± 1.4^{a} (non-overweight), 3.0 ± 1.4^{b} (overweight), 3.1 ± 1.3^{bc} (obese) ($p < 0.001$), ^{a,b,c} indicates differences as determined by Post Hoc Analysis (Scheffe test).

5.5. Discussion

This study examined the presence of diabetes risk factors in a large sample of adolescents and assessed differences among age, sex and BMI groups. Although type 2 diabetes is most commonly seen among adults, early onset of the disease has been reported in increasing numbers in recent years (Dabelea et al. 1998; Hale and Rupert 2006; Urakami et al. 2005; Zdravkovic et al. 2004). The prevalence of obesity, one of the leading risk factors for diabetes, has also been increasing at alarming rates among youth (Shields 2006), leading to concern among health professionals about the future prevalence of diabetes both in youth and in the adult population. Results of diabetes prevention programs have shown that type 2 diabetes can be prevented through modification of lifestyle-related diabetes risk factors (Lindstrom et al. 2003; Ratner 2006). This study examined diabetes risk factors among youth and provides regionally specific information about the present lifestyle behaviours of Alberta adolescents and possible risk factors that could be targeted to reduce diabetes risk.

In the present study, 19% of boys and 11% of girls were overweight and 8% of boys and 5% of girls were obese. This is lower than the national prevalence of overweight and obesity reported by the Canadian Community Health Survey (CCHS) which found that in 2004, 32% of boys and 26% of girls were overweight and 11% of boys and 7% of girls were obese among youth aged 12 to 17 years (Shields 2006). Possible reasons for these differences include the use of self reported weights and heights, different definitions of overweight and obesity and the sampling technique used in the present study. Under-reporting of

body weight and over-reporting of height are frequent problems when using self-reported measurements. The Canadian Community Health Survey recorded both self reported and measured heights and weights and the self-reported prevalence of overweight and obesity were lower than the measured prevalence, with 24% of boys and 14% of girls being overweight and 6% of boys and 3% of girls being obese according to self-reported values (Shields 2006). A validation of the Web-SPAN survey, conducted on a subsample of 459 students, assessed both measured and self reported heights and weights. This validation study showed that using self reported heights and weights, 12% of students were considered overweight and 3% were obese and using measured heights and weights 17% were overweight and 6% were obese (Calengor 2007). This suggests that much of the difference between the results of the present study and those of the CCHS may be due to self-reporting. Another possible reason for differences between the present study and the CCHS were the different cut-offs used to assess overweight and obesity. The CCHS used data derived from the NHANES survey from the United States (Shields 2006), whereas the present study used IOTF (International Obesity Task Force) cut-offs, which are known to result in slightly different estimates of overweight and obesity (Wang and Wang 2002). Finally it is possible that, because of the non-random sampling technique used, response bias in this survey led to a lower obesity prevalence than would be seen in a truly random sample.

Weight status is a significant concern among adolescents in Alberta. Obesity is the strongest risk factor for diabetes in adults with relative risks for those who are obese ranging from 3.5 to 20 compared to normal weight people

(Hart et al. 2007; Hosseinpanah et al. 2007; Hu et al. 2001; Hui and Nelson 2006; Krishnan et al. 2007; Meisinger et al. 2006; Patja et al. 2005; Rana et al. 2007). In addition, obesity is highly prevalent among youth with type 2 diabetes with prevalence rates ranging from 72% to 100% in different clinics (Ehtisham et al. 2004; Hale and Rupert 2006; Harwell et al. 2001; McGrath et al. 1999; Ohki et al. 2004; Perez-Perdomo et al. 2005; Scott et al. 1997). Preventing obesity among adolescents is important for reducing risk of type 2 diabetes both during their youth and in adulthood.

In the present study, high GI and GL diets were frequently reported with 39% of boys and 33% of girls reporting a high GI diet and 56% of boys and 35% of girls reporting a high GL diet. Although this is the first study to assess the occurrence of high GI and GL diets among youth, previous studies from the United States and Europe have reported similar mean values with GIs, ranging from 56 to 60 and GLs ranging from 115 to 310 (Buyken et al. 2006; Davis et al. 2007; Ebbeling et al. 2003; Nielsen et al. 2005; Scaglioni et al. 2005; Verduci et al. 2007). The frequent reporting of high GI and GL diets seen in the present study indicates that the quality of carbohydrate being consumed by the adolescent population is not optimal. However, it should be noted that the cut-offs used were derived from adult data, and it is possible that adult recommendations are not appropriate for youth. In particular, dietary GL is highly related to total food intake, therefore high GL diets would be expected among growing youth with high energy needs. Because of this, an energy adjusted GL value may be more applicable, particularly to adolescent boys who have the highest energy needs.

Food and nutrient intakes observed in this study, including dietary fibre, magnesium intake, vegetable and fruit intake and the percent of energy coming from fat were similar to intakes observed in other North American studies. For example, results of the NHANES study in the United States showed that the mean fibre, magnesium and percent fat intakes of youth aged 12 to 19 were 13.9g/day, 253mg/day and 34%, respectively in the 2005-2006 data collection period (U.S.Department of Agriculture 2008). Results of the Canadian Community Health Survey have also shown similar levels of vegetable and fruit consumption as seen in the present study with approximately 48 % of youth in the 12 to 19 year age range consuming less than 5 servings of vegetables and fruit per day (Statistics Canada 2005).

The high proportion of youth reporting low fibre intakes in the present study is of concern, particularly in light of the conservative fibre cut-off used (the Adequate Intake for fibre in this age group is much higher - 38g/day for 14 to 18 year old boys and 26g/day for girls aged 9 to 18 years (Institute of Medicine 2002)). This suggests that high fibre foods such as vegetables, fruit, whole grains and legumes are not consumed by adolescents in the quantities needed for health. High fibre intake has been linked to decreased risk of type 2 diabetes (Meyer et al. 2000; Schulze et al. 2004). High fibre foods increase satiety (Nilsson et al. 2008), help to prevent obesity (Lindstrom et al. 2006), have lower GI values (Foster-Powell et al. 2002) and contain many beneficial nutrients such as magnesium and antioxidants (Zhou et al. 2004); all of which may help to decrease diabetes risk.

Magnesium is important in the insulin signalling pathway (Suarez et al. 1995) and low plasma levels and low intakes have been linked to insulin resistance and type 2 diabetes (Huerta et al. 2005; Lopez-Ridaura et al. 2004). The high frequency of low magnesium intakes observed in this study could put adolescents at risk of disease. Magnesium is commonly found in vegetables and fruits, legumes and whole grains. Again, these results show that the diets of adolescents do not contain adequate amounts of these nutrient dense foods.

Low vegetable and fruit intake was quite common in our sample, even with the conservative cut-off used of 2 servings per day. Vegetable and fruit intake has been shown to be protective against diabetes (Harding et al. 2008). Vegetables and fruit are high in fibre, have low energy density and a low GL and are also sources of antioxidants, all of which may contribute to their effect on diabetes risk.

High dietary fat intakes have been shown to increase diabetes risk. Much of this effect may be due to the effect of fat intake on body weight (Harding et al. 2004; van Dam et al. 2002), however, fat intake also affects circulating free fatty acid levels, which may affect both insulin sensitivity and beta-cell function (Dubois et al. 2004; Goodpaster and Wolf 2004; Kabir et al. 2005). High fat intakes were commonly reported in the present study and this may contribute to future disease risk in this population.

Physical activity scores seen in the present study were similar to those reported in other studies of Canadian youth using the PAQ-C. For example, among students with a mean age of 13 years, one study found that boys had a

mean PAQ-C score of 3.1 and girls had a mean score of 2.7 (Carter et al. 2001). As was observed in the CCHS, over 50% of youth in the present study were considered inactive. Physical activity decreases diabetes risk by helping to regulate body weight and body composition and by increasing insulin sensitivity. Short term increases in insulin sensitivity occur after every bout of physical activity (Nesher et al. 1985) and physical activity training increases long term insulin sensitivity (O'Gorman et al. 2006).

This study has shown that, in order to decrease the proportion of adolescents reporting diabetes risk factors, youth should maintain a healthy weight, consume more high fibre, high magnesium and low GI foods such as vegetables, fruit, legumes and whole grains, should limit high fat foods and should increase levels of physical activity.

5.5.1. Diabetes Risk Factors: Boys Versus Girls

The findings of the present study showed that boys were more likely than girls to be overweight or obese; a pattern also seen in the CCHS (Shields 2006). In addition, a study of adolescents in Quebec found that boys were more likely to be overweight or obese when they were 9 or 13 years of age, but rates were similar among boys and girls by age 16 (Lambert et al. 2008). Possible mechanisms for this difference include different patterns of growth and maturation between boys and girls or social or behavioural factors. It is well known that girls are more concerned about their body weight compared to boys (Field et al. 2001) and boys have also been found to have poorer dietary quality compared to girls (Hurley et al. 2009), but further research examining the reasons

behind these differences in overweight and obesity between the sexes is warranted. Boys were also more likely to have high GI and GLs and high fat diets. Also of concern for boys was the finding that, in spite of greater energy intakes, magnesium and vegetable and fruit intakes were not greater among boys, indicating that nutrient density may be lower in the diets of the boys. These results suggest that, a greater emphasis on weight management, carbohydrate quality and fat intake may be particularly beneficial for boys.

Girls were more likely than boys to have low fibre intakes and low physical activity levels. Lower energy requirements of girls may it difficult to achieve the same fibre intake as boys, however, promoting a high fibre diet among adolescent girls could be important for diabetes prevention. Lower physical activity levels among girls compared to boys is a pattern that is consistently seen in studies of children and adolescents (Koezuka et al. 2006). Promoting novel physical activity options for girls is challenging, but is especially important in this group.

On average, girls reported fewer diabetes risk factors than boys, suggesting that boys may be at higher risk of developing type 2 diabetes, based on their lifestyle habits. However, studies of type 2 diabetes among adolescents have shown that significantly more girls than boys are diagnosed with type 2 diabetes (Hale and Rupert 2006; Holl et al. 2003; Zdravkovic et al. 2004). It has been hypothesized that this is due to a greater drop in insulin sensitivity during puberty rather than because of differences in lifestyle habits between the sexes (Ball et al. 2006).

5.5.2. Diabetes Risk Factors by Age

The results of this study showed that older boys were more likely than younger boys to have a high GI, a low magnesium intake, a high fat diet and low physical activity levels. Older girls were more likely than younger girls to have a high GI, low vegetable and fruit intake and low physical activity levels. Older students also reported a greater total number of risk factors compared to their younger peers. This suggests that dietary quality and physical activity both decrease with age, indicating that the promotion of health behaviours is particularly important in the 14 to 17 year old age group.

5.5.3. Diabetes Risk Factors by BMI Categories

When students were categorized as being non-overweight, overweight or obese according IOTF cut-offs, it was found that fat intake increased across BMI categories. Overweight youth were more likely to have low fibre intakes than non-overweight or obese youth and a similar pattern was seen with magnesium (boys only). Non-overweight boys were more likely to have a high GL than overweight or obese boys and the proportion of boys reporting low physical activity levels increased with increasing BMI category.

Increasing fat intakes with increasing BMI is a pattern that is frequently, but not consistently, seen in the literature (Johnson et al. 2008; Storey et al. 2003). Previous studies have shown a negative linear trend between fibre intake and adiposity (Johnson et al. 2008), making the finding that more overweight students reported low fibre and magnesium intakes than obese students appear contradictory. A possible explanation for this result could be that the higher fibre

and magnesium intake is due to a higher caloric intake among obese youth. Alternatively, this effect may have been a result of a greater effort by obese students to eat more high fibre and high magnesium foods to control their weight.

The finding that a high GL was more common among non-overweight boys compared to overweight or obese boys, was also unexpected. The glycemic load is a measure that takes into account both carbohydrate quality and quantity. The observed result, therefore, may be due to carbohydrate quantity rather than quality. Higher carbohydrate intakes (and thereby higher GLs) may be indicative of a low fat diet. High fat intakes and lower carbohydrate intakes have been related to obesity in previous studies of adolescents (Storey et al. 2003). The result of the present study that high GLs were more common among non-overweight students may be indicative of a high carbohydrate, low fat dietary pattern.

The proportion of students with low physical activity increased with BMI category among boys but not among girls. The Canadian Community Health Survey observed similar results in its 2004 rotation (Shields 2006). Although there was a trend towards an increasing proportion of students with low physical activity levels with increasing weight among girls, this was not significant. It is possible that because physical activity levels are both low and less variable in girls, it is a less significant contributor to body weight control than in boys.

Overall, this analysis showed that overweight and obese youth had a greater number of risk factors for diabetes than their non-overweight peers. This suggests that overweight groups may be important targets for diabetes prevention

programs and risk factors that are particular problems for overweight and obese youth including fat and fibre intake for both boys and girls and magnesium intake and physical activity for boys.

5.5.4. Strengths and Limitations

This was a large study of Alberta adolescents that used validated tools to assess dietary intake and physical activity. To date, there have been few Canadian studies of this size evaluating the lifestyle practices of youth in this age group. The web-based method was also beneficial as it allowed students throughout a wide geographical area to participate in the study and allowed for complete anonymity.

One limitation of the present study was that our sample was not randomly selected. Although schools were randomly selected to participate, schools and students within those schools were able to opt out of the study. Therefore the present study represents a convenience sample. Our survey is also self-reported data. As discussed above, self reported heights and weights may have led to a lower reported proportion of overweight or obese students. Another limitation was that some variables important to diabetes risk were not part of the study. This survey did not include questions about ethnic background, family history of diabetes or socioeconomic status which are important contributors to diabetes risk. However the purpose of this study was to examine modifiable lifestyle risk factors for diabetes and to determine opportunities for disease prevention. In addition, several dietary variables such as whole grain intake and polyunsaturated fat intake were not available due to limitations of the dietary analysis database.

Finally, cut-offs for diabetes risk were based on values from adult literature and it is not known if these cut-offs are appropriate for a younger age group.

5.6. Conclusions

This study found that, in this large sample of youth from Alberta, Canada, lifestyle risk factors for type 2 diabetes were commonly reported between both sexes and among all age and BMI groups. Boys reported more risk factors compared to girls, older students reported more risk factors compared to younger students and students with a higher BMI reported more risk factors than students with a lower BMI. These findings suggest that the dietary and physical activity habits of Alberta youth are not optimal for the prevention of type 2 diabetes. Greater consumption of vegetables, fruit, legumes and whole grains and lower fat intakes and higher levels of physical activity would greatly improve the risk profile of this group.

5.7. References

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Chapter 6: Dietary and Physical Activity Diabetes Risk Factors and Insulin Sensitivity Among Alberta Adolescents

6.1. Preface

Previous studies (Chapters 3-5) showed that diabetes risk factors were commonly reported among Alberta youth, suggesting that their dietary and physical activity habits are not conducive to diabetes prevention. However, the health consequences of these risk factors were not clear. We therefore aimed to examine the link between diabetes risk factors and a physiological measure of diabetes risk: insulin sensitivity as measured by a Carbon 13 (C-13) glucose breath test.

The following chapter is based on combined data from the Healthy Hearts Initiative and the Web Survey of Physical Activity and Nutrition 2 (Web-SPAN 2). The Healthy Hearts Initiative is a prospective study of the health and fitness of Alberta youth that is being conducted in one Alberta school board district that encompasses several communities outside of the city of Edmonton. This study has been ongoing since 2000, but the present study used only data collected in the spring 2008 rotation of this program. Web-SPAN 2 was a study that employed the Web-SPAN survey (the same survey used in Chapters 4 and 5) to collect nutrition and physical activity information from a large sample of Alberta youth between January and December, 2008. Web-SPAN participants included in this analysis were students aged 10 to 14 who completed both the Web-SPAN 2 survey and completed a Carbon 13 (C-13) glucose breath test as part of the Healthy Hearts Initiative.

6.2. Introduction

Type 2 diabetes is a disease caused by an interaction between genetic predisposition and lifestyle factors. Among adults, the relationship between lifestyle factors and type 2 diabetes risk has been thoroughly studied. Lifestyle factors that influence diabetes risk among adults include obesity (Rana et al. 2007), high glycemic index (GI) and glycemic load (GL) diets (Barclay et al. 2008), low fibre intake (Meyer et al. 2000), low magnesium intake (Lopez-Ridaura et al. 2004), low vegetable and fruit intake (Liu et al. 2004), high fat intake (van Dam et al. 2002) and low physical activity levels (Hu et al. 1999). Risk factors for diabetes are important to examine as they help to identify those at greater risk for disease, provide evidence for the need to intervene in those at high risk and inform strategies to decrease disease risk.

Although type 2 diabetes has traditionally been considered a disease of adulthood, the prevalence of this disease in the adolescent population has risen in recent years (Dabelea et al. 1998; Hale and Rupert 2006; Urakami et al. 2005; Zdravkovic et al. 2004). Because early onset type 2 diabetes is a new and relatively uncommon occurrence, risk factors for type 2 diabetes in youth, particularly lifestyle factors, are not as well defined as for adults. When examining diabetes risk factors among youth, it is necessary to define risk factors by adult standards and extrapolate to children. Although this approach is not ideal, current evidence suggests that the adult and early forms of the disease have similar risk factors, with both adult and child studies finding obesity, family

history and race, to be strong risk factors of type 2 diabetes (Meigs et al. 2000; Morrison et al. 2008; Zdravkovic et al. 2004).

