Diet Quality in Children and Adolescents with Gastrointestinal and Liver Disease

by

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ABSTRACT

Assessment of overall diet quality (DQ), rather than single nutrient intake analysis, provides a broader view of an individual's nutrition status. Overall DQ is assessed using DQ tools that evaluate overall nutritional quality including Adequacy, Moderation and Variety. The association between overall DQ and nutritional status and health related outcomes were reported using different DQ tools in healthy children and adolescents. The objectives of this thesis were to assess and compare overall DQ between children and adolescents with chronic gastrointestinal (Celiac Disease [CD] following a gluten-free diet) or liver disease (Non-Alcoholic Fatty Liver Disease [NAFLD]) and (children post-liver transplantation [LTX]) to lean children or disease control populations and to assess the interrelationships between overall DQ and anthropometric, body composition, health related quality of life (HRQOL) and cardio-metabolic dysregulation in children and adolescents with gastrointestinal and liver disease. Three studies were conducted to assess DQ between children with CD (n=30) and gastrointestinal disease no-CD control (CON) (n=49) (**Chapter 3**), between children five years post-LTX (n=27) and healthy controls (n=28) (**Chapter 4**), and between children with NAFLD (n=18) and healthy control (n=19) (**Chapter 5**). Overall DQ was assessed in different methods: DQ tools [Healthy Eating Index-Canada (HEI-C), Dietary Guideline Index for Children and Adolescents (DGI-CA), Diet Quality Index-International (DQI-I)], glycemic index (GI) and glycemic load (GL). DQ tools were adapted based on the Canadian recommendations for nutrients and the Alberta Nutrition Guidelines for Children and Youth. Data regarding anthropometric, HRQOL (self-reported and parent proxy), body composition, and/or markers of cardio-metabolic dysregulation were measured. In **Chapter 3**, the majority of children with CD were adherent to the gluten-free diet. No significant difference was found in age or Kcal intake between children with CD and CON. Children with CD had higher GI

than CON but no significant difference in DQ scores and GL between children with CD and CON. Around 40-60% of children with CD and CON had moderate-to-poor DQ score. Children with CD reported higher HRQOL scores in physical, psychological, school and average scores than CON. The present of gastrointestinal symptomology, child age (>9 years) and gender (females) were negatively associated with HRQOL. **Chapter 4** illustrates that no significant difference was found in age, Kcal, GI, GL and DQ between children post-LTX and healthy controls. Around 50-80% of children post-LTX and healthy controls had moderate-to-poor DQ scores. **Chapter 5** shows no significant difference in age or Kcal intake between children with NAFLD. The majority of children with NAFLD and healthy controls 60-80% had poor DQ scores. Children with NAFLD had significantly lower total DQ, Adequacy and Moderation scores than healthy controls. Adequacy and Moderation scores are associated with obesity and cardio-metabolic dysregulation. This thesis demonstrates that children with CD, CON, and post-LTX have poor DQ. Children with NAFLD have reduced DQ compared to healthy controls. Poor DQ is indirectly associated with poor HRQOL in children with CD. In children with NAFLD, poor DQ is associated with obesity and cardio-metabolic dysregulation.

PREFACE

All of the work "**Diet Quality in Children and Adolescents with Gastrointestinal and Liver Disease**" presented in this dissertation was conducted at the University of Alberta. The standard operating procedures related to glycemic index, glycemic load, food groups, diet quality development and adaptation were done by Abeer S Alzaben, Diana Mager, Krista MacDonald and Kristin Radmanovich. All statistical analysis related to these variables were completed by Abeer S Alzaben.

The thesis chapter entitled "**Diet Quality of The Gluten-Free Diet and Quality of Life in Ethnically Diverse Populations of Children and Adolescents with Celiac Disease**" is a part of a national study conducted at Stollery Children's Hospital, Edmonton, Alberta; The Hospital for Sick Children, Toronto, Ontario; McMaster Children's Hospital, Hamilton, Ontario; and the Regina Qu'Appelle Region in Saskatoon, Saskatchewan. Protocol for study was approved by the Human Research Ethics Board (Pro00033867) at the University of Alberta and covered part of the research described in **Chapter 3**. Dr. Diana Mager designed and wrote the grant that funded the study (Canadian Celiac Association and Canadian Foundation for Dietetic Practice and Research). Recruitment and data collection for **Chapter 3** was completed by Abeer S Alzaben, Michelle Hoffmann MSc, Ingrid Rivera MSc and other members of the research team. Data entry and auditing for this thesis was completed by Kristin Radmanovich and Abeer S Alzaben.

The study presented in **Chapter 4** "**Diet Quality in Children Post Liver Transplantation**" was approved by the Human Research Ethics Board (Pro00026331) at the University of Alberta. Dr. Diana Mager, Dr.Jason Yap and Abeer S Alzaben designed and wrote the study protocol and this study was initiated prior to initiation of the doctoral program. Recruitment and data collection were completed by Abeer S Alzaben. Data entry and auditing was

completed by Abeer S Alzaben, Krista MacDonald and Kristin Radmanovich. **Chapter 4** was accepted *to Journal of Pediatric Transplantation in April 2017 entitled* "**Diet Quality Of Children Post Liver Transplantation Does Not Differ From Healthy Children**", Abeer S Alzaben MSc, Krista MacDonald BSc, Cheri Robert MSc CCRP, Andrea Haqq MD MSc, Susan M Gilmour MD MSc FRCP, Jason Yap MBChB FRACP, Diana R Mager RD MSc PhD (DOI: 2017;00:e12944. https://doi.org/10.1111/petr.12944). All authors reviewed the manuscript, provided editing and feedback and approval of its submission. **Chapter 4** represents a component of the accepted paper.

The research project entitled "**Altered Fat Metabolism as a Contributor of Hepatic Steatosis in Children and Adolescents with Non-Alcoholic Fatty Liver Disease**" was approved by the Human Research Ethics Board (Pro00000512) at the University of Alberta. **Chapter 5** was a secondary analysis for this study which focused on the dietary data of this study. Dr. Diana Mager designed the study and wrote the grant that funded the study (Canadian Liver Foundation, American Society for Parenteral and Enteral Nutrition, and Canadian Foundation for Dietetic Practice and Research). Recruitment, data collection, and all lab work was completed by Carla Rodriguez and Ingrid Rivera. Dietary analysis, GI and GL calculations, data entry and auditing were completed by Krista MacDonald, Abeer S Alzaben, Kristin Radmanovich and Ruby Bhutani. Data analysis of food groups, and Diet Quality analysis and auditing were completed by Abeer Alzaben and Kristin Radmanovich.

Abeer S Alzaben has received the *J. A. Campbell Young Investigator Award* from The Canadian Celiac Association-National Chapter May 2016 as a co-investigator of the "**Development of a Gluten Free Food Guide for Canadian Children and Youth**" (Pro00065489).

DEDICATION

To my Dad

Dadi, I would not have been able to achieve all my accomplishments without you. Thank you for all the time that you had spent to teach me science, important skills and how to be a good human. I have learned from you work ethic, respect others, and how to be a mature and responsible person. I am lucky to have a father like you.

