INTERRELATIONSHIPS AMONG BODY COMPOSITION, NUTRIENT INTAKE, PHYSICAL ACTIVITY, MEDICAL MANAGEMENT AND GLYCEMIC CONTROL IN CHILDREN WITH TYPE 1 DIABETES

BY

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A Thesis Submitted to the Faculty of Graduate Studies in Partial Fulfilment of the Requirements for the Degree of

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ABSTRACT

Objective: To investigate if children with type 1 diabetes, compared to those without, had higher weight for height, higher fat mass, and/or a more central fat distribution, and to examine the relationship of these variables with age, nutrient intake, physical activity, medical management and glycemic control

Study Design: Females (n=27) and males (n=24) with type 1 diabetes, were compared to control females (n=34), and males (n=34), between the ages of 8 and 17 years, for weight, height, body mass index (BMI), percent total and regional body fat in a cross-sectional design. Percent body fat, percent abdominal fat, and trunk to leg fat ratio (TLFR) were measured by dual-energy x-ray absorptiometry. Height was measured to the nearest cm with a Harpenden stadiometer. Weight was measured to the nearest g with a standard upright balance. Weight and height were corrected to age by calculating Z-scores using the 1977 National Centre for Health Statistics data set. Body Mass Index (BMI) was calculated as kg/m^2 and as Z-scores using data complied by Rosner et al (1998). Nutrient Intake was assessed using one 24 hour recall interview and one 3 day food record. Physical activity was determined using a questionnaire and clinical information for children with diabetes was taken from the medical chart. Relationships among body composition, nutrient intake, physical activity, medical management and glycemic control were examined with correlation and linear regression.

Results: Children in each group were of similar age, weight, weight Z-score, height, height Z-score, percent body fat, percent of body fat in the abdomen, and TLFR. BMI and BMI Z-score were significantly higher in females with diabetes compared to controls. Indicators of central fat distribution increased across age groups in females with diabetes but not in controls.The number of injections of insulin per day and the dosage were not related to percent body fat in females with diabetes, while the use of Lispro insulin was associated with a lower percent body fat. No differences in body composition were found between males with or without diabetes.

Conclusion: Female children with type 1 diabetes are overweight for height compared to the control group as indicated by BMI. Expression of data as group means masks the relationships with age, since indicators of a central body fat distribution increase across age groups in girls with diabetes, but not in the control group. This higher BMI in females with diabetes appears to be mainly fat mass, however this could not be confirmed. Lispro may have a positive effect on body composition and should be investigated further.

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LIST OF ABBREVIATIONS

AB:	abdomen
ANOVA:	analysis of variance
ALFR:	arm to leg fat ratio
BIA:	bioelectric impedance analysis
BMI:	body mass index
CHO:	carbohydrate
CT:	computed tomography
DCCT:	diabetes control and complications trial
DXA:	dual energy x-ray absorptiometry
HbA1c:	Hemoglobin A1c
kcal:	kilocalorie
kg:	kilogram
MRI:	magnetic resonance imaging
PRO:	protein
SD:	standard deviation
SEM:	standard error of the mean
TLFR:	trunk to leg fat ratio

1. Rationale, hypotheses and objectives

Over 400 children in Manitoba have type 1 diabetes and the average annual incidence in children aged 0-14 years in Manitoba is 20.4 per 100,000, which is higher than reported previously in other urban regions of Canada (Blanchard et al, 1997). Type 1 diabetes mellitus is due to absolute insulin deficiency and most cases result from autoimmune destruction of beta cells of the pancreas. There are two peaks for age at diagnosis, namely in preschool and pre-puberty (Reviewed in Kordonouri et al, 1998). Recent studies indicate, that different immunological markers may characterize these patients at the onset of the disease. Kordonouri et al (1998), found that adolescents with diabetes onset during or after puberty have a more benign long-term course of the disease compared to children with a pre-pubertal manifestation of diabetes. The difference appears to be due to the more severe deficit of endogenous beta cell function in patients with long-standing diabetes, rather than the different immunological markers (Kordonouri et al, 1998). Ketoacidosis has been reported to be more frequent at diabetes onset in younger patients (Vanelli et al, 1997), although this was not found by Kordonouri et al (1998).

Children diagnosed with diabetes prior to puberty seem to be the most vulnerable to growth impairment (Holl et al, 1998; Brown et al, 1994; Wise et al, 1992). This may be due to the fact that prepubertal children with type 1 diabetes have lower levels of insulin-like growth factor-1 and higher levels of serum growth hormone concentrations than their non-diabetic peers (Holl et al, 1998;

Wise et al, 1992). When metabolic control improves, growth hormone concentrations fall, insulin-like growth factor-1 levels increase, and growth acceleration occurs (Wise et al, 1992).

While the optimal goal would be to find a cure for diabetes, such is not likely to become immediately available and thus it becomes imperative to achieve optimal management to prevent complications in order to maintain quality of life and health. Current goals for management of diabetes in children and adolescents are to 1) achieve normal physical and emotional growth, 2) reduce the symptoms of diabetes that result from hypoglycemia or hyperglycemia, and 3) lessen the risk of long-term complications such as retinopathy, neuropathy and nephropathy. (Kaufman, 1997). The tools for management include monitoring glycemia, and providing the type and amount of insulin that allows for the best glycemic control, which includes adjusting the insulin dose based on short term changes in glycemia, food intake and exercise. The basic insulin dose also needs to be adjusted to reflect longer term changes in growth.

Large scale studies of metabolic control in young (>14 years of age) subjects with type 1 diabetes were lacking until the Diabetes Control and Complications Trial (DCCT). The results from the DCCT showed that better glycemic control achieved by intensive diabetes management is associated with significantly fewer microvascular complications in adults and adolescents (DCCT Research Group, 1994).This relationship is likely also true for children

(Reviewed by Brink, 1997).Therefore, tight metabolic control, as achieved by intensified insulin treatment used in the DCCT is recommended today for most type 1 patients. However since the DCCT showed a 2-4 fold increase in the risk of hypoglycemia in subjects achieving lower centile mean blood glucose and glycated hemoglobin (HbA1c) levels, there is debate on whether these lower blood glucose and HbA1c targets should be the goal of diabetes management in children.

While the adolescents participating in the intervention group were compliant, HbA1c concentrations were on average higher than in adults receiving similar therapy; regardless of conventional or intensive diabetes management. This suggests that treatment regimens for type 1 diabetes are not yet ideal for adolescents and possibly younger children with diabetes. No differences in absolute growth or growth velocity were observed between the intensively managed adolescents, and those treated with conventional therapy, but a twofold increased risk for becoming overweight was observed in the intensively managed group (DCCT, Trial Research Group, 1994). The DCCT failed to indicate the composition of this weight gain and this issue deserves complete investigation because of the potential long term consequences of adiposity to insulin resistance (Capiro et al, 1994; Colberg et al, 1995; Coppack et al, 1996).

Understanding the relationship between growth, quality of growth and glycemic status is of fundamental importance to providing improved dietary

management for diabetes in childhood. In previous years, type 1 diabetes was not associated with excess weight. However, intensive diabetes management in childhood to control glycemic status, and prevent the debilitating complications, may be associated with disproportionately high weight for height (DCCT, Trial Research Group, 1994). In some cases, insulin dosage is high (units per kilogram). Over time this might result in excess fat mass which is associated with decreased insulin sensitivity and glucose intolerance (Colberg et al, 1995; Coppack et al, 1996; Goodyear et al, 1995)

Recent large scale cross-sectional studies in children and adolescents have found that multiple insulin injections with or without a high dose of insulin per unit body weight are associated with weight gain (Mortensen et al,1998; Danne et al, 1997; Dorchy et al, 1997; Pietilainen et al, 1995). Furthermore the number of insulin injections had no effect on HbA1c. This questions the current management of using multiple insulin injections in the majority of patients and underlines the importance of focusing on the target blood glucose level instead of the number of insulin injections. This also suggests that the cause of weight gain is multifactorial.

This thesis research will investigate the relationships among body composition, nutrient intake, physical activity, glycemic control, and medical management in children with type 1 diabetes, compared to healthy controls. The results will provide the foundation upon which to develop future strategies for dietary and medical management specific to children and adolescents.

Hypothesis: high insulin dose (U/kg) and/or frequency of injection during childhood and adolescence adversely affect body composition such that fat mass is higher than normally expected for age.

The **objectives** of this research in children from 8-18 years of age are to:

1) characterize body composition, nutrient intake, and physical activity in relation to glycemic control and medical management, in children with type 1 diabetes and compared to children without diabetes, and
2) examine possible influences of body composition, diet, physical activity, and medical management on glycemic control in children.

2. Present State of Knowledge

2.0 Metabolic control in children and adolescents with type 1 diabetes

Metabolic control is generally worse in adolescents than in children with type 1 diabetes. (Mortensen et al, 1998). This may be due to several factors, including decreasing compliance with different aspects of the treatment regimen (Lernmark et al, 1996) and decreased insulin sensitivity of peripheral tissues during adolescence perhaps caused by hypersecretion of growth hormone (Bloch et al, 1987). Results of the DCCT proved that adolescents with diabetes, like adults, can reduce the development of diabetic complications by achieving near-normal HbA1c levels with intensive insulin therapy. Retinopathy and nephropathy occur in adolescents with conventionally treated diabetes at an absolute rate of 23 and 6.3 per 100 patient years at risk, respectively (DCCT, Trial Research Group, 1994). Near-normal HbA1c levels, as achieved by

intensified insulin treatment, reduced the risk by 30% for retinopathy and by 10% for nephropathy.

Intensified insulin treatment usually requires multiple daily insulin injections, but the number of insulin injections is less important than the ability to target and achieve near-normal blood glucose values without severe episodes of hypoglycemia. The technique for achieving normal levels of HbA1c is not likely to be as important as the end result (Malone, 1994). In fact, several studies have shown that there is no significant relationship between HbA1c and insulin injection frequency in adolescents (Mortensen et al, 1998; Dorchy et al, 1997). Dorchy et al (1997) found that after 2 years of diabetes, the frequency of home blood glucose monitoring was the only "objective" parameter promoting good HbA1c levels.

Despite the increase in severe hypoglycemia, there were no long-term neurocognitive consequences seen in the DCCT study population, in either the adults or the adolescents (DCCT Research Group, 1994). In addition, quality of life was not adversely affected by following the intensive regimens that were used in the study. Therefore, the DCCT study group recommended that intensive therapy of diabetes should be the treatment of choice for patients with type 1 diabetes who were 13 years of age or older (DCCT Research Group, 1994).

Applying the results of the DCCT to children under the age of 13 is problematic since this group was not included in the study. However, the advice to improve overall glucose control and to do so safely and without excessive

hypoglycemia clearly applies to all children with type 1 diabetes, based upon studies in Berlin, Pittsburg, Sydney and also in Linkoping which detailed the long-term consequences in broader pediatric patients over long periods of time (Reviewed in Brink, 1997). Because young children may be more sensitive to severe hypoglycemia, it is controversial whether the risk of recurrent hypoglycemia is too high to justify advocating these lower blood glucose and glycated hemoglobin targets. In practice, target blood glucose levels are set on an individual basis.

2.1. Assessment of metabolic control

Both the diagnosis of diabetes and the assessment of metabolic control depend on assays of the concentration of blood glucose. The ability to accurately assess present and prior glucose control has undoubtedly benefitted the treatment of patients with diabetes. Methods used to assess blood glucose levels include the oral glucose tolerance test, urine testing, home blood glucose self-monitoring, and HbA1c. The hyperinsulinemic-euglycemic and hyperglycemic clamp techniques are used to measure tissue sensitivity to insulin and beta-cell sensitivity. Laboratory tests done in this thesis research will include urine glucose testing and HbA1c, and the methods used will be described in detail. The remaining tests warrant a brief description since other studies cited have used these procedures.

The oral glucose tolerance test is the current gold standard for diagnosing diabetes. (Singer et al, 1989). The test involves measuring plasma glucose

before and after ingesting a standard 75 g dose of glucose for adults or 1.75 g/kg for children. The patient must have fasted overnight, preceded by 3 days of a typical diet. A sample of the fasting blood is introduced into a tube containing fluoride for baseline glucose estimation (Higgins, 1994). The patient drinks 75 g of glucose dissolved in 300 ml of water and blood is taken for glucose estimation at set intervals at 2 or 3 hours. Plasma glucose levels >11 mmol/L at 1 and 2 hours are diagnostic of diabetes.

Patients can test their urine for the presence of glucose using reagent strips, such as Bmstix and Diastix. A positive urine test for glucose demonstrates that the glucose concentration in blood has risen above the renal threshold of approximately 10 mmol/L, above which glucose is no longer reabsorbed by the blood but is excreted via urine. Urine glucose monitoring is not an accurate measure of blood glucose for several reasons. Urine glucose measurements are influenced by the variability of the renal threshold for glucose, urine accumulation time in the bladder, influence of drugs and other substances. Urine testing also provides no information on blood glucose fluctuation below the renal threshold of approximately 10 mmol/L (Singer et al, 1989).

For laboratory testing, a 24 hr urine sample is preferable, but is difficult to obtain. Instead, first voided fasting morning urine specimen or nonfasting casual urine sample is often used. When a first-voided or casual urine specimen is collected, urinary excretion of glucose is expressed as a molar ratio of the nutrient to urinary creatinine, to correct for fluctuations in urine volume (Gibson,

1990).

The concentration of albumin in urine is measured in a sample from a 24 hour urine collection and the result expressed as albumin excretion rate. The detection of microalbuminuria is used to predict those type 1 patients at risk of diabetic nephropathy, which is the most common cause of renal failure in those with diabetes and accounts for significant levels of morbidity and mortality (Watkins, 1985).

Home blood glucose monitoring is not subject to the limitations of urine glucose testing and few technical difficulties are encountered. Blood glucose determinations are sufficiently accurate for ordinary clinical and home use. This has been made possible by the development of glucose oxidase based reagent strips and reflectance meters since 1978 (Sonksen et al, 1978).

Glycated hemoglobin is the generic term referring to a series of minor hemoglobin components that are formed by the attachment of various sugars to the hemoglobin molecule. Improved techniques have allowed for measurement of the various hemoglobin components such as HbA1, which can be further separated into its constituent parts, including HbA1c. Glucose is the sugar in the major fraction, HbA1c, while other sugars, constitute the other fractions, making HbA1c the most specific indicator of long term glycemic control. (Kilpatrick, 1997). While HbA1c is regarded as the gold standard of long term metabolic control, glycated hemolglobin and HbA1 are also acceptable measurements, as they all reflect the mean blood glucose concentration over

the life of the hemoglobin molecule (six to eight weeks) (Higgins, 1994). Glycated hemoglobin, HbA1, and HbA1c also correlate with various other measures of glycemic control, including fasting plasma glucose and mean postprandial plasma glucose (Nathan et al, 1984). Home blood glucose monitoring is complimentary to HbA1c measurements as home blood glucose monitoring defines the extent of glycemia excursions while HbA1c reflects integrated glycemia control during the lifespan of the hemoglobin molecule. However there are a number of different methods of measuring HbA1c which can give varying results with patient samples. A number of different approaches have been used to address the issue. European guidelines (established before the DCCT report) have suggested that glycemic control be classified according to how many standard deviations a patient's HbA1c lies from the non-diabetic mean value for the particular assay (European IDDM Policy Group, 1993). Another approach is comparing local laboratory values with those obtained when the same samples are measured by the DCCT central HbA1c laboratory (Reviewed by Kilpatrick, 1997).

A less common method of assessing blood glucose is to measure fructosamine in blood. Fructosamine is essentially a measure of glycosylated albumin. Because albumin has a shorter half-life in blood than hemoglobin, fructosamine reflects glucose levels over a shorter period, generally one to three weeks (Higgins, 1994).

Determination of serum fructosamine is a technically simple, reproducible (intra-

and inter-assay variation was 0.5-0.8 and 1.5-2.9%, respectively), and moderately inexpensive method for the assessment of glycemic control in type 1 diabetes mellitus (Koskinen et al, 1987). Many studies have found that fructosamine values correlate well with HbA1c, as well as other measures of glycemic control (Hom et al, 1998; Gomo Z, 1992; Sridama, 1990; Prior et al, 1989; Jerntorp et al, 1988; Koskinen et al, 1987) .
However, HbA1c is slightly more sensitive (Hom et al, 1998; Sridama, 1990; Prior et al, 1989; Jerntorp et al, 1988). Physiological states which alter serum proteins also need to be considered in the interpretation of fructosamine levels (Koskinen et al, 1987).

The hyperinsulinemic-euglycemic and hyperglycemic clamp techniques offer a highly reproducible, physiological method of quantifying both tissue sensitivity to insulin and beta-cell sensitivity to glucose (DeFronzo et al, 1979). In both techniques two intervenous catheters are inserted; one into an antecubital vein for infusion of insulin and glucose, and the second is placed in a vein on the dorsum of the contralateral heated hand for sampling of arterialized venous blood.

The goal of the euglycemic insulin clamp is to raise the plasma insulin concentration acutely to a new plateau and to maintain it at that level. This would result in hypoglycemia if the plasma glucose concentration were not maintained at its euglycemic level. Thus, the euglycemic clamp consists of an insulin infusion of predetermined fixed dosage and a variable rate glucose infusion.

This allows the calculation of the metabolic clearance rate of insulin. Both the hyperglycemic and euglycemic clamp studies assume that basal hepatic glucose production is suppressed by the infusion of glucose and insulin.

The goal of the hyperglycemic clamp technique is to raise the plasma glucose concentration acutely to a fixed hyperglycemic plateau and to maintain it at that level for 2 hours. This allows for the assessment of beta-cell sensitivity to glucose as well as quantification of the amount of glucose metabolized by the body following a controlled hyperglycemic stimulus.

2.1. Growth:

Growth may be affected even prior to diagnosis. Early weight gain and rapid growth have been cited as risk factors for type 1 diabetes (Reviewed in Connors, 1997). Several studies have reported that at the onset of diabetes, children are taller than their non-diabetic peers (Danne et al, 1997; Holl et al 1994; Brown et al, 1994; Price & Burden, 1992; Salardi et al, 1987; Songer et al, 1986; Edelsten et al, 1981; Drayer, 1974). Others have found normal stature (Du Caju et al, 1995; Thon et al, 1992), or short stature (Hoskins et al, 1985; Leslie et al, 1991) at diagnosis of diabetes. Some of the studies lack proper controls, such as correction for secular trends and for mid-parent heights. One well controlled study compared heights of children as many as 3 years before the onset of diabetes and found them to be significantly taller than the controls during each of those years. They were taller than their siblings, who were similar to controls. (Price & Burden, 1992). If a genetic factor were operating, then one

would expect the siblings to be similarly affected.

While children may or may not be taller at diagnosis, reduced longitudinal growth has been observed in the years following diagnosis (Holl et al, 1998; Bognetti et al, 1998; Salerno et al, 1997; Danne et al, 1997; Holl et al, 1994; Brown et al, 1994;). This decrease in growth velocity was found to be more severe in children who were prepubertal at diagnosis, and had worse metabolic control (Danne et al, 1997; Jos et al, 1996; Wise et al, 1992;). Growth acceleration has also been associated with good glycemic control (Holl et al, 1998; Gunczler et al, 1996; Wise et al, 1992; Rudolf et al, 1982). In a number of studies no relationship was found between growth and diabetes control (Pitukcheewanont et al, 1995; Salardi et al, 1987; Herber & Dunsmore, 1988). The reason for these differences may be the arbitrary classification of good, fair and poor control.

While some studies found that poor glycemic control was associated with decreased final height (Danne et al, 1997; Penfold et al, 1994), most studies have found that final height is not reduced in patients with type 1 diabetes (Bognetti et al, 1998; Zachrisson et al, 1997; Salardi et al, 1997; Holl et al, 1994; Brown et al, 1994).

However height for age does not provide information on the quality of growth, or impinge on subsequent ability to control blood glucose levels. It is necessary to look at height and weight together as well as the composition of that weight. Children with diabetes have been increasingly recognized as

overweight for height. (Pietilainen, 1995; Holl et al, 1994; Thon et al, 1992; Wise et al, 1992; Herber & Dunsmore, 1988).

In otherwise healthy children, obesity is known to promote longitudinal growth (Reviewed in Holl et al, 1994 & Thon et al, 1992). In contrast, children with diabetes seem to be gaining weight at a much greater rate than height. In fact, it is the children with the most distinct loss in relative height who exhibited a significantly higher BMI (Danne et al, 1997). This pattern of growth is similar to that found in disease states such as Prader-Willi, Laurence-Moon-Bardet-Biedl syndromes or in untreated hypothroidism or Cushing disease. Most studies indicate weight gain is a problem for both male and female children with type 1 diabetes (Holl et al, 1998; Danne et al, 1997; Jos et al, 1996; Holl et al, 1994; Thon et al, 1992), while others suggest pubertal females are more likely to be overweight for height than males or pre pubertal females (Domargard et al, 1999; Du Caju et al, 1995; Gregory et al, 1992). Exacerbation of diabetes control by excess fat mass could pose a significant problem to the long term management and outcome of diabetes.