Further study of diabetes risk factors among youth is limited by the relative rarity of type 2 diabetes in this age group. A possible solution to this problem is to assess the relationship between lifestyle factors and a measure of diabetes risk that is more commonly seen in the adolescent population, such as insulin resistance. Adolescents with insulin resistance are at greater risk of developing type 2 diabetes in the future (Morrison et al. 2008).

The gold standard for measuring insulin resistance is the hyperinsulinemic euglycemic clamp method. However, this method is costly, time consuming and invasive. Other methods of measuring insulin resistance have been created, the most commonly used in epidemiological settings being measures such as HOMA (Homeostatic Model Assessment) and QUICKI (Quantitative Insulin Sensitivity Check Index) which use fasting blood glucose and insulin to calculate insulin sensitivity scores. However, these methods still require blood samples which are not ideal when assessing a large population of adolescents. Another method of measuring insulin sensitivity that has recently been used is the Carbon 13 (C-13) glucose breath test. In this procedure, C-13 labelled glucose is ingested and the speed with which it is oxidized is assessed by measuring the appearance of the labelled carbon exhaled in the breath. The link is made between the results of this test and insulin sensitivity based on the assumption that decreased insulin sensitivity results in a reduced rate of glucose oxidation. Previous studies have shown that breath test results correlate with insulin resistance as measured by

clamp methods (Lewanczuk et al. 2004). The purpose of the present study was to evaluate the ability of different statistical models to assess the relationship between previously identified lifestyle risk factors for type 2 diabetes (Chapter 5) and insulin sensitivity as measured by the C-13 glucose breath test.

6.3. Methods

This study was a secondary analysis of data collected as part of the Healthy Hearts Initiative. The Healthy Hearts Initiative is an annual survey of the health and fitness of over 2000 school children aged 6 to 18 within one Alberta School District that has been ongoing since 2004. This school district encompasses several rural and urban communities surrounding the city of Edmonton, Alberta. Data used in the present study were collected in the spring 2008 rotation of the study. Ethical approval for the Healthy Hearts study was obtained from the Health Research Ethics Review Board for the Faculty of Medicine and Dentistry at the University of Alberta (see Appendix E).

6.3.1. Participants

Participants for the present analysis consisted of a subset of participants aged 10 to 14 years from the Healthy Hearts Initiative who completed both a Web Survey of Physical Activity and Nutrition (Web-SPAN) and a C-13 glucose breath test for insulin sensitivity during the 2008 data collection period. Before participation in the study, written informed consent was obtained from parents and students provided verbal assent.

6.3.2. Measures

Variables assessed in this study included measured height and weight, dietary intake and physical activity status of the students as measured by the Web-SPAN, and a C-13 glucose breath test for insulin sensitivity.

6.3.2.1. Height, Weight and BMI

Height and weight were measured on site at the schools in duplicate, using a medical stadiometer (Seca Portable Model 214) and a digital scale (Seca 882 Digital Floor scale) and the mean of the two measured values was used. Body Mass Index (BMI) was then calculated (kg/m^2).

6.3.2.2. Web-SPAN Survey

The Web Survey of Physical Activity and Nutrition is an on-line tool that measures dietary intake, physical activity and environmental and social determinants of health behaviours through a series of questionnaires. In the present analysis, only the dietary intake and physical activity assessment portions of the tool were used.

6.3.2.2.1. Dietary Intake

Dietary Intake is assessed in the Web-SPAN questionnaire by the *Food Behaviour Questionnaire;* a tool developed by Dr. Rhona Hanning from the University of Waterloo (Hanning et al. 2003). The Food Behaviour Questionnaire is a web-based 24-hour recall tool, in which students record all food and beverages consumed in the previous 24 hours, selecting from a list of over 500 foods. This tool also includes cues for frequently missed foods such as toppings, and beverages. Nutrient analysis of the recalled dietary intakes was conducted

using the ESHA Food Processor (version 7.9, ESHA Research, Salem, OR) and the 2001 Canadian Nutrient File (Health Canada 2001) database. In addition, the number of servings consumed from each of the food groups according to Eating Well with Canada's Food Guide (Health Canada 2007) was calculated.

Dietary GI and GL were also calculated by the Web-SPAN. For this calculation, each carbohydrate containing food in the Web-SPAN database was assigned a GI value based on published values (Foster-Powell et al. 2002; University of Sydney 2005). As outlined below, daily dietary GI and GL were calculated by the method described by (Sahyoun et al. 2005).

GL/svg = GI x available carbohydrate /100

Where available carbohydrate = total carbohydrate - fibre

The daily GL for each subject was calculated by multiplying the number of servings of each food by the GL/serving value, and the GL values from all the foods eaten were summed.

Daily GL = $\sum$(GL per serving x # servings of each food)

Where GL per serving is the GL of the portion size of each food in the Food Behviour Questionnaire (1 serving was usually equal to 1 serving from Canada's Food Guide to Healthy Eating); and the number of servings equals the number of servings that were reported to be eaten by the student.

Daily GI was calculated as:

Daily GI = (Daily GL/available carbohydrate) x 100

6.3.2.2.2. Physical Activity

Physical activity was measured using an on-line version of the Physical Activity Questionnaire for Older Children (PAQ-C) (Kowalski et al. 2004). Physical activity is assessed by this tool based on self reported physical activities performed in the last 7 days. Activities assessed include sport participation, active transport, activity during the school day, activity after school and activity on the weekends. The PAQ-C scores range from 1 to 5 with 1 indicating a low level of physical activity and 5 indicative of a high level. A second measure of physical activity was also calculated from variables in the PAQ-C score. Previous studies have shown that it is possible to assign a relative Metabolic Equivalent of Task (MET) score to the self reported frequencies of different physical activities as reported by youth (Klentrou et al. 2003; McMurray et al. 2000). The method used for calculating a relative MET score from PAQ-C values can be found in Appendix F.

6.3.2.3. C-13 Glucose Breath Test for Insulin Sensitivity

The C-13 glucose breath test was used as a measure of insulin sensitivity (Lewanczuk et al. 2004). Participants provided a baseline breath sample following an overnight fast by exhaling one normal breath of air through a straw into a 10ml gas sampling tube. Participants then consumed a 100ml beverage containing 25mg of C-13 labelled glucose, 15g of unlabelled dextrose and orange flavouring. After 90 minutes, a second breath sample was taken. The C-13 content of all breath samples was measured at the Isodiagnostika laboratories using an AP2003 isotope ratio mass spectrometer (Analytical Precision Limited,

Cheshire, U.K.). The Insulin Sensitivity Score (ISS) for each participant was calculated as the difference in the C-13 content between the baseline breath sample and the 90 minute sample (δo/oo).

6.3.3. Statistical Modeling of Lifestyle Risk Factors for Diabetes

The association of diabetes risk factors with ISS was tested in three ways: (1) using continuous risk factor variables (2) using dichotomous variables and (3) using composite diabetes risk scores. These methods were used to determine which model best explained changes in ISS and, in the case of dichotomous variables, to test the effectiveness of cut-offs used in Chapter 5. Risk factors included in each of these models included obesity, GI, GL, fibre, magnesium, vegetable and fruit intake, fat intake and physical activity (as seen in Chapter 5). The methods for creating the dichotomous risk factors and the composite diabetes risk scores are outlined below.

6.3.3.1. Defining Dichotomous Diabetes Risk Factors

Dichotomous diabetes risk factors were defined according to the method discussed in Chapter 5. Briefly, all large, longitudinal cohort studies examining the relationship between dietary and physical activity risk factors and type 2 diabetes risk were compiled and summarized. A table containing these summaries for each risk factor can be found in Appendix C. Based on the findings of these studies and expert consultation, cut-offs for each variable were determined as outlined in Table 6.1 (See Chapter 5 and Appendix D for detailed rationale for these cut-offs).

6.3.3.2. Creating a Composite Diabetes Risk Score

To determine the best method for constructing a composite diabetes risk score based on dietary and physical activity risk factors for diabetes, a literature search was conducted to determine what diabetes risk scores exist for the adult population and to evaluate their ability to be used as a model for our composite diabetes risk score (Chapter 2; Table 2.1). As the variables used in these scores were not comparable to data available in the Web-SPAN survey, none of these scores could be used as the basis of our composite diabetes risk score for youth. Therefore, diabetes risk factors identified in Chapter 5 were used to create the composite diabetes risk score. As the best method of weighting these risk factors in a composite diabetes risk score was unclear, three methods of weighting the variables were used:

1. Each risk factor could be weighted equally so the risk score for each person would be the sum of the number of risk factors they reported.
2. Each risk factor could be weighted according to the reported relative risk of diabetes associated with the cut-off chosen according to unadjusted models (adjusted for only age and sex).
3. Each risk factor could be weighted according to the reported relative risk of diabetes associated with the cut-off chosen according to multivariate adjusted models (adjusted for a wide variety of variables including such factors as age, sex, ethnicity, family history of diabetes, blood pressure, blood lipids, dietary intake and physical activity).

For the variables of obesity and physical activity, a wide range of weights for their effects on diabetes risk were evident from the literature. For these two variables the range of possible weights was tested by creating different variations of the composite risk score using the strongest and weakest weights suggested in the literature. In addition, when data collection was complete, it was found that only a small subset of the total sample had completed the physical activity portion of the Web-SPAN survey. Therefore, different variations of the composite risk score either including or excluding physical activity made it possible to both use the full sample and determine if including physical activity in the composite score was beneficial. The decisions made for each risk factor are described in detail in Appendix D and cut-offs, weighting, references and rationale are summarized in Table 6.1.

Table 6.1 Cut-offs and Relative Risks for Diabetes Risk Factors

Variable	Cut-off	Unadjusted Relative risk	Adjusted Relative Risk	Reference	Reason for using
Overweight and Obesity	IOTF cut-offs for overweight and obesity by age and sex.	Overweight: 2.6-7.0 Obese: 5.8 – 18.6	Overweight: 1.8-7.6 Obese: 3.5-20	Hart, 2007, Krishnan, 2007, Hosseinpanah, 2007, Rana, 2007, Hu 2001, Meisinger, 2006	Appropriate for children. Reference values come from an international sample. Studies have shown that there is increasing diabetes risk with increasing BMI category, however, for children, only overweight and obese classifications exist (no class I, II, III obesity).
High GI	> 58	n/a	1.4	Barclay, 2008	This study was the best available source of information. As a meta-analysis, it included information from many studies.
High GL	> 142	n/a	1.3	Barclay, 2008	This study was the best available source of information. As a meta-analysis, it included information from many studies.
Low Fibre Intake	< 14.8g	1.89 (0.53)	1.28 (0.78)	Schulze, 2004	Both of these studies are North American and had similar results therefore the mean value between the two studies was taken.
Low Magnesium Intake	< 220mg/d < 280mg/d males	1.82 (0.55)	1.39 (0.72)	(Lopez-Ridaura et al. 2004)	This study was the best study available that measured magnesium in units comparable to the Web-SPAN survey (mg/d).
Low Vegetable and Fruit Intake	< 2 servings/day	n/a	1.3 (0.77)	Liu, 2004	This study used portion sizes similar to sizes from Canada's food guide.
High Fat Intake	> 39% of calories	1.88	1.27	Van Dam, 2002	Due to the characteristics of our dataset, only total fat could be used. This study was the best study that showed the risk that could be attributed to total fat intake.

Low Physical Activity	< 3	1.7 – 3.3 (0.3-0.6)	1.16 -1.96 (0.51-0.86)	Plotnikoff, 2009	This value has been used in a previous study assessing overall chronic disease risk in the same sample (Plotnikoff et al. 2009). A MET (Metabolic Equivalent of Task) value was not available from the PAQ-C. Also, this cut off results in a inactivity rate similar rates in the Canadian Community Health Survey (CCHS) (Koezuka et al. 2006).

As mentioned above, several composite risk factor scores, each using different combinations of risk factors and weights, were calculated. In total there were 14 composite diabetes risk score variations to be tested:

Equal weights

DRS #1 = Overweight + Obesity + High GI + High GL + Low Fibre + Low Mg + Low V&F + High fat + Low PA

DRS #2 = Overweight + Obesity + High GI + High GL + Low Fibre + Low Mg + Low V&F + High fat

Unadjusted Weights

DRS #3 (weighted low for overweight and obesity and low for PA) = Overweight * 2.6 + Obesity * 5.8 + High GI * 1.4 + High GL * 1.3 + Low Fibre * 1.89 + Low Mg * 1.82 + Low V&F * 1.3 + High fat * 1.88 + Low PA * 1.7

DRS #4 (weighted low for overweight and obesity and high for PA) = Overweight * 2.6 + Obesity * 5.8 + High GI * 1.4 + High GL * 1.3 + Low Fibre * 1.89 + Low Mg * 1.82 + Low V&F * 1.3 + High fat * 1.88 + Low PA * 3.3

DRS #5 (weighted low for overweight and obesity and PA not included) = Overweight * 2.6 + Obesity * 5.8 + High GI * 1.4 + High GL * 1.3 + Low Fibre * 1.89 + Low Mg * 1.82 + Low V&F * 1.3 + High fat * 1.88

DRS #6 (weighted high for overweight and obesity and low for PA) = Overweight * 7 + Obesity * 18.6 + High GI * 1.4 + High GL * 1.3 + Low Fibre * 1.89 + Low Mg * 1.82 + Low V&F * 1.3 + High fat * 1.88 + Low PA * 1.7

DRS #7 (weighted high for overweight and obesity and high for PA) = Overweight * 7 + Obesity * 18.6 + High GI * 1.4 + High GL * 1.3 + Low Fibre * 1.89 + Low Mg * 1.82 + Low V&F * 1.3 + High fat * 1.88 + Low PA * 3.3

DRS #8 (weighted high for overweight and obesity and PA not included) = Overweight * 7 + Obesity * 18.6 + High GI * 1.4 + High GL * 1.3 + Low Fibre * 1.89 + Low Mg * 1.82 + Low V&F * 1.3 + High fat * 1.88

Adjusted Weights

DRS #9 (weighted low for overweight and obesity and low for PA) = Overweight * 1.8 + Obesity * 3.5 + High GI * 1.4 + High GL * 1.3 + Low Fibre * 1.28 + Low Mg * 1.39 + Low V&F * 1.3 + High fat * 1.27 + Low PA * 1.16

DRS #10 (weighted low for overweight and obesity and high for PA) = Overweight * 1.8 + Obesity * 3.5 + High GI * 1.4 + High GL * 1.3 + Low Fibre * 1.28 + Low Mg * 1.39 + Low V&F * 1.3 + High fat * 1.27 + Low PA * 1.96

DRS #11 (weighted low for overweight and obesity and PA not included) = Overweight * 1.8 + Obesity * 3.5 + High GI * 1.4 + High GL * 1.3 + Low Fibre * 1.28 + Low Mg * 1.39 + Low V&F * 1.3 + High fat * 1.27

DRS #12 (weighted high for overweight and obesity and low for PA) = Overweight * 7.6 + Obesity * 20 + High GI * 1.4 + High GL * 1.3 + Low Fibre * 1.28 + Low Mg * 1.39 + Low V&F * 1.3 + High fat * 1.27 + Low PA * 1.16

DRS #13 (weighted high for overweight and obesity and high for PA) = Overweight * 7.6 + Obesity * 20 + High GI * 1.4 + High GL * 1.3 + Low Fibre * 1.28 + Low Mg * 1.39 + Low V&F * 1.3 + High fat * 1.27 + Low PA * 1.96

DRS #14 (weighted high for overweight and obesity and PA not included) = Overweight * 7.6 + Obesity * 20 + High GI * 1.4 + High GL * 1.3 + Low Fibre * 1.28 + Low Mg * 1.39 + Low V&F * 1.3 + High fat * 1.27

6.3.4. Statistical Analysis

Mean values for each of the risk factors were calculated and differences between girls and boys were determined with student's t-tests. In addition, t-tests were used to assess differences in mean values between those who did and did not complete the PAQ-C questionnaire. The proportion of students reporting each risk factor was also determined and differences between the sexes were assessed using chi-square tests. Differences in the proportion of students reporting each risk factor between those who did and did not complete the PAQ-C questionnaire were also assessed using chi-square tests.

The associations between risk factors for diabetes to and ISS were assessed using three models; using continuous risk factor variables, using dichotomous diabetes risk factors and using the composite diabetes risk scores. The relationship between continuous risk factor, as well as age and sex and ISS

were assessed using multiple linear regression. Separate models were used for the whole sample, for boys and for girls. In addition, a multiple regression model including only those who had completed the PAQ-C questionnaire was constructed. Separate models were not used for sex in this sample as the small sample size greatly reduced the power of this analysis. The relationship between dichotomous risk factors for diabetes and ISS was also assessed using multiple linear regression models. Again, separate models were used for boys and girls and for students who completed the PAQ-C questionnaire.

The association between each version of the composite diabetes risk score with ISS was assessed using separate multiple regression models for each version of the composite diabetes risk score and the percentage of variance explained by the models was compared. Hierarchical analysis was used to determine how much of the variability of the ISS could be explained by the composite diabetes risk score in addition to the variance explained by age and sex. Analyses were not divided by sex as the sample size for models containing physical activity were too small to have adequate power.