To my Mom

I dedicate my thesis to my angel, my mom, who trusted my potential and loved me unconditionally. Your smiles and your hugs gave me strength on the hard days. Thank you for teaching me good morals in life. No school, college or university can teach the wisdom given to me by the best teacher in the world. Yes, you are right, there is always light at the end of tunnel. Your prayers and love were surrounding me and protecting me all the time. Love you.

To my Brother Mohammad Salman Alzaben

I dedicate this thesis to my brother and my partner. Your graduation was the happiest day in the last 8 years. I am and will always be proud of you. Thank you for trusting me, caring about my health, being there and trying to make me laugh on the hard days.

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LIST OF ABBREVIATION

γGT: γ-glutamyltransferase
ACARFS: Australian Child and Adolescent Recommended Food Score
AI: Adequate Intake
ALA: α Linolenic Acid
ALP: Alkaline Phosphatase
ALT: Alanine Aminotransferase
AMDR: Acceptable Macronutrient Distribution Range
ANGCY: Alberta Nutrition Guideline for Children and Youth
AST: Aspartate Aminotransferase
ATTG: Tissue Transglutaminase Antibodies
BA: Biliary Atresia
BMI: Body Mass Index
BMI-z: BMI for-age z- score
BMR: Basal Metabolic Rate
BP: Blood pressure
CAT: Category
CCA: Canadian Celiac Association
CD: Celiac Disease
CDC: Centers for Disease Control
CNF: Canadian Nutrient File
CONT: Continuous
DBP: Diastolic blood pressure
CDDUX: Celiac Disease DUX
CRP: C-reactive Protein
DDI: Dietary Diversity Index
DGA-CA: Dietary Guidelines Index for Children and Adolescents
DHA: Docosahexaenoic Acid
DQ: Diet Quality
DQI: Diet Quality Index
DQI-I: Diet Quality Index-International
DQS: Diet Quality Score
DRI: Dietary Reference Intake
DFE: Dietary Folate Equivalent
EI: Energy Intake
ELISA: Enzyme Linked Immunosorbent Assay
E-KINDEX: Electronic Kids Dietary Index
EPA: Eicosapentaenoic Acid
ESLD: End Stage Liver Disease
F: Fruit
F/V: Fruits and Vegetables
FA: Fatty Acids
FAO: Food and Agriculture Organization of the United Nations
FFQ: Food Frequency Questionnaire
GI: Glycemic Index

GF: Gluten Free
GFD: Gluten Free Diet
GL: Glycemic Load
GS: Gastrointestinal Symptomology
GSS: Gastrointestinal Symptomology Score
HDL: High Density Lipoprotein
HEI-C: Healthy Eating Index- Canada
HFFQ: Harvard Youth/Adolescent Food Frequency Questionnaire
HOMA-IR: Homeostasis Model of Assessment of Insulin Resistance
HRQOL: Health Related Quality of Life
Ht-z: Height-for-age z-score
ICC: Intra Class Correlation
IL-6: Interleukin-6
IL-10: Interleukin-10
INR: International Normalized Ratio
IQ: Inter-quartile Range
ISAK: International Society for the Advancement of Kinanthropometry
KINDL: Celiac Disease quality of life scale
LA: Linoleic acid
LDL: Low Density Lipoprotein
LTX: Liver Transplant
Med DQI-I: Mediterranean Diet Quality Index-International
MUFA: Monounsaturated Fatty Acid
NAFLD: Non-Alcoholic Fatty Liver Disease
NASH: Nonalcoholic Steatohepatitis
n: Sample size
NS: Not significant
OMD: Optimized Mixed Diet
PedsQL: Pediatric Quality of Life
PUFA: Polyunsaturated Fatty Acid
RAE: Retinol Activity Equivalents
RDA: Recommended Daily Allowance
RTX: Renal Transplant
SFA: Saturated Fatty Acid
SBP: Systolic blood pressure
SD: Standard Deviation
SPLIT: Studies of Pediatric Liver Transplantation
SS: Simple Steatosis
TG: Triglyceride
TNF-α: Tumor Necrosis Factor–α
USDA: U.S. Department of Agriculture
V: Vegetables
WHO: World Health Organization
WT-z: Weight-for-age z-score
YHEI: Youth Healthy Eating Index

Publications not related to the PhD Thesis:

- Hoffmann MR, Senior PA, Jackson ST, Ferland G, Presse N, Kailash J, Li P, Alzaben AS, Mager DR "**Vitamin D and vitamin K1 intake improves vitamin D status and bone mineral density in an ambulatory adult population with diabetes and chronic kidney disease**" Can J Diet Prac & Res. 2017, 78(1): 11-19, 10.3148/cjdpr-2016-023. Role: assisted with data collection and the development of standard operating procedures related to assessment of vitamin K using the USDA database, and mentorship of summer student who performed dietary intake analysis.
- Grace Hubert, Theresa Tam Chung, Connie Prosser, Dale Lien, Justin Weinfauf, Neil Brown, Marianne Schafenaker, Kathy Jackson, Joan Tobak, Josette Salgado, Abeer Salman Alzaben, Diana R Mager "**Bone mineral density and fat soluble vitamin status in adults with Cystic Fibrosis undergoing lung transplantation: a pilot study**" Can J Diet Prac Res. 2016, 77(4): 199-202, 10.3148/cjdpr-2016-014. Role: performed statistical analysis with DRM.
- Diana Mager, Abeer Salman Al-zaben, Cheri Robert, Susan Gilmour, Jason Yap. "**Bone mineral density and growth in children having undergone liver transplantation with corticosteroid-free immunosuppressive protocol**" JPEN J Parenter Enteral Nutr. 2015,41 (4): 632-640. pii: 0148607115609524. (related to MSc thesis).
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- AS Alzaben, JM Turner, L Shirton, Samuels T, R Persad, DR Mager "**Assessing Nutritional Quality in The Gluten-free Diet in Children and Adolescents with Celiac Disease**". Canadian Journal of Dietetic Practice and Research. Jun;76 (2):56-63. DOI: 10.3148/cjdpr-2014-040. (pilot study with data collected during MSc program with other members of the research team).
- S Rajani, A Alzaben, L Shirton, R Persad, HQ Huynh, DR Mager, JM Turner. "**Exploring anthropometric and laboratory differences in children of varying ethnicities with celiac disease**". Canadian Journal of Gastroenterology & Hepatology. 2014 Jul-Aug;28 (7):351-4. Role: Performed some statistical analysis.

Publications in progress not related to the PhD Thesis

"**Differences in Long Chain Poly-Unsaturated Fatty Acid Content In Parenteral Lipid Emulsions Influence Hepatic Fatty Acid and Phytosterol Composition in A Neonatal Piglet Model of Intestinal Failure"** Isaac DM, Alzaben AS, Yap J, Mazurak VC, Wizzard P, Josephson J, Nation PN, Sergi C, Wales P, Turner JM, Mager DR. The Study was approved by the Faculty of Agriculture, Life and Environmental Sciences Animal Policy and Welfare Committee (ISO110834) at University of Alberta. The lab work related to hepatic lipidomics, statistical analysis, and writing a draft of the manuscript were completed by Abeer Salman Alzaben. Dr. Justine Turner and Dr. Diana Mager designed and wrote the grant that funded the study.