Routine measurements collected at scheduled clinical appointments at the Manitoba Diabetes Education Resource for Children and Adolescents (DER-CA) indicate that children within Manitoba are experiencing weight gain with specific emphasis in adolescent girls (see Figure 1). In Manitoba during 1995, all children with type 1 diabetes had an average Z-score of 0.41 for height and 1.37 for weight suggesting excess weight and potentially disproportionate fat

distribution (Manitoba Diabetes Education Program, 1995). Z scores are the number of standard deviations above or below the 50th percentile for a specific age (and sex) using data from the National Center for Health Statistics. More recently, growth of 151 children over the past year followed that same trend, but when expressed as Z scores separated by sex, only females appeared to be overweight for height and age (Figure 1.1). Since it remains unknown if this additional weight is fat or lean mass and a complete data set is not available, this thesis research will investigate the composition of excess weight gain and include a comparison group of children without diabetes.

At present the cause of weight gain and its composition are unknown. It is not uncommon for adolescent and young adult females with type 1 diabetes to omit insulin injections to maintain body weight which is associated with impaired metabolic control and a higher risk of diabetes-related complications (Bryden et al, 1999; Daneman et al, 1998 ;Rydall et al, 1997). Since the intensive management of the DCCT is associated with weight gain (DCCT, Trial Research Group, 1994) , it may not be well accepted and glycemic status will be compromised. The present study will help to identify the factors related to weight gain and provide information upon which to base future dietary management of type 1 diabetes.

2.1.0. Assessment of Growth

Body weight indicates short term growth in response to nutritional and medical care of children with diabetes. Standing height offers information on

chronic nutritional status and is also valuable to monitoring growth progress and quality of growth. Measurement of weight and height can also be used to assess appropriateness of growth by calculating weight to height ratios. Standard deviation scores (Z scores) for weight and height indicate growth of a subject compared to a large population of similar genetic and cultural background. As is commonly done, the National Centre for Health Statistics data set will be used to compare growth of these children. However, it is important to include a group of children without diabetes to reflect current trends as the data set is dated and childhood obesity is increasing in general (VanItallie, 1996).

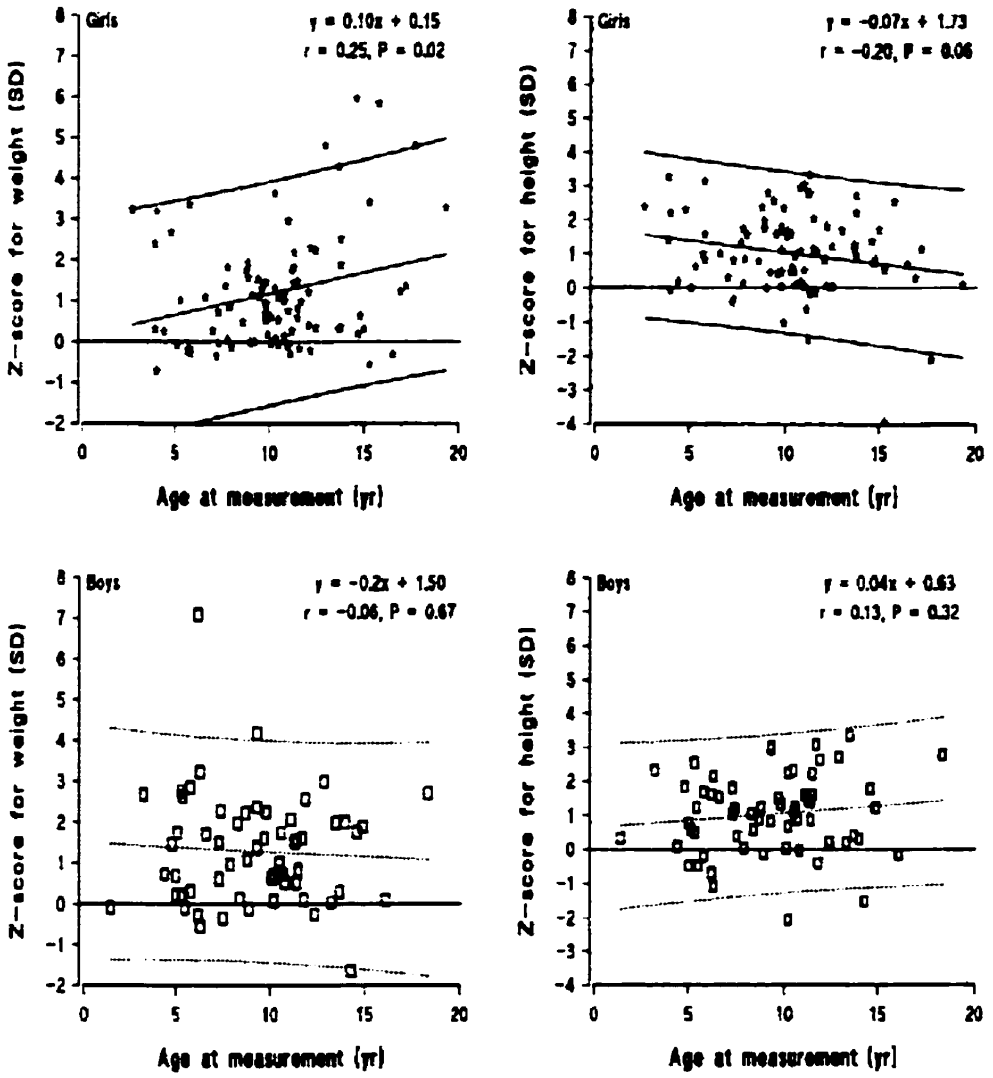

Figure 1.1. Weight and height z-score expressed to age at measurement and separated by sex. The line at zero represents the 50th centile for weight or height from the National Centre for Health Statistics. The solid line and dashed lines represent the regression line and 95% confidence interval for the growth data.

2.2. Body Composition

A twofold increased risk for becoming overweight exists with intensive insulin treatment (DCCT, Trial Research Group, 1994). One small study by Carlson & Campbell (1993) investigated the composition of this weight in 6 adults who experienced weight gain as a result of intensive management in the DCCT. Body weight increased by 2.6±0.8 kg (from 70.3±6.8 to 72.9±6.3) during 2 months of intensive management. All of the weight gain could be attributed to an increase in body fat as measured by underwater weighing. Reduction in glycosuria and the decrease in the 24 hour energy expenditure (measured by open-circuit, indirect calorimetry) accounted for all of the weight gain. These results are of great concern and this issue deserves further investigation because of the potential long term consequences of increased fat mass, and the distribtuion of that fat mass, on insulin resistance (Capiro et al, 1994; Colberg et al, 1995; Coppack et al, 1996).

Existing data on lean and fat mass in children with type 1 diabetes are preliminary at best. Sinha et al, (1996) used DXA to measure total body fat and lean mass in 9 subjects with newly diagnosed type 1 diabetes greater than 14 years of age, over 6 months. Based on small sample sizes, separate evaluation of the young subjects was not feasible. As a group, new onset type 1 diabetes was associated with greater weight gain than in new onset type 2 diabetes. Weight gain associated with type 1 was predominantly lean mass when expressed as percent body weight and weight gain in type 2 was predominantly

fat. However, absolute gain in fat mass (kg) was greater in type 1 diabetes than in type 2 which may play a key role in evaluating the effectiveness of insulin dosage; the importance of not only percent body fat but absolute kilograms of fat and its distribution can not be stressed enough in preventing insulin resistance. The extent and duration of weight gain and alterations in body composition past 6 months of therapy were not assessed.

Similar results were found by Bartz et al (1997) who used bioelectric impedance to measure total fat and lean mass in 157 male, and 117 female children with type 1 diabetes. The average age was 17.6 with a duration of diabetes of 8.9 years. There was no significant difference in percent body fat between the diabetic and control group. However, the fat free mass (FFM) was significantly higher in the diabetics compared to the controls. Unfortunately, change in percent body fat over time, and metabolic control were not assessed.

On the other hand, several studies indicate that weight gain in type 1 diabetes is a result of mainly fat mass. In one study, 68 children (6-18 years) with type 1 diabetes were studied for body fat using skin fold thickness and bioelectrical impedance measurements (Gregory et al, 1992). Body fat was highly variable (4-47% of weight) and dependent on age and sex. Unfortunately abdominal versus limb adiposity was not determined. This is important because a central distribution of fat has been associated with decreased insulin sensitivity in children (Freedman et al, 1987). Pubertal females had a significantly higher percentage body fat than younger females and males of all

ages (Gregory et al, 1992). Girls in late puberty also received more insulin on a per kilogram basis than younger females and had a significantly greater HbA1 than prepubertal girls. But since there was no control group studied, evaluation against the normal increase in body fattness during puberty could not be assessed.

In another study by Tuvemo et al, (1997) 34 children less than 15 years of age were studied during the first 5 years after diagnosis of type 1 diabetes. All children were intensively managed using 3 or more injections daily after the second year of diagnosis. Height, weight and body mass index (BMI) did not differ from the control group, however girls with diabetes increased their triceps and subscapular fat significantly despite normal BMI. This was not the case for males. Since BMI does not provide information regarding body composition, the fact that the 2 skinfold measurements were significantly larger in the girls with diabetes suggests that excess fat was accumulated, or that fat distribution was abnormal. Unfortunately only the 2 upperbody skinfold measurements were made, abdominal fat was not measured and total percent body fat was not calculated. A negative association between skinfold thickness and insulin dose was observed suggesting that dosages were withheld to maintain body weight. This study indicates that acquisition, or distribution of, fat mass in females is altered by intensive management of type 1 diabetes (Tuvemo et al, 1997). The consequence of this to glycemic control will be further investigated by the present research where a larger sample size will be used and both whole body

and regional fat mass assessed. In addition the comparison group will help to define if increases in fat mass are due to normal physiological maturation or management of type 1 diabetes.

Finally, Pietilaninen et al, (1995), found that 48 girls with type 1 diabetes between the ages of 10 and 19 years had a higher BMI and %body fat (determined by skinfold thickness) than the control group. Most (96%) of these girls took 3 or more insulin injections per day. The number of insulin injections was not found to be related to adiposity but the insulin dose was correlated positively with BMI and percent body fat. Percent body fat and intake of saturated fat were also significantly related to HbA1c. Unfortunately, only 3 upper body skinfold thickness measurements were made (triceps, biceps and subsacpular), and fat distribution was not addressed.

2.2.0 Assessment of Body Composition

Dual-energy x-ray absorptiometry provides whole body as well as regional measurements of bone, lean, and fat mass (Mazess et al, 1990). The only other methods which directly measure body composition are computed tomography or magnetic resonance imaging. However, these methods are impractical due to the high cost, high radiation exposure in the case of computed tomography, and limited access to equipment.

The most common and frequently used methods of measuring body composition are based on a two-compartment model comprising fat and fat-free mass. These methods have shortcomings or are indirect in the sense that they

rely on physical properties or chemical constants of the body which are derived from limited human cadaver studies (Pintauro et al, 1996). Another limitation is that these methods can not determine regional fat distribution. The three most common methods used to calculate body composition based on the two-compartment model are under-water weighing, bioelectrical impedance analysis, and skinfold-thickness measurements. Underwater weighing is impractical for children since many children find the breathing maneuver too difficult to perform. In addition, the amount and composition of fat free mass in a maturing child changes with growth, leading to uncertainties concerning the constants that are used to convert density to percentage fat (Gutin et al, 1996). Likewise, DXA was found to have better precision and accuracy than skin fold measures (Coefficient of variation 3.3%) or bioelectric impedance (Coefficient of variation 3.5%) (Gutin et al, 196). DXA also offers the ability to specify the region for assessment. After a review of many validation studies, Kohrt (1998) recently concluded that DXA is less dependent on assumptions about biological consistency than are other methods.

DXA (Hologic QDR-4500W) operates using a pulsed, dual-energy x-ray source switched between 70 kVp and 140 kVp. These energies have been shown to be optimal for precision and maximizing bone/soft tissue contrast. The x-ray beam passes through a calibration disk and scans the subject longitudinally. A detector passing simultaneously under the subject feeds a computer with the absorption data recorded as pixel (picture element) by pixel.

For each pixel corresponding to a surface of 0.151 cm length x 0.064 cm width, weight, fat mass percentage and mineral bone mass are determined from beam attenuation analysis, which depends on the relevant tissue composition (Pietrobelli et al, 1996). The fat mass percentage of each pixel is calculated in reference to internal standards of variable thickness, simulating various fat mass percentages. Their attenuation coefficient is standardized with those of a stearate (standard of acrylic resin) and of a water-stearate mixture (standard of acrylic resin with aluminum overlapping). The sum of all pixel values gives the whole-body composition in terms of fat mass, boneless lean mass and mineral bone mass. A daily calibration with reference to internal standards is required.

The major advantages of DXA for examination of children are that the measurement time is relatively short (6 min), the precision is generally good (<1-2%) and the radiation dose is minimal (1.5 R or 2.6 μSv for one whole body scan). Coefficients of variation for whole body fat (g) and lean body (g) mass using the DXA (Hologic QDR-4500W) at the Manitoba Clinic are 1.2% and 0.2% respectively (preliminary data in 14 young adults ranging from 38 to 80 kg). These measurement errors are compatible with cross-sectional studies of body composition in young children. In addition, DXA measures indicate the distribution of fat and lean mass in regions such as trunk, forearms and limbs. This information will be important to define the relationship between fat distribution and glycemic control. Variations in DXA results exist based on the model used (Ellis et al, 1994). The largest Canadian data base regarding growth

and body composition (Faulkner et al, 1996) is based on DXA measurements by a 2000W Hologic model compared to the 4500W Hologic model used in the present study. These two machines give similar results but variation of up to 2-3% could alter interpretation of results. Madsen et al, (1997) measured the reproducibility of total and regional body composition measurements performed on DXA using Norland XR-26 equipment. The precision errors, expressed as coefficients of variation were 1.4 % for lean mass of whole body and 1.7% for fat mass of whole body. In addition, Madsen et al, (1997) examined the ability of DXA to measure changes in lean mass and fat mass was examined by placing 11.1 and 22.3 kg porcine lard on the body of 11 subjects. Percentage fat of exogenous lard was 81.3 (SD 3.5%) as assessed by DXA which corresponded well with the result of chemical analysis (82.8%).

Several studies compared DXA with carcass analysis in pigs. Svendsen et al (1993) found that the lean and fat components of seven pigs (weight: 35-95 kg) measured by DXA (using Lunar DPX-L instrument in the adult medium scan mode) were highly correlated ($r>0.97$)to the values determined by chemical fat extraction. Brunton et al (1993) measured 10 pigs (approximately 6 kg) using DXA (Hologic QDR-1000W, pediatric mode). There was good agreement with the carcass analysis for lean tissue ($r=0.96$), and fat tissue ($r= 0.83$). Pintauro et al, (1996) measured 18 pigs (15-35 kg) using DXA (Lunar DPX-L, adult fast-detail mode). Carcass lean and fat contents were highly correlated with DXA measurements ($r=0.99$). Jensen et al (1993) evaluated the accuracy of DXA-

predicted fat and lean mass by comparison to chemical analysis of meat block phantoms. The correlation was excellent (r>0.99). Going et al (1993) evaluated the ability of DXA (Lunar, DPX model) to detect small changes in body composition during a dehydration-rehydration protocol in 17 subjects aged19-31. The results suggest that DXA provides better estimates of small changes in body composition than do dual photon absportiometry and hydrodensitometry and it seems reasonable to expect DXA to provide accurate estimates of changes in body composition in studies of longer duration in which grater changes in body mass occur.

Gutin et al (1996) compared the reliability of DXA (Hologic QDR-2000), BIA and anthropometry in the measurement of body composition of 43 children ages 9-11 The range of trial-to-trial differences were smallest with DXA. The largest single trial-to-trail difference for the DXA measurement was 1.1% fat units. This implies that DXA may be especially well-suited for repeated-measures studies in which small differences need to be detected.

2.3 Total fat mass and it's distribution in relation to insulin resistance

In Adults, insulin resistance is frequently associated with overall accumulation of fat in the body, however there is growing evidence that the distribution of fat may have an additional role (Abate, 1996). In the 1980's it was reported that a measure of central body fat distribution, the waist-to-hip ratio was independently and additively predictive of abnormalities in glucose and lipid metabolism (Reviewed in Jensen, 1997). Krotkiewshi et al (1983) reported that

fasting plasma glucose and insulin concentrations were independently associated with waist-to-hip ratio, and were additive to the degree of obesity.

One recent study examined the relationship of abdominal fat to insulin sensitivity by direct and indirect measurement of regional fat (by DXA and anthropometry). Carey et al (1996) found that the strong relationship between insulin resistance and central adiposity in non-obese women was not seen with traditional anthropometry but was evident when both insulin sensitivity and abdominal fat were measured by DXA. The region measured by DXA contained tissue from lumbar vertebra 2-4, an area which has been shown by MRI to contain a relatively high visceral and low subcutaneous fat content (Ross et al, 1993). Anthropometric indicators of central fat (waist-to-hip ratio and subscapular-to-triceps ratio) were no better than estimates of total fat (eg. BMI, percentage total fat from skinfolds) in predicting insulin sensitivity and central abdominal fat. This may be because intra-abdominal fat in women, measured by CT, has been shown to correlate better with the BMI (Seidell et al, 1987) than with the waist-to-hip ratio, except in the obese and very obese. In contrast to the anthropometric data, DXA central fat measurements (which included visceral and some subcutaneous fat) had significant metabolic associations, independent of total and nonabdominal adiposity. Increased abdominal, rather than nonabdominal, fat was associated not only with impaired insulin sensitivity but also with reduced glycogen synthesis. Other studies which have used direct measures of abdominal fat, such as computed tomography (CT) or magnetic

resonance imaging (MRI), have found that the amount of intra-abdominal fat was strongly correlated with the plasma glucose response to oral glucose tolerance testing, even after adjustment for gender and body mass index (Sparrow et al; 1986; Fujioka et al, 1987; Despres et al, 1989, Macor et al, 1997).

Few studies have been done on the relationship between insulin resistance and body fat content or body fat distribution in children, and the results are conflicting. Travers et al (1995) found that the best predictor of insulin sensitivity in 97 children aged 9.5 to 14.5 years, was body fatness as assessed by BMI, skinfold measurements, underwater weighing, and bioelectric impedance analysis. Body fat distribution measured by waist-to-hip ratio and umbilicus to hip ratio was not associated with insulin sensitivity when total body fatness was accounted for. However studies that have used magnetic resonance imaging to assess visceral fat in children have not found that waist-to-hip ratio is a good indicator of visceral fat (De Ridder et al, 1992).

Freedman et al (1987) examined the relation of body fat distribution as assessed by skin fold measurements, to plasma levels of glucose and insulin during an oral glucose tolerance test, in 355 Black and White children aged 6-18 years. Central body fat was more strongly related to the 1-h insulin response than peripheral fat ($r=0.35$ vs 0.26); this association remained significant for central fat independent of peripheral fat ($r=0.18$). The significant relation of central fat to insulin response was noted in both races and sexes but not in either sexually immature or relatively thin children.

Gower et al (1998), examined the relation between fat distribution and insulin in 73 African American and White children aged 5-10 years. Fasting and postchallenge insulin concentrations were determined by oral-glucose-tolerance test, total body fat by DXA, and subcutaneous abdominal and intraabdominal adipose tissue by computerized tomography. In multiple linear regression, fasting insulin was independently related to total fat within both ethnic groups, with subcutaneous abdominal adipose tissue being independently related to insulin area under the curve only in African American children, and intraabdominal adipose tissue being independently related to 30-min insulin concentration only in White children. As most children with type 1 diabetes in Manitoba are Caucasian, being able to measure the amount of intra-abdominal fat is more relevant to this thesis. Once again, it is unfortunate that the authors did not measure regional fat distribution with DXA. It would have been interesting if they had compared the results from DXA with those found by CT.

2.4. Nutrient Intake

Despite the recognition that dietary management is an important component of overall care for children with type 1 diabetes, published literature provides little about these children's actual dietary intakes. Some investigators have reported that diabetic children and adults with poor metabolic control made 50% more deviations from the number of planned exchanges than those with good metabolic control (Christensen et al, 1983).

Care in carbohydrate estimation, consistency in the timing of meals and

snacks and compliance with the recommended intake of complex carbohydrates have been associated with lower HbA1c values in diabetic subjects (Reviewed in Virtanen, 1992).

Wolever et al, (1999) also found that consistency in amount and source of carbohydrate from day to day was associated with lower HbA1c in 272 subjects with type 1 diabetes. In British diabetic children and adolescents, HbA1c was associated positively with energy intake, deviation from the prescribed carbohydrate intake and day-to-day variation in energy intake, and inversely with energy-adjusted intake of dietary fiber (Hackett et al, 1986).