6.4. Results

A total of 318 students aged 10 to 14 were included in this analysis. However, it should be noted that only about a quarter (n = 82) of the students completed the physical activity portion of the Web-SPAN survey. Therefore, analyses including physical activity were conducted separately with this smaller group and differences between students who did and did not complete the physical activity questionnaire were assessed. Analyses conducted using the

whole sample (n = 318) were separated by sex, as initial analyses showed differences in results between the sexes. Analyses conducted in the smaller group who completed the PAQ-C were not separated by sex as the smaller sample size greatly reduced the power of this sub-sample. The presence of outliers was assessed by examining Cook's distances and leverage values. Participants who had leverage values twice that of the mean were considered possible outliers, however, as none of these possible outliers significantly affected the outcome of the multiple regression models when removed, all participants were included in the final analysis.

6.4.1. Characteristics of Participants and Risk Factor Frequency

Students in this study ranged in age from 10 to 14 years with a mean age of 11.7 years. The characteristics of participants and mean values for each of the risk factors assessed are shown in Table 6.3. Results of student's t-tests showed that boys had higher dietary GLs compared to girls ($p = 0.03$) and girls had a higher mean ISS compared to boys ($p = 0.02$).

Table 6.2 Participant Characteristics and Mean Values for Risk Factor Variables by Sex

Variable	Total N = 318	Boys N = 137	Girls N = 181	P-value
Age	11.6 ± 1.5	11.7 ±1.2	11.6 ± 1.2	0.786
BMI (kg/m^2)	19.8 ± 3.7	19.9 ± 3.8	19.7 ±3 .7	0.590
GI	55.6 ± 6.8	55.7 ± 7.5	55.5 ± 6.28	0.782
GL	132.5 ± 63.2	141.3 ± 72.6	125.7 ± 54.9	0.030
Fibre (g)	14.2 ± 8.3	14.8 ± 9.1	13.8 ± 7.9	0.314
Magnesium (mg)	262.4 ± 131.9	272.0 ± 144.2	255.3 ± 122.9	0.265
Vegetable and Fruit (Servings)	4.8 ± 3.6	4.9 ± 3.6	4.9 ± 3.7	0.998
Percent Fat (% kcal)	31.0 ± 8.5	30.6 ± 7.9	31.1 ± 8.9	0.549
Insulin Sensitivity Score	17.2 ± 5.0	16.5 ± 4.7	17.8 ± 5.0	0.022

Data are means ± SD

Differences between boys and girls were assessed using student's T-tests.

Characteristics of participants who had completed the PAQ-C portion of Web-SPAN were determined. As observed in the whole sample, of those who completed the PAQ-C, boys had a significantly higher GL than girls ($p = 0.014$). The difference observed in ISS between the sexes was not significant in the smaller group. Comparisons between students who did and did not complete the PAQ-C showed that participants who completed the PAQ-C were slightly older ($p = 0.003$) and had a higher GL ($p = 0.030$) compared to those who did not (data tables for these analyses can be found in Appendix G).

The proportion of students reporting each of the diabetes risk factors are found in Table 6.3 for the whole sample ($n = 318$). Chi-squared analysis showed that boys were more likely to report the risk factors of high GL and low magnesium intake compared to girls. Students who had completed the PAQ-C portion of the Web-SPAN questionnaire ($n = 82$) were less likely to have low magnesium intakes than those who had not completed the PAQ-C (Data tables for these analyses can be found in Appendix G).

Table 6.3 Proportion of Students Reporting Diabetes Risk Factors by Sex

Variable	Total N = 318 % (n)	Boys N = 137 % (n)	Girls N = 181 % (n)	P-Value
Not Overweight Overweight Obese	75.8 (241) 18.2 (58) 6.0 (19)	74.5 (102) 17.5 (24) 8.0 (11)	76.8 (139) 18.8 (34) 4.4 (8)	0.401
High GI	36.2 (115)	35.6 (48)	37.0 (67)	0.441
High GL	33.6 (107)	41.5 (56)	28.2 (51)	0.009
Low Fibre	60.1 (191)	57.8 (78)	62.4 (113)	0.212
Low Magnesium	52.2 (166)	61.5 (83)	45.9 (83)	0.005
Low Vegetable and Fruit Servings	23.0 (73)	23.7 (32)	22.7 (41)	0.479
High Percent Fat	15.4 (49)	14.1 (19)	16.6 (30)	0.318

Differences between boys and girls were assessed using chi-square tests

6.4.2. Associations between Continuous Risk Factors for Diabetes and Insulin Sensitivity

Multiple regression analysis was performed to evaluate the associations between each of the risk factor variables and ISS. Three models were used: one for the whole sample, one for boys and one for girls (see Table 6.4). The model including both boys and girls accounted for 53% of the variation in ISS ($F [9, 306] = 38.837$, $p < 0.001$). Results of this analysis showed that, age and sex contributed significantly to the model (age: $\beta = -0.446$, $p < 0.001$; sex: $\beta = 0.096$, $p = 0.017$), but of the risk factors, only BMI was significantly associated with ISS. However, the contribution made by GI to the model approached significance ($p = 0.082$). When the analysis was separated by sex, the model for boys explained 55% of the variation in ISS ($F[8, 126] = 18.975$, $p < 0.001$) and the model for girls accounted for 53% ($F[8, 172] = 23.873$, $p < 0.001$). BMI continued to be significantly associated with ISS in both boys and girls (boys: $\beta = -0.520$; girls: $\beta = -0.413$, $p < 0.001$ for boys and girls) and GI was significantly associated with ISS for boys ($\beta = -0.185$ $p = 0.02$) but not for girls.

Table 6.4 Associations between Continuous Dietary Diabetes Risk Factor Variables and Insulin Sensitivity Score for Boys and Girls

	Insulin Sensitivity								
	Total			Boys			Girls		
Variable	β	Partial R^2	P-value	β	Partial R^2	P-value	β	Partial R^2	P-value
Age (yrs)	-0.446	0.279	<0.001	-0.427	0.266	<0.001	-0.463	0.284	<0.001
Sex	0.096	0.018	0.017	n/a	n/a	n/a	n/a	n/a	n/a
BMI (kg/m^2)	-0.457	0.291	<0.001	-0.520	0.354	<0.001	-0.413	0.241	<0.001
GI	-0.086	0.010	0.082	-0.185	0.041	0.022	-0.027	0.001	0.675
GL	-0.057	0.002	0.425	-0.081	0.004	0.471	-0.014	<0.001	0.822
Fibre (g)	-0.064	0.003	0.348	0.072	0.003	0.523	-0.139	0.014	0.117
Magnesium (mg)	0.016	<0.001	0.839	-0.089	0.004	0.500	0.058	0.002	0.558
Vegetable and Fruit Intake (servings)	0.021	<0.001	0.707	-0.029	0.001	0.735	0.049	0.003	0.513
Percent Fat (% kcal)	-0.011	<0.001	0.797	0.012	<0.001	0.857	-0.027	0.001	0.623

β = Standardized Coefficient

Total: F [9, 306] = 38.837, $p < 0.001$, $R^2 = 0.533$; boys: F[8, 126] = 18.975, $p < 0.001$, $R^2 = 0.546$; girls: F[8, 172] = 23.873, $p < 0.001$, $R^2 = 0.526$

Because the PAQ-C portion of the Web-SPAN questionnaire was not completed by all participants, a separate multiple regression model was used to determine if physical activity was related to ISS in the smaller group of participants who completed this portion of the study. The analysis in this group was not divided by sex due to the smaller sample size. This model (Table 6.5) explained 54% of the variation in ISS, and similar to results of the whole sample, age and BMI were significantly associated with ISS and GI approached significance ($p = 0.072$). However, in this analysis, sex was not significantly related to ISS. This model also showed that PAQ-C score was not significantly associated with ISS. The relationship between a second measure of physical activity, a MET score calculated from PAQ-C variables, and ISS was also assessed. As seen with the PAQ-C, the MET score was not associated with ISS (Table 6.6).

Table 6.5 Associations between Continuous Dietary and Physical Activity Diabetes Risk Factor Variables and Insulin Sensitivity Score Using the PAQ-C to Measure Physical Activity

Variable	β	Partial R^2	P-value
Age (yrs)	-0.381	0.214	<0.001
Sex	0.021	0.001	0.805
BMI (kg/m^2)	-0.460	0.275	<0.001
GI	-0.193	0.045	0.072
GL	-0.108	0.008	0.441
Fibre (g)	-0.165	0.020	0.229
Magnesium (mg)	-0.016	<0.001	0.918
Vegetable and Fruit Intake (servings)	0.099	0.013	0.332
Percent Fat (% kcal)	0.023	0.001	0.795
PAQ-C Score	-0.014	<0.001	0.877

β = Standardized Coefficient

$F[10, 71] = 8.365$, $p < 0.001$, $R^2 = 0.541$

Table 6.6 Associations between Continuous Dietary and Physical Activity Diabetes Risk Factor Variables and Insulin Sensitivity Score Using a MET Score to Measure Physical Activity

Variable	β	Partial R^2	P-value
Age (yrs)	-0.400	0.190	<0.001
Sex	0.043	0.003	0.617
BMI (kg/m^2)	-0.374	0.194	<0.001
GI	-0.120	0.017	0.230
GL	-0.041	0.001	0.740
Fibre (g)	-0.147	0.015	0.248
Magnesium (mg)	-0.042	0.001	0.773
Vegetable and Fruit Intake (servings)	0.143	0.022	0.168
Percent Fat (% kcal)	-0.018	<0.001	0.839
MET Score	-0.058	0.006	0.484

β = Standardized Coefficient, SE = Standard Error
$F[10, 87] = 8.226$, $p < 0.001$, $R^2 = 0.486$

6.4.3. Associations between Dichotomous Risk Factors for Diabetes and Insulin Sensitivity

The relationship between dichotomized risk factors for type 2 diabetes and ISS was examined using two multiple regression models. Table 6.7 shows the regression model for the whole sample and Table 6.8 shows the model including only participants who had completed the PAQ-C questionnaire. Results were not separated by sex as no significant differences between the sexes were observed when this analysis was conducted. These results showed that age ($\beta = -0.570$, $p < 0.001$), sex ($\beta = 0.111$, $p = 0.012$), overweight ($\beta = -0.295$, $p < 0.001$), obesity ($\beta = -0.238$, $p < 0.001$) and GI ($\beta = -0.096$, $p = 0.028$) were significantly associated with ISS in the model using the whole sample, explaining 47% of the variation in ISS ($F[10, 305] = 26.861$, $p<0.001$). Among participants who completed the physical activity questionnaire, only age, overweight and obesity were significantly associated with ISS ($F[11, 69] = 4.930$, $p<0.001$, $R^2 = 0.440$).

Table 6.7 Associations between Dichotomous Dietary Diabetes Risk Factors and Insulin Sensitivity Score

Variable	β	Partial R^2	P-value
Age	-0.570	0.367	< 0.001
Sex	0.111	0.021	0.012
Overweight	-0.295	0.135	< 0.001
Obesity	-0.238	0.092	< 0.001
High GI	-0.096	0.016	0.028
High GL	0.013	<0.001	0.796
Low Fibre	0.013	<0.001	0.809
Low Magnesium	0.014	<0.001	0.781
Low Vegetable and Fruit	0.074	0.009	0.092
High Fat	-0.021	0.001	0.615

β = Standardized Coefficient, SE = Standard Error
$F[10, 305] = 26.861$, $p<0.001$, $R^2 = 0.468$

Table 6.8 Associations between Dichotomous Dietary and Physical Activity Diabetes Risk Factors and Insulin Sensitivity Score

Variable	β	Partial R^2	P-value
Age	-0.544	0.311	< 0.001
Sex	0.085	0.011	0.379
Overweight	-0.268	0.103	0.006
Obesity	-0.233	0.079	0.018
High GI	-0.155	0.035	0.118
High GL	-0.085	0.008	0.444
Low Fibre	0.024	0.001	0.852
Low Magnesium	-0.019	<0.001	0.862
Low Vegetable and Fruit	0.126	0.025	0.188
High Fat	-0.021	0.001	0.825
Low Physical Activity	-0.047	0.004	0.619

β = Standardized Coefficient

$F[11, 69] = 4.930$, $p<0.001$, $R^2 = 0.440$

6.4.4. Associations between Composite Diabetes Risk Scores and Insulin Sensitivity

Table 6.9 shows the associations between of each composite diabetes risk score and ISS. Model 14 explained the greatest amount of the variation in ISS at 43% however; models 6, 7, 12 and 13 resulted in the greatest change in R^2 with the composite diabetes risk score after the inclusion of age and sex in the model, explaining 11.5 – 12.6% of the variation in ISS ($p < 0.001$ for change in R^2 for each model).

Table 6.9 Variance in Insulin Sensitivity Score Explained by Each Version of the Composite Diabetes Risk Score

Composite Diabetes Risk Score	R^2 Total	R^2 for Age and Sex	Change in R^2 with DRS	P-value for the change in R^2
Equal Weights				
1	0.326	0.279	0.046	0.016
2 [c]	0.360	0.334	0.026	< 0.001
Unadjusted Weights				
3 †[a]	0.348	0.279	0.068	0.003
4 †[b]	0.343	0.279	0.064	0.005
5 †[c]	0.383	0.334	0.049	< 0.001
6 ‡[a]	0.397	0.279	0.117	< 0.001
7 ‡[b]	0.395	0.279	0.115	< 0.001
8 ‡[c]	0.426	0.334	0.092	< 0.001
Adjusted Weights				
9 †[a]	0.341	0.279	0.062	0.005
10 †[b]	0.339	0.279	0.060	0.006
11 †[c]	0.373	0.334	0.038	< 0.001
12 ‡[a]	0.406	0.279	0.126	< 0.001
13 ‡[b]	0.405	0.279	0.126	< 0.001
14 ‡[c]	0.432	0.334	0.097	< 0.001

† low weighting of obesity, ‡ high weighting of obesity, [a] low weighting of physical activity, [b] high weighting of physical activity, [c] no physical activity

6.5. Discussion

This is the first study to examine the relationship between lifestyle variables and insulin sensitivity in Canadians adolescents based on a C-13 glucose breath test. Results of this study showed that age, sex, and BMI were significantly associated with ISS as measured by a C-13 glucose breath test in a sample of Alberta adolescents, and in addition, among boys, GI was significantly related to ISS. In addition this study showed that examining an aggregated risk score was not more helpful in accounting for variation in ISS compared to testing each risk factor separately, indicating that there does not appear to be a synergistic effect among the risk factors.

6.5.1. Associations between Continuous Risk Factors for Diabetes and Insulin Sensitivity

In the present study, age was significantly related to ISS with insulin sensitivity decreasing with increasing age. Our participants ranged in age from 10 to 14 years; a time period in which puberty generally occurs. Studies have established that insulin sensitivity decreases during puberty with the nadir occurring in mid-puberty (Tanner Stage 2-3) and rebounds in late puberty (Ball et al. 2006). The relationship observed with decreasing ISS with age in the present study is consistent with the pattern we would expect to observe in this age group as a result of puberty. The inclusion of a direct measure of pubertal development might have been beneficial to include in our models, however, this information was not available for this study.

Previous studies examining insulin sensitivity among youth have found differences between boys and girls. One study that used the euglycemic clamp technique, the gold standard of insulin sensitivity measurement, to assess insulin sensitivity among over 350 adolescents aged 10- to 14 found that girls are less insulin sensitive than boys at all pubertal stages (Moran et al. 1999). Similarly, a study that used HOMA to measure insulin resistance found that girls were less insulin sensitive than boys (Lee et al. 2006). However, in the present study, it was found that girls had higher insulin sensitivity scores than boys. A previous pilot study using the C-13 breath test to determine insulin sensitivity in adolescents reported a similar pattern, with girls having higher ISSs compared to boys; however, in this small study (n = 39), differences between the groups were not significant (unpublished data, Jetha et al). It is possible that this difference is related to variables not included in this study, such as family history of diabetes, pubertal stage and ethnicity; however further investigation of this observed pattern is warranted.

Studies examining insulin sensitivity and insulin resistance in youth have found obesity to be the variable most strongly related to insulin resistance (Lee et al. 2006; Lobstein and Jackson-Leach 2006), with one study showing that body weight explained 29% of the variation in IR as measured by HOMA (Lee et al. 2006; Lobstein and Jackson-Leach 2006). Similarly, in the present study, BMI accounted for 29% of the variation in ISS in the multiple regression model including both sexes. It accounted for 35% of the variation in ISS in boys and 24% of the variation for girls.

The present study showed that, for boys, higher GI diets were associated with lower ISS. High glycemic index diets result in high postprandial insulin levels (Del Prato et al. 1994), high fatty acid concentrations (Kallio et al. 2008) and they may trigger inflammation (Qi et al. 2006); all of which could lead to a decrease in insulin sensitivity. Several studies of adults have shown a relationship between GI and insulin sensitivity (Du et al. 2008; McKeown et al. 2004; Ostman et al. 2006); however, this pattern is not consistently shown in the literature (Lau et al. 2005; Liese et al. 2005). To our knowledge, only one study has examined the relationship between dietary GI and insulin sensitivity in youth, and that study did not find a relationship between GI and insulin sensitivity as measured by a frequently sampled intravenous glucose tolerance test (FSIVGTT) in a sample of overweight Latino youth aged 10 to 17 years (Davis et al. 2007). The smaller sample size (n = 120) and characteristics of the participants in this study may account for the differences in results.