Abstract Submitted (and Published) Related to PhD Thesis

- "**Diet Quality and Quality of Life in Children and Adolescents with Celiac Disease**" Abeer Salman Alzaben MSc PhD (candidate), Margaret A. Marcon MD, Herbert Brill MD, Heather Mileski RD, Rabin Persad MD FRCPC, Justine Turner MD PhD, Diana Mager PhD RD. The 5th World Congress of Pediatric Gastroenterology, Hepatology and Nutrition (WCPGHAN). October 2016. Montreal, QC, Canada. Oral presentation; presenter: DRM.
- "**The Cost of The Gluten Free Diet: Household Food Expenditures in Families with a Child or Adolescent with Celiac Disease"** Abeer Salman Alzaben, Justine Turner, Margaret A. Marcon, Sven Anders, Diana Mager. The Canadian Paediatric Society (CPS) 93rd Annual Conference. June 2016. Prince Edward Island, Canada. Poster; presenter: DRM
- "**Ethnicity Influences Quality of Life in Youth with Celiac Disease on The Gluten Free Diet**" Abeer Alzaben, Leanne Shirton, Rabin Persad, Justine Turner, Diana Mager. "WCHRI Research Day", October 2015, Edmonton, Alberta, Canada. Poster; presenter: AA.
- "**Adherence to Micronutrient Supplementation in Children with Celiac Disease**" Mager DR, Alzaben AS, Hoffmann MR, Enns, S, Turner JT. The 16th International Celiac Disease Symposium (ICDS2015). June 2015. Prague. Czech Republic. Poster; presenter: DRM.
- "**Parental Perceptions and Adherence to Micronutrient Supplementation in Children and Adolescents with Celiac Disease"** Alzaben AS, Hoffmann MR, Alsaif M, Nikopoulus H, Turner JT, Mager DR. The Canadian Foundation for Dietetic Research. Dietitians of Canada Conference. June 2015. Quebec City, Quebec, Canada. Poster; presenter: DRM.
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- "**Interrelationships between High Fructose Corn Syrup Intake and Markers of Liver Dysfunction, Insulin Resistance and Inflammation in Children and Adolescents with Non-Alcoholic Fatty Liver Disease"** Abeer Alzaben, Irene Kim, Ingrid Iñiguez, Vera Mazurak, Susan Gilmour, Jason Yap, Diana Mager. WCHRI Research Day, November 2013, Edmonton, Alberta, Canada. Poster; presenter: AA.

Other Abstracts

- **"Micronutrient Monitoring and Bone Health in Adults with Cystic Fibrosis Undergoing Lung Transplant"** G.L. Hubert, T. Tam Chung, C. Prosser, D. Lien, J. Weinkauf, N.Brown, M. Goodvin, K. Jackson, J. Tabak, J. Salgado, A.S. Alzaben, D.R. Mager. The Journal of Heart and Lung Transplantation. April 2017; 36(4) Supplement, Page S177. Presenter: GLH.

Chapter 1 Literature Review

1.1 Introduction

In recent decades, the definition of diet quality (DQ) has shifted from a "single nutrient" approach to an "overall DQ" approach (1). The focus on a single nutrient, or food, as the cause of disease does not take into account the combination of foods and nutrients that humans consume. Therefore, research has shifted towards studying the effects of "whole foods" and dietary patterns (1-5). To assess dietary pattern, the "overall DQ" approach is a comprehensive method for assessing the role of diet in disease promotion and prevention (1-5).

DQ tools are used to measure overall DQ and compare an individual's dietary intake to age- and gender-specific dietary guidelines and Dietary Reference Intakes (DRI) (3-5). DQ tools are used to assess intake of essential nutrients, foods, and food groups by comparing the consumption of food and nutrient to the recommendations, and link to nutritional adequacy and risk of chronic diseases (3-10). In adults, DQ tools are linked to disease-specific morbidity (e.g. cardiovascular disease) and mortality from specific diseases (e.g. cancer) (3-5). In children, DQ tools are mainly used to evaluate either overall DQ and adherence to dietary recommendations, or to examine the associations between DQ and nutritional status (e.g. malnutrition, growth), specifically in healthy children (9). Determining the associations between DQ and health-related outcomes, such as obesity, using DQ tools has not been comprehensively applied in children with chronic gastrointestinal diseases (9).

1.2 Diet Quality Tools

DQ tools are used to score overall DQ and to compare an individual's dietary intake to age- and gender-matched dietary recommendations (3-5, 9, 10). DQ tools were mainly developed to assess an individual's overall DQ and evaluate optimal balanced diet from macro and

micronutrient intake (3-5, 9-11). Due to the increased risk of obesity and chronic disease, DQ tools (such as Healthy Eating Index (HEI) and Diet Quality Index (DQI)) have been revised based on new dietary recommendations (5). For example, the DQI was developed in 1994 based on the dietary recommendations of the National Research Council Food and Nutrition Board in 1989 and focused on only 8 components (total fat, saturated fat, cholesterol, fruit and vegetables, complex carbohydrates, protein, sodium and calcium) (12, 13). Later, a revised DQI was released based on new dietary recommendations, including the Food Guide Pyramid, the 1995, Dietary Guidelines for Americans, and the DRI (12, 13). The revised DQI included 10 components, total fat, saturated fat, cholesterol, fruit, vegetables, grains, calcium, iron, dietary diversity and dietary moderation (consumption of added sugar, sodium, and alcohol) (12, 13). Moreover, some of the DQ tools were modified for nutrients and food intakes for specific diets; for example, the DQI have been validated to measure the Mediterranean-Diet (Mediterranean-Diet Quality Index) (5).

1.2.1 The Components of Diet Quality Tools

Table 1-1 and **Figure 1-1** describe the components and the scores of some existing DQ tools available to use in children and adolescents. The main components of DQ tools are dietary diversity, moderation and nutritional adequacy (3-5, 9-11). The measured components of DQ tools are diverse between tools, which may lead to different total scores, hence, different interpretation and evaluation of an individual's diet. Further research is needed to address this concern.