Virtanen (1992) examined the associations between metabolic control and dietary intake as measured by a 48 hour recall method in 105 diabetic adolescents past partial remission. Several dietary factors associated with good metabolic control were: an adequate time interval between insulin injection and eating, high number of daily eating occasions, and high day-to-day variation in energy intake. These factors probably reflect the importance of good coordination between insulin regimen and dietary intake.

Randecker et al, (1996) assessed the dietary intakes of 66 children with type 1 diabetes aged 4-9 years. Three 24 hour dietary recalls were collected within a 2-week period via telephone interviews with the child and one of the child's primary caregivers. Overall the sample met the recommendations for protein and most vitamins and minerals. The intake of saturated fat exceeded the recommendations. Similar results were found by Schober et al, 1999, using 2

day weighed food records. 63 Austrian children with type 1 diabetes aged 10 to 14, as well as healthy controls, had a mean intake of carbohydrate lower than recommended, while the total fat and cholesterol intake exceeded recommendations. Using a 48 hour recall interview, Pietilainen et al, (1995), also found that 48 girls with type 1 diabetes aged 10-19, as well as 48 age and sex matched controls had higher intakes of total and saturated fat than recommended. This is of concern because diabetic children are already at an increased risk of cardiovascular disease. The diabetic girls also had higher energy intake, BMIs and percentage body fat than control girls. Furthermore, a high percentage body fat and high intake of saturated fat were found to be associated with poor metabolic control.

Multiple insulin injection regimens were not related to adiposity but daily insulin dose per unit body weight correlated positively with BMI and percentage body fat. The authors suggest that an unnecessarily high insulin dose leads to increased energy intake and increased storage of extra energy as the cause of greater adiposity in girls with type 1 diabetes. This conclusion is surprising since energy intake did not correlate with measurements of adiposity, and no results were provided regarding insulin dose and energy intake. Unfortunately, only 3 upper body skinfold thickness measurements were used to determine percentage body fat and the effects of regional fat distribution were not investigated. Thus it is possible that had whole body and regional fat been measured a significant correlation may have been observed.

Up to one third of young women with type 1 diabetes have eating disturbances, which may affect the management of diabetes (Reviewed in Rydall et al, 1997). The coexistence of eating disorders and diabetes is associated with noncompliance with treatment for diabetes, omission or under dosing of insulin to induce glycosuria and promote weight loss, and impaired metabolic control (Reviewed in Rydall et al, 1997).

This thesis research will compare the diets of children with type 1 diabetes to non-diabetic children and examine dietary factors that are associated with metabolic control using a 24 hour dietary recall interview and 3 day food record.

2.4.0. Nutrient Intake and Adiposity

Several studies examined the relationship between diet composition and body fatness in children without diabetes. All of these studies used skinfold measurements to determine body fatness. After adjusting for resting energy expenditure and physical activity in 48 children, aged 9-11, Gazzaniga & Burns, (1993) found the percentage of body fat correlated positively with intakes of total fat and negatively with carbohydrate intake, and total energy intake adjusted for body weight. Diet was assessed with three 24 hour telephone recalls using the Dietary Intervention study in children Food Record Guidebook . Similar results were found by Tucker et al, (1997), who included 262 children in their study between the ages of 9 and 10 years. Diet was assessed using the National Cancer Institute food frequency questionnaire. Ricketts, (1997), also found that

body fatness and BMI correlated positively with high fat food preferences in 88 children aged 9-12.

It is a popular belief that excessive energy intake is the primary cause of obesity in children and adults, however, this has not been supported by published research (Reviewed in Gazzaniga & Burns, 1993). Several studies have found a negative correlation between sum of skinfold measurements and total energy intake, suggesting that fatter children consume fewer calories than thinner children (Stewart et al, 1999; Tucker et al, 1997; Maffeis et al, 1996; Gazzaniga & Burns, 1993). These results indicate reduced physical activity or a systematic underestimation of energy intake by fatter children. Maffeis et al, (1996) also found that fat intake as a percentage of energy was significantly higher in the obese than in the non-obese group. However, in a subsequent study, this author found that diet composition did not contribute to explain the children's adiposity when the parents' degree of overweight (BMI) was taken into account (Maffeis et al, 1998).

One study used DXA to measure body composition in 66 male and female children (45 African American and 21 Caucasian), aged 4 to 10 years. Dietary intake was assessed using two 24 hour recall interviews with one parent present. There was no significant correlation between dietary fat and body fat indices after adjusting for nonfat energy intake and total lean tissue mass (Ku et al, 1998). The fact that no relationship was found in this study may be due to the inaccuracies of assessing diet with only two 24 hour recalls, as well as the small

sample size. The wide variability in age range may have also been a factor. However, this study is the only study published to date which examined the relationship of dietary fat with body fat distribution in children. Ku et al, (1998) found that subcutaneous abdominal adipose tissue and intra-abdominal adipose tissue, determined by computed tomography, were not related to dietary fat. It is unfortunate that the authors did not compare the ability of DXA to measure fat distribution with the results obtained by computed tomography.

Similar results have been found in the few studies done on adults. Samaras et al, (1998), examined the relationship between diet (measured by food frequency questionnaire) and total and central body fat (measured by DXA) in 436 middle-aged female twins. There was no relationship between dietary fat and body fat, however, a significant negative association between carbohydrate intake and total adiposity, and in paired analyses, the twin with the higher intake of total sugars had significantly lower total body and central abdominal adiposity. Larson et al, (1996) also found that dietary fat was not related to intraabdominal adipose tissue, as assessed by 3 day food records and computed tomography respectively, in 135 men and 214 women. These studies suggest that physical activity is a more important determinant of total and central fat distribution than diet (Samaras et al, 1999; Larson et al, 1996).

2.4.1. Assessment of Nutrient Intake

Direct chemical analysis of exact duplicates of all food eaten during a specific time period is required for precise information on nutrient intakes of

individuals (Gibson, 1990). However, this method is extremely time consuming and expensive, and is therefore not routinely used to determine nutrient intake. Traditional methods to assess nutrient intake include dietary history, food frequency questionnaires, 24 hour recalls, and food records.

The dietary history is used to estimate the usual food intakes of individuals over a relatively long period of time. This method is very labor intensive and unsuitable for large groups (Gibson, 1990). As the name implies, the aim of the food frequency questionnaire is to assess the frequency with which certain food items or food groups are consumed during a specified time period.

The 3-7 day food record, with or without weighing, provides an accurate quantitative account of a person's diet during a specific period and is considered by some to be the gold standard for dietary assessment (Rockett and Colditz, 1997). Crawford et al, (1994) found that the 3-day food record correlated better with observed intake in 9 and 10 year old girls compared to a 24 hour recall and a 5-day food frequency questionnaire. However, food records are intrusive, which may cause an individual to change his/her diet. Food records also require that the individual is literate and motivated, and may result in a lower response rate because it requires more effort on the part of the participant. (Gibson, 1990).

The 24 hour recall is most appropriate for assessing average intakes of foods and nutrients for large groups. The primary disadvantage is that a single

24 hour recall is limited in its ability to characterize usual intakes of individuals. Another limitation is its reliance on memory which may lead to inaccuracies.

The strengths of the 24 hour recall are that it is inexpensive and quick to administer, and can provide detailed information on specific foods (Block, 1989). It is well accepted by respondents because they are not asked to keep records and their expenditure of time and effort is relatively low. The 24 hour recall is a good method for children because it does not require skill in reading, writing, or measuring. The method is considered by some to be more objective than the dietary history and food frequency questionnaire, and its administration does not alter the usual diet (Guenther, 1994).

2.5. Physical Activity

Exercise is routinely recommended to children with diabetes mellitus as a means of improving glycemic control, limiting excessive weight gain, increasing sense of well-being, and helping in the prevention of cardiovascular disease. There have however been conflicting reports on the effect of physical training programs and physical fitness on insulin sensitivity, glucose tolerance and glycemic control (Reviewed in Sackey & Jefferson, 1996).

Gutin et al, (1994) examined whether body fatness, aerobic capacity, and fat distribution were associated with risk factors of cardiovascular disease in 57 non-diabetic children 7 to 11 years of age. The percentage of body fat was measured by DXA, maximal aerobic capacity was measured by open-circuit spirometry on a treadmill, and fat distribution was expressed as the waist-to-hip

ratio. The most striking finding was the magnitude of the correlation between percentage of body fat and insulin. Although maximal aerobic capacity was associated with lower fasting insulin, it was not a significant predictor of fasting insulin when fatness was included in the multiple regression models, which suggests that the influence of aerobic capacity was expressed through its impact on fatness.

Fat distribution did not explain significant proportions of the variance in fasting insulin, however, as previously mentioned, waist-to-hip ratio has not been shown to be a good indicator of central fat distribution or visceral fat in children (DeRidder et al, 1992). It is surprising that the authors did not use DXA to measure fat distribution since DXA has been shown to accurately measure regional as well as total fat distribution. In fact studies using magnetic resonance imaging (MRI) have found that a specific region (lumbar vertebra 2-4) measured by DXA was shown to contain a relatively high visceral fat content (Ross et al, 1993).

Sackey & Jefferson (1996), examined the relationship of physical activity, skinfold thickness, and glycemic control in 53 children with type 1 diabetes aged 4-18. Activity was recorded over a one week period and 8 blood tests were taken over 24 hours on one of those days. Levels of activity were assessed using a semi-quantitative scoring scheme. Subcapular skinfold thickness was lower in the high activity group ($p=0.02$) which suggests exercise reduces fat accumulation. However the authors did not investigate percentage body fat or

regional fat distribtuion. Activity before 9 am significantly correlated with mean blood glucose (p=0.005) and fructosamine (p=0.04). This indicates that timing of exercise with the period of highest blood glucose may be important in improving glycemic control. Secondly, compensatory eating is probably less likely to accompany activity early in the morning compared to later in the day.

Arslanian et al,(1990) examined the relationship of in vivo insulin-mediated glucose utilization to the state of physical fitness and the degree of glycemic control in 27 adolescents with type 1 diabetes compared to 10 non-diabetic adolescent control subjects. In vivo total-body insulin-mediated glucose metabolism was evaluated by the hyperinusulinemic-euglycemic clamp. Physical fitness was assessed by maximal oxygen consumption (VO_2 max) measured by a metabolic cart during cycle ergometry. There was a strong direct correlation between glucose metabolism and physical fitness in both diabetic ($r = 0.83$, $p<0.001$) and control subjects ($r = 0.81$, $p<0.05$). In addition, there was an inverse correlation ($r = -0.63$. $p<0.001$) between glucose metabolism and HbA1c in diabetic subjects.

There was no relationship between total-body insulin-mediated glucose metabolism and BMI, age, and duration of diabetes. The lack of an association between BMI and insulin-mediated glucose metabolism in diabetic subjects could have resulted for many reasons. First, BMI only measures weight in relation to height and may not be a good indicator of adiposity. Second, the small sample size and narrow range of BMIs present in the sample. Third, other

factors related to the diabetic state (e.g. degree of glycemic control) may overshadow the relationship of BMI to insulin-mediated glucose metabolism.

2.5.0. Assessment of physical activity

Physical activity assessment tools have been used to measure various dimensions and attributes of physical activity. Most assessment tools used to measure physical activity have focused on the amount of energy expended (Laporte et al, 1985). Epidemiologic studies have typically used subjective measures, such as the questionnaire, to assess physical activity in populations. Such studies then used objective measures to validate the subjective activity measures. The most precise objective activity assessment tools include measures of total energy expenditure, such as the doubly labeled water technique and the respiratory chamber or metabolic cart. Open-circuit spirometry has also been found to be accurate and reliable (Montoye et al, 1996).

There are a number of advantages to the questionnaire/interview technique compared to other approaches (observation, heart rate recording, diaries, etc.). It is relatively inexpensive, easy to administer and well accepted by subjects. At present it is the only method feasible for large population surveys. The procedure does not alter the behavior of the individual being surveyed, it can be adapted to suit a specific population, and it is both reliable and valid. By employing energy expenditure tables, it may be possible to estimate total energy expenditure. (Laporte et al, 1985; Montoye et al, 1996). The estimates obtained by the activity questionnaire are valuable in relative terms and can be used to

rank individuals or groups of subjects within a population from the least to the most active. The ranking can then be examined with respect to physiologic parameters (Kriska & Bennett, 1992).

There are also limitations to the method. Subjects do not necessarily recall their activities accurately; they may tend to overestimate time or intensity. A self-administered questionnaire must be suited to respondents' ages and education levels. Detailed questionnaires and interviews place a considerable burden on subjects (Reviewed by Montoye et al, 1996).

3. Methods

3.0. Study Design: Cross-sectional study

3.1. Population: 51 children (27 female and 24 male) with type 1 diabetes and 68 (34 male and 34 female) age matched controls between the ages of 8 and 17 were recruited. The original goal was 50 children in each of the 4 groups (males and females with diabetes, and without). As this goal proved impossible to attain, given the time frame, the revised goal became 30 subjects per group. This goal was achieved in the control male and female control groups, but not in the diabetic groups.

3.2. Ethical Approval: This study was reviewed and approved by The Faculty of Medicine Committee on the use of Human Subjects in Research, University of Manitoba.

3.3. Recruitment: Children with type 1 diabetes were recruited over 1 year at the DER-CA. As clinic appointments are scheduled every six months, all children had the opportunity to participate. The study was advertised in the quarterly DER-CA newsletter. The control group was recruited from the Manitoba Clinic patient base; after each subject with diabetes was recruited a comparison child was sought from the Manitoba Clinic; the largest pediatric base within Winnipeg and representative of both inner-city and rural populations.

3.4. Inclusion criteria: Children aged 8-18 years with type 1 diabetes for at least 12 months were eligible for the study following informed written consent from the parent and assent from the subject. Children with diabetes combined

with Celiac disease, hypothyroidism, Addison's disease, Down's Syndrome, cystic fibrosis or other chronic diseases were excluded from this study. The control group inclusion criteria were normal growth, free of major disease and informed consent. The subjects were remunerated for their time by giving them one $10 gift certificate for their clinic visit and one $5 gift certificate for completion of the 3-day food record and activity questionnaire.

3.5. Indicators of Growth: Weight was measured to the nearest kg using a standard upright balance. Children wore light clothing (usually a T-shirt and jeans). Footwear and sweaters or sweatshirts were removed. Height was measure to the nearest cm using a Harpenden stadiometer, and was measured in triplicate. Weight was expressed in relation to height as BMI (kg/m^2) to determine appropriateness of growth. Z scores were calculated for BMI using data compiled by Rosner et al, (1998). The calculation was done by subtracting the mean (BMI) for the age and sex of the child from the actual measurement and then dividing by the standard deviation for that child's age and sex. Z scores were also calculated for weight and height using the National Centre for Health Statistics (NCHS) data to indicate "normal" growth patterns in both groups of children. Age at menarche was self-reported.

3.6. Body composition: Whole body scans were performed by one trained individual, using whole body DXA (Hologic 4500W, Hologic Inc, Waltham, MA). Children wore a T-shirt and shorts, or a hospital gown, and were positioned as recommended by the manufacturer. Lean and fat mass were measured in grams

and as percent of total mass for the total body and 4 standard regions (trunk, arms, legs, and head plus neck). In addition, the amount of fat in the abdomen was determined by measuring the region including lumbar vertebra 2-4 as suggested by Carey et al (1996). Central fat distribution was examined by calculating the percentage of body fat located in this region and by the ratio of trunk to leg fat (TLFR). A TLFR ratio greater than 0 indicates that there is a larger proportion of fat in the trunk region compared to the lower limbs. Another indicator of body fat distribution is the ratio of arm to leg fat. Since this has not previously been done, there are no published guidelines for interpretation of the results.

3.7. Glycemic Status: Glucose was measured in a non-fasting morning urine sample using a colorimetric assay (procedure #510-A, Sigma Diagnostics, Inc., St. Louis, MO, USA), which is essentially that of Raabo and Terkildsen (1960) with a minor change in the quantity of chromogen to increase sensitivity. The sample is added to a mixture containing glucose oxidase, peroxidase and o-dianisidene. The reaction is allowed to proceed to completion in approximately 30 minutes at 37 degrees Celsius. The final color intensity is proportional to the glucose concentration, read at 450 nm on a Microplate Spectrophotometer (SpectraMax340, Molecular Devices Corporation, California, USA). The coefficient of variation for reproducibility is 3.5%, and accuracy is 95 -102% as provided by the manufacturer. To correct for fluctuations in urine volume, urinary excretion was expressed as the molar ratio of glucose to urinary creatinine.

Creatinine was also measured in the same non-fasting morning urine sample (procedure #555-A, Sigma Diagnostics, Inc., St. Louis, MO, USA). The principle of the test is that color derived from creatinine is destroyed at acid pH. The difference in color intensity measured at 500 nm before and after acidification is proportional to creatinine concentration. The coefficient of variation for reproducibility is 3.6-10.9%, and accuracy is 95 -103% as provided by the manufacturer. Both glucose and creatinine assays were done in triplicate, and any measurements with a coefficient of variation of >10% were repeated.

HbA1c was taken from the medical chart at the DER-CA. Blood is taken at the DER-CA and HbA1c is measured at the Winnipeg Health Sciences Centre Laboratory. The method used was the Abbott Imx Glycated Hemoglobin test, which is a boronate affinity binding assay which measures and reports percent glycated hemoglobin (Ghb) and is also standardized to report percent hemoglobin A1c (HbA1c). Assay reproducibility is provided by Abbott Laboratories for the IMx® Glycated Hemoglobin assay as coefficients of variation for within assay (4.1-4.5%), between assay (4.9-5.1%) and total (6.3-6.8%) assay precision. Accuracy is reported as 97-98%.

The prescribed daily dose of insulin (U/kg/day) was taken from the medical chart at the DER-CA and was calculated by including the total units of all types of insulin used on a daily basis and dividing by weight in kilograms. The injection frequency was also recorded.

3.8. Nutrition: A 24 hour food recall and 3-day food record were taken to help interpret glucose control and growth in both groups of children. To eliminate inter-interviewer bias and effects, all 24 hour food recall interviews and subsequent analysis were conducted by the same investigator. Timing of food intake was recorded and for the children with diabetes, all blood sugar readings and type and amount of insulin taken over the previous 24 hours were also recorded at this time. Portion sizes were determined using food models and standard household measures. Children were asked to draw the size and thickness of a food item on paper if there were no appropriate food models. If children could not remember what they ate, they were asked what they were doing throughout the day to help them remember when and what they ate. Parents were usually present to provide missing information such as brand names and preparation techniques. When parents were not present, details were obtained by phone. The interview was conducted in an objective and standardized manner, as described by Dennis et al, (1980). For example, leading questions and judgmental comments were avoided. Coding was not required as the interviewer made detailed written records and personally entered all information into the nutrient analysis program. Interviews normally took approximately 30 to 45 minutes to complete depending on the amount of probing required.

A 3-day food record was mailed or given to each participant to complete at home and return by mail (see appendix A). Detailed instructions were included

which described how to record everything consumed for 3 non-consecutive days (2 weekdays and one weekend day). The rate of return was 58% and the average time between the 24 hour recall and the 3 day record was approximately 6 months. Any information which was missing or unclear on the 3 day record was obtained by phone. All records were analyzed by the same investigator using a nutrient analysis program equipped with the 1996 Canadian Nutrient File (E. Warwick, PEI, Canada). Foods which were not included in the nutrient analysis program were added to the system using information obtained from food labels and manufacturers. Results of analysis provided total energy (Kcal), total carbohydrate, protein, and fat consumed expressed in grams as well as the relative percent of each contributing to total energy consumed. The average of the 3 day intakes was used for analysis.

3.9. Physical Activity: A modifiable activity questionnaire for adolescents (see appendix B) was mailed or given to each participant with detailed instructions to be completed at home with the help of a parent and returned by mail. This questionnaire was found to be reliable and valid in 1245 adolescents in a metropolitan school district near Pittsburgh, Pennsylvania (Aaron et al, 1993). Subjects were 12-16 years old, with equal numbers of males and females, and 73% were Caucasian, 24% African American, and 3% Hispanic or Asian. Questionnaires were completed on a group basis, during physical education class and reviewed by trained research assistants (Aaron et al, 1993).

For questions 1-4, the subjects were ranked from 0 to 4 based on the

lowest to highest response. The remainder of the questionnaire was analyzed by calculating the total number of hours per year of all types of activities listed. For example, if one subject indicated that he/she played soccer for 4 months per year, 2 days per week and 120 minutes per day, then the calculation would be: 4months/year x 4.3 weeks/month x 2 days/week x 120 min/day = 4128 minutes per year = 68.8 hours/year.

The response rate for the activity questionnaire was 64 out of 119 or 54%, however any information which was missing or unclear on the questionnaire was not included in the analysis. Therefore, 59 to 64 of the responses were usable depending on the question.