Results of the present study suggested that the relationship between GI and ISS existed only for boys and not for girls. It is possible that this difference is due to a greater variability in GI for boys compared to girls. As Table 6.2 shows, the standard deviation for GI for boys is 7.5 and the standard deviation for girls is 6.3. Although this observed difference falls just short of reaching significance ($p = 0.08$), it is possible that the variability in GI for girls is not great enough to see a significant relationship. Another possible explanation of the different result between boys and girls is the day to day variability of GI. A previously conducted validation of the GI value calculated by the Web-SPAN (see Chapter

4) showed that GI was highly variable from day to day (Intra-class Correlation Coefficient (ICC) = 0.28) and the ICC was higher for boys than for girls (ICC = O.30 for boys vs. 0.25 for girls). The difference in ICC values between boys and girls suggests that a GI value from one 24-hour recall may be more representative of usual eating patterns for boys than for girls.

Glycemic load, fibre, magnesium, vegetable and fruit intake, % fat and physical activity were not associated with ISS as measured by a C-13 glucose breath test in this study. Results linking the majority of these variables to insulin sensitivity have been inconsistent in the past as detailed below.

A previous assessment of insulin sensitivity in youth found no relationship between dietary GL and insulin resistance (Davis et al. 2007). Many studies of adults have found no relationship between GL and insulin sensitivity (Du et al. 2008; Lau et al. 2005; Liese et al. 2005). An analysis of the Framingham Offspring Cohort found that GL was related to insulin resistance, but not as strongly as GI (McKeown et al. 2004).

Several studies of adults have found fibre to be associated with insulin sensitivity (Lau et al. 2005; Liese et al. 2005; McKeown et al. 2004), however this effect has not yet been seen among youth. Cereal fibre has been shown to be more strongly related to insulin sensitivity in adults than total fibre (McKeown et al. 2004) and a relationship between whole grain intake and insulin sensitivity has been observed in youth (Steffen et al. 2003). Unfortunately, a measure of cereal fibre or whole grain intake was not available in the present study.

Magnesium intake has been linked to insulin resistance in both adults (Humphries et al. 1999; Rumawas et al. 2006) and youth (Huerta et al. 2005). One study of obese children found that low dietary magnesium intake was related to insulin resistance as measured by QUICKI (Huerta et al. 2005). However, another study that examined the link between diet and insulin resistance in youth did not duplicate this finding (Davis et al. 2007).

Vegetable and fruit intake has not been linked to insulin sensitivity in either adults or youth, however it has been found to be related to the metabolic syndrome in youth (Kelishadi et al. 2008) and to type 2 diabetes risk in adults (Harding et al. 2008; Lindstrom and Tuomilehto 2003).

The link between dietary fat intake and insulin resistance in youth is also not clear. An intervention study found that a low saturated fat diet for children beginning at infancy lead to increased insulin sensitivity at 9 years of age (Kaitosaari et al. 2006). However, other studies of diet and insulin resistance have found no connection between dietary fat and insulin resistance (Davis et al. 2007; Klein-Platat et al. 2005; Sheikh et al. 2008).

Physical activity and fitness have consistently shown a strong link with insulin sensitivity, however that link was not shown in the present study. Various methods of assessing physical activity and fitness (i.e. VO2 max (maximum volume of oxygen), accelerometers, physical activity questionnaires) have been shown to be related to insulin sensitivity as measured by various methods (FSIVGTTs, QUICKI, HOMA) (Allen et al. 2007; Brage et al. 2004; Eisenmann et al. 2007; Imperatore et al. 2006; Ku et al. 2000; Rizzo et al. 2008; Sardinha et

al. 2008; Snitker et al. 2007). However, some studies have found that relationships between physical activity and insulin sensitivity are attenuated and no longer significant after adjusting for body weight (Imperatore et al. 2006). It is possible that the use of a more objective measure of physical activity may have been beneficial in seeing the effect of physical activity on insulin sensitivity in this group. In addition, only a small subsample of our group completed the physical activity questionnaire which may have affected our ability to detect the effects of physical activity on insulin sensitivity. It should also be noted that participants who completed the PAQ-C survey were significantly older and showed some differences in the presence of risk factors compared to those who did not complete the survey. Therefore, the findings in this smaller sample may not be representative of the whole group.

6.5.2. Associations between Dichotomous Risk Factors for Diabetes and Insulin Sensitivity

Dichotomous risk factors resulted in similar associations with ISS as observed with continuous risk factors, however the variance in ISS explained was slightly lower (47% for dichotomous vs. 53% for continuous). This finding suggests that using diabetes risk cut-offs suggested by the adult literature have comparable associations with ISS as continuous risk factors. This provides evidence that examining the presence of these risk factors in a population of youth (as seen in Chapter 5 of this thesis) does give some indication of diabetes risk.

6.5.3. Associations between Composite Diabetes Risk Scores and Insulin Sensitivity

In this group, multivariate models using composite diabetes risk scores based on adult values did not explain as much of the variation in ISS as models that assessed risk factors individually (43% for composite diabetes risk score vs. 47% for dichotomous variables and 53% for continuous variables). This is likely reflective of the finding that not all risk factors tested were significantly associated with ISS in this group. These results show that a composite diabetes risk score taking into account only age, sex, overweight, obesity and GI may be more effective in showing associations with ISS.

6.5.4. Strengths and Limitations

Web-SPAN is a survey comprised of validated tools that collects detailed dietary and physical activity information using a fun, interactive method. The Web-SPAN survey is well received by participants, is easy to administer and the automatic recording of responses decreases measurement error. However, the 24-hour recall portion of the questionnaire only collects information about one day of food intake, which may not be representative of usual intake. Repeated 24-hour recalls may have provided dietary intake estimates that were more representative of usual intake, however the extra time commitments required on the part of schools to execute this method may not have been as acceptable. Time constraints were already a limitation in this study as several schools were not able to complete the physical activity portion of the Web-SPAN questionnaire, resulting in incomplete data for many participants. Another limitation of this

study was that it did not include information on some variables that are known to be related to insulin sensitivity such as pubertal status, ethnicity and family history of diabetes. Inclusion of these variables may have provided a more complete picture of insulin sensitivity in this group.

This study used a novel, non-invasive measure of insulin sensitivity to assess the relationships between diabetes risk factors and insulin sensitivity in a sample of healthy adolescents. The non-invasive nature of the test increased the acceptability to students, parents and schools, which made it possible to collect a larger sample size for this study. This may also have decreased volunteer bias.

Although the C-13 glucose breath test is a well developed method for evaluating carbohydrate metabolism, its use as a measure of insulin sensitivity is relatively new. The C-13 breath test has been shown to be successful in differentiating between healthy participants, those with impaired glucose tolerance and those with diabetes, and values correlate strongly with other measures of insulin sensitivity among adults (Dillon et al. 2009; Lewanczuk et al. 2004). Although similar correlations with other measures of insulin sensitivity have been seen in children (unpublished data, Jetha et al.), this method has not been extensively validated in this age group.

6.6. Conclusions

In this group of Alberta youth aged 10 to 14 years, age, sex and BMI were significantly associated with ISS as measured by a C-13 glucose breath test. In addition, among boys, GI was significantly related to ISS. Glycemic load, magnesium, fibre, vegetable and fruit intake, % fat and physical activity were not

associated with ISS in this group. This suggests that maintaining a healthy body weight is important for insulin sensitivity and following a low GI diet may also be beneficial. This study also found that using dichotomous risk factor variables to explain ISS had similar results compared to continuous variables; and a composite diabetes risk score was not advantageous compared to looking at diabetes risk factors separately.

6.7. References

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Chapter 7: Conclusions and Discussion

7.1. Review of Hypotheses and Conclusions

Hypothesis 1: Youth with type 2 diabetes will differ from those who are overweight in that they will have:

a. a greater frequency of medical history related risk factors for diabetes including:
    i. stronger family history of type 2 diabetes **(Chapter 3)**
    ii. greater frequency of diabetes during gestation **(Chapter 3)**
    iii. greater frequency of high (>4000g) and low (<2500g) birth weights **(Chapter 3)**
b. have greater frequency of symptoms of the metabolic syndrome including:
    i. dyslipidemia, specifically high triglycerides and low High Density Lipoprotein Cholesterol (HDL-C) concentrations **(Chapter 3)**
    ii. higher blood pressure **(Chapter 3)**
c. different dietary and physical activity related behaviours, specifically:
    i. higher dietary fat intakes **(Chapter 3)**
    ii. lower dietary fibre intakes **(Chapter 3)**
    iii. higher rates of inactivity **(Chapter 3)**

Hypothesis 1.a.i. was accepted as those with type 2 diabetes were more likely than controls to have a family history of type 2 diabetes (n = 24, 86 % vs. n = 17, 61 %, p = 0.026). **Hypothesis 1.a.ii.** was not accepted because although more patients with type 2 diabetes were exposed to diabetes during gestation compared to controls (n = 7, 25% vs. n = 3, 11%), the difference was not significant (p = 0.125). **Hypothesis 1.a.iii.** was accepted as those with type 2 diabetes were more likely to have been born with either low (< 2500g) or high (> 4000g) birth weights compared to controls (p = 0.024).

Hypothesis 1.b.i. was accepted as dyslipidemia was more common among those with diabetes compared to those without. In particular, mean triglyceride levels were higher among those with type 2 diabetes (3.4mmol/L vs. 1.6mmol/L, p = 0.048) and those with diabetes were more likely than controls to reach the cut-off for high triglycerides (61% vs. 23%, p = 0.039) and high total cholesterol levels (48% vs. 4%, p = 0.001). **Hypothesis 1.b.ii.** was not accepted as there were no differences between the diabetes and control groups in the proportion of patients with high blood pressure.

Hypotheses 1.c.i. was not accepted as there were no significant differences between those with and without type 2 diabetes in terms of their fat intakes. **Hypothesis 1.c.ii.** was also not accepted. Inter-observer reliability for fibre was too low for comparisons in intake to be made. **Hypothesis 1.c.iii.** could also not be accepted with a high degree of confidence. Although patients with type 2 diabetes were significantly less likely to report being physically activity compared to controls, the inter-observer variability for this variable was slightly

below the acceptable level. The results were suggestive that physical activity levels were lower in those with type 2 diabetes.

Hypothesis 2: The GI and GL of the diets of Alberta adolescents are associated with their macronutrient distribution, food group choices and meal patterns with the following variables being related to:

a. Higher GIs
    i. Macronutrient Distribution
        1. High carbohydrate intakes **(Chapter 4)**
        2. Low fibre intakes **(Chapter 4)**
        3. Low fat intakes **(Chapter 4)**
        4. Low protein intakes **(Chapter 4)**
    ii. Food group choices
        1. High consumption from the "other" categories (particularly the mostly sugar, high salt and fat, high calorie beverage and high sugar and fat categories) **(Chapter 4)**
        2. High consumption from the grain product food group **(Chapter 4)**
    iii. Meal patterns
        1. High frequency of eating away from home **(Chapter 4)**
        2. Low frequency of family meals **(Chapter 4)**
        3. Low meal frequency **(Chapter 4)**
b. Higher GLs

i. Macronutrient distribution

    1. High carbohydrate intakes **(Chapter 4)**
    2. Low fibre intakes **(Chapter 4)**
    3. Low fat intakes **(Chapter 4)**
    4. Low protein intakes **(Chapter 4)**

ii. Food group choices

    1. High consumption from the "other" categories (particularly the mostly sugar, high salt and fat, high calorie beverage and high sugar and fat categories) **(Chapter 4)**
    2. High consumption from the grain product food group **(Chapter 4)**

iii. Meal patterns

    1. High frequency of eating away from home **(Chapter 4)**
    2. Low frequency of family meals **(Chapter 4)**
    3. Low meal frequency **(Chapter 4)**

Hypothesis 2.a.i.1. was accepted as carbohydrate intake was strongly correlated with GI for both boys and girls ($r = 0.110$ and $r = 0.068$, respectively, $p < 0.001$ for both sexes). **Hypothesis 2.a.i.2** was also accepted. Fibre intake was inversely correlated to GI in both boys and girls with Pearson correlations of -0.079 and -0.069, respectively ($p < 0.001$ for both sexes). **Hypothesis 2.a.i.3** was not accepted as there was no relationship between fat intake and GI for either boys or girls. **Hypothesis 2.a.i.4** was accepted as protein intake was inversely correlated

with GI for both boys and girls (boys r = -0.213, girls r = -0.224, p<0.001 for both sexes). **Hypothesis 2.a.ii.1.** was accepted as high intakes of foods in the other category were related to high GI. In particular, high intakes from the mostly sugar (boys: p = 0.032; girls: p <0.001), high salt and fat (boys: p <0.001; girls: p = 0.008), high calorie beverages (boys only p = 0.002) and high sugar and fat (p < 0.001 for both sexes) groups were related to high GI. **Hypothesis 2.a.ii.2.** was also accepted as high consumption of grain products was related to high GI (boys: $\beta = 0.111$, girls: $\beta = 0.167$, p < 0.001 for both sexes). **Hypothesis 2.a.iii.1., Hypothesis 2.a.iii.2. and Hypothesis 2.a.iii.3.** were not supported as eating away from home family meals and meal frequency were not associated with high GI.

Hypothesis 2.b.i.1 was accepted as carbohydrate intake was strongly correlated with GL (boys: r = 0.377and girls: r = 0.424, p < 0.001 for both sexes). **Hypothesis 2.b.i.2** was accepted for girls but not for boys. Fibre intake was positively correlated with GL among girls r = 0.120, p < 0.001) but not significantly correlated with GL for boys. **Hypothesis 2.b.i.3** was accepted as fat intake was inversely associated with GL (boys: r = -0.286, girls r = -0.324, p < 0.001 for both sexes). **Hypothesis 2.b.i.4** was accepted. Protein intake was inversely correlated with GL for both boys and girls (boys r = -0.285, girls r = -0.278, p<0.001 for both sexes). **Hypothesis 2.b.ii.1.** was accepted as high intakes of foods in the other category were associated with high GL. High intakes from the mostly sugar (p < 0.001 for both sexes) and high calorie beverages (boys: p < 0.001; girls: p = 0.002) groups were related to high GL. **Hypothesis 2.b.ii.2.** was also accepted as high consumption of grain products was associated with high GL

(boys: $\beta = 0.066$, $p = 0.007$; girls: $\beta = 0.094$, $p < 0.001$). **Hypothesis 2.b.iii.1** was accepted as eating away from home explained 5% of the variation in GL for boys and 3% of the variation in GL for girls ($p < 0.001$ for both sexes). **Hypothesis 2.b.iii.2.** was not accepted as family meals were related to GL. **Hypothesis 2.b.iii.3.** was not supported as the observed results were opposite to those expected with high meal frequency being related to a higher GL (boys: $\beta = 0.230$; girls: $\beta = 0.232$, $p < 0.001$ for both sexes).

Hypothesis 3: There will be a greater proportion of participants with diet and physical activity related diabetes risk factors (* see below) observed among youth who:

a. are females compared to males **(Chapter 5)**
b. are older (15-16 year olds) compared to younger (13-14 year olds) adolescents **(Chapter 5)**
c. have BMI percentiles in the overweight (>85th percentile) and obese (>95th percentile) categories compared to those who are non-overweight **(Chapter 5)**

Hypothesis 3.a was not supported as boys reported a higher total number of diabetes risk factors on average compared to girls (mean number of risk factors boys: 3.2 vs. girls: 3.0, $p < 0.001$). **Hypothesis 3.b.** was accepted as older boys and girls reported a significantly higher total number of risk factors on average than younger boys and girls (mean number of risk factors per group: 3.3 (older

boys) vs. 3.1 (younger boys), p = 0.059; 3.1 (older girls) vs. 2.9 (younger girls), p = 0.001). **Hypothesis 3.c.** was accepted as students in overweight and obese BMI categories reported a higher mean number of risk factors compared to non-overweight students (mean number of risk factors per group: 2.8 ± 1.4^{a} (non-overweight), 3.0 ± 1.4^{b} (overweight), 3.1 ± 1.3^{bc} (obese), $p < 0.001$).

Hypothesis 4: The insulin sensitivity of Alberta adolescents, as measured by a C-13 glucose breath test, is associated with:

a. continuous diet[4] and physical activity[5] related diabetes risk factor variables **(Chapter 6)**.
b. dichotomous diet and physical activity related diabetes risk factor variables **(Chapter 6)**.
c. a composite diet and physical activity diabetes risk score **(Chapter 6)**.

Hypothesis 4.a. was accepted for some, but not all of the dietary and physical activity risk factors tested. Body mass index (boys: $\beta = -0.520$; girls: $\beta = -0.413$, $p < 0.001$ for both sexes) and GI (boys only $\beta = -0.185$, $p = 0.022$) were significantly associated with insulin sensitivity score (ISS) as measured by a C-13 glucose breath test, but GL, fibre, magnesium, vegetable and fruit intake, dietary fat and physical activity score were not related to ISS. **Hypothesis 4.b.** was also accepted for some, but not all risk factors. When dichotomous variables were used, only BMI category (overweight: $\beta = -0.295$; obese: β -0.238, $p < 0.001$ for

[4] Diet related risk factors for diabetes include: high GI, high GL, low fibre, low magnesium, low vegetable and fruit intake and high fat intake.
[5] Physical activity related diabetes risk factors include: low physical activity score.

both variables) and GI ($\beta = -0.096$, $p = 0.028$) were associated with ISS.

Hypothesis 4.c. was accepted as a composite diabetes risk score was associated with ISS (the best model explained 43% of the variation in ISS $p < 0.001$). However, the composite variable did not explain as much of the variation in ISS as either continuous or dichotomous risk factor variables (Continuous variables explained 53% of the variation ($p < 0.001$) and dichotomous risk factors explained 47% of the variation in ISS ($p < 0.001$)).