Table 1-1: Description of Some Existing Diet Quality Tools Used in Children and Adolescents

Index Author (Year)	Variables and components and scoring system	Age (Years)	Dietary intake	Purpose/Comment
ACARFS Marshall et al (2012) (14)	Food, **Score:** 0–73 **Components:** 8; food groups (grains, F, V, dairy foods, meat protein foods, non- meat protein foods), water, extra food	6-14	FFQ	- Reflects adherence to the 2003 Australian Dietary Guidelines for Children and Adolescents - Adjusted for energy intake
DQI Li et al (2012) (15)	Food and Nutrients, **Score:** 20–150 **Components:** 12; food groups (grains, vegetables, fruit, dairy products, and meat), extra foods, vitamin C, vitamin A, fibre, calcium, protein, % fat, % SFA, FA ratio (omega-6:omega-3)	1-14	FFQ	- Reflects adherence to the Australian Guide to Healthy Eating and Nutrient Reference Values
DQI-I Kim et al (2003) (16)	Food and Nutrients, **Score:** 0–100 **Components:** 4 major components with sub-components **Variety:** Overall food groups and within-group for protein source **Adequacy:** F, V, grains, fibre, calcium, vitamin C, protein, iron **Moderation:** % fat, % SFA, cholesterol, sodium, empty calorie foods **Overall balance:** Macronutrient ratio and FA ratio (PUFA:MUFA:SFA)	Used in children 6-18	24-hour recall	- Reflects worldwide dietary guideline (WHO and US), food pyramid guide(17-19). - Designed to worldwide healthy adults and used in pediatrics (6-18 years) (20-28). - Adjusted for energy intake (23, 27, 29)
Med DQI-I Mariscal-Arcas et al (2007) (20)	Food and Nutrients, **Score:** 0–100 **Components:** 4 major components each with sub-components **Variety:** Overall food group variety and within-group variety for protein source **Adequacy:** F, V, total grain, fibre, calcium, vitamin C, protein, iron **Moderation:** % fat, % SFA, cholesterol, sodium, empty calorie foods **Overall balance:** Macronutrient ratio and FA ratio (PUFA:MUFA:SFA)	6-18	24-hour recall	- Reflects worldwide (WHO, USA and China) adherence to dietary food and nutrient recommendations with specific Mediterranean adaptations
DQS Kohlboeck et al (2012) (30)	Food, **Score:** 0-11 **Components:** 11; beverages, F, V, bread/cereals, potatoes/pasta/rice, milk and milk products, meat/ sausages, eggs, fish, fat/ *other foods* groups	10-13	FFQ	- Reflects adherence to the Optimized Mixed Diet (OMD) for children and adolescents in European countries (Greece Germany, Belgium, France, Hungary, Italy, Sweden, Austria, and Spain). - Adjusted for energy intake

DGI-CA Golley et al (2011) (31)	Food, **Score:** 0–100 **Components:** 11; food groups (grain, F, V, meat, dairy), wholegrain bread, reduced-fat dairy foods, extra foods, food choice, beverage, and diet variety	4-16	24-hour recall	- Reflects adherence to the 2003 Australian Dietary Guidelines for Children and Adolescents - Adjusted for energy intake
DDI Sabbe et al (2008) (32)	Food, **Score:** 0-5 **Components:** 5; food groups (grain, F, V, dairy, meat)	10	FFQ	- Reflects adherence to the 2000 American Food Guide Pyramid
E-KINDEX Lazarou et al (2009) (33, 34)	Food Behavior and Dietary Habits, **Score:** 1–87 **Components:** **Foods E-KINDEX**: 13 items; 11 food groups (bread, cereal and other grains, F and fruits juices, V, legumes, milk, fish and sea food, meat, salted and smoked meat food, sweets and junk food, soft drinks) and 2 aspects of cooking techniques (fried food and grilled food) **Behavior E-KINDEX**: 8 items dietary beliefs and behaviors **Dietary Habits E-KINDEX**: 9 items to evaluate dietary practices	9-13	Semi-quantitative FFQ	- Reflects dietary components, beliefs, habits and practices on the development of obesity in children
HEI-C Woodruff et al (2010**)** (35)	Food and Nutrients, **Score:**0-100 **Components:** 9; food groups (grains, F/V, meat, dairy), *other foods*, % fat, % SFA, cholesterol and variety	≥3	24-hour recall	- Reflects adherence to the 2007 Eating Well with Canada's Food Guide - Adjusted for energy intake (36)
YHEI Feskanich et al (2004) (37)	Food and Behavior, **Score:**0-100 **Components:** 13; whole grains, F, V, ratio from meat and other protein sources, dairy, snack foods, soda and drinks, multivitamin use, margarine and butter, fried foods outside home, visible animal fat, eat breakfast, dinner with family	9-14	FFQ	- Reflects adherence to the Dietary Guidelines

Abbreviations: ACARFS, Australian Child and Adolescent Recommended Food Score; ALA, α Linolenic Acid; DDI, Dietary Diversity Index; DGI-CA, Dietary Guideline Index for Children and Adolescents; DHA, Docosahexaenoic Acid; DQI, Diet Quality Index; DQI-I, Diet Quality Index-International; DQS, Diet Quality Score; E-KINDEX, Electronic Kids Dietary Index; EPA, Eicosapentaenoic Acid; F, Fruit; FA, Fatty Acids; FFQ, Food frequency questionnaire; HEI-C, Canadian Healthy Eating Index; LA, Linoleic Acid; Med DQI-I, Mediterranean Dietary Quality Index-International; MUFA, Monounsaturated Fatty Acid; OMD, Optimized Mixed Diet; PUFA, Polyunsaturated Fatty Acid; SFA, Saturated Fatty Acid; V, Vegetables; WHO, World Health Organization; YHEI, Youth Healthy Eating Index.

Additional References: (3-10).

1.2.1.1 Dietary Diversity or Variety

Dietary diversity (or Variety) is defined as the number of different foods (or food groups) consumed over a period (1-15 days) and can be measured in different ways (38). Variety can be assessed by counting the intake of food items within major food groups (e.g. the number of fruits or vegetables) or can be more specific, such as by counting the food items within minor food groups (e.g. the food source of protein: legumes vs meat vs fish) (38). The association between dietary diversity and DQ, nutritional status, and growth has been reported (38). Diet diversity is a component of most DQ tools (4). However, some DQ tools [e.g. DQI-International (DQI-I)] measure diet diversity as a specific component (overall food groups Variety and within-group Variety for protein source) (4).

1.2.1.2 Nutritional Adequacy and Moderation

Nutritional adequacy is assessed using DQ tools by comparing food group, macronutrient and micronutrient consumption to the selected age- and gender-specific recommendation (e.g. Canadian Food Guide and DRI) (3-5, 9). Several DQ tools assessed the consumption of food groups only, nutrients only, food groups and macronutrients (such as HEI), or food groups and macro and micronutrients (such as DQI-I) (4, 9). The HEI-Canada (HEI-C) and Dietary Guideline Index for Children and Adolescents (DGI-CA) measure fat and saturated fat (as percent of kcal) and cholesterol. The DQI-I evaluates the intake of macronutrients (fat, saturated fat, cholesterol, and protein) and micronutrients (iron, sodium, calcium, vitamin C) (9). The DQI-I includes numerous micronutrients, which can have different availabilities and recommendations in different countries.