3.10. Statistical Analysis:

A contingency table with chi square analysis was used to confirm the number of subjects in each age group was not different between groups. Differences between groups for height, weight, body composition, nutrient intake, and physical activity were determined using ANOVA and using factors of diabetes vs control, and male vs. female. Normality was tested using Kolmogorov-Smirnov equation (with Lilliefors' correction), and the Leven Median test was used to test for equal variances. Student's t-tests were used when only two groups were being compared. Pearson correlation, as well as simple and multiple linear regression analysis were used to examine the relationship of body composition, nutrient intake, physical activity, glycemic control, and medical management in children. Slopes of simple linear regression equations were compared using the

method explained in Chapter 18 of J Zar, Biostatistical Analysis, 2nd edition, Prentice Hall, 1984. Agreement between the 24 hour recall and 3 day food record was tested using the method of Bland & Altman (1986). Outliers were defined by mean ± 3 S.D, and removed. For all tests, a p-value of ≤ 0.05 was considered significant.

4. Results:

4.0 Subject Characteristics

Subject characteristics are presented in Tables 4.1 - 4.3. A contingency table with Chi square analysis (p=0.32) was used to confirm that the number of subjects in each age group (8-17) was similar in all groups (control male and female, diabetic male and female). Race was mainly Caucasian.

4.1 Indicators of Growth and Body Composition

Weights and heights in the control group followed expected patterns. Children were taller than NCHS data, but similar in height and weight to healthy children in Canada (Faulkner et al, 1996).

Using two way ANOVA, with factors diabetes vs control, and female vs male, there were no differences among groups for height, height Z-score, weight, weight Z-score, BMI, BMI Z-score, TLFR. Total percent fat did not differ between diabetic and control groups but was significantly higher ($p<0.001$) in females compared to the males, which is to be expected (See Table 4.1).

Using t-tests, female children with and without diabetes were similar in age (p=0.95), height (p=0.18), height Z-score (p=0.61), weight (p=0.13), weight Z-score (p=0.12), %body fat (p=0.20), %abdominal fat (p=0.37), TLFR (p=0.18), but not in BMI (p=0.02), BMI Z-score (p=0.02), or age at menarche (p=0.02) (See Table 4.1). Since age at menarche was self-reported and most girls could not recall an exact date, these results may not represent a true difference. To control for puberty, girls were separated into groups according to pre- and post-

menarche. Using a t-test, the significant difference in BMI (Control=21.30±0.76 kg/m^2 vs Diabetes=23.30±0.81 kg/m^2, p=0.04), and BMI z-score (Control=0.07±0.20 SD vs Diabetes=0.64±0.20SD, p=0.02) remained between diabetic and control girls when only girls who had reached age at menarche were included.

Using the definition of obesity as ≥85th percentile for BMI 7 out of 34 (21%) of control females would be considered obese while 7 out of 27 (26%) of females with diabetes qualify as obese. However, when using the definition of ≥95th percentile as obese, then only 2 out of 34 (6%) control girls and 1 out 27 (4%) girls with diabetes would be considered obese.

Using two-way ANOVA , females were separated into groups according to pre- vs. post-menarche, and diabetics vs. controls. BMI was not different between the diabetic and control groups, but did differ significantly between pre- and post-menarche (p<0.001). Other factors such as BMI Z-score, percent fat, and percent of body fat in the abdomen were not different for diabetic vs control, or pre- vs post-menarche females (See Table 4.4).

While there was no significant difference between the control and diabetic females, in mean percent body fat, and percent of body fat in the abdomen, group means masked the relationship between age and fat distribution. Using simple linear regression, central fat distribution increased across age groups in female children with type 1 diabetes (as measured by percent of body fat in the abdomen and TLFR). This is not the case for the control group (see Figures 4.1

and 4.2). The slopes of these regression lines were significantly different between diabetic and control females (p=0.009 for both percent of fat in the abdomen and TLFR). Males with diabetes did not have a more central fat distribution than control males and TLFR was not significantly correlated with age in either group. However, percent of fat in the abdomen was significantly positively correlated with age for males with diabetes but not controls (see Table 4.5).

Correlations between age and indices of body composition are shown in Table 4.5, and the relationship between percent body fat and other indicators of body composition are presented in Table 4.6.

The absolute difference from the mean was calculated for height, weight, BMI, and percent body fat for all females. Differences between females with and without diabetes were compared using the absolute difference from the mean. These results were not different from results obtained using Z-scores, therefore, only results from Z-scores are shown in this thesis research.

4.2 Comparison of Nutrient Intake Assessment Methods

The agreement between the results from the 24 hour recall and the 3 day food record was examined using the method of Bland & Altman (1986). For comparing total energy intake (Kcal) between methods, the limits of agreement are: -1500 to 1400 Kcal. This is calculated by determining the mean difference in Kcal between methods plus or minus 2 standard deviations. In this example the mean difference is -39.56 and the standard deviation is 716.35. Thus, the 24

hour recall may be 1500 kcal below or 1400 kcal above the 3 day record which is unacceptable on an individual basis, but acceptable on a group basis. Results for grams of carbohydrate, protein and fat were similar in that the mean difference between methods was not significantly different from zero and therefore the 24 hour recall is acceptable on a group basis. However, the limits of agreement are too large, indicating that the results from the 24 hour recall should not be used to compare individuals (See Figures 4.3 - 4.6).

The mean difference for total grams of carbohydrate was 10.93 grams, with a standard deviation of 111.51, giving limits of agreement of -212 to 234 grams. Results for total grams of protein showed a mean difference of -8.08, with a standard deviation of 32.94, giving limits of agreement of -75 to 58 grams. Finally, total grams of fat had a mean difference of -4.16, with a standard deviation of 33.45 giving limits of agreement -71 to 63 grams.

4.3 Body Composition and Nutrient Intake

In both the diabetes and control groups percent body fat was significantly positively correlated with percent of energy (kcal) from fat (24 hour recall), and negatively with kcal/kg of body weight (24 hour recall and 3-day food record), percent of kcal from carbohydrate (24 hour recall), total grams of carbohydrate (24 hour recall), and grams of protein per kg of body weight (3-day food record). Similar results were found when subjects were separated by diabetes vs control and male vs. female (see Tables 4.7.0 & 4.7.1). Only dietary variables with significant correlations were included in the tables.

Results of correlation analysis of percent body fat in the abdomen with dietary variables are shown in Tables 4.8.0. & 4.8.1. These results were similar to those found for percent body fat, however saturated fat was significantly positively correlated with percent of body fat in the abdomen in the diabetic, and female groups.

All groups were compared using one-way ANOVA, for nutrient intake variables (See Table 4.3). All groups were close to the Canadian recommendations of >55% kcal from carbohydrate, <30% kcal from total fat, <10% energy from saturated fat, and approximately 15% kcal from protein. However, fibre intake was generally lower than the recommendation of age plus 5 grams. Total energy intake (kcal) was also slightly lower than the recommended 2800 (or 56kcal/kg) for a 13 year old male, and 2200 (or 46 kcal/kg) for a 13 year old female. Protein in grams per kg body weight was above the recommended 1 g/kg.

4.4 Physical Activity

The response rate for the activity questionnaire was 64 out of 119 or 54%, however any information which was missing or unclear on the questionnaire was not included in the analysis. Therefore, 59 to 64 of the responses were usable depending on the question. For the number of hours of activity per year, there were no significant differences between subjects who returned usable questionnaires (R) and those who did not (NR): for age (R:12.88 ± 0.30, vs. NR:13.19 ± 0.30; p=0.48), Z-score weight (R:0.44 ± 0.13, vs. NR:0.55 ± 0.13;

p=0.56), Z-score BMI (R:0.15 ± 0.13, vs. NR:0.36 ± 0.13; p=0.25), Z-score % body fat (R:-0.10 ± 0.07, vs. NR:0.02 ± 0.07;p=0.21), or lean/fat ratio (R: 3.77 ± 0.21, vs. NR:3.24 ± 0.21;p=0.08).

Mean hours of activity per year were not significantly different among groups, with an average of 216.16 ± 87.68 in the control female group, to 496.18 ± 77. 08 in the control male group.

Hours of activity were significantly positively correlated with activity question #1 (r=0.38, p=0.004), #4 (r=0.38, p=0.004), and units of insulin per kg body weight (r=0.45, p=0.05). Dietary fibre in grams (r=0.37, p=0.005), and as a percent of kcal (r=0.27, p=0.04), was also positively associated with hours activity until a single outlier was removed. Once this same outlier was removed, the ratio of lean/fat mass became significantly and positively correlated with hours activity (r=0.28, p=0.03). A significant negative correlation was found for percent of kcal from fat (r=-0.34, p=0.01). No other significant correlations were found.

Subjects were ranked from 1 of 4 depending on the hours of yearly activity based on quartiles (1=0-127.5, 2=127.6-221.8, 3=221.9-465.0, and 4=465.1+). Using one-way ANOVA there were no significant differences among groups for body fat Z-score, weight Z-score, BMI Z-score, lean/fat mass, percent of kcal as fat, percent of kcal as carbohydrate, total kcal/kg (see Table 4.9)

Question #1 on the activity questionnaire (see Appendix B) inquired about frequency of vigorous exercise. Subjects were ranked from 0-4 based on the

lowest to highest response. Using one-way ANOVA significant differences were found among groups for percent of kcal as fat (see Table 4.10). No other significant differences were found.

For question # 2, which asked about frequency of light exercise, and #3, which inquired about hours spent watching television and playing video games, no significant differences were found among groups for body fat Z-score, weight Z-score, BMI Z-score, lean/fat mass, percent of kcal as fat, percent of kcal as carbohydrate, total kcal/kg (see Table 4.11 & 4.12).

Question #4, asked about the number of sports which were participated in on a competitive level. Subjects who participated in 4 or more competitive sports in the past year had a significantly higher body fat Z-score than subjects who participated in 1 competitive sport. Subjects who participated in 0 competitive sports had a significantly higher percentage of kcal from fat (from the 3-day food record) compared to subjects who participated in 2 competitive sports. No other significant differences were found (see Table 4.13).

4.5. Medical Management

Children with type 1 diabetes were divided into two groups depending on if they used 2 insulin injections versus 3 or more injections per day. There were no differences between groups for glycemic control (HbA1c), age, weight, height, BMI, percent body fat, percent abdominal fat, percent of body fat located in the abdomen or grams of lean mass. However, when these groups were separated by sex, the females using 3 or more injections per day were taller ($p=0.03$), and

had significantly more grams of total lean body mass (p=0.03) than those using 2 injections per day. There was no significant difference for age (p=0.38), weight (p=0.06), BMI (p=0.22), total grams of fat mass (p=0.29), percent total body fat (p=0.91), or HbA1c (p=0.38).

For children with diabetes as a group, units of insulin per kg was significantly positively correlated with duration of disease (p=0.04), weight (p=0.03), BMI (p=0.007), and grams of total fat mass (p=0.02), and negatively with kcal/kg (p=0.01), and with percent of energy from carbohydrate (p=0.04) using data from the 24 hour recall, but not with percent body fat, or with HbA1c. For the females alone, units of insulin per kg was only significantly positively correlated with BMI (p=0.02), and negatively with kcal/kg (p=0.04). For the males alone, units of insulin per kg was only significantly positively correlated with height Z-score (p=0.03), and negatively with percent of kcal as carbohydrate (p=0.02), and grams of carbohydrate (p=0.04).

There was no significant difference in HbA1c between children who used Lispro (fast acting insulin) versus Regular insulin. However, females who used Lispro had significantly lower percent body fat (p=0.04) than female children who used Regular insulin. There were no differences between females who used Lispro vs Regular insulin for weight, height, BMI, total grams of fat mass, total grams of lean mass, percent fat in abdominal region, percent of body fat located in the abdomen, age, age at onset, or HbA1c.

4.6. Glycemic Control

In the diabetic group as a whole, HbA1c was significantly positively correlated with duration of diabetes, the urine glucose/creatinine ratio, BMI, and total grams of fat mass. In the female diabetic group, HbA1c was significantly positively correlated with age, weight, BMI, total grams of fat mass, and total grams of lean mass. In the male diabetic group only duration of diabetes, and the urine glucose/creatinine ratio were significantly positively correlated with HbA1c (See Table 4.14). None of the dietary variables were significantly correlated with HbA1c, including energy adjusted intake of dietary fibre.

4.7. Interrelationships

Using multiple linear regression, the best equation to explain variation in HbA1c in the entire group with diabetes included weight Z-score, percent of body fat in the abdomen, total hours of activity, and grams of saturated fat (see Table 4.15). Variables which were not included in the model included: units of insulin/kg body weight, use of Lispro insulin, number of injections per day, percent body fat Z-score, abdominal percent fat, duration of diabetes, age at diagnosis, ratio of lean/fat mass, BMI Z-score, sex, age, grams of total fat mass, grams of total lean mass, and TLFR.

Percent of body fat Z-score in all subjects with diabetes was best explained by hours of activity, percent of body fat in the abdomen, and age at diagnosis (see Table 4,16). Variables which did not contribute to the model included: units of insulin/kg body weight, use of Lispro insulin, number of

injections per day, abdominal percent fat, BMI Z-score, sex, age, and TLFR.

Percent of body fat in the abdomen was best explained in all children with diabetes by hours of activity, HbA1c, and BMI Z-score (see Table 4.17). Variables which were not included in the model included: units of insulin/kg body weight, use of Lispro insulin, number of injections per day, percent body fat Z-score, abdominal percent fat, duration of diabetes, age at diagnosis, ratio of lean/fat mass, BMI Z-score, sex, and age.

For females with diabetes the best equation to explain variation in HbA1c included BMI Z-score, percent of body fat in the abdomen, total hours of activity, and units of insulin/kg body weight (see Table 4.18). Variables which were not included in the model were: use of Lispro insulin, number of injections per day, percent body fat Z-score, abdominal percent fat, duration of diabetes, age at diagnosis, ratio of lean/fat mass, age, grams of total fat mass, grams of total lean mass, and TLFR.

Percent of body fat Z-score in females with diabetes was best explained by hours of activity, percent of body fat in the abdomen, use of lispro insulin, and age at diagnosis (see Table 4.19). Variables which did not contribute to the model included: units of insulin/kg body weight, number of injections per day, abdominal percent fat, BMI Z-score, sex, age, and TLFR.

Percent of body fat in the abdomen was best explained in females by the same variables as for the entire group with diabetes (see Table 4.20).

Table 4.1. Subject characteristics

	DF (n= 27)	CF (n=34)	DM (n=24)	CM (n=34)
Age (yr)	13.09 ± 0.44	13.06 ± 0.39	13.63 ± 0.47	12.56 ± 0.39
Race (% White)	96	94	100	97
Age at menarche	12.34 ± 0.2[t] n=19	13.08 ± 0.2[t] n=19	N/A	N/A
Wt (kg)	54.07 ± 3.19	49.95 ± 2.84	55.84 ± 3.38	53.15 ± 2.84
Wt Z-score	0.57 ± 0.23	0.26 ± 0.20	0.42 ± 0.24	0.85 ± 0.20
Ht (cm)	155.41 ± 2.66	155.51 ± 2.37	161.30 ± 2.82	157.63 ± 2.37
Ht Z-score	0.10 ± 0.18	0.23 ± 0.16	0.21± 0.19	0.62 ± 0.16
BMI (kg/m^2)	22.08 ± 0.77[t]	20.23 ± 0.69[t]	20.73 ± 0.82	20.83 ± 0.69
BMI Z-score	0.51 ± 0.19[t]	0.06 ± 0.17[t]	0.11± 0.21	0.35 ± 0.17
Fat (kg)	15.17 ± 1.32[a]	13.51 ± 1.18[a]	10.57 ± 1.40[b]	11.30 ± 1.18[b]
Lean (kg)	35.60 ± 2.14[a]	33.78 ± 1.93[a]	41.89 ± 2.27[b]	37.02 ± 1.90[b]
Fat (%)	28.16 ± 1.31[a]	26.70 ± 1.17[a]	18.57 ± 1.39[b]	21.30 ± 1.17[b]
Fat Z-score	-0.06 ± 0.10	-0.17 ± 0.09	0.01 ± 0.11	0.06 ± 0.09
Ab fat (%)	20.02 ± 1.56[a]	19.32 ± 1.39[a]	12.60 ± 1.66[b]	15.38 ± 1.41[b]
Body fat in ab (%)	8.30 ± 0.45	8.26 ± 0.40	7.70 ± 0.47	8.13 ± 0.40
TLFR	0.65 ± 0.03	0.68 ± 0.02	0.66±0.03	0.70 ± 0.02
ALFR	0.97 ± 0.04[a]	0.93 ± 0.03[a]	0.87±0.04[b]	0.87 ± 0.03[b]
Activity (hrs/yr)	263.80 ± 114.33	216.16 ± 87.68	313.70 ± 114.33	496.18 ± 77.08

Values shown as mean ± SEM

CF: Control Female; CM: Control Male; DF: Diabetes Female; DM: Diabetes Male

Groups with different letters in rows are significantly different at $p<0.05$ as tested by two-way ANOVA (F1= Diabetes vs. Control, F2= male vs. female)

[t]pairs are significantly different at $p<0.05$ as tested by t-tests

Table 4.2. Clinical characteristics of subjects with diabetes

	Diabetes (n=51)	Diabetes Female (n= 27)	Diabetes Male (n=24)
HbA1c*	7.85 ± 0.19	7.89 ± 0.28	7.82 ± 0.27
Age at Onset (yr)	8.71 ± 0.50	8.50 ± 0.69	8.94 ± 0.75
Duration (yr)	4.64 ± 0.49	4.60 ± 0.64	4.69 ± 0.78
Insulin (U/Kg)**	0.97 ± 0.04	1.00 ± 0.06	0.93 ± 0.06
2 injections/day (# of subjects)	20	10	10
3+ injections/day (# of subjects)	30	17	13
Use Lispro (# of subjects)	19	10	9
AM blood glucose (mmol/L)	10.22 ± 0.58	9.47 ± 0.70	11.15 ± 0.95
Urinary Glucose/Creatinine (molar ratio)	29.92 ± 5.80	26.74 ± 6.70	33.39 ± 9.80

Data are mean ± SEM except for values for # of subjects.
Values are not significantly different at $p<0.05$ as tested by t-tests
*Target levels: < 8.3% in children 6-12 years and <7.7% for age 13-18
**Average insulin dosage for this age group is 0.5-1.5 units/kg

Table 4.3. Selected nutrient intake by group as indicated by the average intake from a 24 hour recall or 3 day food record

24 hr Recall	**CF (n=34)**	**CM (n=34)**	**DF (n=27)**	**DM (n=24)**
Total kcal	1901 ± 124^{a}	2504 ± 124^{b}	1949 ± 139^{a}	2390 ± 147^{ab}
Total kcal/kg	40.7 ± 2.8^{a}	51.2 ± 2.8^{b}	37.3 ± 3.2^{a}	40.0 ± 3.4^{b}
Protein g/kg	1.2 ± 0.1^{a}	1.6 ± 0.1^{b}	1.4 ± 0.1^{ab}	1.2 ± 0.1^{a}
Pro (% of kcal)	12.2 ± 0.6^{a}	13.1 ± 0.6^{ab}	15.3 ± 0.7^{b}	13.5 ±0.8^{ab}
Cho (% of kcal)	57.9 ± 1.4^{a}	60.0 ± 1.4^{a}	50.7 ± 1.6^{b}	54.1 ± 1.7^{ab}
Fat (% of kcal)	29.9 ± 1.5	28.9 ± 1.5	34.0 ± 1.7	32.5 ± 1.8
Sat fat (%of kcal)	10.6 ± 0.6^{abc}	8.9 ± 0.6^{b}	11.2 ± 0.7^{c}	11.6 ± 0.7^{c}
Total fibre (g)	10.3 ± 1.4	14.3 ± 1.4	12.2 ± 1.6	15.0 ± 1.7
3 Day Record	**CF (n=20)**	**CM (n=23)**	**DF (n=13)**	**DM (n=13)**
Total kcal	2025 ± 116^{a}	2458 ± 108^{b}	1747 ± 144^{a}	2408 ± 144^{ab}
Total kcal/kg	45.0 ± 3.5^{ab}	51.2 ± 3.2^{a}	34.8 ± 4.3^{b}	49.7 ± 4.3^{ab}
Protein g/kg	1.5 ± 0.1	1.8 ± 0.1	1.3 ± 0.2	1.9 ± 0.2
Cho (% of kcal)	54.5 ± 1.3	58.1 ± 1.2	55.2 ± 1.6	53.0 ± 1.6
Pro (% of kcal)	14.0 ± 0.6	14.4 ± 0.6	15.6 ± 0.8	14.9 ± 0.8
Fat (% of kcal)	33.5 ± 1.0	28.9 ± 1.0	31.3 ± 1.3	33.5 ± 1.3
Total fat (g)	75.2 ± 5.1^{ab}	78.6 ± 4.8^{ab}	62.3 ± 6.4^{a}	90.6 ± 6.4^{b}
Saturated fat (g)	27.8 ± 2.2^{ab}	28.4 ± 2.0^{ab}	19.7 ± 2.7^{a}	32.6 ± 2.7^{b}
Sat fat (%of kcal)	12.4 ± 0.6^{a}	10.5 ± 0.5^{ab}	10.0 ± 0.7^{b}	12.0 ± 0.7^{ab}
Total fibre (g)	11.5 ± 1.2	14.2 ± 1.1	13.8 ± 1.5	16.0 ± 1.5