7.2. Review of Research Questions

Some of the research questions posed in this thesis were exploratory in nature and were therefore not addressed in hypotheses. The findings pertaining to these questions will be reviewed below.

Research Question 2: What are the Glycemic Index and the Glycemic Load of the diets of youth in Alberta? **(Chapter 4)**

We found that the mean daily GIs and GLs were 56 and 168 for boys and 55 and 128 for girls. Boys had significantly higher mean GIs ($p < 0.001$) and GLs ($p < 0.001$) compared to girls.

Research Question 4: How commonly are diet and physical activity related diabetes risk factors reported among Alberta youth? **(Chapter 5).**

Overweight was reported by 19% of boys and 11% of girls and obesity was reported by 8% of boys and 5% of girls. High GI was reported by 39% of boys and 33% of girls. High GL was reported by 56% of boys and 35% of girls. Low fibre intakes were particularly common with 53% of boys and 64% of girls reporting this risk factor. Low magnesium intakes were reported by 48% of boys and 50% of girls and low vegetable and fruit intakes were reported by 30% of both boys and girls. High fat intakes were reported by 22% of boys and 18% of girls and low physical activity scores were seen in 50% of boys and 63% of girls.

7.3. Discussion

This thesis has examined the presence of diabetes risk factors among several unique populations of Alberta youth; those who had type 2 diabetes, those who were overweight, and the general population. This thesis has also examined some consequences of these risk factors including type 2 diabetes and insulin sensitivity as measured by a C-13 glucose breath test. The main findings of the research suggest that dietary and physical activity diabetes risk factors are common among Alberta teens and these unhealthy lifestyle behaviours may lead to early changes in carbohydrate metabolism in this population. These changes may put youth at greater risk of developing type 2 diabetes in the future.

7.3.1. Presence of Diabetes Risk Factors

Chapters 3, 4 and 5 examined the presence of diabetes risk factors in youth with type 2 diabetes and in the general population. Commonly reported risk factors among youth with type 2 diabetes included obesity and low physical activity levels. These findings are consistent with previous studies of youth with type 2 diabetes from around the world (Faulkner et al. 2005; Hale and Rupert 2006; Harwell et al. 2001; Likitmaskul et al. 2005).

All dietary and physical activity risk factors for diabetes examined in this thesis were quite commonly reported in the general population of Alberta teens (Chapters 4, 5 and 6). Most frequently reported risk factors included low fibre intakes, low physical activity levels and low magnesium intakes. Although mean intakes of many nutrients examined in the Web Survey of Physical Activity and Nutrition (Web-SPAN) survey were similar to values seen in previous studies

(Buyken et al. 2006; Davis et al. 2007; Ebbeling et al. 2003; Nielsen et al. 2005; Scaglioni et al. 2005; U.S. Department of Agriculture 2008; Verduci et al. 2007), this was the first to examine the presence of diabetes risk factors in a large group of Canadian adolescents. The findings of Chapter 5 also showed that although diabetes risk factors were commonly reported by adolescents in all sex, age and BMI categories, a greater number of risk factors were seen among boys, older youth and those in a higher BMI category.

In summary, a major theme emerged in this thesis in terms of the presence of risk factors for type 2 diabetes. It was consistently shown in chapters 3, 4, 5 and 6 that risk factors for type 2 diabetes were commonly reported among Alberta youth. These findings were of particular concern in light of the increasing rates of early onset type 2 diabetes (Toth 2005; Zdravkovic et al. 2004) and obesity in this age group (Shields 2006) that have been seen in recent years and have stimulated interest in examining early consequences of dietary and physical activity diabetes risk factors in this age group.

7.3.2. Health Consequences of Diabetes Risk Factors

The results of Chapters 3 and 6 showed some of the consequences of dietary and physical activity risk factors for type 2 diabetes among Alberta youth. Both chapters highlighted the importance of obesity as a risk factor for type 2 diabetes with nearly all type 2 diabetes patients being obese and with BMI having the strongest relationship with ISS among healthy adolescents. This is consistent with the findings of other studies of early onset diabetes from around the world (Hale and Rupert 2006; Harwell et al. 2001; Likitmaskul et al. 2005) and studies

of insulin sensitivity in this age group (Lee et al. 2006; Lobstein and Jackson-Leach 2006).

Chapters 3 and 6 also examined the impact of dietary risk factors for type 2 diabetes. Dietary risk factors such as dietary fat and fibre did not differ between youth with type 2 diabetes and control subjects which may suggest a limited effect of these factors, however, these data collected from medical charts were not recorded by clinic staff using validated methods which may have limited our ability to detect differences between the groups. Previous studies of youth with type 2 diabetes have identified dietary variables as possible contributors to diabetes risk. One study that compared the diets of youth with type 2 diabetes to those with type 1 diabetes found that children with type 2 diabetes had lower intakes of magnesium, vitamin C and iron, and higher intakes of vitamin E and simple sugars. This study also found that both children with type 1 and type 2 diabetes had high intakes of fat and saturated fat (Mayer-Davis et al. 2006).

In Chapter 6, this research showed that, among healthy youth, dietary GI was significantly related to ISS among boys. This suggests that high GI diets contribute to early changes in carbohydrate metabolism in this group and that low GI diets may be a useful dietary target for future interventions for diabetes prevention. Chapter 4 of this thesis examined dietary patterns related to dietary GI and GL and these patterns may provide useful guidelines for the promotion of low GI and GL diets among Alberta youth. However, further study is required to determine if promoting these dietary patterns will lead to changes in GI or GL. Although links between insulin sensitivity and GI have previously been observed

among adults (Du et al. 2008; McKeown et al. 2004; Ostman et al. 2006), this is the first study to observe this pattern among teens.

Although the intra-observer variability was too high in Chapter 3 to make conclusions regarding differences in physical activity levels between those with and without type 2 diabetes, inactivity was common among of youth with type 2 diabetes, suggesting that this may also be an important risk factor in the pathogenesis of this disease. To date, few studies have examined the physical activity habits of youth with type 2 diabetes. However, one study that compared physical fitness and physical activity between patients with type 1 and type 2 diabetes found that those with type 2 diabetes had a significantly lower peak volume of oxygen (VO2) score, lower reported levels of physical activity and a lower exercise belief score compared to those with type 1 diabetes (Faulkner et al. 2005). The results of Chapter 6 showed no relationship between ISS and physical activity, which was surprising as previous studies have consistently shown a link between these variables (Allen et al. 2007; Brage et al. 2004; Eisenmann et al. 2007; Imperatore et al. 2006; Ku et al. 2000; Rizzo et al. 2008; Sardinha et al. 2008; Snitker et al. 2007). However, it should be noted that a large portion of our study population did not complete the physical activity questionnaire which may have limited our ability to detect relationships between physical activity and ISS.

In terms of the consequences of risk factors for type 2 diabetes, the variable most consistently related to diabetes risk was obesity. Obesity has been shown, both in this thesis and in other studies to be the most important risk factor for type

2 diabetes in youth. Preventing overweight and obesity in this age group may be the best strategy for preventing type 2 diabetes in this age group.

7.3.3. Strengths and Limitations

The Web-SPAN survey allowed diet and physical activity variables to be assessed in a large population of youth from throughout the entire province of Alberta using validated tools. However, the nature of the study made random selection of participants unfeasible; therefore the sample may not be representative of the whole population of Alberta youth. In addition, the Web-SPAN survey relies on self-reported data which may contain some inaccuracies (Guenther et al. 1997). However, validations of Web-SPAN's dietary and height and weight information showed good correlation with dietitian administered 24-hour recalls (Vance et al. 2008) and measured height and weight (Calengor 2007). A further limitation was that the Web-SPAN study did not collect information about some variables important to diabetes risk such as family history of diabetes, polyunsaturated fat intake and cereal fibre intake.

This research used a novel C-13 glucose breath test to examine relationships between diabetes risk factors and insulin sensitivity. This made it possible to evaluate a larger sample of youth than would otherwise be feasible. The non-invasive nature of this test was particularly appealing to students, parents and schools. This method is relatively new and although C-13 glucose measures correlate well with other measures of insulin sensitivity (Dillon et al. 2009; Lewanczuk et al. 2004), it has not been extensively validated in youth.

7.4. Implications, Recommendations and Future Research Directions

The results of Chapter 3 showed that type 2 diabetes is a concern among Alberta youth and greater efforts are needed for the prevention of this disease. Results of both this chapter and other studies suggest that factors such as obesity, high or low birth weight and family history are associated with early onset type 2 diabetes. Prevention of obesity among youth, particularly among those with a family history of type 2 diabetes or with a high or low birth weight may be important target groups for future policies and interventions aiming to prevent early onset type 2 diabetes.

Although Chapter 3 provided information on the dietary patterns of Alberta youth with type 2 diabetes and age, sex and BMI matched controls, dietary and physical activity data were not collected by validated tools. Therefore, further investigation of the diets of Alberta teens with type 2 diabetes is warranted. It should be noted that the burden of dealing with a chronic disease in youth is challenging for both patients and their families. Therefore, integration of validated dietary and physical activity measures into clinical practice may be one way to obtain additional evidence-based information about this population.

The results of Chapter 4 revealed that high GI and GL diets were common among Alberta youth and Chapter 6 showed that high GI diets were related to ISS. These findings suggest that GI and GL may be important variables to consider when assessing the diets of youth. Future policies that promote the consumption of low GI and GL foods may be beneficial for this group. Lower GI and GL diets could be promoted by encouraging food manufacturers to formulate

more low GI foods or by providing GI information on food labels. In addition, this thesis identified dietary patterns related to dietary GI and GL. Future interventions could determine if dietary GI and GL can be reduced among Alberta youth by promoting these dietary patterns. In addition, future studies could determine if lowering dietary GI and GL has an effect on insulin sensitivity as measured by a C-13 glucose breath test.

Diabetes risk factors were commonly reported among Alberta youth and boys, older youth, and those with in higher BMI categories were more likely to report a greater number of risk factors. This suggests that programs, policies or interventions aiming to decrease diabetes risk among Alberta adolescents could target commonly reported diabetes risk factors such as low physical activity levels and low fibre intakes. In addition, although diabetes risk factors were of concern in all groups, boys, older youth and youth with high BMIs may benefit most from intervention.

Finally, the results of Chapter 6 showed that BMI was significantly related to ISS. This suggests that promoting healthy body weights may lead to increases in insulin sensitivity in this group and may be good targets for future programs or interventions. School or community programs that help youth control their body weight by incorporating physical activity and healthy eating into their daily lives could greatly impact diabetes risk in this population.

This chapter used a novel tool to assess insulin sensitivity in this group and further research is needed to determine the link between ISS as measured by the C-13 glucose breath test and diabetes risk. In addition, a more thorough

examination of the link between ISS and physical activity than was possible in this study is warranted.

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List of Appendices and Contents

Appendix A: Ethical Approval: Chart Review Study

Health Research Ethics Board

213 Heritage Medical Research Centre
University of Alberta, Edmonton, Alberta T6G 2S2
p.780.492.9724 (Biomedical Panel)
p.780.492.0302 (Health Panel)
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ETHICS APPROVAL FORM

Date: April 2006

Name(s) of Principal Investigator(s): Dr. Linda McCargar

Department: Agricultural, Food and Nutritional Sciences

Title: Chart review of the nutritional status, lifestyle factors and metabolic indicators in youth with Type 2 Diabetes.

The Health Research Ethics Board (Biomedical Panel) has reviewed the protocol involved in this project which has been found to be acceptable within the limitations of human experimentation.

Specific Comments:

The Research Ethics Board assessed all matters required by section 50(1)(a) of the Health Information Act. The REB Panel determined that the research described in the ethics application is a retrospective chart review for which subject consent for access to personally identifiable health information would not be reasonable, feasible or practical. Subject consent therefore is not required for access to the personally identifiable health information described in the ethics application.

J. S. Bamforth, M.D.
Associate Chairman, Health Research Ethics Board
Biomedical Panel

APR 2 4 2006
Date of Approval Release

This approval is valid for one year

Issue #6325

UNIVERSITY OF ALBERTA Capital Health CARITAS HEALTH GROUP

Appendix B: Information Letters, Consent Forms and Ethical Approval for the Web-SPAN Survey

B.1 Information Letter for Board Recruitment

[Date]

Dear [Name]:

We would like to invite the [Board Name] to participate in a continuing study examining food, activity, and general health behaviours in Alberta youth. This research will investigate the nutrition, physical activity, and behavioural choices of students in grades seven through ten by using a web-based survey. Each student will receive brief individual feedback immediately upon completion of the computer-based survey. This web-based survey complements the Comprehensive School Health Model and new curriculum. Class group data will be provided to the teacher with suggestions on how to incorporate the feedback into the grade-specific curriculum and relevant learning resources.

As you know, students in grades seven through ten experience many physiological and psychological milestones, including the adolescent growth spurt with rapid bone development, and increasing autonomy in food and activity choices. There is little information on the diet and physical activity behaviours of Alberta youth, however dietary surveys elsewhere indicate that teens consume insufficient amounts of energy, calcium, iron, and may have low levels of physical activity. Obesity is particularly concerning as many overweight and obese children become obese adults, at risk for diabetes and heart disease. Thus the lifestyle behaviours of Alberta youth are of tremendous interest.

The web-based tool was developed by Dr. Rhona Hanning at the University of Waterloo, and has previously been used to survey over 1500 Alberta students. We are planning to survey 5000 additional Alberta students, creating the most comprehensive assessment of Alberta youth's diet and physical activity. Your board and schools within your board have been randomly selected to participate in this survey. Please find attached copies of the following: 1) a summary of the project with details on the design, objectives and measures to be used for this study, 2) the survey questions, 3) the information letter and consent form that will be sent to parents, 4) the information letter for the students, and 5) our ethics approval letter.

The following schools from within your board were selected: [School Names]. In the event an insufficient number of schools from you board can participate, we have selected back-up schools, which may be required in order to complete the

research survey. These schools have been selected as back-up schools: [School Names].

This study has been reviewed by, and received ethics clearance from the Faculty of Agriculture, Forestry and Home Economics Research Ethics Board at the University of Alberta. The research is funded by the Canadian Institutes of Health Research.

We would like an opportunity to speak with you to discuss our project and your school board's protocol for the approval of research projects. We appreciate the strain on school boards and schools at this time and do not wish to create more pressure. If there is anything we can do to make it easy for your schools to participate, please let us know. One of our staff will call you to determine your interest. In the meantime, if you have any questions, please call either Kate Calengor or Laura Kennedy at (780) 492-3700 or by e-mail at either calengor@ualberta.ca or lek1@ualberta.ca. We look forward to further collaboration with you on this project.

Sincerely,

Kate Calengor, PhD Student Project Coordinator, Dept of Agricultural, Food & Nutritional Science University of Alberta Phone: 780-492-3700	Laura Kennedy, MSc Candidate Project Coordinator, Dept of Agricultural, Food & Nutritional Science University of Alberta Phone: 780-492-3700	Linda McCargar, PhD, RD Professor, Dept of Agricultural, Food & Nutritional Science University of Alberta Phone: 780-492-9287

B.2 Information Letter for School Recruitment

[Date]

Dear [Name]:

The University of Alberta has the approval of your school board to invite [school name] to participate in a continuing study examining food, activity, and general health behaviours in Alberta youth. The research will investigate the nutrition, activity, and behavioural choices of students in grades seven through ten using a web-based survey. This web-based survey complements the Comprehensive School Health Model and new curriculum. Feedback from the survey will be available to the individual students, and teachers will receive group feedback and suggestions for incorporating the results into the curriculum, including relevant learning resources.

As you know, teenagers experience many physiological and psychological milestones, including the adolescent growth spurt with rapid bone development, and increasing autonomy in food and activity choices. There is little information on the diet and physical activity behaviours of Alberta youth, however dietary surveys elsewhere indicate that teens consume insufficient amounts of energy, calcium, iron, and may have low levels of physical activity. These have the potential to exert a strong deleterious impact on future health and increase the risk of chronic disease in later life. Through better understanding of the lifestyle patterns of Alberta youth, and variables that influence this pattern, targeted healthy eating and active living programs and strategies can be designed.

The web-based tool was developed by Dr. Rhona Hanning at the University of Waterloo, and has previously been used to survey over 1500 Alberta students. We are planning to survey 5000 additional Alberta students, creating the most comprehensive assessment of Alberta youth's nutrition and physical activity. Your school has been randomly selected to participate in this survey. Please find attached copies of the following: 1) a summary of the project with details on the design, objectives and measures to be used for this study, 2) the survey questions, 3) the information letter and consent form that will be sent to parents, 4) the information letter for the students, and 5) our ethics approval letter. Upon your approval of this research study, we would ask you to randomly select four classrooms in grades seven and eight (if possible), and four classrooms in grades nine and ten (if possible) to participate in the nutrition and physical activity survey.

The research has been reviewed by and received ethics clearance from the Faculty of Agriculture, Forestry, and Home Economics Research Ethics Board at the

University of Alberta. This research is funded by the Canadian Institutes of Health Research.

We would like an opportunity to speak with you to discuss this project and the possibility of your school's participation. We appreciate the strain on schools at this time and do not wish to create more pressure. If there is anything we can do to make it easy for your school to participate, please let us know. One of our staff will call you to determine your interest. In the meantime, if you have any questions, please call either Kate Calengor or Laura Kennedy at (780) 492-3700, or by email at either calengor@ualberta.ca or lek1@ualberta.ca. We look forward to further collaboration with you on this project.