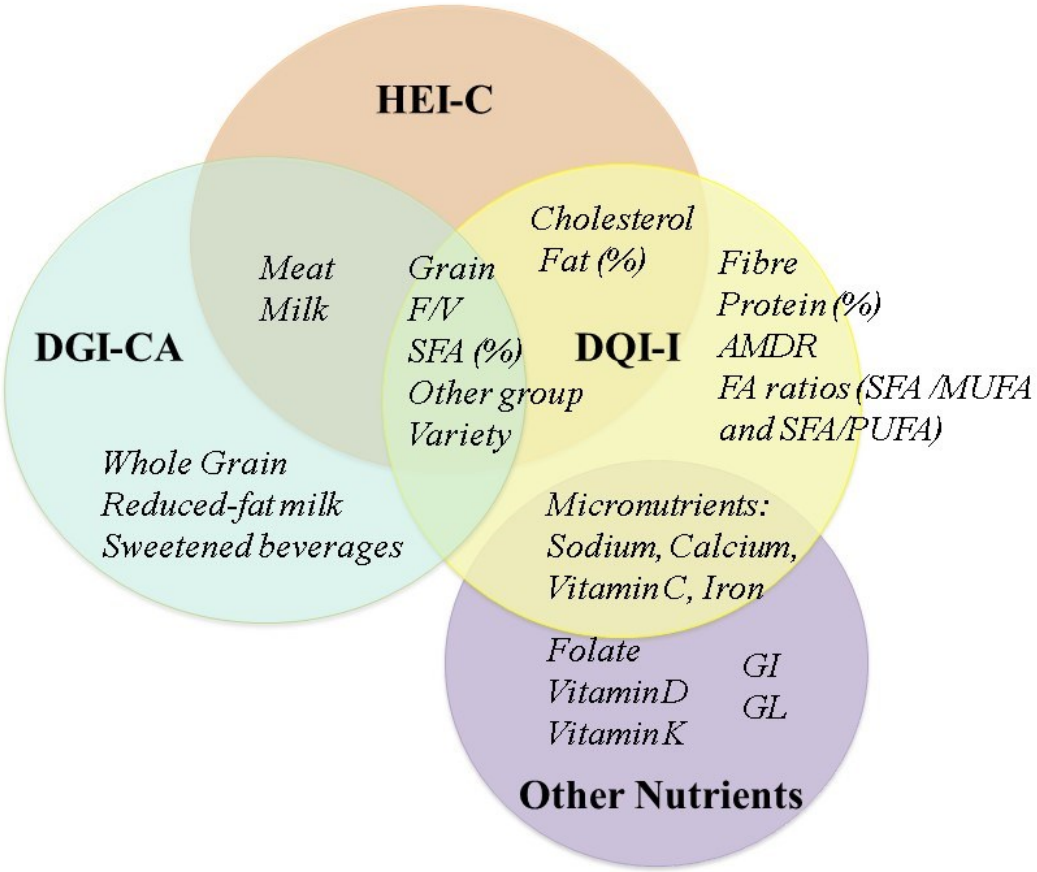


Figure 1–1: The Components of Diet Quality Tools That Will Be Measured in the Present Thesis. This figure shows the foods and nutrients component of diet quality tools [Healthy Eating Index-Canada (HEI-C), Dietary Guideline Index for Children and Adolescents (DGI-CA) and Dietary Quality Index-International (DQI-I)]. The diet quality tools lack other important nutrients such as folate, Glycemic Index (GI) and Glycemic Load (GL).
Abbreviations: AMDR, Acceptable Macronutrient Distribution Range; F/V, Fruit and Vegetables; MUFA, Monounsaturated Fatty Acids; PUFA, Polyunsaturated Fatty Acids; SFA, Saturated Fatty Acids.

Micronutrient components of DQ tools are included based on the dietary pattern of varying populations. DQ tools were used to assess several micronutrients that are at risk of over- or under-consumption in healthy populations such as sodium, iron and calcium. In Australia, sodium was included in the DGI due to the high consumption of sodium as compared to the recommendations, which can lead to several chronic diseases (2). However, other essential micronutrients were not included as components of the DQ tools, because they are not nutrients of concern in the general

population. However, there may be micronutrient at risk for several therapeutic diets [e.g. folate in the gluten-free diet (GFD)] for individuals with chronic diseases. Individuals following therapeutic diets are at risk of under or over-consumption of some essential nutrients, which may lead to reduced DQ scores. Under-reporting and/or consumption of some nutrients in therapeutic diets may occur as a result of the altered nutritional quality of therapeutic diets, lack of fortification and enrichment policies, or due to difficulties in assessing nutrient intake due to a lack of information on specialized food product labels. Therefore, DQ tools should be modified by: 1) including nutrients or foods of concern in therapeutic diets and 2) adjusting the cut-off values to determine adequacy and based on the scoring system. For example, individuals following a ketogenic diet have high fat intake (>40% of Kcal) and the cut-off values of fat in DQ tools need to be adjusted for this population. In addition, this issue presents challenges for the use of food based DQ tools in children with food allergies. Modifying of DQ tools to evaluate overall DQ of individuals following a lifelong therapeutic diet has not previously examined.

1.2.1.3 *Other Foods* Category in Nutrition Guidelines

Due to an increase in the risk of obesity, DQ tools include components related intake of *other foods*. *Other foods* is defined as any edible products not classified into the main food groups (i.e. fruit and vegetables, grain products, milk and alternatives, meat and alternatives), based on *Eating Well with Canada Food Guide* (39). For example, foods contain added sugar (candies), added fat (butter), salty snacks (potato chips), and alcoholic, and non-alcoholic beverages (soft drinks) (39). Several DQ tools contain *other foods* as a DQ component; however, scoring methodology of *other foods* varies greatly between DQ tools. HEI-C scores the intake of *other foods* based on the number of servings intake related to kcal intake (35). DGI-CA measures the intake of the *other foods* as the consumption of sweetened beverages and DQI-I scores the intake

of the *other foods* as percent of kcal (16, 31).

1.2.2 Factors Influencing the Assessment of Diet Quality among Diet Quality Tools

Although vast differences exist between DQ tools (**Table 1-1),** no studies have evaluated the differences in DQ scores between DQ tools in children with chronic disease and/or consuming therapeutic diets (3-5, 9, 10).

1.2.2.1 Age

One major variation between DQ tools is the age of the studied population (infants, children, adults) (5, 9, 10). DQ tools were validated for specific age groups. For instance, the Child Feeding Index was validated in infants and children (between 6-36 month) and includes questions about feeding frequency, bottle feeding, breast feeding and other questions specifically related to infants and young children (40).

1.2.2.2 Country Specific

DQ tools were established to evaluate overall DQ in developed countries (e.g. the HEI) or in developing countries (e.g. diet variety score). Components of DQ tools were established based on the diversity in dietary pattern between developed and developing countries (10). One obvious example is the increased consumption of added sugar and fat in developed countries. Nevertheless, added sugar may be a nutrient of concern in some developing countries as it may displace more nutritiously dense foods, which are more expensive and less available to the general population (9, 10). In developing countries, food variety and dietary diversity are the main components of DQ tools used to assess the nutritional adequacy of macro and micronutrients (9).