Data are mean ± SEM

CF: Control Female; CM: Control Male; DF: Diabetes Female; DM: Diabetes Male

Groups with different letters in rows are significantly different at $p<0.05$ tested by one-way ANOVA

Table 4.4. Body composition in females: Results of two way ANOVA

	Diabetes pre-menarche	Diabetes post-menarche	Control pre-menarche	Control post-menarche
Wt (kg)	40.26 ± 3.87[a]	59.89 ± 2.51[b]	39.71 ± 2.93[a]	57.12 ± 2.45[b]
Wt Z-score	0.26 ± 0.36	0.66 ± 0.23	0.22 ± 0.26	0.63 ± 0.22
Ht (cm)	144.3 ± 3.0	160.1 ± 2.0	144.6 ± 2.3	163.1 ± 1.9
Ht Z-score	-0.12 ± 0.35	0.19 ± 0.23	0.00 ± 0.27	0.39 ± 0.23
BMI	19.18 ± 1.15	23.30 ± 0.75	18.69 ± 0.87	21.30 ± 0.73
BMI Z-score	0.20 ± 0.30	0.64 ± 0.20	0.05 ± 0.23	0.07 ± 0.19
Fat (kg)	10.50 ± 2.20[a]	17.13 ± 1.43[b]	10.70 ± 1.67[a]	15.47 ± 1.39[b]
Lean (kg)	27.42 ± 1.87[a]	39.04 ± 1.21[b]	26.85 ± 1.47[a]	38.28 ± 1.18[b]
Body fat (%)	26.54 ± 2.38	28.84 ± 1.54	26.69 ± 1.80	26.71 ± 1.50
Z-score fat	-0.08 ± 0.16	-0.05 ± 0.10	-0.04 ± 0.12	-0.25 ± 0.10
Ab fat (%)	15.71 ± 2.95	21.84 ± 1.91	19.61 ± 2.23	19.11 ± 1.86
ALFR	0.96 ± 0.08	0.98 ± 0.05	1.03 ± 0.06	0.87 ± 0.05
TLFR	0.56 ± 0.05	0.69 ± 0.03	0.71 ± 0.04	0.67 ± 0.03
% of fat in abdomen	6.98 ± 0.85	8.76 ± 0.50	8.73 ± 0.60	7.93 ± 0.50*

Data shown as mean ± SEM

Groups with different letters in rows are significantly different at $p<0.05$ tested by two-way ANOVA (F1= Diabetes vs. Control, F2= Pre vs. post menarche)

*Significant interaction between F1 and F2 ($p<0.05$)

Table 4.5. Relationship between age and indices of body composition

	D n=51	C n=68	DM n=24	DF n=27	CM n=34	CF n=34
Wt (kg)	**r=0.73 p<0.0001**	**r=0.69 p<0.0001**	**r=0.74 p<0.0001**	**r=0.71 p=0.0001**	**r=0.72 p<0.0001**	**r=0.69 p<0.0001**
Wt Z-score	r=0.09 p=0.52	r= -0.04 p=0.72	r=0.08 p=0.70	r=0.13 p=0.51	r= -0.07 p=0.71	r=0.04 p=0.80
Ht (cm)	**r=0.83 p<0.0001**	**r=0.87 p<0.0001**	**r=0.89 p<0.0001**	**r=0.71 p<0.0001**	**r=0.92 p<0.0001**	**r=0.84 p<0.0001**
Ht Z-score	r=0.02 p=0.86	r=0.03 p=0.80	r=0.04 p=0.86	r= -0.01 p=0.97	r= -0.21 p=0.24	r=0.26 p=0.14
BMI	**r=0.53 p<0.0001**	**r=0.37 p=0.002**	**r=0.55 p=0.005**	**r=0.57 p=0.002**	**r=0.37 p=0.03**	**r=0.41 p=0.02**
BMI Z-score	r=0.13 p=0.35	r= -0.02 p=0.89	r=0.14 p=0.53	r= 0.21 p=0.29	r= 0.00 p=1.00	r= -0.01 p=0.97
Fat Mass (g)	**r=0.45 p=0.001**	**r=0.32 p=0.009**	**r=0.47 P=0.02**	**r=0.60 p=0.0009**	r=0.18 p=0.31	**r=0.44 p=0.009**
Lean Mass (g)	**r=0.76 p<0.0001**	**r=0.62 p<0.0001**	**r=0.80 p<0.0001**	**r=0.72 p<0.0001**	**r=0.60 p=0.0002**	**r=0.79 p<0.0001**
Body Fat (%)	r=0.08 p=0.57	r= -0.04 p=0.76	r=0.08 p=0.70	r=0.37 p=0.06	r= -0.25 p=0.16	r=0.11 p=0.55
Fat Z-score	r=0.07 p=0.64	r= -0.21 p=0.085	r=0.06 p=0.78	r=0.06 p=0.75	r= -0.21 p=0.23	r= -0.17 p=0.33
Ab fat (%)	**r=0.29 p=0.04**	r=0.005 p=0.97	r=0.28 p=0.19	**r=0.54 p=0.004**	r= -0.09 p=0.60	r=0.04 p=0.82
Trunk fat (%)	r=0.17 p=0.23	r= -0.02 p=0.90	r=0.14 p=0.52	**r=0.46 p=0.02**	r= -0.12 p=0.49	r=0.03 p=0.88
TLFR	**r=0.35 P=0.01**	r=0.09 p=0.47	r=0.17 p=0.43	**r=0.56 P=0.002**	r=0.33 p=0.06	r= -0.15 p=0.40
% body fat in ab	**r=0.50 P=0.0002**	r= -0.07 p=0.56	**r=0.51 p=0.01**	**r=0.59 P=0.001**	r= -0.06 p=0.75	r= -0.10 p=0.58
ALFR	r= -0.14 p=0.34	**r= -0.30 p=0.01**	r= -0.37 p=0.076	r=0.28 p=0.16	**r= -0.41 p=0.02**	r= -0.30 p=0.08

r=Pearson Correlation Coefficient, D: Diabetes; C: Control; DM: Diabetes Male; DF: Diabetes Female; CM: Control Male; CF: Control Female

Table 4.6. Relationship between percent body fat and body composition

Y variable	D n=51	C n=68	MD n=24	FD n=27	MC n=34	FC n=34
Wt (kg)	**r=0.40 p<0.004**	**r=0.36 p=0.003**	**r=0.52 p=0.009**	**r=0.64 p=0.0003**	r=0.29 p=0.10	**r=0.59 p=0.0002**
Wt Z-score	**r=0.57 p<0.0001**	**r= 0.53 p<0.0001**	**r=0.68 p=0.0002**	**r=0.71 p<0.0001**	**r=0.71 p=0.0001**	**r= 0.61 p=0.0001**
Ht (cm)	r=0.05 p=0.75	r= -0.02 p=0.87	r=0.21 p=0.31	r=0.30 p=0.12	r= -0.13 p=0.48	r= 0.17 p=0.34
Ht Z-score	r=0.16 p=0.25	r=0.14 p=0.26	r=0.31 p=0.15	r=0.23 p=0.25	r=0.36 p=0.04	r=0.11 p=0.55
BMI	**r=0.64 p<0.0001**	**r=0.60 p<0.0001**	**r=0.65 p=0.0006**	**r=0.74 p<0.0001**	**r=0.57 p=0.0005**	**r=0.81 p<0.0001**
BMI Z-score	**r=0.63 p<0.0001**	**r=0.66 p<0.0001**	**r=0.75 p=0.0006**	**r=0.92 p<0.0001**	**r=0.73 p=0.0005**	**r=0.82 p<0.0001**
Fat mass (g)	**r=0.84 p<0.0001**	**r=0.84 p<0.0001**	**r=0.85 p<0.0001**	**r=0.87 p<0.0001**	**r=0.83 p<0.0001**	**r=0.87 p<0.0001**
Lean Mass (g)	r=0.04 p=0.76	r=0.06 p=0.65	r=0.30 p=0.15	r=0.37 p=0.056	r=0.06 p=0.72	r=0.24 p=0.19
Fat Z-score	**r=0.63 p<0.0001**	**r= 0.78 p<0.0001**	**r=0.92 p<0.0001**	**r=0.92 p<0.0001**	**r= 0.91 p<0.0001**	**r= 0.88 p<0.0001**
Ab Fat (%)	**r=0.93 p<0.0001**	**r=0.94 p<0.0001**	**r=0.93 p<0.0001**	**r=0.92 p<0.0001**	**r=0.94 p<0.0001**	**r=0.95 p<0.0001**
Trunk Fat (%)	**r=0.97 p<0.0001**	**r= 0.97 p<0.0001**	**r=0.96 p<0.0001**	**r=0.97 p<0.0001**	**r= 0.97 p<0.0001**	**r= 0.97 p<0.0001**
TLFR	**r=0.36 p=0.009**	**r=0.55 p<0.0001**	r=0.30 p=0.15	**r=0.70 p<0.0001**	**r=0.49 p=0.003**	**r=0.71 p<0.0001**
% body fat in ab	**r=0.56 p<0.0001**	**r=0.56 p<0.0001**	**r=0.48 p=0.02**	**r=0.69 p<0.0001**	**r=0.51 p=0.002**	**r=0.68 p<0.0001**
ALFR	**r=0.55 p<0.0001**	**r= 0.62 p<0.0001**	**r= 0.57 p=0.003**	r=0.34 p=0.08	**r= 0.78 p<0.0001**	**r= 0.57 p=0.0005**

r=Pearson Correlation Coefficient
Significant correlations (p<0.05) are shown in bold
D: Diabetes; C: Control; DM: Diabetes Male; DF: Diabetes Female; CM: Control Male; CF: Control Female

Table 4.7.0. Relationship between percent body fat and nutrient intake

24 hr Recall	**D (n=51)**	**C (n=68)**	**M (n=58)**	**F (n=61)**
Total kcal/kg of body weight	**r= -0.29, p=0.03**	**r= -0.33, p=0.006**	r= -0.16, p=0.22	**r= -0.34, p=0.007**
Protein/kg of body weight(g)	r= -0.14, p=0.32	r= -0.22, p=0.07	r= -0.23, p=0.83	**r= -0.35, p=0.006**
Fat (% of kcal)	**r= 0.30, p=0.03**	**r= 0.26, p=0.03**	r= 0.22, p=0.10	**r= 0.31, p=0.01**
Protein (% of kcal)	r= 0.19, p=0.17	r= 0.17, p=0.17	**r= 0.44, p=0.0006**	r= -0.03, p=0.82
Carbohydrate (% of kcal)	**r= -0.35, p=0.01**	**r= -0.37, p=0.002**	**r= -0.35, p=0.007**	r= -0.21, p=0.10
3 Day Record	**D (n=51)**	**C (n=68)**	**M (n=36)**	**F (n=33)**
Total kcal/kg of body weight	**r= -0.51, p=0.008**	r= -0.24, p=0.12	r= -0.11, p=0.54	r= -0.24, p=0.17
Protein /kg body weight	**r= -0.49, p=0.01**	r= -0.26, p=0.09	r= -0.13, p=0.44	r= -0.28, p=0.12

D: Diabetes; C: Control; M: Males; F: Females
r=Pearson Correlation Coefficient
Significant correlations ($p<0.05$) are shown in bold

Table 4.7.1. Relationship between percent body fat and nutrient intake

24 hour Recall	**DM (n=24)**	**DF (n=27)**	**CM (n=34)**	**CF (n=34)**
Total Kcal/kg of body weight	r= -0.35, p=0.09	r= -0.29 p=0.14	r= -0.18, p=0.32	**r= -0.35, p=0.04**
Protein/kg of body weight(g)	r= -0.30, p=0.15	r= -0.35, p=0.07	r= -0.14, p=0.43	**r= -0.42, p=0.01**
Total CHO (g)	**r= -0.48, p=0.02**	r= -0.22, p=0.26	r= -0.18, p=0.31	r= -0.07, p=0.69
Fat (% of Kcal)	r= 0.25, p=0.23	r= 0.33 p=0.09	r= 0.26, p=0.13	r= 0.27, p=0.12
Protein (% of Kcal)	**r= 0.42, p=0.04**	r= -0.16, p=0.43	**r= 0.50, p=0.003**	r = -0.01, p=0.94
CHO (% of Kcal)	**r= -0.42, p=0.04**	r = -0.15, p=0.47	**r= -0.47, p=0.005**	r= -0.21, p=0.23
3 Day Record	**DM (n=13)**	**DF (n=13)**	**CM (n=23)**	**CF (n=20)**
Total Kcal/kg of body weight	r= -0.32, p=0.29	r= -0.16, p=0.60	r= -0.07, p=0.75	r= -0.31, p=0.18
Protein /kg body weight	r= -0.25, p=0.41	r= -0.33, p=0.27	r= -0.09, p=0.67	r= -0.27, p=0.25

DM: Diabetes Male; DF: Diabetes Female; CM: Control Male; CF: Control Female

r=Pearson Correlation Coefficient

Significant correlations ($p<0.05$) are shown in bold

Table 4.8.0. Relationship between percent of body fat in the abdomen and nutrient intake

24 hr Recall	D (n=51)	C (n=68)	M (n=58)	F (n=61)
Total Kcal	r= 0.21, p=0.14	r= 0.16, p=0.19	r= 0.19, p=0.15	r= 0.25, p=0.06
Total Kcal/kg of body weight	**r= -0.47, p=0.0005**	r= -0.14, p=0.25	**r= -0.27 p=0.04**	r= -0.15 p=0.26
Protein (g)	**r= 0.31, p=0.03**	**r= 0.25, p=0.04**	**r= 0.33, p=0.01**	r= 0.22, p=0.08
Protein/kg of body weight(g)	**r= -0.35, p=0.01**	r= -0.09 p=0.47	r= -0.18, p=0.19	r= -0.16 p=0.22
Fat (g)	r= 0.26, p=0.06	**r= 0.26, p=0.03**	r= 0.22, p=0.10	**r= 0.31, p=0.02**
Fat (% of kcal)	r= 0.12, p=0.42	**r= 0.34, p=0.005**	**r= 0.30 p=0.02**	r= 0.23, p=0.07
Saturated fat (g)	**r= 0.38, p=0.006**	**r= 0.32 p=0.008**	**r= 0.30 p=0.02**	**r= 0.36 p=0.005**
Sat fat (% of kcal)	**r= 0.31 p=0.03**	r= 0.22 p=0.08	r= 0.19 p=0.15	**r= 0.25 p=0.05**
Protein (% of kcal)	r= 0.19, p=0.17	r= 0.13, p=0.30	**r= 0.27, p=0.05**	r= 0.03, p=0.80
CHO (% of kcal)	r= -0.20, p=0.17	**r= -0.24, p=0.05**	r= -0.19, p=0.16	r= -0.18, p=0.16
3 Day Record	**D (n=51)**	**C (n=68)**	**M (n=36)**	**F (n=33)**
Total kcal/kg of body weight	r= -0.30, p=0.13	r= -0.23, p=0.14	**r= -0.38, p=0.02**	r= -0.12, p=0.52

r=Pearson Correlation Coefficient
Significant correlations ($p<0.05$) are shown in bold
D: Diabetes; C: Control; M: Males; F: Females

Table 4.8.1. Relationship between percent of body fat in the abdomen and nutrient intake

24 hour Recall	DM (n=24)	DF (n=27)	CM (n=34)	CF (n=34)
Total kcal	r= 0.10, p=0.63	**r= 0.46, p=0.02**	r= 0.22, p=0.20	r= 0.14, p=0.45
Total kcal/kg	**r= -0.69, p=0.0002**	r= -0.27 p=0.18	r= -0.17, p=0.33	r= -0.10, p=0.57
Protein (g)	r= 0.28, p=0.19	**r= 0.39, p=0.05**	**r= 0.40, p=0.02**	**r= 0.33, p=0.01**
Protein g/kg	**r= -0.69, p=0.0002**	r= -0.13, p=0.50	r= -0.01, p=0.95	**r= -0.42, p=0.01**
Carbohydrate (g)	r= 0.02, p=0.91	r= 0.32, p=0.10	r= 0.05, p=0.79	r= 0.09, p=0.63
Fat (% of kcal)	r= -0.07, p=0.75	r= 0.23 p=0.24	**r= 0.40, p=0.02**	r= 0.24, p=0.16
Saturated fat (g)	r= 0.17 p=0.42	**r= 0.58 p=0.002**	**r= 0.43 p=0.01**	r= 0.18 p=0.31
Sat fat (% of kcal)	r= 0.13 p=0.54	**r= 0.47 p=0.01**	r= 0.33 p=0.06	r= 0.12 p=0.49
Protein (% of kcal)	r= 0.25, p=0.15	r= 0.06, p=0.78	r= 0.25, p=0.15	r = 0.01, p=0.94
Carbohydrate (% of kcal)	r= 0.37, p=0.08	r = -0.15, p=0.47	r= -0.28, p=0.10	r= -0.21, p=0.23
3 Day Record	**DM (n=13)**	**DF (n=13)**	**CM (n=23)**	**CF (n=20)**
Total kcal/kg	r= -0.37, p=0.22	r= -0.26, p=0.40	**r= -0.41, p=0.05**	r= -0.08, p=0.75

r=Pearson Correlation Coefficient
Significant correlations ($p<0.05$) are shown in bold
DM: Diabetes Male; DF: Diabetes Female; CM: Control Male; CF: Control Female

Table 4.9. Body composition and nutrient intake data by ranked hours of activity for all subjects

	0-127.5 hrs/yr (n=14)	127.6-221.8 (n=15)	221.9-465.0 (n=15)	>465.0 (n=15)
Wt Z-score	0.12 ± 0.26	0.54 ± 0.25	0.43 ± 0.25	0.66 ± 0.25
Body fat (%)	23.55 ± 2.11	22.33 ± 2.04	22.93 ± 2.04	21.95 ± 2.04
Fat Z-score	-0.18 ± 0.14	-0.12 ± 0.14	-0.10 ± 0.14	-0.008 ± 0.14
BMI Z-score	-0.07 ± 0.25	0.21 ± 0.24	0.09 ± 0.24	0.35 ± 0.24
Lean/fat mass	3.17 ± 0.49	3.61 ± 0.47	3.86 ± 0.47	4.38 ± 0.47
Ab fat (%)	15.48 ± 2.17	15.43 ± 2.10	16.47 ± 2.10	15.89 ± 2.10
% fat in ab	7.18 ± 0.56	7.93 ± 0.54	8.23 ± 0.54	8.26 ± 0.54
kcal/kg	43.43 ± 4.63	50.87 ± 4.63	46.30 ± 4.63	47.20 ± 4.47
Carbohydrate (% of kcal)	56.21 ± 1.63	53.29 ± 1.63	54.57 ± 1.63	56.40 ± 1.58
Fat (% of kcal)	31.86 ± 1.36	31.21 ± 1.36	32.14 ± 1.36	29.53 ± 1.31

Data are mean ± SEM
No significant differences as tested by one-way ANOVA

Table 4.10. Question #1 of activity questionnaire: Number of days with at least 20 minutes of vigorous exercise in the past 14 days for all subjects

	none (n=2)*	1-2 days (n=8)	3-5 days (n=15)	6-8 days (n=17)	≥9 days (n=21)
Wt Z-score	0.28, 0.67	0.44 ± 0.33	0.20 ± 0.23	0.46 ± 0.21	0.38 ± 0.20
Body fat (%)	11.20, 23.30	25.25 ± 2.53	24.45 ±1.79	19.73 ± 1.64	23.44 ± 1.56
Fat Z-score	-0.54, 0.35	-0.20 ± 0.18	-0.05 ± 0.13	-0.20 ± 0.12	0.01 ± 0.11
BMI Z-score	-0.80, 0.86	-0.20 ± 0.31	0.24 ± 0.22	-0.13 ± 0.20	0.37 ± 0.19
lean/fat mass	3.30, 7.62	3.01 ± 0.57	3.43 ± 0.40	4.32 ± 0.38	3.65 ± 0.35
Ab fat (%)	7.50, 20.40	17.68 ± 2.65	17.51 ± 1.88	12.71 ± 1.72	16.46 ± 1.64
% body fat in ab	7.63, 9.98	7.30 ± 0.72	8.81 ± 1.43	8.81 ± 1.43	7.81 ± 0.44
kcal/kg	39.16, 45.93	45.74 ± 6.04	45.59 ± 4.41	47.11 ± 4.14	48.13 ± 3.73
Cho (% of kcal)	47.00, 50.00	55.13 ± 2.02	55.40 ± 1.47	54.71 ± 1.38	56.67 ± 1.25
Fat (% of kcal)	37.00, 40.00[a]	33.12 ± 1.62[ab]	32.60 ± 1.18[ab]	31.65 ± 1.11[bc]	29.29 ± 1.00[bc]