Sincerely,

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B.3 Web-Survey of Physical Activity and Nutrition (WEB-SPAN) Information Sheet

The purpose of the project is to examine food behaviours, physical activity, and general health behavior patterns in Alberta adolescents using an Internet-based 24-hour diet recall in conjunction with a food behavior, and physical activity questionnaire.

WHY A SCHOOL SURVEY?

- Nutritional Problems in youth have the potential to exert a deleterious impact on future health and increase the risk of chronic disease in later life.
- Results from small research studies in Canada and the U. S. suggest that children and adolescents are not consuming adequate amounts of meat and meat alternates and subsequently, iron and zinc intakes (especially in females) are low to marginal.
- The same studies suggest that youth Canadians are not consuming the number of servings of milk and dairy products recommended by Canada's Food Guide to Healthy Eating. Hence, calcium intakes are not being met during a time of bone growth.
- Children and teens are also not meeting the minimum requirements for vegetables & fruit consumption and some related nutrients, like folate, may be low.
- Previous studies have not looked at some of the factors associated with youths' food consumption that may be important in designing relevant educational materials.
- School-based surveys are an effective way to collect information about this age group.

WHY USE THE INTERNET?

- The ability to provide immediate feedback to participants regarding their food behavior.
- An interactive tool that is fun and easy for participants to use.

- ❖ The flexibility and universality of the Internet allows a large number of participants to complete the survey concurrently, in many different locations.

WHO IS INVOLVED IN THE PROJECT?

- ❖ The project is being conducted by Dr. Linda McCargar, Professor, Department of Agricultural, Food & Nutritional Sciences, of the University of Alberta. Dr. McCargar teaches and conducts research in the field of nutrition.
- ❖ Kate Calengor and Laura Kennedy are the project coordinators. Kate and Laura are graduate students in Nutrition at the University of Alberta. The project coordinators will be accessible by phone during the time period that each class is completing the Internet survey.
- ❖ Participants will come from grades seven through ten from schools across Alberta.
- ❖ The research survey is funded by the Canadian Institutes of Health Research.

WHAT IS INVOLVED IN THE PROJECT?

- ❖ Teachers of students in grades seven through ten will be asked to facilitate the completion of the "Web-SPAN".
- ❖ Completing the survey requires approximately one class period and may be incorporated into a Mathematics, Health and Physical Education, or Computer Usage class.
- ❖ Surveys should only be done Tuesday through Friday to obtain weekday food intake. If Monday is a holiday, then surveys should only be done Wednesday through Friday.
- ❖ Upon completing the initial survey at school, students may go back to the website on another day, where the same set of questions about their eating habits will be available. This second portion of the project is optional.
- ❖ Teachers will receive group feedback and suggestions for incorporating the information into the grade-specific curriculum, and relevant learning resources.

CONSENT AND CONFIDENTIALITY MEASURES

- ❖ Information letters and consent forms will be provided to be sent home to parents.
- ❖ Parents must complete, sign and return a consent form before their child can participate in the survey.
- ❖ The survey is anonymous.
- ❖ All students will have a unique identification code and password; unauthorized users will not have access to the survey.

WHAT ARE THE BENEFITS TO THE STUDENTS AND SCHOOLS?

- ❖ School Feedback Report: Teachers will receive group feedback of their classrooms' data based on Canada's Food Guide to Healthy Eating, and suggestions for incorporating the results into the curriculum, including relevant learning resources. Feedback reports may be used by teachers to plan future lessons and to examine current students' eating and physical activity behaviours.
- ❖ Individual Feedback: Upon completing the food intke recall, students will receive information about their diets for that day, based on Canada's Food Guide to Healthy Eating. Studnets will develop a better understanding of their eating patterns, ways to improve their diets, and the benefits to healthy living.

FOR MORE INFORMATION, CONTACT:

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& Nutritional Science
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Phone: 780-492-9287

B.4 Letter and Information Package for Teachers

[Date]

Dear Teacher:

Thank you for agreeing to participate in a "Web-Survey of Physical Activity and Nutrition (Web-SPAN)". The contribution that you and the students in your school will make is invaluable. The information gathered from this project may be used to develop nutrition and healthy lifestyle education programs targeting "risk" behaviours or at-risk populations. By identifying the factors that are associated with "risk" behaviours, we hope to indicate potential areas for preventive programs, and reduce the health and economic burdens associated with poor nutrition and low physical activity. Data may also be used to compare food consumption and activity patterns across populations, provinces and even internationally.

Preparing for the Survey:

This web-based survey complements the Comprehensive School Health Model and new curriculum and may be directly incorporated into Health, Science, Math, Physical Education, or Computer classes. The survey can be implemented during any class period.

If there are sufficient computer facilities, it would be most efficient for all of your students to complete the survey simultaneously. Otherwise students may complete the survey as an independent activity or however you deem appropriate. It is expected that students will require approximately one class period to complete the survey.

Parental information letters and consent forms are included with this mailing. We are asking you to have the students take the letter and consent form home to parents, or have your school mail the letters and consent forms to all parents of potential participants. **Once the signed and completed consent forms have been returned to you, please mail them back to the University of Alberta in the prepaid envelope(s) addressed to Laura Kennedy included with this mailing.** You will also have received an envelope containing student information letters. Please distribute these to students in your class.

Participation in the study is voluntary, and the decision to participate is made by each student and his or her parents. If parents do not complete, sign and return the consent forms to the teachers, students cannot participate in the research study. **Parents must answer "yes" to all questions included on the consent form in order for their son/daughter to participate in the research study.**

Logins and passwords will be provided to you to access the survey once the signed consent forms have been returned to the University of Alberta.
Randomly distribute these to each student who is participating, on the day of the survey. If you require more logins and passwords than are supplied, please contact Laura Kennedy at (780) 492-3700. Please keep a record of the assigned logins and passwords on the sheet provided, noting those logins and passwords that were not assigned. To sustain anonymity, please do not include the students' names with their logins and passwords. If a student chooses to withdraw please note that on the same sheet.

One of our nutrition research assistants working on this project will be accessible by phone during the time that your class is completing the survey.

Completing the Survey
The survey is located at http://survey.afns.ualberta.ca. The web site is best viewed using Internet Explorer, but any web browser will suffice.

The survey is available for teachers to visit before students input their food records.
Your login name is: s
Your password is: s

Students are able to complete the survey independently. It is important to note that:

- The survey is confidential and anonymous. Students' names are not on the survey. Every participant has a unique identification and password; only the researchers at the University of Alberta will see their answers. No one at the school will know students' answers.
- We would like to know what students ate ***yesterday***. We would like them to remember as much as possible.
- Surveys should only be done Tuesday through Friday to obtain weekday food intake. If Monday is a holiday, then surveys should only be done Wednesday through Friday.
- Surveys must be completed between the hours of 8 a.m. to 4 p.m. in order for technical support to be available.
- We have tried to include as many foods as possible, but we have not been able to include ***every*** food. Please ask the students to choose a food item that most closely resembles what he/she ate. If in doubt, please call the researcher on call during the survey period.
- The web site is available should students want to repeat the survey on a different day. This is of course optional, and would be done on the student's own time.

- Students may complete the survey only once each day. Twenty-four hours needs to lapse before students can input more data.
- Students should store their logins/password cards in a safe place. Students must remember their logins and passwords if they wish to return on another day to complete the survey.
- Participation in the survey is completely voluntary.

Directions for Accessing the Food Behaviour Questionnaire:

1. Open the Internet browser on your computer (Explorer or Netscape).
2. On the address line, enter the address: **http://survey.afns.ualberta.ca**
3. Enter assigned login identification code.
4. Enter assigned password, hit the launch button.
5. The survey is open and ready to go. Follow the directions on the screen.

Your feedback regarding this survey is invaluable. We would appreciate your time in completing an online evaluation form using a login name and password that we will provide you on the day of the survey. However, if the online evaluation is not completed, a one-page question sheet will be faxed to you after the survey to obtain your feedback.

If you have any questions or concerns, please contact Laura Kennedy at (780) 492-3700 or by email at lek1@ualberta.ca. A nutrition research assistant involved in this project will be available by phone on the day(s) that your school completes the survey.

Thank you for your participation in the project, we look forward to sharing the results with you.

Sincerely,

Kate Calengor and Laura Kennedy,

Project Coordinators (Web-SPAN),
Department of Agricultural, Food and Nutritional Science
University of Alberta
Phone: (780) 492-3700
Fax: (780) 492-4320
Email: calengor@ualberta.ca, lek1@ualberta.ca

B.5 Parent Information Letter

Title of Research Project: Web-Survey of Physical Activity and Nutrition (Web-SPAN)

This letter describes research being conducted at your son or daughter's school by the University of Alberta (Department of Agricultural, Food & Nutritional Science). Dr. Linda McCargar is the researcher leading the study, and Kate Calengor and Laura Kennedy are the coordinators of the study. We would like to give you some information about the study to help you to decide if your son or daughter should be a part of it.

Your school board and principal have given us permission to conduct this research. This study has received ethics clearance from the Faculty of Agriculture, Forestry, and Home Economics Research Ethics Board at the University of Alberta.

Why is the study being done?
Teenagers are going through a time of physical and emotional changes. They are experiencing the final stages of the adolescent growth spurt with rapid bone development and increasing independence in food and activity behaviours. Previous surveys have shown that children and teens do not get enough food energy, calcium, iron, and are becoming less active. However, there is very little information on the diet and activity levels of Alberta youth.

Who are we looking for?
Teachers of eligible classrooms in your son or daughter's school are being invited to participate in this research. The study will involve 5000 grade seven through ten students throughout Alberta. If you are the parent/guardian of a student invited to take part in this research study, we hope you will agree to his or her participation in the research.

What does my son/daughter have to do?
A student will not be included in the study if a parent or guardian indicates that he or she does not want the student to participate, or if the student does not agree to take part. In order to participate in this survey, your son/daughter **must return a signed and completed consent form** to their teacher.

All of the students in participating classes will be invited to complete a nutrition and physical activity survey on the Internet during class time. This survey is designed to examine food and physical activity habits. We want to know what types of food your son/daughter eats and how they feel about certain foods. Upon completing the survey, your son or daughter will receive immediate feedback on their diet based on Canada's Food Guide to Healthy Eating. If your son or daughter wishes to revisit the web site on another day, the same set of questions

about his/her food behaviour will be available. Revisiting the survey is optional, and may be done on a computer at school, at home, or in the community.

It will take approximately one class period (~45 minutes) to learn about the web site and complete the on-line survey.

Why is the survey web-based?

In the past, other nutrition surveys have included only a small number of participants due to practical issues such as cost. The proposed research will use a web-based tool to deliver a nutrition and physical activity survey to a large number of Alberta children and adolescents. This will result in the most complete assessment of the diet and physical activity of Alberta youth to date.

What will the data be used for?

The information collected from the web-based survey will be used to increase our understanding of the nutrition and physical activity habits of adolescents in Alberta. It will also be used to make recommendations about the types of programs needed to improve the health of Alberta youth. All responses will be anonymous and research journal articles and reports will be written based on the group results obtained from this study; individual results will not be referred to in any publication, report, or presentation. We will compare our results to those of a similar study done in Alberta and Ontario. As well, if we re-administer this survey in the future, we will use the results from this study as a comparison for other data. Your son or daughter's involvement in this project does not obligate them in any way to participate in future surveys.

What if I change my mind about participation?

Being in the study is completely voluntary. Your son or daughter is free to refuse to answer any question(s). Being in the study does not pose any risks for your son or daughter. If you and your son or daughter agrees now to participate, but either of you change your mind later, either you or your son or daughter can withdraw at any time, up until the point when your son or daughter submits their survey on the Internet.

The final decision to participate in this study must be made by the individual student and his/her parent(s) or guardian(s). Your co-operation in permitting your son or daughter to take part in this research is greatly appreciated. However, there is no penalty of any kind if he/she does not participate. If you have any questions or concerns, please contact either Kate Calengor or Laura Kennedy at (780) 492-3700.

Will information about the student go back to the school?

Student names will not be included on the survey; the survey is anonymous. Individual student responses will be kept completely confidential and no individual results will be made available to school or other personnel. Each

student will have a unique identification and password. The web site will be password protected so that unauthorized users will be unable to gain access.

Only the researchers at the University of Alberta will have access to the locked computer files on which we will keep your information. These computers are located in locked offices. The data will be permanently stored on CD in electronic form, which will be held in locked offices at the University of Alberta. Funders and the Advisory Committee will not have access to this information.

Identification codes, not participant names, will be used in the data analysis. All data are published in group form so that it will not be possible to determine the responses from any individual student. The teacher will have access to the group results and we will provide feedback to their class. This ensures that the study can support and enhance the curriculum.

Who is funding this project?
This research is funded by the Canadian Institutes of Health Research.

How do I include my son/daughter in the project?
If you would like to include your son or daughter in this research project, please complete and sign the attached consent form and have your son/daughter return it to their teacher as soon as possible.

<u>If we do not receive a signed and completed consent form from you, your son/daughter will not be able to participate in the survey</u>.

Sincerely,

Kate Calengor, PhD Student
Project Coordinator,
Dept of Agricultural, Food
& Nutritional Science
University of Alberta
Phone: 780-492-3700

Laura Kennedy, MSc Candidate
Project Coordinator,
Dept of Agricultural, Food
& Nutritional Science
University of Alberta
Phone: 780-492-3700

Linda McCargar, PhD, RD
Professor,
Dept of Agricultural, Food
& Nutritional Science
University of Alberta
Phone: 780-492-9287

B.6 Student Information Letter (Grades Seven and Eight)

This letter is a request for your help in a study we are doing at the University of Alberta. We would like to give you some information about the study and what you need to do to take part.

Why is the study being done?
We want to collect information on what pre-teens and teenagers in Alberta are eating, how active they are and other factors that influence nutrition and physical activity.

What do I have to do?
If you wish to participate, your parents and/or guardians have to sign and complete the study consent form. After the signed consent form is given to your teacher, he/she will give you a login and password. This login and password will let you sign in to our web survey. We will first ask you to complete the survey on the Internet at school.

What if I want to quit being in the study?
Being in the study is completely up to you. You are free to say you don't want to answer any question. You can also decide to stop all together at any time before you submit your survey on the Internet. If you have any questions about the study, please contact Laura Kennedy at (780) 492-3700 or lek1@ualberta.ca.

Will information about me go back to my school?
Your name will not be on the survey. All the information that you give to the research group will be kept private. No one at your school will know your answers. Your classroom's average group results will be provided to your teacher.

The final decision to be in this study must be made by you and your parents. We hope you enjoy this survey – and learn from the information you get from the survey. However, there are no consequences any kind if you do not participate.

Sincerely,

Laura Kennedy, MSc Candidate	Linda McCargar, PhD, RD
Project Coordinator,	Professor,
Dept of Agricultural, Food	Dept of Agricultural, Food
& Nutritional Science	& Nutritional Science
University of Alberta	University of Alberta
Phone: 780-492-3700	Phone: 780-492-9287

B.7 Student Information Letter (Grades Nine and Ten)

This letter is a request for your help in a study we are carrying out at the University of Alberta. Dr. Linda McCargar is the researcher leading the study. Kate Calengor is the coordinator of the study. We would like to give you some information about the study and what you need to do to take part.

Why is the study being done?
There is only a little information available of the diet and physical activity of Alberta teenagers. Your diet and activity can affect your growth and health. Students throughout Alberta, ingrades nine and ten, will be asked to participate in thie project. This will provide us with a better understanding of eating patterns of adolescents and things that influence these patterns. We hope to use this information to make recommendations of how to improve the health of teenagers. As well, since a similar project was conducted in Alberta and Ontario (investigators: Dr. Linda McCargar and Dr. Rhona Hanning), the results obtained from this survey will be compared to the results from other Alberta and Ontario students to see if there is a difference in how teenagers are eating. As well, if we re-create this survey in the future, we will use the results from this study as a comparison for other data. Your involvement in this project done not require that you participate in future surveys.

Who are we looking for?
Teachers of eligible classrooms in your school are being invited to participate in the research. If you are a student in one of these classrooms, we would welcome your help with the research.

What do I have to do?
If you wish to participate, your parents and/or guardians have to sign and complete the study consent form that was delivered to them either by you or the school. This form needs to be given to your teacher before you can complete the survey. Your teacher will assign you a login and password that will allow you to sign in to our web survey. We will ask you to complete the survey on the Internet at school. This survey is designed to examine food and physical activity habits. We want to know what types of food you eat and how you feel about certain foods. It should require approximately one period (~ 45 minutes) of class time. If you wish to complete the survey again on another day, you can. This is completely optional.

Why is the survey web-based?
A web-based survey was selected so that we could have a very large number of students from Alberta fill out the survey. This will result in the biggest survey of adolescent diet and physical activity to date.

What if I want to quit being in the study?
Being in the study is completely voluntary. You are free to say you don't want to answer any question. You can also decide to stop all together at any time before you submit your survey on the Internet. Being in this study does not have any risks for you. If you have any questions about the study, please contact Kate Calengor at (780) 492-3700 or calengor@ualberta.ca.

We have received permission from the school board and your school principal to conduct this research. This study has been reviewed by, and received ethics clearance from the Faculty of Agriculture, Forestry, and Home Economics Research Ethics Board at the University of Alberta.