1.2.2.3 Dietary Guidelines and Dietary Recommendations

The dietary guidelines used to develop DQ tools are “country specific” guidelines typically

based on nutrient databases reflective of the nutrient content of foods available in the individual country (5, 9). HEI is based on U.S. Department of Agriculture (USDA) recommendations, Diet Quality Score is based on the Optimized Mixed Diet for Children and Adolescents in European countries, and the DGI-CA is based on the Australian Dietary Guidelines (4, 9). Furthermore, dietary guidelines for countries are specified to ensure nutritional adequacy of essential nutrients to prevent chronic diseases, such as obesity (41). When using a specific DQ tool, the nutritional recommendation should be adapted based on the nutritional recommendation of the studied populations such as HEI. For example, the HEI-C was adapted to address the nutritional recommendations for Canadians (35).

In addition, the cut-off values of the DQ components are based on the dietary recommendations of the country, as reported by Kim et al (2003) for developing DQI-I. DQI-I was developed to compare DQ between China and the US. The cut-off values were based on the DRI in the US and the Recommended Nutrient Intake (RNI) or Adequate Intakes (AI) in China. Therefore, adjusting the cut-off values based on the dietary recommendations of the country is necessary for adapting DQ tools.

1.2.2.4 Scoring System and Cut-off Values of Diet Quality Tools

The rationale of scoring system approach and cut-off values establishment to evaluate DQ has not been reported in the literature and it requires extensive study. The scoring values of the components of DQ tools are divided into four main types: dichotomous, scaled-based, category-based, or a combination. HEI-C is both scaled-based in food-based components and dichotomous in variety, compared to the Healthy Dietary Indicator, which is dichotomous-based methodology (35). A dichotomous scoring system lacks the ability to discriminate differences in DQ due to differences in adherence between individuals. This means that the individual either meets or does

not meet the cut-off values for the recommended level of intake within each different category of the tool. The drawback of this method is that it may not be possible to distinguish the percentage of individuals who meet, or do not meet, the recommended level of intake for that particular component in the DQ tool, and therefore may be assigned a lower DQ value (4).

Two methods have been reported to determine the cut-off value for particular components of DQ tools. The first method is to choose the median as a cut-off value, which results in 50% of the sample having a positive score and 50% having a negative score (4). The disadvantage of this method is that it is unable to distinguish precisely between subjects. Therefore, it may not be valid for populations with chronic diseases because the median of DQ in populations with chronic disease may be lower than in healthy populations (4). The second method is to use the recommended reference intakes. This method enables 1) the cut-off value of DQ tools to be adapted based on age-and gender-specific recommendations; 2) different ways to assess recommended intakes of nutrients globally for developed vs developing countries or for healthy populations vs populations with chronic diseases; and 3) discriminate an individual's diet by assessing how much an individual has met the dietary recommendation for a specific component. The main advantage of this method is the ability to adapt the DQ tools for different recommendations based on the country or health condition.

1.2.2.5 Relative Contribution of Individual Component Scores within a Diet Quality Score to the Total Diet Quality Score in Diet Quality tools

In most DQ tools, the components have the same score, which contributes equally to the total DQ score. Other DQ tools such as HEI-C, DGI-CA, and DQI-I have assigned different scores to different DQ components. The rationale for assigning different scores to various DQ components has not been reported (4). One potential solution for component scoring is to assign scores using weighting factors based on the impact of the DQ component on health. Two

limitations of this approach are the difficulty determining the contribution of different dietary components to health outcomes, and the applicability to varying ages or diseases. Future research is needed to determine the contribution of DQ components to the total score of DQ tools using weighting factors in children with chronic disease (42).

1.2.2.6 The Method of Dietary Intake Assessment

The dietary intake assessment method is the first method that was used to evaluate DQ. Three methods have been used to estimate actual/usual dietary intake; 24-hour recall, or food records, or validated food frequency questionnaires (FFQ) (4, 5, 9). In general, the literature has reported several errors related to reporting of dietary intake in children and adolescents including portion size estimation and food recall bias. These sources of error can potentially lead to: 1) under-reporting (missing foods), 2) over-reporting (overestimation of portion size), and 3) incorrect identification of foods (43). Other specific limitations have been reported when using FFQ to assess dietary intake such as random error, overestimation, and fewer details about food preparation (44-46). Several DQ tools have been validated using a specific FFQ. The number of food items included in a FFQ can vary widely between studies (47). The food items present in FFQs are included to capture only the nutrients and the foods that are assessed by the DQ tool. Therefore, using a FFQ to measure DQ using several DQ tools may not practical. In addition, misreporting of energy intake has been observed in children and adults using FFQ and/or 24-hour recalls (48, 49). A multi-pass approach for the 24-hour recall method was developed to reduce under-reporting of energy intake, by providing respondents with multiple prompts to recall additional food intake (49). Under-reporting of energy intake was demonstrated in 28% and 15% of healthy adults using FFQ and a multi-pass 24-hour recall, respectively (48). To minimize under-reporting dietary intake, studies have found multiple days 24-hour recalls may be helpful to

estimate actual food intake (50). There is some evidence reported that energy, macro and micronutrient intake is different between weekend vs weekday day which may lead to some variation of DQ between weekend vs weekday day (51, 52).

Although the majority of DQ tools use one or multiple 24-hour recall days to assess dietary intake, limited studies have compared the DQ scores using two different dietary intake assessment methods (53). A recent study compared nutrient intake and HEI-2005 scores of self-administrated (online) two-day 24-hour recalls to 4-day food records in 93 adults (53). Macro and micronutrients intake and HEI-2005 scores were not significantly different between self-administrated 24-hour recalls and 4-day food records. Highly significant Pearson correlation and moderate agreement (using weighted *k* coefficients values) was observed in nutrient intake and HEI-2005 between self-administrated 24-hour recalls and 4-day food records (53). Further studies are required to compare DQ score between different dietary intake methods: multi-pass 24-hour recalls, food records and FFQs.

1.2.2.7 Components of Diet Quality Tools

Based on the purpose of the specific DQ tool, DQ tools have been established using three major approaches: nutrient-based, food group-based, or based on a combination of nutrients and food groups (3-5, 9). Other tools include additional nutritional components related to eating beliefs and behaviors such as the Electronic Kids Dietary Index (33). The Electronic Kids Dietary Index has 3 main components: food groups, eating beliefs and behaviors (e.g. feelings during eating), and dietary practices (meal patterns and behaviors) (33). Including eating behaviors and dietary practices as components of DQ may be important component for specific populations (such as obese children), but not as necessary in other populations (such as inborn metabolic errors). Improving eating behaviors and dietary patterns can be the treatment used to improve DQ in

children with obesity, but would not be useful for improving DQ in children consuming therapeutic diets.

1.2.2.8 Food Groups and The Definition of Mixed Dishes

Food-based DQ tools have been developed based on food consumed that are part of a food guide (4). A Food Guide is a reference of food groups, food components, and nutritional recommendations. The main food guide in Canada is called "Canada's Food Guide", and in the United States it was called the "Food Pyramid". One major difference between food guides is the classification of food groups and, potentially, food portion sizes. The Canadian Food Guide includes fruits and vegetables as one food group, whereas these are considered separate food groups in the Food Pyramid (54, 55). This may affect the components and the scoring of Canadian vs US DQ tools. For example, fruits and vegetables are separate components in the original HEI. HEI was adapted based on The Canadian Food Guide and resulted in fruits and vegetables being grouped together as one component (54).