Data are mean ± SEM

*Data in Column are presented as range due to small sample size

Groups with different letters in rows are significantly different at $p<0.05$ tested by one-way ANOVA

Table 4.11. Question #2 of activity questionnaire: Number of days with at least 20 minutes of light exercise in the past 14 days for all subjects

	1-2 days (n=2)*	3-5 days (n=20)	6-8 days (n=10)	≥9 days (n=32)
Wt Z-score	0.13, 0.28	0.56 ± 0.21	0.62 ± 0.29	0.20 ± 0.16
Body fat (%)	23.30, 29.30	23.63 ± 2.12	22.96 ± 1.22	23.46 ± 2.21
Fat Z-score	0.07, 0.35	-0.23 ± 0.11	0.10 ± 0.16	-0.07 ± 0.09
BMI Z-score	0.64, 0.86	-0.08 ± 0.20	0.42 ± 0.28	0.06 ± 0.16
lean/fat mass	2.32, 3.30	3.88 ± 0.37	3.64 ± 0.52	3.50 ± 0.29
Ab fat (%)	18.00, 20.40	14.67 ± 1.71	17.57 ± 2.42	15.78 ± 1.35
% body fat in abdomen	7.92, 9.98	7.61 ± 0.43	8.76 ± 0.61	7.51 ± 0.34
kcal/kg	20.89, 45.93	42.62 ± 3.82	47.07 ± 5.55	50.46 ± 2.99
Cho (% of kcal)	54.00, 47.00	53.05 ± 1.29	56.56 ± 1.87	56.61 ± 1.01
Fat (% of kcal)	27.00, 40.00	33.47 ± 1.06	30.67 ± 1.54	30.94 ± 0.83

Data are mean ± SEM
*Data in Column are presented as range due to small sample size
No significant differences as tested by one-way ANOVA

Table 4.12. Question #3 of activity questionnaire: Hours per day of television viewing and video game use during a normal week for all subjects

	none (n=1) *	≤1 (n=11)	2-3 (n=34)	4-5 (n=11)	≥6 (n=5)
Wt Z-score	0.67	0.56 ± 0.25	0.31 ± 0.15	-0.06 ± 0.25	1.27 ± 0.39
Body fat (%)	11.2	23.63 ± 2.12	22.96 ± 1.22	23.46 ± 2.21	21.60 ± 3.28
Fat Z-score	-0.54	-0.13 ± 0.15	-0.07 ± 0.08	-0.06 ± 0.15	-0.20 ± 0.23
BMI Z-score	-0.8	0.06 ± 0.26	0.04 ± 0.15	0.42 ± 0.26	0.21 ± 0.40
lean/fat mass	7.62	3.54 ± 0.54	3.69 ± 0.28	3.28 ± 0.48	4.34 ± 0.75
Ab fat (%)	7.5	14.80 ± 2.23	15.97 ± 1.28	16.16 ± 2.23	16.52 ± 3.45
% body fat in ab	7.63	6.98 ± 0.58	7.81 ± 0.33	8.23 ± 0.58	8.94 ± 0.90
kcal/kg	39.16	47.82 ± 5.09	48.63 ± 2.89	41.61 ± 4.87	45.73 ± 7.55
Cho (% of kcal)	50	52.64 ± 1.69	56.38 ± 0.96	56.58 ± 1.62	52.80 ± 2.51
Fat (% of kcal)	37	33.09 ± 1.46	31.09 ± 0.83	29.82 ± 1.46	33.40 ± 2.17

Data are mean ± SEM

*Data in column are values for a single subject

No significant differences as tested by one-way ANOVA

Table 4.13. Question #4 of activity questionnaire: Number of competitive sports in the past year for all subjects

	0 (n=14)	1 (n=19)	2 (n=10)	3 (n=6)	≥4 (n=14)
Wt Z-score	0.09 ± 0.24	0.47 ± 0.20	0.34 ± 0.29	1.29 ± 0.38	0.27 ± 0.25
Body fat (%)	22.45 ± 1.95	21.68 ± 1.65	22.41 ± 2.39	20.07 ± 3.08	26.72 ± 2.02
Fat Z-score	-0.14 ± 0.12^{ab}	-0.23 ± 0.10^{a}	-0.14 ± 0.15^{ab}	-0.17 ± 0.19^{ab}	0.30 ± 0.13^{b}
BMI Z-score	-0.19 ± 0.22	0.00 ± 0.19	0.06 ± 0.27	0.20 ± 0.35	0.64 ± 0.23
lean/fat mass	3.52 ± 0.46	3.96 ± 0.39	3.79 ± 0.56	4.51 ± 0.72	3.09 ± 0.47
Ab fat (%)	15.69 ± 2.03	14.87 ± 1.72	14.74 ± 2.49	14.22 ± 3.21	19.30 ± 2.10
% body fat in ab	7.83 ± 0.53	7.58 ± 0.45	7.68 ± 0.65	7.98 ± 0.84	8.35 ± 0.55
kcal/kg	43.87 ± 4.39	44.63 ± 3.77	48.84 ± 5.19	60.10 ± 6.70	45.84 ± 4.39
Cho (% of kcal)	51.93 ± 1.51	56.05 ± 1.30	56.80 ± 1.79	56.50 ± 2.31	57.14 ± 1.51
Fat (% of kcal)	35.14 ± 1.23^{a}	30.68 ± 1.06^{ab}	28.90 ± 1.46^{b}	30.50 ± 1.88^{ab}	30.43 ± 1.23^{ab}

Data are mean ± SEM

Groups with different letters in rows are significantly different at $p<0.05$ tested by one-way ANOVA

Table 4.14. Relationship between HbA1c and body composition

Y variable	D n=50	DM n=23	DF n=27
Wt (kg)	r=0.24, p=0.09	r=0.11, p=0.63	**r=0.41, p=0.03**
Wt Z-score	r=0.12, p=0.41	r=0.01, p=0.96	r=0.22, p=0.26
Ht (cm)	r=0.16, p=0.27	r=0.04, p=0.84	r=0.33, p=0.10
Ht Z-score	r= -0.02, p=0.91	r= -0.16, p=0.46	r= -0.10, p=0.62
BMI	**r=0.28, p=0.05**	r=0.17, p=0.43	**r=0.37, p=0.05**
Total Fat Mass (g)	**r=0.31, p=0.03**	r=0.23, p=0.30	**r=0.40, p=0.04**
Total Lean Mass (g)	r=0.14, p=0.34	r=0.02, p=0.93	r=0.37, p=0.06
Body Fat (%)	r=0.24, p=0.10	r=0.30, p=0.17	r=0.28, p=0.15
Fat Z-score	r=0.10, p=0.48	r=0.11, p=0.60	r=0.11, p=0.59
Ab Fat (%)	r=0.25, p=0.09	r=0.24, p=0.28	r=0.28, p=0.15
Trunk Fat (%)	r=0.20, p=0.16	r=0.20, p=0.36	r=0.24, p=0.22
Leg fat (%)	r=0.24, p=0.10	r=0.33, p=0.13	r=0.30, p=0.13
Arm fat (%)	r= -0.18, p=0.21	r=0.21, p=0.33	r=0.23, p=0.25
TLFR	r= -0.01, p=0.94	r= -0.17, p=0.44	r=0.10, p=0.62
ALFR	r= -0.19, p=0.90	r= -0.04, p=0.86	r= -0.18, p=0.93
Onset (yr)	r= -0.11, p=0.45	r= -0.35, p=0.11	r=0.08, p=0.70
Duration (yr)	**r= 0.29, p=0.04**	**r= 0.45, p=0.03**	r= 0.15, p=0.45
Age (yr)	r=27, p=0.55	r=0.16, p=0.48	**r=0.41, p=0.04**
Insulin (U/kg)	r=0.13, p=0.37	r=0.097, p=0.66	r=0.15, p=0.46
Am blood glucose	r=0.11, p=0.44	r=0.36, p=0.10	r= -0.70, p=0.73
Glucose/creatinine	**r=0.41, p=0.004**	**r=0.50, p=0.02**	r=0.35, p=0.09

D: Diabetes; DM: Diabetes Male; DF: Diabetes Female
r=Pearson Correlation Coefficient
Significant correlations ($p<0.05$) are shown in bold

Table 4.15. Multiple linear regression analysis of factors related to HbA1c for all subjects with diabetes

Variable	Coefficient	SE	t-ratio	p-value
HbA1c (R=0.74, Radj=0.67) Constant	14.716	1.187	12.402	<0.001
Activity (hrs/yr)	0.002	0	1.553	0.141
Body fat in abdomen (%)	-0.806	0.168	-4.789	<0.001
Wt Z-score	1.178	0.274	4.301	<0.001
Saturated fat (g) (24 hour recall)	-0.047	0.018	-2.673	0.017

HbA1c = constant + Activity (mean) - Body fat in abdomen (mean) + Wt Z-score (mean) - Saturated fat (mean) = 14.716 + 0.002 (288.8) - 0.806 (8.02) + 1.178 (0.50) - 0.047 (28.0)

Table 4.16. Multiple linear regression analysis of factors related to percent body fat Z-score for all subjects with diabetes

Variable	Coefficient	SE	t-ratio	P-value
Percent fat Z-score (R=0.87, Radj=0.72) Constant	-0.35	0.292	-1.198	0.248
Activity (hrs/yr)	-0.001	0	-2.92	0.01
Body fat in abdomen (%)	0.163	0.04	4.102	<0.001
Age at diagnosis (yr)	-0.098	0.015	-6.489	<0.001

Percent fat Z-score = constant - Activity (mean) + Body fat in abdomen (mean) - Age at diagnosis (mean) = -0.350 -0.001 (288.8) + 0.163 (8.02) -0.098 (8.71)

Table 4.17. Multiple linear regression analysis of factors related to percent of body fat in the abdomen for all subjects with diabetes

Variable	Coefficient	SE	t-ratio	P-value
%body fat in abdomen(R=0.813, Radj=0.66) Constant	11.876	1.17	10.153	<0.001
Activity (hrs/yr)	0.003	0	3.038	0.008
HbA1c	-0.634	0.144	-4.394	<0.001
BMI Z-score	0.859	0.301	2.858	0.011

%body fat in abdomen = constant + Activity (mean) - HbA1c (mean) + BMI Z-score (mean) = 11.876 + 0.003 (288.8) - 0.634 (7.85) + 0.859 (0.32)

Table 4.18. Multiple linear regression analysis of factors related to HbA1c for females with diabetes

Variable	Coefficient	SE	t-ratio	P-value
HbA1c (R=0.95, Radj=0.84) Constant	11.042	1.687	6.545	0.001
Activity (hrs/yr)	0.003	0	2.03	0.098
Body fat in abdomen (%)	-1.078	0.163	-6.607	0.001
BMI Z-score	1.178	0.274	4.301	<0.001
Insulin (units/kg)	4.019	1.614	2.491	0.055

HbA1c = constant + Activity (mean) - Body fat in abdomen (mean) + BMI Z-score (mean) + Insulin (mean) = 11.042 + 0.003(263.8) - 1.078(8.30) + 1.178(0.51) + 4.019(1.0)

Table 4.19. Multiple linear regression analysis of factors related to percent body fat Z-score for females with diabetes

Variable	Coefficient	SE	t-ratio	P-value
Percent fat Z-score (R=0.98, Radj=0.91) Constant	0.478	0.266	0.793	0.147
Age at diagnosis (yr)	-0.063	0.013	-4.701	0.009
Body fat in abdomen (%)	0.11	0.028	3.87	0.018
Use of lispro (yes/no)	-0.318	0.084	-3.808	0.019
Activity (hrs/yr)	0.001	0	2.374	0.077
Insulin dose (units/kg)	-0.928	0.23	-4.027	0.016

Percent fat Z-score = constant - Age at diagnosis (mean) + Body fat in abdomen (mean) - Use of lispro (mean) + Activity (mean) - Insulin dose (mean)= 0.478 - 0.063(8.50) + 0.11(8.30) - 0.318(?) + 0.001(263.8) - 0.928(1.0)

Table 4.20. Multiple linear regression analysis of factors related to percent of body fat in the abdomen for females with diabetes

Variable	Coefficient	SE	t-ratio	P-value
%body fat in abdomen(R=0.97, Radj=0.88) Constant	9.609	1.6	6.004	0.002
BMI Z-score	1.566	0.391	4.009	0.01
Activity (hrs/yr)	0.003	0	2.457	0.057
Insulin dose (units/kg)	3.595	1.385	2.595	0.049
HbA1c	-0.832	0.126	-6.607	0.001

%body fat in abdomen = constant + BMI Z-score + Activity (mean) + Insulin dose (mean) - HbA1c (mean) = 9.609 + 1.566(0.51) + 0.003(263.8) + 3.595(1.0) - 0.832(7.89)

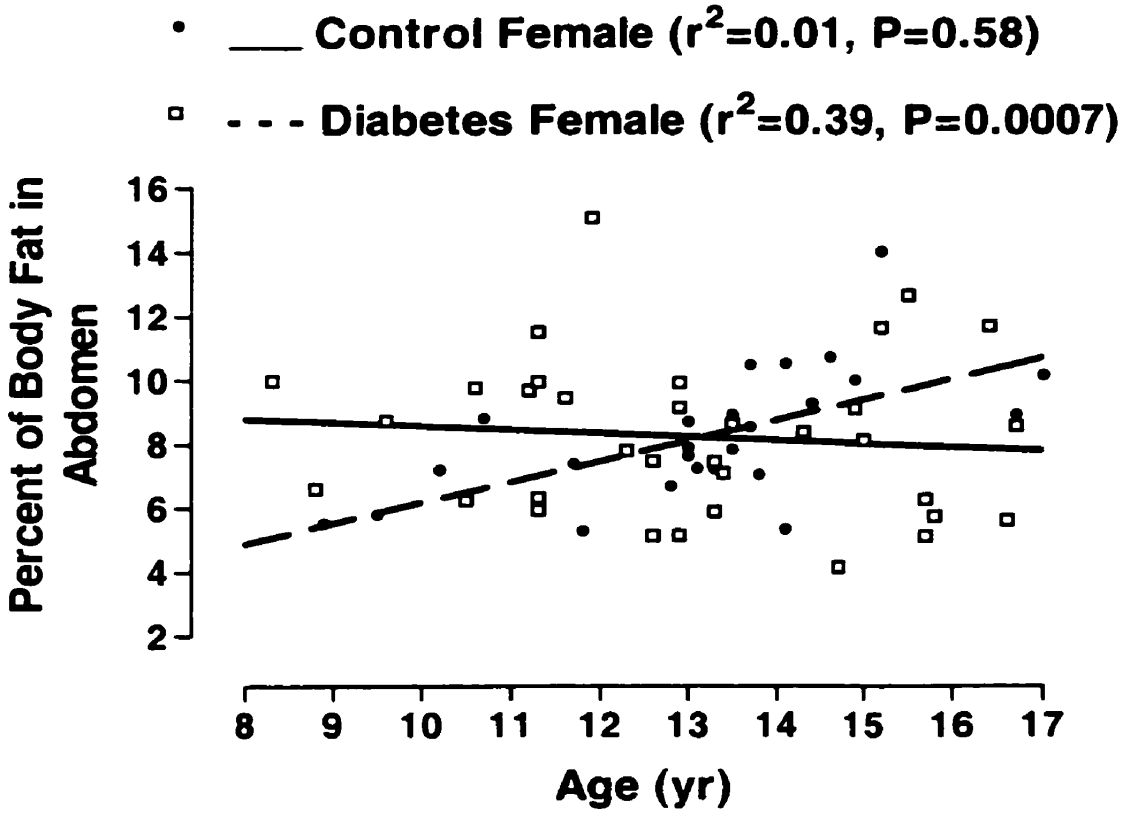

Figure 4.1. Linear regression of percent of body fat in the abdomen vs age for females with (n=27) and without (n=34) type 1 diabetes. Slopes are significantly different at p=0.009

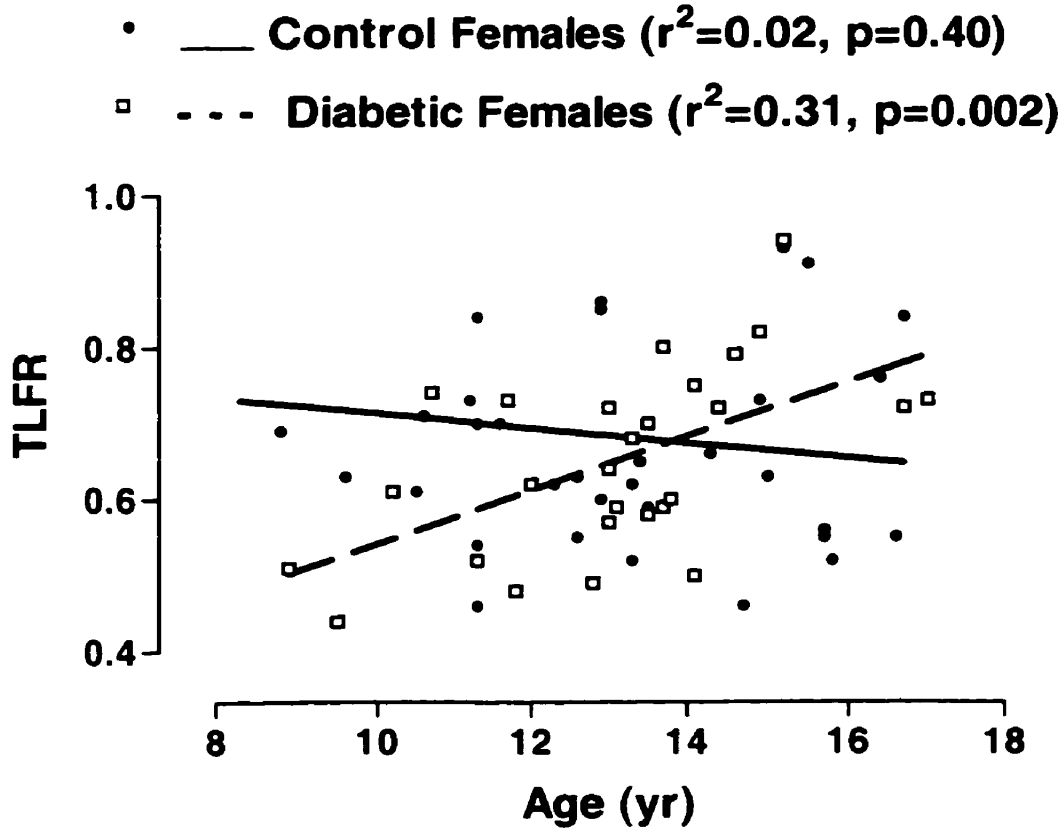

Figure 4.2. Linear regression of trunk to leg fat ratio vs age for females with (n=27) and without (n=34) type 1 diabetes. Slopes are significantly different at p=0.009

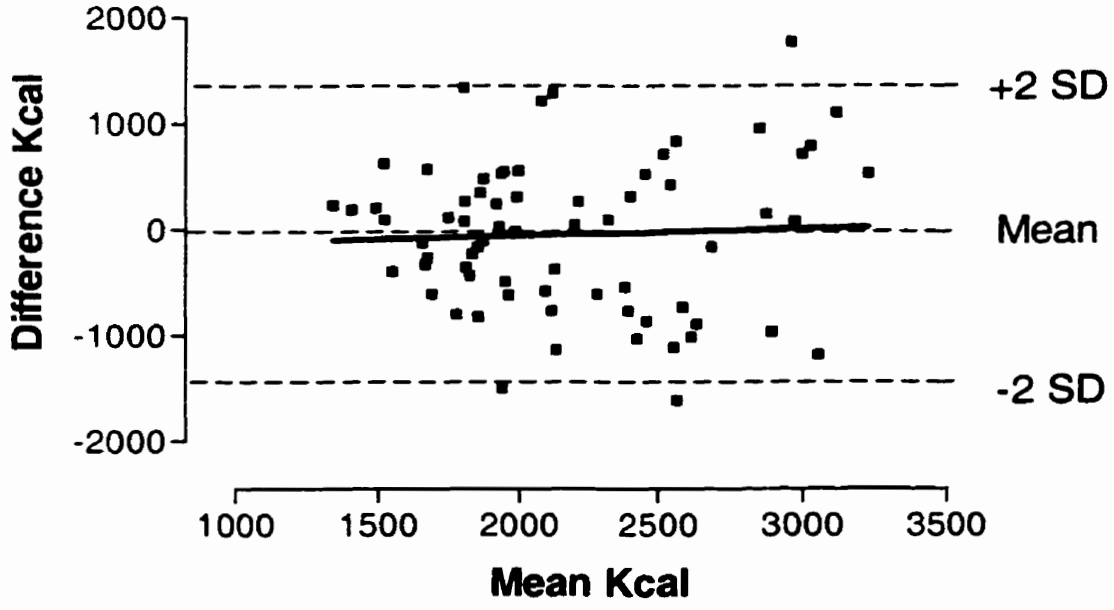

Figure 4.3. Linear regression of the difference in total energy intake (kcal) between the 24 hour recall and 3-day food record vs. the mean kcal for both methods combined (r^2= 0.002, p=0.73), n=69