Will information about me go back to my school?
The survey is anonymous. This means that your name will not be on the survey. You will have a unique identification and password. The web site will be password protected so that unauthorized users will be unable to gain access. All the information that you give to the research group will be kept private. We will not give information about your answers to any other group, including your school. No one at your school will know your answers. When we report survey results, no individuals will be identified. Only the researchers at the University of Alberta will have access to the locked computer files on which we will keep your information. These computers are located in locked offices. Your teacher will receive group averages for your class as a whole.

The final decision to be in this study must be made by you and your parents. We hope you enjoy participating in this survey – and learn from the information on your diet that you receive at the end of the survey based on Canada's Food Guide to Healthy Eating. However, there are no consequences of any kind if you do not participate.

Sincerely,

Kate Calengor, PhD Student
Project Coordinator,
Dept of Agricultural, Food
& Nutritional Science
University of Alberta
Phone: 780-492-3700

Linda McCargar, PhD, RD
Professor,
Dept of Agricultural, Food
& Nutritional Science
University of Alberta
Phone: 780-492-9287

B. 8 Consent Form

CONSENT FORM

Please COMPLETE, sign, date and <u>return this form</u> to your son/daughter's teacher

Consent Form
(Please COMPLETE, sign, date and <u>return this form</u> to your son/daughter's teacher)

Title of Research Project: Web-Survey of Physical Activity and Nutrition (Web-SPAN)

Investigators:

Laura Kennedy, MSc Candidate Project Coordinator, Dept of Agricultural, Food & Nutritional Science University of Alberta Phone: 780-492-3700	Kate Calengor, PhD Student Project Coordinator, Dept of Agricultural, Food & Nutritional Science University of Alberta Phone: 780-492-3700	Linda McCargar, PhD, RD Professor, Dept of Agricultural, Food & Nutritional Science University of Alberta Phone: 780-492-9287

Consent: Please circle your answers:

Do you understand that you have been asked to include your son or daughter in a nutrition and physical activity research study that will require approximately 45 minutes of class time?

Yes **No**

Have you read and received a copy of the attached Information Letter?

Yes **No**

Do you understand that there are no risks involved in including your son or daughter in this research study?

Yes **No**

Do you understand that your son or daughter can quit taking part in this study at any time up until the point he or she submits their survey on the Internet? Neither you nor your child has to say why and it will not affect the benefits your son or daughter will receive.

Yes **No**

Was confidentiality adequately explained to you in the information sheet?

Yes **No**

Do you understand who will be able to access the nutrition information collected from this study?

Yes **No**

Do you understand that the information obtained from this project (group results) may be compared to results obtained from a similar survey conducted in Alberta and Ontario and that the information may also be compared to results from future surveys?

Yes **No**

WILL YOU CONSENT TO HAVING YOUR SON OR DAUGHTER TAKE PART IN THIS RESEARCH STUDY?

Yes **No**

Please sign and date below:

Date: _____

Signature of parent/guardian:_____ Name of parent/guardian:_____

As per research guidelines, the anonymous data will be stored for seven years following time of collection. There will be no paper copies of the data. All data will be stored electronically (on CD) and kept in locked offices on password-protected computers.

B.9 Web-SPAN Assent (part of web-survey)

This questionnaire is designed to examine your food habits and those of other students your age. We want to know what sorts of things you eat, what you like to eat, and how you feel about certain foods. We know that not everyone feels the same way, or eats the same things, but we are very interested in your answers to the following questions.

The questionnaire is strictly confidential. No one except the researchers will see your finished questionnaire, so please be as honest as you can. If there is a question that you don't know how to answer or don't want to answer, that's okay, just go on to the next one.

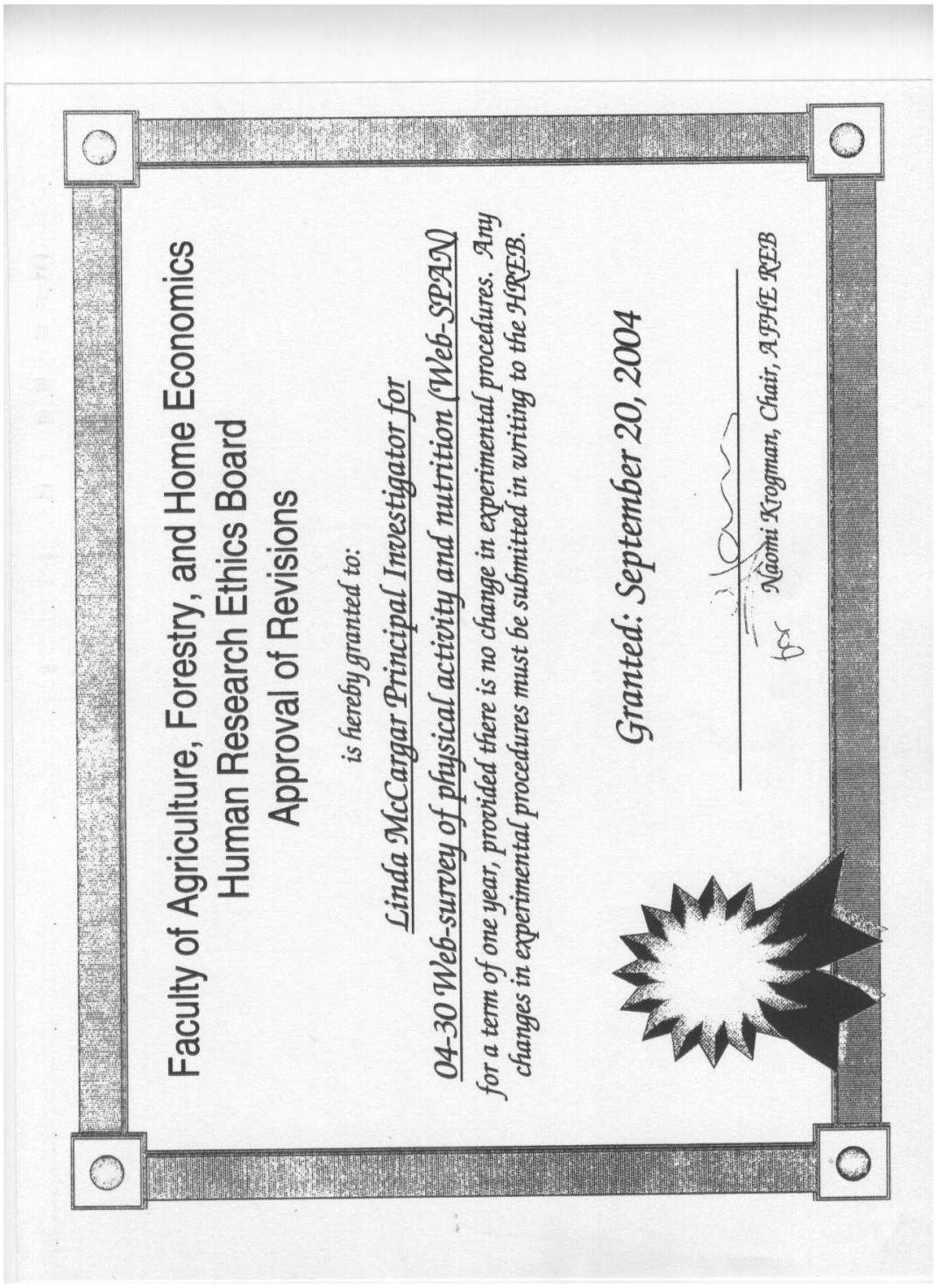
Thanks for helping us with this very valuable research!

Do you agree to participate in this survey?

Yes No

***Note: If student did not choose "yes", they could not proceed with the survey*

B.10 Ethical Approval: Web-SPAN



Faculty of Agriculture, Forestry, and Home Economics
Human Research Ethics Board
Approval of Revisions

is hereby granted to:

Linda McCargar Principal Investigator for

04-30 Web-survey of physical activity and nutrition (Web-SPAN)

for a term of one year, provided there is no change in experimental procedures. Any changes in experimental procedures must be submitted in writing to the HREB.

Granted: September 20, 2004

Naomi Krogman, Chair, AFHE REB

Appendix C: Results of Literature Searches: Longitudinal Studies of Diabetes Risk Factors

Table C-1. Results for Obesity

Reference	N, sex, age, location, length follow-up	Variable/measure	Cut-off vs. reference	Unadjusted Relative risk	Adjusted Relative Risk	Variables adjusted for
(Hart et al. 2007)	19147, men& women, 45-56, Scotland, 30y	Obesity BMI	25-30 >30 vs. 18.5-24.9	OR 2.7m, 2.5w OR 7.3m, 5.8w	OR 2.5m, 2.6w OR 6.4m, 5.4w	Age, class, smoking, BP, cholesterol
(Krishnan et al. 2007)	Black women's health study 49, 766, black women 21-69, USA, 8y	Obesity BMI	25-29 30-34 35-39 40-44 >45 vs. <23	5.5 10 18 20 28	5 8.8 15 16 23	Age, family history, physical activity, smoking, education, time of data collection
(Hosseinpanah et al. 2007)	4728, men & Women, Tehran, >20yrs. 3.6 y	Obesity BMI	25-30 >30 vs. 18.5-25	2.57 5.79	1.76 3.54	Family history, age, TG, BP
(Rana et al. 2007)	Nurses Health Study 68,907, women, 30-55 yrs, USA, 16 yr	Obesity BMI	25-27 27-29 30-33 33-35 35-39 >40 vs. < 21	6.26 11.67 18.62 25.31 32.56 40.28	5.51 9.8 14.8 19.1 24 28	Age, family history, smoking, menopause, physical activity, alcohol

(Hu et al. 2001)	Nurse's health study 121700, women, 30-55, USA, 16 y	Obesity BMI	25-29 30-35 >35 vs. <23	n/a	7.6 20 39	Age, time family history, menopause, dietary score, exercise, smoking, alcohol
(Meisinger et al. 2006)	6012 men & women,35-74, Germany,9.2y	Obesity BMI	26-29 >29 vs. < 25.1	7.0 17.9	4.9 10.6	Age, survey, education, family history, hypertension, lipids, smoking, alcohol, physical activity

Table C-2. Results for GI and GL

Reference	N, sex, age, location, length follow-up	Variable/measure	Cut-off vs. reference	Unadjusted Relative risk	Adjusted Relative Risk	Variables adjusted for
(Barclay et al. 2008)	Meta-analysis mostly 50ish	GI FFQ GL	58 vs. 49 142 vs. 92 (~100units/1000kcal) Patel, 2007 (120/1000kcal) Zang et al., 2006, Liu et al, 2000 Energy adjusted GL?	n/a	1.4 1.3	Age sex, family history, BMI, smoking, alcohol, PA, dietary fibre, medication, supplement use.

Table C-3. Results for Fibre

Reference	N, sex, age, location, length follow-up	Variable/measure	Cut-off vs. reference	Unadjusted Relative risk	Adjusted Relative Risk	Variables adjusted for
(Meyer et al. 2000)	Iowa Women's health study 35,988, women, 55-69y, Iowa, 6y	Total fibre FFQ	>23.6g vs.<15.3	n/a	0.78	Age total energy, BMI, waist to hip ratio, education, smoking, alcohol, physical activity
(Schulze et al. 2004)	Nurse's health study 91,249, women, 24-44, USA, 8y	Total Fibre FFQ	>22g vs. <14.2	0.53	0.78	Age and BMI
(Montonen et al. 2003)	Finnish examination survey 10,054 men and women, 40-69y, Finland, 10y	Diet History Interview	>33g vs. <19.2	0.57	0.51	Age, sex, geography, smoking, BMI, energy, fruit and berries, vegetables

Table C-4. Results for Magnesium

Reference	N, sex, age, location, length follow-up	Variable/measure	Cut-off vs. reference	Unadjusted Relative risk	Adjusted Relative Risk	Variables adjusted for
(Lopez-Ridaura et al. 2004)	Nurses Health Study, 85,060 women 30-55y, USA, 18y Health professionals follow-up study, 42,872 men 40-75y, USA, 12y	Magnesium intake FFQ	377 (women) 458 (men) vs. 222(women) and 280 (men)	0.55-0.56	0.72-0.73	Energy, family history, BMI, PA, smoking, alcohol, hypertension, hypercholesterolemia, GL, cereal fibre, polyunsaturated fats, trans fats, processed meats
(Larsson and Wolk 2007)	Meta-analysis	Magnesium FFQ	Per 100mg increase in Mg intake/day	n/a	0.85	

Table C-5. Results for Vegetables and Fruit

Reference	N, sex, age, location, length follow-up	Variable/measure	Cut-off vs. reference	Unadjusted Relative risk	Adjusted Relative Risk	Variables adjusted for
(Harding et al. 2008)	EPIC-Norfolk, 21,831 men and women 40-75 yrs. UK,12 yr	Fruit and vegetable intake FFQ	3-4 vs. 5-6 Low vs. high quintile	0.87	0.78	Age, sex, family history, alcohol, PA, smoking, education, class, supplements, BMI
(Villegas et al. 2008)	SWHS 64,191 women, 40-70, China, 4.6y	G vegetable intake FFQ	428g/d veg. vs. 181 g/d	n/a	0.72	Age, energy, meat, BMI, WHR, smoking, alcohol, PA, income, education, job status, hypertension
(Liu et al. 2004)	Women's Health Study 39,876, women, ≥40, USA, 8,8y	Total fruit and veg. servings FFQ	10 vs. 2	n/a	0.77	Age smoking total calories
(Lindstrom and Tuomilehto 2003)	FINRISK study 4746 men & women, 35-64, Finland, 5y	Total fruit, veg. and servings FFQ	< 33 servings per month	n/a	1.18	BMI, age, WC, blood pressure, history high blood glucose, PA included in model

Table C-6. Results for Fat

Reference	N, sex, age, location, length follow-up	Variable/measure	Cut-off vs. reference	Unadjusted Relative risk	Adjusted Relative Risk	Variables adjusted for
(van Dam et al. 2002)	Health Professionals follow-up study 42504, men, 40-75y, USA, 12y	FFQ Total fat	39% of calories vs. 24 %	1.88	1.27	Age, energy, time period, PA, smoking, alcohol, hypercholesterolemia, hypertension, family history, fibre and magnesium, NOT BMI
(Salmeron et al. 2001)	Nurses Health Study 84,204 women, 34-59y, USA, 14y	FFQ	Every 5% increase in PUFA	n/a	0.63	Age, time period, BMI, smoking, family history, alcohol, AP, protein and total energy
(Harding et al. 2004)	EPIC- Norfolk, 25631, men & women, 40-74, UK, 3-7yrs	FFQ P:S ratio	0.518 vs. 0.475	n/a	0.38	Age, BMI, Waist to hip ratio and total energy intake in the same model.

Table C-7. Results for Physical Activity

Reference	N, sex, age, location, length follow-up	Variable/measure	Cut-off vs. reference	Unadjusted Relative risk	Adjusted Relative Risk	Variables adjusted for
(Hsia et al. 2005)	Women's Health Initiative observational study, 93676 women, mean age 61, US, 5.1y	Physical activity quintile METS	Not reported	0.67	0.78	Alcohol, education, smoking, hypertension, hypercholesterolemia, dietary fibre, % energy from CHO BMI and age
(Villegas et al. 2006)	Shanghai Women's Health Study 70,658 women, 40-70, Shanghai, 4.6y	PA METS quartile	>15.2 METs vs. <7.85/day	n/a	0.86	Age, energy, education, in come, occupation, smoking, alcohol, hypertension
(Weinstein et al. 2004)	Women's Health Study 38,878 women, ≥45, US, 6.9y	PA Met score	> 1500 kcal per week vs. 0-199 kcal/week	0.6	0.82	Age, family history, alcohol, smoking, hormone, hypertension, cholesterol, dietary factors, BMI
(Hu et al. 1999)	Nurses Health Study 70,102 women, 40-65, US, 8y	MET score	35.4 METs vs. 0.8 METs/week	0.43	0.74	Age, time period, smoking, menopause, hormone, family history, alcohol, hypertension, high cholesterol, BMI
(Wannamethee et al. 2000)	British Regional Heart Study 7735 men 40-59yrs. UK, 16.8 y	Physical activity questionnaire score	Moderately vigorous vs. inactive	0.36	0.51	Age, smoking, alcohol, class, BMI, CHD, insulin

Table C-8. Results for Sedentary Activity

Reference	N, sex, age, location, length follow-up	Variable/measure	Cut-off vs. reference	Unadjusted Relative risk	Adjusted Relative Risk	Variables adjusted for
(Hu et al. 2003)	Nurses Health Study 50,277 women, 30-55, US, 6y	Sitting TV Sitting Work Sitting home	>40 hours vs. 0-1 hour	2.00 1.24 1.06	1.94 1.25 1.11	Age, smoking, hormone, alcohol, METS, total fat, GL, total calories

C.1 References

Barclay, A. W., Petocz, P., Millan-Price, J., Flood, V. M., Prvan, T., Mitchell, P., and Brand-Miller, J. C.2008. Glycemic index, glycemic load, and chronic disease risk--a meta-analysis of observational studies. Am.J Clin.Nutr. 87(3): 627-637.