Foods and food components can be handled differently between DQ tools. Two different examples are explored. First, beans are treated differently between some DQ tools and food guides (16, 39). Beans have been categorized as a separate food group, and are clustered with "meat" within one food group, or grouped with "dairy" as part of one food group in another DQ tool (16, 39). Second, categorizing mixed foods into food groups is challenging due to the difficulty for estimating ingredient portion size. Children consume food as mixed dishes rather than as separate, single food items (56). One method to address this is to establish a standard protocol for estimating the serving size of each food group to prevent over or underestimation of food group intake. Another method for categorizing mixed dishes was reported by Golley et al (2011) to establish DGI-CA (31). Golley et al (2011) weighed mixed foods to account for the primary food component

toward the servings of the main food group such as >70% of the weight of macaroni and cheese being counted toward servings of bread and cereal (31). The Golley approach can lead to underestimation especially in the energy-dense food *other foods*. For example, French fries are a mixed dish that combines both vegetables and fat as *other foods.* On the other hand, using the Golley approach may lead to an underestimation of vegetable intake; ≈50% of total vegetable consumption in children and adolescents is accounted for by mixed dishes (56). A recent study found that chilli consumption accounts for 9-16% of vegetable intake in children. Golley approach may underestimate up to 16% of vegetable intake (56). Furthermore, underestimating vegetable intake may account for up to 20% of DQ score discrepancies.

1.2.2.9 Confounding by Energy Intake

Prior to scoring an individual's DQ, dietary intake is analyzed to assess energy, and macro- and micronutrient intake. Misreporting dietary intake is linked with DQ scores and leads to over or underestimation of the servings of food groups, macro-and micronutrient intake and energy intake (3, 4). Under-reporting energy intake is frequently observed in children and adolescents for studies that use food records rather than 24-hour food recall, to assess dietary intake (57). To explore misreporting energy intake, studies report methods to estimate the degree that energy intake is misreported, based on the proportion between reported energy intake and the estimated energy expenditure (57, 58).

Misreporting of energy intake may influence assessment of DQ in children and adolescents by 20-50% (57, 59). Misreporting energy intake may have a greater influence on nutrient components than food components. The influence of misreporting energy intake can be high, especially for nutrients-based DQ compared to food-based DQ. For example, the consumption of wholegrain

bread in DGI-CA may not be affected by misreporting energy intake. To our knowledge, only one study in adults adjusted the Mediterranean Diet Score for under-reporting energy intake (60). After adjusting for under-reporting energy intake, the study reported a negative association between obesity and Mediterranean Diet Score (60). However, several studies that assessed dietary intake and DQ in children and adolescents omitted misreporting from the analysis. The definition of misreported intake varies between DQ studies in children. Golley et al (2011) defined misreporting using the Goldberg method (energy intake/basal metabolic rate <0.87) (31, 61). Woodruff and Hanning (2010) and Chan et al (2013) explored misreported intake in children (9-17 years old) and treated energy intake for children <200-700 kcal or >4700-6000 kcal as outliers (35, 62). It has been reported that this method may lead to bias because this method may not capture over or underweight children with low dietary intakes, respectively (63). Another method to handle misreporting when assessing the intake of several nutrients is to use energy adjustment methods (nutrient density) (64). A study found that the effect of energy adjustment varied with some micronutrients (64).

1.3 Diet Quality Tools and Parameters of Nutritional Status and Quality of Life and Health Related Outcomes in Children and Adolescents

1.3.1 Healthy Eating Index–Canada (HEI-C)

The HEI was developed by Kennedy in 1995 to measure compliance to the 1990 dietary guidelines for Americans (55). In 2005, the dietary guidelines were revised due to an increase in chronic diseases (65). Therefore, a revised Healthy Eating Index became necessary (65). In 2010, Woodruff et al adapted the Canadian version of the HEI (HEI-C) for children (**Table 1-3)** (35). HEI-C is the adapted version of Healthy Eating Index, based on the Canadian dietary recommendations and The Canada's Food Guide. HEI-C scores were found to be tightly ranged

between 55-77 (needs improvement category). This may be a result of using one method to measure of dietary intake assessment (24-hour recall).

The HEI-C has not been extensively used to measure the relationship between DQ and health-related outcomes, especially in children with chronic diseases. Only one study in our group examined the HEI-C in children with celiac disease (CD) (66). Poor DQ (HEI-C ≤80) was observed in more than 50% of children with CD and a healthy control group (67, 68). In addition, HEI-C was widely used to assess the relationship between the child's DQ and dietary habits and practices (such screen time and evening snacks) in Canadian children (36, 68).

Dubois et al (2000), who adapted the HEI-C in adults, reported a stronger correlation between the Canadian version of Healthy Eating Index and the mean adequacy ratio (the proportion of dietary recommendations met for each nutrient) compared to other DQ tools (Healthy Diet Indicator and DQI) (69). However, the HEI-C has been tested but not validated in healthy children. A validation of the HEI-C in Canadian children and adolescents against nutritional biomarkers such as serological biomarker of some antioxidants (carotenoids) is necessary (70). Although HEI-C is a simple tool to assess DQ, HEI-C lacks important foods and nutrients that have a big impact on health e.g. sodium, fibre, water, omega-3 fatty acids or fish consumption, the consumption of green leafy vegetables. Finally, HEI-C has limited use for the evaluation of DQ in therapeutics diets. **Table 1-2** presents the strengths and the limitations of HEI-C use in assessing DQ in children.

1.3.2 Dietary Guideline Index for Children and Adolescents (DGI-CA)

DGI-CA was developed by Golley et al (2011) to measure adherence to the 2003 Australian Dietary Guidelines for Children and Adolescents (**Table 1-3)** (31). DGI-CA was validated against

body mass index z-score, waist circumference, and socio-economic variables (household income, number of children in household, and food security) in children aged 4-16 years (31). Only five studies have examined DQ in children using DGI-CA (31, 71-74). The average DGI-CA scores in healthy Australian children fall between 47-77. Variations in the DGI-CA scores are due to age and the method of dietary intake assessment. Hendrie et al (2014) examined the reliability and the validity of using the Short Food Survey to measure DGI-CA scores (74). The study found a 16% overestimation of DGI-CA using the Short Food Survey (mean DGI-CA score=78) compared to 24-hour recall (mean DGI-CA score=62) (74). Only three studies examined the interrelationships between DGI-CA scores and health-related outcomes (31, 62, 72). Several relationships were observed between DGI-CA score and markers of cardio-metabolic dysregulation, abdominal fat, and markers of vitamins and serum fatty acids (31, 62, 72). Poor DQ (lower DGI-CA score <60) was associated with poor insulin sensitivity, high triglyceride/plasma stearic acid (c18:0) levels, low serum omega-3 fatty acids, and high in waist to hip ratio in healthy children compared to children with a high DGI-CA score (**Table 1-3)**.