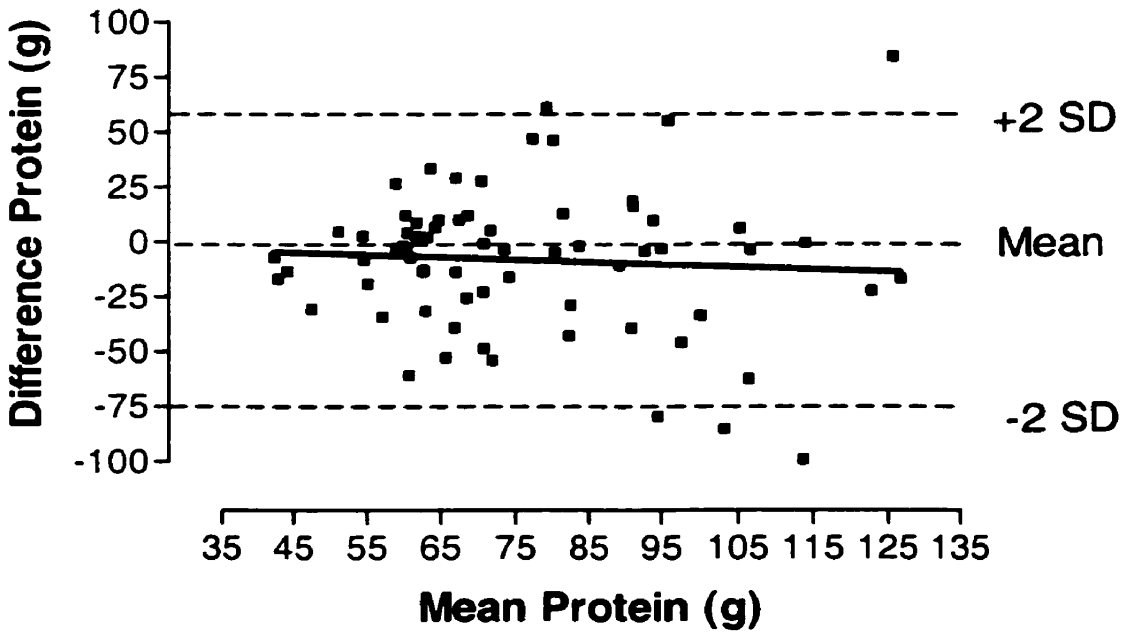

Figure 4.4. Linear regression of the difference in protein intake between the 24 hour recall and 3-day food record vs. the mean kcal for both methods combined (r^2= 0.005, p=0.58), n=69

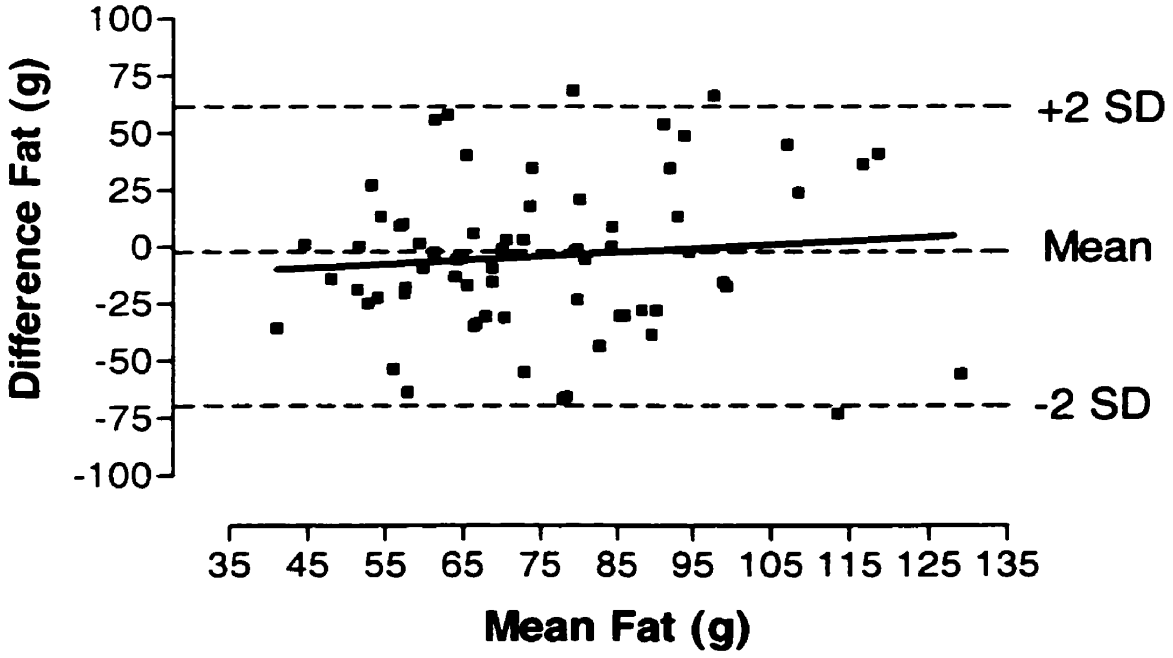

Figure 4.5. Linear regression of the difference in fat intake between the 24 hour recall and 3-day food record vs. the mean kcal for both methods combined (r^2= 0.010, P=0.42), n=69

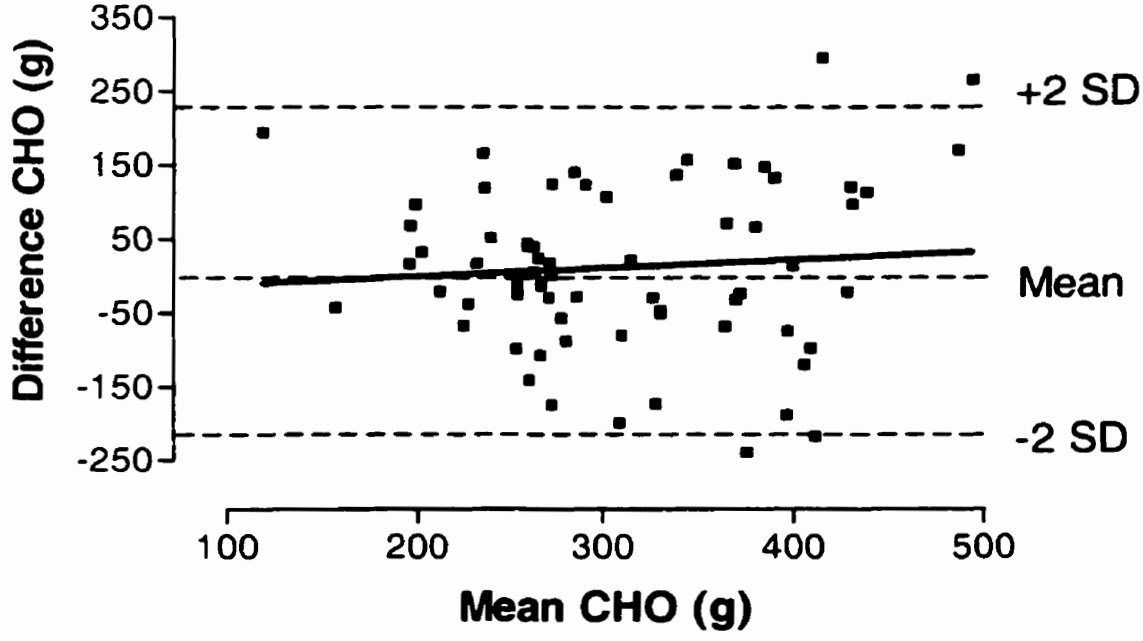

Figure 4.5. Linear regression of the difference in carbohydrate (CHO) intake between the 24 hour recall and 3-day food record vs. the mean kcal for both methods combined (r^2= 0.006, P=0.51), n=69

5. Discussion:

Results from the DCCT proved that better glycemic control achieved through intensive management resulted in significantly fewer long term complications. Therefore, achieving glycemic control as close to normal as possible without causing hypoglycemia, has become the goal of management of type 1 diabetes in children over the age of 6 years. This is referred to as intensive management and often requires three or more insulin injections per day. However, intensive management in the DCCT was also associated with weight gain. Therefore, it is not surprising that in recent years children with type 1 diabetes have been increasingly found to be overweight for height (Pietilainen, 1995; Holl et al, 1994; Thon et al, 1992; Wise et al, 1992; Herber & Dunsmore, 1988). Most studies indicate weight gain is a problem for both male and female children with type 1 diabetes (Holl et al, 1998; Danne et al, 1997; Jos et al, 1996; Holl et al, 1994; Thon et al, 1992), while others, including data from Manitoba, suggest that only adolescent females are overweight for height (Domargard et al, 1999; Du Caju et al, 1995; Gregory et al, 1991). Recent large scale cross-sectional studies in children and adolescents have found that multiple insulin injections with or without a high dose of insulin per unit body weight are associated with weight gain (Mortensen et al,1998; Danne et al, 1997; Dorchy et al, 1997). Investigations into the composition of this weight have produced conflicting results. Studies on newly diagnosed children and adults with type 1 diabetes have found that weight gain is largely lean mass (

Rigalleau et al, 1999; Sinha et al,1996). One study by Bartz et al, (1997) found similar results in 157 male, and 117 female children with type 1 diabetes with an average age of 17.6, and duration of diabetes of 8.9 years. However, several other studies found that weight gain in type 1 diabetes is predominately fat mass (Tuvemo et al, 1997; Pietilainen et al, 1995; Carlson et al, 1993; Gregory et al, 1992). Exacerbation of diabetes control by excess fat mass could pose a significant problem to the long term management and outcome of diabetes. Therefore, the hypothesis of this thesis research was: **high insulin dose (U/kg) and/or frequency of injection during childhood and adolescence adversely affect body composition such that fat mass is higher than normally expected for age**. The objectives of this research in children from 8-18 years of age were to:

1) characterize body composition, dietary patterns, and physical activity in relation to glycemic control and medical management, in children with type 1 diabetes and compared to children without diabetes, and
2) examine possible influences of body composition, diet, physical activity, and medical management on glycemic control in children.

Children with diabetes as a group were not overweight for height compared to controls. When separated by sex, there were no differences between males with or without diabetes, but females with diabetes did have a significantly higher BMI than control females. When females were separated into groups according to pre- or post-menarche, the significant difference in BMI

remained between the control and diabetic post-menarche but not the pre-menarche girls. These results are similar to other studies which found that pubertal females were overweight for height, but males and pre-pubertal females were not (Domargard et al, 1999; Du Caju et al, 1995; Gregory et al, 1992) .

While girls with diabetes did have a higher BMI than the control group, how important is this difference? One way to answer that question is to look at how many children in each group would be classified as obese. Using the definition of obesity as $\geq 85^{th}$ percentile for BMI 7 out of 34 (21%) of control females would be considered obese while 7 out of 27 (26%) of females with diabetes qualify as obese. However, when using the definition of $\geq 95^{th}$ percentile as obese, then only 2 out of 34 (6%) control girls and 1 out 27 (4%) girls with diabetes qualify as obese. Using the former definition of obesity, both groups fall within the reported range of 15-30% of children (Rosner et al, 1997). However BMI does not provide information on body composition and fat distribution, and we do not have data for abdominal fat so we can only assume or speculate.

The higher BMI found in the females with diabetes could not be explained by a significantly higher amount of fat or lean mass than the control group. However, there were indications that the higher BMI in females with diabetes could be mainly due to fat rather than lean mass. For example, while not statistically significant, %fat, and total grams of fat were higher in the girls with diabetes compared to controls, while the ratio of lean/fat mass was somewhat higher in the control group.

While there was no significant difference between the control and diabetic females in mean percent body fat, and percent of body fat in the abdomen, group means masked the relationship between age and fat distribution. Using simple linear regression, central fat distribution increased across age groups in female children with type 1 diabetes (as measured by percent of body fat in the abdomen and TLFR). This was not the case for the control group (See Figures 2 and 3). The slopes of these regression lines were significantly different between diabetic and control females (P=0.009 for both percent of fat in the abdomen and TLFR). These results are interesting because it is normal for males to develop an android or central fat distribution (measured by TLFR) as they age, while females generally develop a more gynoid distribution. (Cowell et al, 1997). Studies in adults (Sparrow et al, 1986; Fujioka et al, 1987; Despres et al, 1989; Macor et al, 1997), and children (Stephen et al, 1999; Daniels et al, 1999; Freedman et al, 1987) have found a central fat distribution, independent of gender or obesity, is associated with decreased insulin sensitivity and increased blood lipids. If it is true that females with type 1 diabetes develop a more central fat distribution with age, then this could add to the already increased risk of cardiovascular disease. It is important to note that while percent of body ft in the abdomen increased with age in girls with diabetes and decreased in girls without, post-menarche females with diabetes did not have a significantly higher percentage of fat in the abdomen than post-menarche females without diabetes. This may be due to the small sample size of post-

menarche girls which did not allow for a high enough power to detect a significant difference where one existed, or it may be more important to examine if and why the pre-pubescent girls with diabetes had less fat in the abdomen than those without diabetes. One possible explanation could be that they were newly diagnosed with diabetes and had not regained the weight they lost prior to diagnosis, and that fat in the abdomen is the most easily lost and gained. However percent of body fat in the abdomen was not positively correlated with duration of diabetes which does not support this explanation.

Males with diabetes did not have a more central fat distribution than control males and TLFR was not significantly correlated with age in either group. However, percent of fat in the abdomen was significantly positively correlated with age for males with diabetes but not controls. Unlike in females, the slopes of these regression lines were not significantly different. The fact that females with diabetes have a higher BMI than controls, but no difference was found for males may be a result of several factors. While males did not have a higher HbA1c than females, there were some indications that males may have worse metabolic control than females. For example, although not statistically significant, males had higher morning (AM) home blood glucose tests and urinary glucose/creatinine ratio on the morning of the 24 hour recall (see Table 4.2). Furthermore, significant positive correlations were found only for males between HbA1c and urinary glucose/creatinine ratio, as well as duration of diabetes (see Table 4.15). For girls, HbA1c was significantly positively correlated with weight

in kg, BMI, total grams of fat mass, and total grams of lean mass as well as age. These results indicate that age is the most important factor related to HbA1c in girls, but not in boys. This could mean that girls reach puberty earlier than boys and may be experiencing the increased insulin resistance which comes with puberty, while most boys in this study have not yet reached puberty.

For children with diabetes as a group, insulin dose (U/kg) was significantly positively correlated with duration of disease, weight, BMI and grams of total fat mass but not with HbA1c, percent body fat, percent of fat located in the abdomen, or TLFR. These results make sense, since insulin dose is usually based on weight or BMI, rather than percent body fat. However, HbA1c does not decrease as insulin dose increases, therefore, a higher insulin dose does not produce better glucose control.

When children with diabetes were separated into groups according to 2 or 3+ injections per day, there were no differences in indices of body composition between groups. However, when these groups were separated by sex, the females using 3 or more injections per day were taller, and had significantly more grams of total lean body mass than those using 2 injections per day. There was no significant difference for age, weight, BMI, total grams of fat mass, percent total body fat, or HbA1c. While age was not significantly different, the females using only 2 injections per day were on average 7 months younger than those using 3 or more injections (2 injections = 12.66 ± 0.61 yrs, 3+ injections = 13.35 ± 0.47 yrs). This difference may be enough to affect the results. On the

other hand it is possible that more frequent injection of insulin could lead to higher lean mass. Although most studies suggest that multiple insulin injections result in excess fat mass (Tuvemo et al, 1997; Pietilainen et al, 1995; Carlson & Campbell, 1993; Gregory et al, 1992), no studies have been done which directly compare the body composition between children with type 1 diabetes who use 2 injections daily to those who use 3 or more.

The results that females using fast-acting (Lispro) insulin instead of Regular had a lower percent body fat were interesting. Lispro mimics the normal physiological response to glucose as it begins to work immediately after injection and peaks 30-90 minutes later. It is normally no longer effective after 2-3 hours. This is in contrast to Regular insulin which must be injected at least 30 minutes prior to eating, peaks 2.5 to 5 hours later, and could still be affecting blood sugar levels for several more hours. Lispro allows for greater flexibility in timing and amount of food consumed throughout the day, since it can be taken immediately before eating or even shortly after food is consumed. This gives the patient the ability to eat based on hunger cues rather than having to eat according to peak insulin activity, which could result in a lower caloric intake. Lispro also allows more flexibility to include activity throughout the day since Lispro is out of the system after 2-3 hours and will be less likely to produce hypogycemia with activity between meals. Therefore, activity may also be increased with Lispro. However, the lower percent body fat was not explained by this theory, as there was no significant difference in calorie intake or hours of activity between girls

using Lispro and Regular insulin. However, this could be due to the lower power to detect significant differences due to the low response rate for the 3-day food record and activity questionnaire.

The method of a 3-day food record was chosen due to the higher accuracy and reliability compared to 24 hour recalls. However, the small gain in accuracy was offset by the low return rate. Therefore, it might have been more useful to perform 3 or 4 separate 24 hour recalls. The first one would still have been done in person and the other 2-3 by telephone. However, this would have changed the way portion sizes were estimated. For example, we could have used two dimensional food models during the face-to-face interview and then given each child a package of these food models to take home and use during the telephone interviews. Having the children complete the activity questionnaires at the initial interview would also have increased the return rate as well as accuracy as we would have been available to answer any questions and review the questionnaire for completeness or clarification of responses.

Nutrient intake was compared among groups and to Canadian recommendations. All groups were close to Canadian recommendations of >55% kcal from carbohydrate, <30% kcal from total fat (<10% energy from saturated fat), and approximately 15% kcal from protein. However, fibre intake was generally low. The recommendation for fibre intake for children is age plus 5 g. (Dwyer, 1995). If we consider that the average age of participants in this study was 13 years, then the average recommendation would be 18 grams. The

average fibre intake across groups was 14 grams or 77% of the recommendation. Total energy intake (kcal) was also slightly lower than the recommended 2800 (or 56kcal/kg) for a 13 year old male, and 2200 (or 46 kcal/kg) for a 13 year old female. This may indicate systematic underreporting of food intake for both the 24 hour recall and 3 day food record. Protein in grams per kg body weight was above the recommended 1 g/kg.

Children in this thesis research had slightly higher intakes of total and saturated fat than recommendations, with an average of 32% of energy coming from total fat and 11.23% of energy from saturated fat. However these results are much closer to recommendations than those found in other studies including children with and without diabetes (Schober et al, 1999; Randecker et al, 1996; Pietilainen et al, 1995; Shatenstein & Ghadirian,1996). Macronutrient intake in this thesis research was similar to a study done in Saskatchewan by Whiting et al, (1995), which examined nutrient intake in 228 school children aged 8-15 (111 males; 115 females) using six 24 hour recalls. Percent of energy from carbohydrate, fat and protein was approximately 53, 32, and 15% for girls, and 51, 34, and 15% for boys.

Results of correlation analysis between dietary variables (from 3-day food records) and indicators of body composition for all subjects with diabetes were similar to other studies in that total energy/kg of body weight was negatively correlated with percent body fat (Stewart et al, 1999; Gazzaniga & Burns, 1993). Grams of protein per kg of body weight was also negatively correlated with

percent body fat for children with diabetes, which has not been previously reported. Neither of these results were significant for the children without diabetes. Many studies also found a significant positive correlation between percent of kcal from fat and percent body fat (Tucker et al, 1997; Ricketts, 1997; Maffeis et al, 1996; Gazzaniga & Burns, 1993). In this thesis research, a significant correlation was found between percent of kcal from fat and percent body fat in children with and without diabetes with 24 hour recall data. It is generally agreed that results of a single 24 hour recall are not representative of usual intakes of individuals and therefore should not be used in correlation analysis, regression, or to ranking individuals by nutrient intake. This was confirmed by the results of the Bland & Altman method. However, it is interesting that the results from the 24 hour recall were more similar to findings from other studies than those of the 3 day food record. This might be explained by the fact that these other studies also used only one or two 24 hour recalls, or that a single 24 hour recall actually provides more accurate information on food intake because subjects do not change their eating behaviour. Another reason may be that the sample size of the 24 hour recall was much larger than the 3 day record and therefore had a higher power to detect significant results. It is also important to note that it may have been better to use a paired t test rather than the method by Bland & Altman (1986) to compare methods of assessing nutrient intake. Namely because the two measures of nutrient intake are both attempts to operationalize the same variable. Hence, the

comparison of their respective levels of precision needs to measure variability in the mean difference of the two estimates. The inference test for this comparison is the paired t test, which uses SEM, not the comparison which uses SD of the differences between the two estimates. However, even if the paired t test found no differences between the results of the 24 hour recall and the 3 day food record, it can not be stressed enough that a single 24 hour recall is generally considered inappropriate to assess intakes of individuals. Furthermore, in this study, the 24 hour recall was not representative of the different days of the week since most interviews were done on Saturday, which means Friday was over represented.