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Appendix D: Detailed Rationale for the Selection of Cut-offs and Weights for Diabetes Risk Factors

D.1 Method of Decision Making

When determining which cut-offs and weights to use for each of the risk factors, several steps were taken in the decision making process. First, the results of each longitudinal study for each risk factor were considered (See Appendix A). Studies were excluded from being considered if the variables used were not comparable to the ones available in the Web-SPAN survey (example: for magnesium, the units used in the meta-analysis by (Larsson and Wolk 2007) was change in risk/100mg increase in magnesium intake. This unit could not be applied to the Web-SPAN dataset.). A panel of experts was also consulted during the decision making process. Experts included an expert in the GI and GL, two experts in childhood obesity, two experts in physical activity measurement and one expert in statistical analysis. After expert advice, if several similar possible cut-offs existed, a mean of these values was used.

D.2 Obesity

The most appropriate cut-offs for overweight and obesity to use for this tool were determined to be the WHO (World Health Organization) cut-offs or the IOTF (International Obesity Task Force) cut-offs, rather than the CDC (Centers for Disease Control) criteria. The WHO and IOTF cut-offs are both measures intended for population-based studies and international use (Cole et al. 2000; de Onis et al. 2007). It was decided that the IOFT guidelines were most appropriate as the WHO cut-offs are relatively new and have not yet been thoroughly validated (Norris et al. 2009).

D.3 Glycemic Index and Glycemic Load

The meta-analysis by Barclay et al., 2008 considered many longitudinal studies of diabetes risk and was chosen as the best source of information to base GI and GL cut-offs and weighting on. The GL is based on both on quality and quantity of carbohydrate and a high GL score can either indicate a high quantity or a low quality of carbohydrate, which could have very different metabolic effects. Thus, we were advised to remove it from the analysis. However, having taken this into consideration, we decided to keep GL in the score because, in spite of its complicated meaning, it is an independent risk factor for type 2 diabetes (Barclay et al. 2008). The theory behind the GL and diabetes risk is that any high carbohydrate load, whether from low quality or high quantity, require more insulin to be secreted from the beta cells of the pancreas (Brand-Miller et al. 2003; Wolever and Bolognesi 1996), which may promote beta-cell exhaustion in cells genetically prone to dysfunction. The role of GL in the progression of disease therefore does appear plausible. The final cut-offs used for GI and GL were >58 and >142, respectively.

D.4 Fibre

The cut-offs for low fibre intake used in the study by (Larsson and Wolk 2007) were much higher than those used in North American studies and using this cut-off would have resulted in nearly all participants having low fibre intake as a risk factor, which would not be helpful in identifying those at greater risk. The remaining two American studies (Meyer et al. 2000; Schulze et al. 2004) had similar cut-offs and relative risk values, therefore the mean of the values reported

by these two studies were used to create a cut-off value and weight. The final cut-off for low fibre was < 14.8g.

D.5 Magnesium

The best study for determining the effect of low magnesium intake on diabetes risk was determined to be the study by Lopez-Ridaura et al. (Lopez-Ridaura et al. 2004). This study employed longitudinal data from both the Nurses Health Study and the Health Professionals Follow-up Study. The meta-analysis by Larsson and Wolk 2007 also provided helpful information, but the units of measuring magnesium intake in this meta-analysis (RR/100mg change in magnesium intake) were not comparable to that collected in the Web-SPAN study. Therefore the cut-offs and relative risks determined in the study by Lopez-Ridaura et al. (2004) were used for this study. The final cut-offs for magnesium were < 220mg for girls and < 280mg for boys.

D.6 Vegetables and Fruit

The units used to measure vegetable and fruit intake in the study by (Villegas et al. 2008) (g/day) were not comparable to the units used by Web-SPAN (servings per day), therefore the results of this study were not considered when determining a cut-off for vegetable and fruit intake. In addition, serving sizes of fruits and vegetables were considered to have greater similarity to the serving sizes of Canada's food guide in the study by (Liu et al. 2004) compared to the remaining two studies (Harding et al. 2008; Lindstrom and Tuomilehto 2003). Therefore, the study by Liu et al. was used for determining the cut-off and

weighting of the vegetable and fruit risk factor. The final cut-off for low vegetable and fruit intake was <2.0 servings.

D.7 Fat Intake

When the Web-SPAN results for polyunsaturated fatty acids (PUFA) were examined, it was found that reported PUFA intakes were unrealistically low due to frequent occurrences of missing PUFA data for many of Web-SPAN's ~500 food choices. Therefore, the only measure of dietary fat that could be used with accuracy was total fat. For this reason, the cut-offs and level of risk for total fat intake suggested in the study by Van Dam (2002) was used. The final cut-off for high fat intake was <39% of total kcal.

D.8 Physical Activity

In the diabetes literature, the most commonly used variable to used for determining the ability of physical activity to predict diabetes risk is a daily MET score. Physical activity in our cohort was measured using the PAQ-C questionnaire which results in activity scores ranging from 1 to 5, with a score of 1 being low and a score of 5 being high. Unfortunately, it is not possible to convert these scores to MET scores. The possibility of using some PAQ-C variables to create a relative MET score was considered but because the relative MET score calculated from the selected PAQ-C variables was not a true daily MET value, it could not be compared to the values in the diabetes literature. The relative MET score was used as a continuous variable to determine its ability to predict changes in ISS but was not included in the analysis of risk factor cut-offs or the composite risk variable analysis. An indirect method of determining a cut-

off using the full PAQ-C score was therefore used. The results of the Canadian Community Health Survey (CCHS) found that approximately 50% of boys and 68% of girls were not physically active (did not expend 3 kcal per kg body weight per day – about the amount of energy expended in 60 minutes of brisk walking). Using these values as a guide, cut-offs were chosen for the total PAQ-C score. A cut-off of 3 resulted in a similar percentage of students with low physical activity scores, therefore this was the final cut-off used for low physical activity.

D.9 Sedentary Activity

Although sedentary activity was considered as a possible risk factor to include in this analysis, it has only been shown to be related to diabetes risk in one study, which does not constitute firm evidence. Therefore, sedentary activity was not included in the final analysis.

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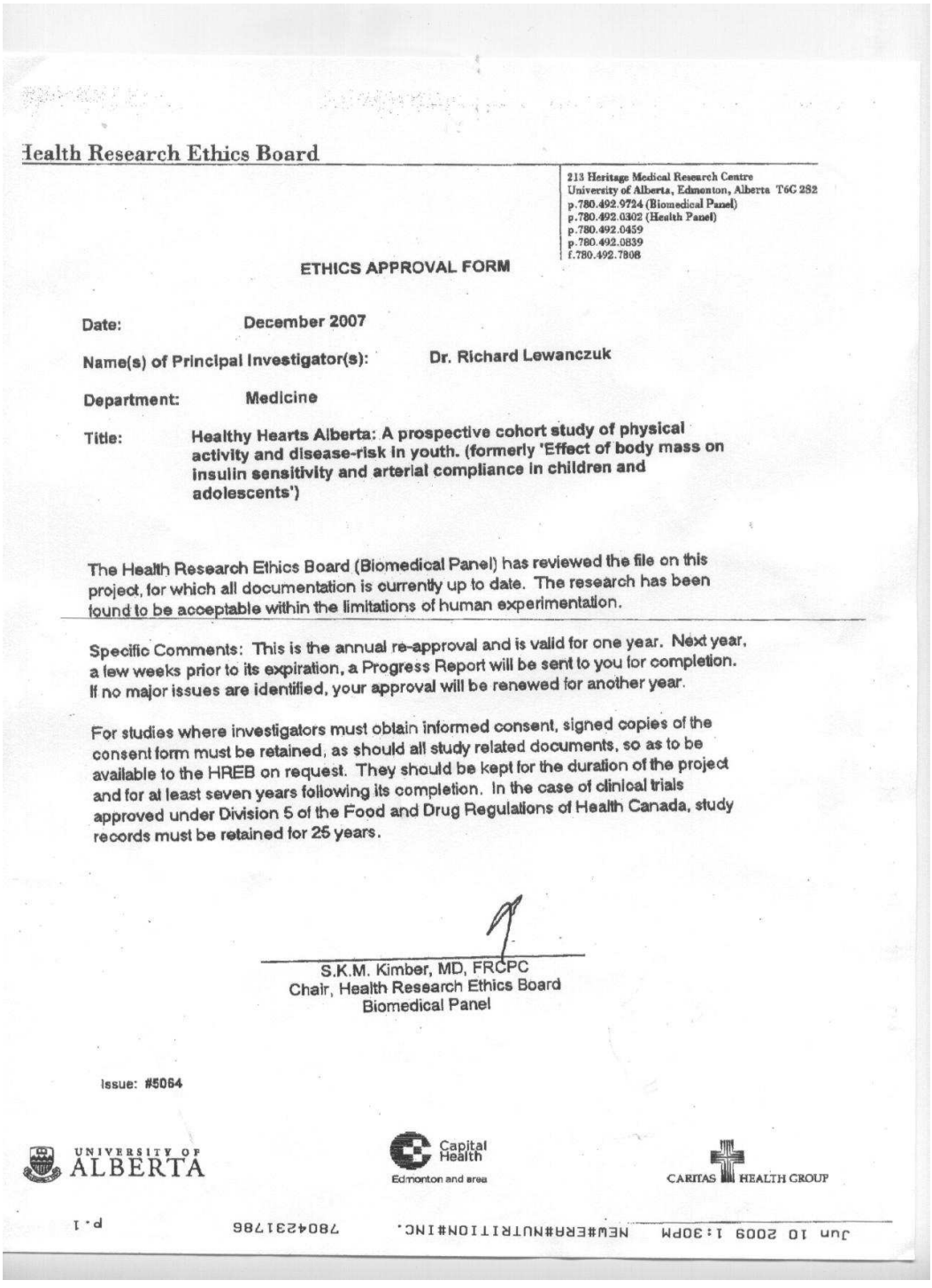
Appendix E Ethical Approval: Healthy Hearts Study



Health Research Ethics Board

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ETHICS APPROVAL FORM

Date: December 2007

Name(s) of Principal Investigator(s): Dr. Richard Lewanczuk

Department: Medicine

Title: Healthy Hearts Alberta: A prospective cohort study of physical activity and disease-risk in youth. (formerly 'Effect of body mass on insulin sensitivity and arterial compliance in children and adolescents')

The Health Research Ethics Board (Biomedical Panel) has reviewed the file on this project, for which all documentation is currently up to date. The research has been found to be acceptable within the limitations of human experimentation.

Specific Comments: This is the annual re-approval and is valid for one year. Next year, a few weeks prior to its expiration, a Progress Report will be sent to you for completion. If no major issues are identified, your approval will be renewed for another year.

For studies where investigators must obtain informed consent, signed copies of the consent form must be retained, as should all study related documents, so as to be available to the HREB on request. They should be kept for the duration of the project and for at least seven years following its completion. In the case of clinical trials approved under Division 5 of the Food and Drug Regulations of Health Canada, study records must be retained for 25 years.

S.K.M. Kimber, MD, FRCPC
Chair, Health Research Ethics Board
Biomedical Panel

Issue: #5064

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Appendix F: Method Used to Assign a Relative MET Value to PAQ-C Variables

F.1 Rationale

Metabolic Equivalent of Tasks, or METs are a measure of the intensity of physical activities. One MET (measured in kcal/kg body weight/hour) is the amount of energy expended per hour when sitting quietly. A daily MET value, a measure of total daily physical activity, can be calculated by multiplying the duration of activities by their MET value. Daily MET values are commonly used in epidemiological studies to examine the link between physical activity and disease risk.

Although a true daily MET score could not be calculated from data collected through the PAQ-C questionnaire, previous studies have used similar information to assign a relative MET score to the self reported frequencies of different physical activities as reported by youth (Klentrou et al. 2003; McMurray et al. 2000).

Table F-1 Method for Recoding Frequency of Physical Activities to Activity Weight

Value From PAQ-C	Recoded Activity Frequency Weight
No	0
1-2 Times per week	1.5
3-4 Times per week	3.5
5-6 Times per week	5.5
7 Times or more	7

Table F-2 Met Values for Activities in the PAQ-C

Activity	MET Values (From (Ainsworth et al. 1993) kcal/kg body weight/hr
In-Line Skating	12.5
Tag	5
Walking for Exercise	4
Bicycling	8
Jogging or Running	8
Swimming	7
Baseball, Softball	5
Dance	5
Football	8
Skipping	10
Soccer	7
Racquet ball	6
Volleyball	4
Basketball	7
Ice Skating	7
Skateboarding	5
Ice Hockey/Ringette	8
Gymnastics	4
Martial Arts (Judo)	10
Other	5

F.2 Method for Calculating Relative MET Score

For each participant, relative MET scores for each sport were calculated by multiplying the weight for the reported frequency by the MET value. The total relative MET score was calculated by taking the sum of all the MET scores for each individual physical activity. It should be noted that, using this method, it is assumed that the duration of one bout of activity is similar between people and no true duration of activity is reported. Because of this assumption, a true MET score can not be calculated using this method; the result is a relative MET score.

F.3 References

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Appendix G: Characteristics of Participant who Completed the PAQ-C Questionnaire and Differences Between Participants who Did and Did Not Complete the Questionnaire

Table G-1 Participant Characteristics and Mean Values for Risk Factor Variables for Participants who Completed the PAQ-C

Variable	Total n = 79	Boys n = 33	Girls n = 46	P-value
Age	12.0 ± 1.1	11.9 ± 1.1	12.0 ± 1.1	0.589
BMI (kg/m^2)	19.8 ± 3.2	19.9 ± 3.5	19.8 ± 3.1	0.989
GI	55.9 ± 6.8	57.1 ± 7.9	55.0 ± 5.8	0.204
GL	148.1 ± 65.4	170.5 ± 75.4	132.0 ± 52.3	0.014
Fibre (g)	14.8 ± 7.9	16.3 ± 8.2	13.7 ± 7.6	0.145
Magnesium (mg)	284 ± 119	308 ± 135	266 ± 104	0.129
Vegetables and Fruit (Servings)	5.2 ± 3.6	5.7 ± 4.1	4.8 ± 3.2	0.263
Percent Fat (% kcal)	31.6 ± 8.0	29.9 ± 6.2	32.8 ± 9.0	0.113
PAQ-C Score	2.6 ± 1.0	2.6 ± 1.0	2.6 ± 1.0	0.823
MET Score	204 ± 134	224 ± 127	191 ± 138	0.311
Insulin Sensitivity Score (δ o/oo)	16.6 ± 4.6	16.1 ± 5.1	17.0 ± 4.3	0.438

Data are means ± SD
Differences between boys and girls were assessed using student's T-tests.

Table G-2 Differences in Mean Values Between Participants Who Did and Did Not Complete the Physical Activity Portion of the Questionnaire

Variable	No PAQ-C n = 239	PAQ-C n = 79	P-value
Age	11.5 ± 1.6	11.9 ± 1.1	0.003
BMI (kg/m^2)	19.8 ± 3.8	19.9 ± 3.5	0.786
GI	55.6 ± 6.7	55.8 ± 7.1	0.845
GL	128.0 ± 61.86	145.4 ± 65.4	0.030
Fibre (g)	14.0 ± 8.5	14.6 ± 7.8	0.602
Magnesium (mg)	256.5 ± 135.7	279.4 ± 119.4	0.174
Vegetable and Fruit (Servings)	4.8 ± 3.7	5.1 ± 3.6	0.530
Percent Fat (% kcal)	30.7 ± 8.6	31.6 ± 8.3	0.392
Insulin Sensitivity Score (δ o/oo)	17.3 ± 5.1	16.7 ± 4.7	0.303

Data are means ± SD

Differences between those who did and did not complete the PAQ-C were assessed using student's T-tests.

Table G-3 Proportion of Students Reporting Diabetes Risk Factors by Sex for Participants Who Completed the PAQ-C

Variable	Total N = 82 % (n)	Boys N = 36 % (n)	Girls N = 46 % (n)	P-Value
Non-Overweight Overweight Obese	74.4 (61) 19.5 (16) 6.1 (5)	72.2 (26) 16.7 (6) 11.1 (4)	76.1 (35) 21.7 (10) 2.2 (1)	0.229
High GI	36.6 (30)	36.1 (13)	37.0 (17)	0.561
High GL	41.6 (34)	52.8 (19)	32.6 (15)	0.053
Low Fibre	54.9 (45)	50.0 (18)	58.7 (27)	0.287
Low Magnesium	36.6 (30)	41.7 (15)	32.6 (15)	0.269
Low Vegetable and Fruit Servings	22.0 (18)	22.2 (8)	21.7 (10)	0.583
High Percent Fat	14.6 (12)	8.3 (3)	19.6 (9)	0.132
Low Physical Activity	65.9 (54)	66.7 (24)	65.2 (30)	0.595

Differences between boys and girls were assessed using chi-square tests.

Table G-4 Differences in the Proportion of Students Reporting Diabetes Risk Factors Between Participants who Did and Did Not Complete the PAQ-C

Variable	No PAQ-C N = 234 % (n)	PAQ-C N = 82 % (n)	P-value
Non-Overweight Overweight Obese	76.9 (180) 17.9 (42) 6.0 (14)	74.4 (61) 19.5 (16) 6.1 (5)	0.924
High GI	37.6 (88)	37.8 (31)	0.516
High GL	32.1 (75)	41.5 (34)	0.074
Low Fibre	64.1 (150)	54.9 (45)	0.115
Low Magnesium	58.1 (136)	36.6 (30)	0.001
Low Vegetable and Fruit Servings	23.9 (56)	22.0 (18)	0.443
High Percent Fat	17.1 (40)	14.6 (12)	0.398

Differences between those who did and did not complete the PAQ-C were assessed using chi square tests.