When physical activity was examined in relation to dietary variables and indices of body composition, hours of activity were significantly negatively correlated with percent kcal from fat, and once a single outlier was removed, the ratio of lean/fat mass was significantly positively correlated with hours of activity. These results are similar to those found by Deheeger et al, (1997), in that active children consumed a lower percentage of kcal from fat. Deheeger et al, (1997) also found that active children consumed more energy, and percent of kcal as carbohydrate than less active children. This thesis research did find that total kcal correlated positively with hours of activity (when one outlier was removed), however when total energy was adjusted for body weight (kcal/kg), this relationship was no longer significant. Percent of energy as carbohydrate was also not significantly related to hours of activity. Results of body composition

found by Deheeger et al, (1997) were that while more active children had similar BMIs as less active children, they did have a higher percentage of lean mass and lower percentage of fat mass as measured by triceps skinfold thickness.

Ranking of subjects from 1 to 4 based on quartiles of hours activity did not produce any significant differences among different levels of physical activity. The lack of significant differences among the groups may indicate that dividing groups based on quartiles may not have been the most effective way to measure differences among groups. The group with the lowest level of activity averaged 0 to 127.5 hours of activity per year or 0 to 2.45 hours per week during the previous year. It is possible that differences in body composition may occur within this group alone.

Question #1 on the activity questionnaire asked about the frequency of vigorous activity in the past 14 days (see Appendix B). Significant differences were found among groups for percent of kcal as fat with subjects who responded "none" (0) having a significantly higher intake of fat as a percentage of kcal than those who responded "6 to 8 days" (3) and "9 or more days" (4). The subjects with the highest level of activity (4) had a significantly lower consumption of fat as a percentage of kcal compared to level 0, 1, and 2, but not 3. These results agree with the significant negative correlation of hours of activity with percent of kcal as fat, which makes sense because the results for question 1 were significantly positively correlated with hours of activity. Question 1 was also significantly positively correlated with question 2, and question 4, and negatively

with percent of kcal as fat.

For question # 2, which asked the frequency of hours of light exercise, and #3, which inquired about the number of hours per day spent watching television or playing video games, no significant differences were found among groups for dietary variables or indices of body composition. These results do not agree with several recent studies that have found that fatness was significantly and positively associated with time spent watching television (Hernandez et al, 1999; Maffeis et al, 1998, Deheeger et al, 1997;), and video games (Deheeger et al, 1997).

For question #4, which asked about the number of competitive sports in the past year, significant differences were found for percent of kcal as fat (3-day food record), and for body fat Z-score (see Table 4.13). No other significant differences were found. These results are surprising in that the subjects who competed in 4 or more sports had a significantly higher body fat Z-score than those who competed in only 1 sport. It is possible that subjects who participated in only 1 sport may have spent more time and/or intensity participating in one activity than those who participated in 4 or more sports.

As is commonly done, Z-scores were used in this thesis research to indicate height, weight, % fat and BMI in relation to the mean for a specific age and sex. However, recent unpublished work by Stoltzfus (2000), indicates that it is better to use the absolute difference from the mean instead of Z-scores because the variability around the mean is very much inflated throughout the

period of pubertal growth. This is because the timing and shape of the pubertal growth spurt varies considerably, both between and within populations. While pubertal growth is associated with large standard deviations, variation in childhood growth is relatively small from 3-11 years of age. The result is that 2 standard deviations above or below the mean for age, becomes progressively further from the typical value with age. Therefore a child who is tracking along a negative Z-score is becoming progressively shorter than the reference population in terms of mean height.

Differences between females with and without diabetes for height, weight, BMI, and percent body fat were compared using the absolute difference from the mean. Since these results were not different from results obtained using Z-scores, only results from Z-scores were included in this thesis research.

Using Pearson correlation analysis, for the diabetic group as a whole, HbA1c was significantly positively correlated with duration of diabetes, the urine glucose/creatinine ratio, BMI, and total grams of fat mass. In the female diabetic group, HbA1c was significantly positively correlated with age, weight, BMI, total grams of fat mass, and total grams of lean mass. In the male diabetic group only duration of diabetes, and the urine glucose/creatinine ratio were significantly positively correlated with HbA1c (See Table 4.14). None of the dietary variables were significantly correlated with HbA1c, including energy adjusted intake of dietary fibre. Similar results were found by Dorchy et al (1997), in that HbA1c was positively correlated with diabetes duration in a study including 73 boys and

71 girls under the age of 18. However, contrary to this thesis research, Dorchy et al (1997), also found that HbA1c was positively correlated to the insulin dose.

Results of multiple linear regression analysis of factors related to HbA1c for all subjects with diabetes included hours of activity, percent of body fat in the abdomen, weight Z-score, and grams of saturated fat (see Table 4.15). The equation is: HbA1c = 14.716 + 0.0015 (288.8) - 0.806 (8.02) + 1.178 (0.50) - 0.047 (28.0). This means that for every unit increase in HbA1c, hours of activity contributes by .43, percent of body fat in the abdomen contributes by -6.46, weight Z-score contributes by .59, and grams of saturated fat by - 1.32. These results are surprising in that both percent of body fat in the abdomen and grams of saturated fat had a positive relationship when simple linear regression was used, and it would be expected that hours of activity would be negatively related to HbA1c. It was expected that results would be similar to those found by a nationwide study of French children with type 1 diabetes aged 1-19 years by Rosilio et al (1998). This study was able to explain 94% of the variance in HbA1c with a limited number of independent variables. Multiple regression analysis identified age, daily insulin dosage, mother's age, diabetes duration, and in-hospital days as being positively correlated with HbA1c, and, frequency of glucose measurements and number of consultations as being negatively correlated. Factors which were included in the regression but did not contribute to the model were BMI, and number of insulin injections. Another study by Garancini et al (1997), used multiple linear regression to determine factors

associated with HbA1c in 573 patients with type 1 diabetes >13 years old (mean age 35.8 ±13.2). Only number of insulin injections per day and insulin dose per kg contributed to the model. Other variables which were included but did not contribute to the model were age, sex, disease duration, fundus examination, and qualified employment.

Percent of body fat Z-score in all subjects with diabetes was best explained by hours of activity, percent of body fat in the abdomen, and age at diagnosis (see Table 4.16). The equation is: Percent fat Z-score = -0.350 - 0.001(288.8) + 0.163(8.02) -0.098(8.71). This means that for every unit increase in percent fat Z-score, hours of activity contributes by -.29, percent of body fat in the abdomen by 1.31, and age at diagnosis by -0.85.

Percent of body fat in the abdomen was best explained in all children with diabetes by hours of activity, HbA1c, and BMI Z-score (see Table 4.17). The equation is: Percent body fat in the abdomen = 11.876 + 0.003 (288.8) - 0.634 (7.85) + 0.859 (0.32). This means that for every unit increase in percent body fat in the abdomen, hours of activity contributes by .87, HbA1c by -4.98, and BMI Z-score by .27.

For females with diabetes, factors which best explained HbA1c in multiple linear regression included hours of activity, percent body fat in the abdomen, BMI z-score, and units of insulin per kg body weight (see Table 4.18). The equation is: HbA1c = 11.042 + 0.003(263.8) - 1.078(8.30) + 1.178(0.51) + 4.019(1.0). This means that for every unit increase in HbA1c, hours of activity

contributes by 0.79, percent of body fat in the abdomen contributes by -8.95, BMI Z-score contributes by .60, and units of insulin per kg body weight by 4.02.

Percent of body fat Z-score in females with diabetes was best explained by hours of activity, percent of body fat in the abdomen, use of lispro insulin, and age at diagnosis (see Table 4.19). The equation is: Percent fat Z-score = 0.478 - 0.063(8.50) + 0.11(8.30) - 0.318(?) + 0.001(263.8) - 0.928(1.0). This means that for every unit increase in percent fat Z-score, hours of activity contributes by .26, percent of body fat in the abdomen by .91, and age at diagnosis by -0.54.

Percent of body fat in the abdomen was best explained in females with diabetes by BMI Z-score, hours of activity, insulin units/kg body weight, and HbA1c (see Table 4.20). The equation is: Percent body fat in the abdomen = 9.609 + 1.566(0.51) + 0.003(263.8) + 3.595(1.0) - 0.832(7.89). This means that for every unit increase in percent body fat in the abdomen, BMI Z-score contributes by .80, hours of activity by .79, insulin units/kg body weight by 3.60, and HbA1c by -6.56.

Interpretation of the results of the multiple linear regression is difficult at best. For example, we would expect physical activity to have a beneficial effect on body composition and glycemic control. Results of the above multiple linear regression did not seem to support this assertion. In fact, the only results of this thesis research which found a beneficial effect of physical activity were that a higher lean/fat ratio was associated with a higher number of hours of physical activity per year. One possible explanation for these contradictory results is the

limitations of the method used to measure physical activity. In addition to the limitations of using questionnaires discussed in section 2.5.0. of this thesis, this particular questionnaire was validated in a group of junior high school students who completed the questionnaire under the supervision of research assistants. It may not have been appropriate for subjects to complete the questionnaire at home, or to use this questionnaire for subjects under 12 years of age. In addition, in this thesis research, hours of physical activity were not multiplied by the metabolic cost of that activity as was done by Aaron et al, (1993). This may also have contributed to the limitations of estimating the true level of physical activity.

It is also possible that most of the subjects in this study were within a healthy range for percent body fat, and/or physical fitness. This raises two important questions: 1) When does the percentage or distribution of body fat have a negative impact on glycemic control?, and 2) If a person is physically fit, is body fat important?

It is also crucial to remember that many tests of significant differences in data were done which will lead to some differences showing up as significant by chance. And finally, some of these variables may interact in a non-linear manner and further exploration should include non-linear approaches to describing the data observed.

Strengths and Limitations

This study was the first to examine whole body and regional fat distribution in children with diabetes compared to those without. Strengths of this study include the use of DXA to measure body composition. DXA has been found to have better precision and accuracy than other methods used to measure body composition in children, such as skin fold thickness and bioelectric impedance (Gutin et al, 1996). This thesis research also has the advantage over many other studies in that it goes beyond the examination of group means to look at relationships with other variables. Nutrient intake was measured with a 24 hour recall and a 3 day food record. Physical activity was also assessed using a questionnaire which had been previously found to be reliable and valid in this age group (Aaron et al, 1993). However, as previously discussed, there are many limitations involved in the methods chosen to assess nutrient intake and physical activity, as well as the appropriateness of the tests used to compare methods of assessing nutrient intake. Another limitation is the cross-sectional design of this study, which does not allow for repeated measures, comparison over time, or cause and effect. The study population was also self-selected, which may produce a bias towards leaner subjects than the general population, in that fatter children may not want to participate due to embarrassment. However, this possible bias towards leaner children should affect both groups equally. Another limitation was that puberty was not assessed according to tanner stages in both girls and boys. It was also a limitation that

blood was not taken so we could measure HbA1c, as well as other biochemical indicators rather than taking information from the medical chart.

In conclusion, this study did not find that high insulin dose (U/kg) and/or frequency of injection during childhood and adolescence adversely affect body composition such that fat mass is higher than normally expected for age.

6. Future Investigations

The contributions of this research in identifying the interrelationships among body composition, medical management, glycemic control, diet, and physical activity, have provided the groundwork upon which to base future studies. Children with diabetes as a group were not overweight for height compared to controls. When separated by sex, there were no differences between males with or without diabetes, but females with diabetes did have a significantly higher BMI than control females. When females were separated into groups according to pre- or post-menarche, the significant difference in BMI remained between the control and diabetic post-menarche but not the pre-menarche girls.

This difference in BMI between girls with and without diabetes may not be very important when children are classified according to the definition of obesity as $\geq$the 85th percentile for BMI and both groups fall within the reported range of 15-30% of children (Rosner et al, 1997). However BMI does not provide information on body composition and fat distribution.

The higher BMI found in the females with diabetes could not be explained by a significantly higher amount of fat or lean mass than the control group. However, there were indications that the higher BMI in females with diabetes could be mainly due to fat rather than lean mass. For example, while not statistically significant, %fat, and total grams of fat were higher in the girls with diabetes compared to controls, while the ratio of lean/fat mass was somewhat

higher in the control group.

While there was no significant difference between the control and diabetic females in mean percent body fat, and percent of body fat in the abdomen, group means masked the relationship between age and fat distribution. Using simple linear regression, central fat distribution increased across age groups in female children with type 1 diabetes but not in controls. Future studies need to examine fat distribution in pubertal and post-pubertal subjects and determine if insulin sensitivity and HbA1c are being compromised. It would also be interesting to investigate if and why pre-pubertal girls with diabetes have a lower percent fat in the abdomen than girls without diabetes, and why this trend changes with age/puberty.

Contrary to the results of the DCCT, subjects using 3+ insulin injections did not weight more, or have better glycemic control than those using 2 injections per day. In addition, females using 3+ insulin injections per day were significantly taller and had higher lean mass than females using 2 injections per day. However, while age was not significantly different, subjects using 3+ injections per day were slightly older and this may have affected the results. A larger study comparing subjects of the same age using intensive compared to conventional insulin management should be done.

It is also important to compare different types of insulin. In this study, females using Lispro had a lower percent body fat than those using Regular insulin. While this makes sense since Lispro is more physiological than Regular

insulin, again, larger studies are needed to confirm these results.

Regarding the difference in body composition between children with diabetes and those without, the results of this research suggest that overweight for height is only a problem for pubertal and post-pubertal females and future studies should focus on this group. Such a study could also confirm if this excess weight is mostly fat mass as was suggested by these results. However, when the sample sizes needed were calculated, the number of subjects required are very high (see Table 6.1 below), which may make future studies unfeasible unless multi-centre studies are conducted. It is also important to recognize that the standard error of the mean used to calculate these sample sizes was based on the smaller sample sizes and that as the sample size increases, the standard error of the mean will decrease. The other factor which makes these calculated sample sizes so high is the wide age range included in this study which also contributed to the large standard error used to calculate the sample sizes needed. Therefore, these sample sizes are likely larger than necessary.

Table 6.1 The sample sizes needed to detect significant differences in body composition

	Females (8-17 years)	Females (post-menarche)
Weight (kg)	327	271
Body fat (%)	327	154
Body fat Z-score	291	85
% of fat in abdomen	62899	99

Assuming alpha <0.05, power = 0.80

Appendix A

Dear participant and parent(s): January 30, 1999

Re: Study: Body Composition in Children

University of Manitoba and the Manitoba Clinic

Thank you for your past participation in this project. Instead of asking you to return to the clinic for a six month and one year visit, we would like you to complete the enclosed three day food record and physical activity questionnaire, and return them to us in the enclosed addressed and stamped envelope. We have also enclosed a 5$ gift certificate for your important contribution to this research.

We are asking parents to assist their children with completing and mailing the enclosed forms. If you have any questions or concerns, please do not hesitate to call one of the investigators listed below. To make the information useful to us, the accuracy of the recorded information we receive from you is essential. In order to complete the food record properly, please follow the instructions outlined below.

III. Choose 2 week days and 1 weekend day to keep records of everything you eat or drink on those days. Please try to choose non-consecutive days (e.g. Tuesday, Thursday and Saturday would be good choices). Do not use a day when you are feeling sick.

IV. For reasons of confidentiality, we have written your subject number on each form, therefore, please do not write your name on any of the forms.

V. Record all foods/liquids consumed each day starting when you wake-up, making sure to write down the time when any food /liquid is consumed. Start a new line for each food/liquid recorded. Try to list foods/liquids immediately after eating/drinking.

VI. Indicate the food/liquid type in detail, including brand names if appropriate and any toppings or spreads. If you are eating a mixed dish such as a stir fry, please write the recipe on the back of the food record.

VII. If you run out of space please write on the back or attach another piece of paper.

VIII. Indicate the amount of food/liquid consumed in one of the following ways: 1)using standard household measuring cups/spoons, 2)recording the weight of the food eaten in grams or ounces, or 3)by drawing a picture of the food eaten on the back of the food record, or on a separate piece of paper. This picture should also indicate how thick the food is (see the back of the example food record).

IX. **For children who have diabetes**, please indicate your blood sugar readings and insulin type and amount used in the column marked **Sugar/Insulin.**

X. If you take any vitamins/supplements/medications on a regular basis, please write them down at the bottom of the food record and indicate the amount taken.

XI. Please complete the physical activity questionnaire by following the directions printed on the questionnaire.

When you are finished the three day food record and the physical activity questionnaire, please return it to us by mail, in the addressed and stamped envelope. Thank you for your continued support. If you have any questions, please call one of the following investigators:

Laela Janzen (204) 452-9480
Kathy Green (204) 269-0932
Dr. Hope Weiler (204) 474-6798

EXAMPLE **Food Record - Day 1**

Subject:_____ **Date and day of week:** **Tuesday, Feb 1, 1999**

Time	Food	Brand	Amount	Sugar/ Insulin
0.3125	TOAST	COUNTRY HARVEST CRACKED OAT	2 SLICES	6.4/ 8R + 17NPH
	MARGARINE	REGULAR BECEL	2 TSP.	
	JAM	DIET RASPBERRY	1 TBSP.	
	PEANUT BUTTER	KRAFT LIGHT SMOOTH	2 TBSP.	
	BANANA		1 SMALL	
	MILK	SKIM	½ CUP	
0.41667	CHEESE	KRAFT 27% M.F. CHEDDAR	2 OZ.	
	CRACKERS	SODA	4	
0.5	SOUP	CAMPBELL'S CREAM OF MUSHROOM - HALF THE FAT, MADE WITH SKIM MILK	1 CUP	8.9/ None
	½ HAM SANDWICH			
	BREAD		1 SLICE	
	HAM	DELI SHAVED	1 OZ	
	MUSTARD	YELLOW	1 TSP	
	MAYONNAISE	KRAFT LIGHT MIRACLE WHIP	1 TSP	
	APPLE		1 MED.	
0.16667	BANANA BREAD WITH NUTS (NO ICING)	HOMEMADE	SEE PICTURE	
	MARGARINE	REGULAR BECEL	1 TSP	

Vitamins/Supplements/Medications: Flinstones chewable multivitamin/mineral - 250mg tablet daily

Food Record - Day 1

Subject:_____ **Date and day of week:**_____

Time	Food	Brand	Amount	Sugar/Insulin

Vitamins/Supplements/Medications:_____

Food Record - Day 2

Subject:_____ **Date and day of week:**_____

Time	Food	Brand	Amount	Sugar/Insulin

Vitamins/Supplements/Medications:_____

Food Record - Day 3

Subject:_____ **Date and day of week:**_____

Time	Food	Brand	Amount	Sugar/Insulin

Vitamins/Supplements/Medications:_____

Appendix B

Modifiable Activity Questionnaire for Adolescents

1. How many times in the past 14 days have you done at least 20 minutes of exercise hard enough to make you breathe heavily and make your heart beat fast? (Hard exercise includes, for example, playing basketball, jogging, or fast bicycling; include time in physical education class)

   ( ) None
   ( ) 1 to 2 days
   ( ) 3 to 5 days
   ( ) 6 to 8 days
   ( ) 9 or more days

2. How many times in the past 14 days have you done at least 20 minutes of light exercise that was not hard enough to make you breathe heavily and make your heart beat fast? (Light exercise includes playing basketball, walking or slow bicycling; include time in physical education class)

   ( ) None
   ( ) 1 to 2 days
   ( ) 3 to 5 days
   ( ) 6 to 8 days
   ( ) 9 or more days

3. During a normal week how many hours a day do you watch television and videos, or play computer or video games before or after school?

   ( ) None
   ( ) 1 hour or less
   ( ) 2 to 3 hours
   ( ) 4 to 5 hours
   ( ) 6 or more hours

4. During the past 12 months, how many team or individual sports or activities did you participate in on a competitive level, such as varsity or junior varsity sports, intramurals, or out-of-school programs.

   ( ) None
   ( ) 1 activity
   ( ) 2 activities
   ( ) 3 activities
   ( ) 4 or more activities

   What activities did you compete in?

   _____
   _____
   _____
   _____
   _____
   _____

From Aaron et al, 1993

PAST YEAR LEISURE-TIME PHYSICAL ACTIVITY

Check all activities that you did at least 10 times in the **PAST YEAR**. Do not include time spent in school physical education classes. Make sure you include all sport teams that you participated in during the Last year.

Aerobics	Gymnastics	Swimming (Laps)
Band/Drill Team	Hiking	Tennis
Baseball	Ice Skating	Volleyball
Basketball	Roller Skating	Water Skiing
Bicycling	Running for Exercise	Weight Training (Competitive)
Bowling	Skateboarding	Wrestling
Cheerleading	Snow Skiing	Others:
Dance Class	Soccer	_____
Football	Softball	_____
Garden/Yard Work	Street Hockey	_____

List each activity that you checked above in the "Activity" box below.
Check the months you did each activity and then estimate the amount of time spent in each activity.

Activity	Jan	Feb	Mar	Apr	May	Jun	Jly	Aug	Sep	Oct	Nov	Dec	Months per Year	Days Per Week	Minutes Per Day

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