The strength of this tool is based on the updated recommendations. DGI-CA is a mainly food-based tool; some components are related to the quantity vs the quality of food consumed such as “low fat milk” and “wholegrain bread”. On the other hand, DGI-CA may not a valid tool to assess other dietary patterns, such as veganism. Moreover, the consumption of bread in children may not be consistent on a daily bases and this may affect the “wholegrain bread” score. In addition, Golley et al (2011) handled mixed dishes based on the primary food component (31). The drawback of this approach is the under or over estimation of the food groups in mixed dishes. Finally, the DGI-CA tool has not been used to assess DQ of therapeutic diets. **Table 1-2** represents the strengths and the limitations of the DGI-CA to assess DQ in children.

1.3.3 Dietary Quality Index–International (DQI-I)

Kim et al (2003) developed the DQI-I to measure several nutrition-related diseases (over and under-nutrition) (16). The DQI-I was validated in healthy adults against food (servings of fruits and vegetables) and nutrient intakes (% energy from fat and from saturated fat, fibre, riboflavin, vitamin C, calcium, iron, sodium, and zinc) intakes (16). The DQI-I was used for children in different countries such as Canada, Greece, Spain, Portugal and Tunisia (20-22, 27-29, 75). The association between DQI-I and nutritional status and quality of life has been examined in several studies (**Table 1-3)**. Poor DQ (DQI-I score <60) was linked with low weight for age z-score, height for age z-score, and body mass index z-score (76). Poor DQ (low DQI-I score <60) was associated with poor academic performance and feeling worried, sad, or unhappy (25, 27, 75). The DQI-I can be a useful tool to evaluate "overall DQ" in health promotion and intervention programs. A randomized clinical trial examined the DQ of healthy children (6-12 years) after 6 months of a nutrition educational intervention program (29). The intervention program focused on nutrition, healthy eating, and healthy cooking. The study found improvements in some DQI-I components (sodium and vegetables).

The DQI-I was used internationally with children and adolescent to examine the associations between DQ and nutritional status and quality of life (**Table 1-3)**. In addition, the DQI-I can be adapted based on the nutritional recommendations of countries or dietary patterns (Mediterranean diet), but may not be useful in assessing DQ of therapeutic diets. Another limitation of the DQI-I is the classification of beans and dairy products in one food group; however, beans are treated as a part of meat or as a separate food groups in American, Australian and Canadian food guides (16, 17, 39, 77, 78).

Table 1-2: The Strengths and The Limitations of Diet Quality Tools for Children and Adolescents

DQ Tool	Strength	Limitations
HEI-C	• Adapted for Canadian children based on the Canadian recommendations • Scoring: the majority is proportional • Components: adequacy and variety • Used to measure the association between overall DQ, socioeconomic variables and nutritional status in children	• Components: the majority are nutrient based • Varity: includes overall food groups only and the scoring of this component is dichotomous • Not validated against nutrient biomarkers • Does not assess micronutrient intake • Variety: not evaluate within food groups • Failure to assess micronutrients (vitamin K, folate, sodium), omega-3 fatty acids and the quality of carbohydrate (GI, GL, fructose, added sugar)
DGI-CA	• Based on the new Australian dietary recommendations • Validated against nutritional biomarker • Used to measure the association between overall DQ and socioeconomic variables, cardio-metabolic risk, and nutritional status in children	• Components: the majority are food based and can be difficult to adapt for therapeutic diets • Not used in other countries • Variety: does not evaluate within food groups • Failure to assess micronutrients (vitamin K, folate, sodium), omega-3 fatty acids and the quality of carbohydrate (GI, GL, fructose, added sugar)
DQI-I	• Used to measure DQ internationally • Used to evaluate DQ in healthy children • Variety: evaluated overall and within food groups (protein) • Measures the intake of some micronutrients • Measures the quality of fat intake • Components: adequacy (macro and micronutrient), moderation, variety, and overall balance • Varity: overall and within food groups	• Based on old dietary recommendations • Not validated against nutrient biomarkers • Not validated for children • The variety within fruit and vegetables and grains was not evaluated • Failure to assess micronutrients (vitamin K, folate, sodium), omega-3 fatty acids and the quality of carbohydrate (GI, GL, fructose, added sugar) • Cut-off values based on old recommendation (World Health Organization 1996 and U.S. Department of Agriculture1992)

Abbreviations: DGI-CA, Dietary Guideline Index for Children and Adolescents; DQ, Diet quality; DQI-I, Diet Quality Index-International; GI, Glycemic Index; GL, Glycemic Load, HEI-C, Healthy Eating Index-Canada.

Table 1-3: Cross Sectional Studies of Diet Quality Tools and Parameters of Nutritional Status, Quality of Life and Health Related Outcomes

Author (Year) Country	Sample Size, Age	Dietary Assessment	Results
		HEI-C	
Woodruff et al (2010) Ontario, Canada (67)	n=1288, 10-11 year	Two days 24-hour recall	**Mean HEI-C score:** 65 ± 13 BMI:NS
		DGI-CA	
Golley et al (2015) Australia (72)	n=130, 4-13 year	Three days 24-hour recall	**Mean DGI-CA score**: 47-51 (depends on age, gender and weight) Positive associations with plasma lutein, α-carotene, β-carotene, and omega-3 fatty acid. Inverse associations with plasma lycopene and stearic acid (c18:0) NS associations with α -tocopherol, n–6 fatty acids and serum lipid profile
Chan et al (2015) Australia (62)	n=2262, 10-17 year	FFQ	**Mean DGI-CA score**: 47 ± 10 Positive association with BMI z-score and negative association with insulin, heart rate, waist to hip ratio and triglyceride
Golley et al (2011) Australia (31)	n=3416, 4-6 year	Two days 24-hour recall	**Mean DGI-CA score:** 54 4 – 7years: positive associations with BMI z-score and WC z-score 8 – 11years: NS associations with BMI z-score and WC z-score 12 – 16years: positive associations with BMI z-score and WC z-score
		DQI-I	
Setayeshgar et al (2016) Quebec, Canada (79)	n=546, 8-10 years	Three days 24-hour recall	**Mean DQI-I score:** 58±7 Inverse associations with central fat mass index and percentage body fat. Each unit of improvement in DQI-I was associated with lower gain in fat mass index, central fat mass index and percentage central body fat
McMartin et al (2013) Alberta, Canada (25)	n=6528, 10-11 year	HFFQ	Inverse associations with children's feelings of worried, sad or unhappy
McMartin et al (2012) Nova Scotia, Canada (80)	n=3757, 10-14 year	HFFQ	Emotional and behavioral disorder: NS
Wu et al (2012) Alberta, Canada (75)	n=3421, 10-11 year	HFFQ	**Tools:** Using EQ-5D-youth (components: walking, looking after myself, doing usual activities, having pain or discomfort, and feeling worried, sad or unhappy) and visual analogue scale Positive association with visual analogue scale and negative association with pain & discomfort dimension

Karagiozoglou-Lampoudi et al (2012) Greece (28)	n=42 with cerebral palsy, 8±4 years	Two days dietary record	**Mean DQI-I score:** 60 Positive correlation with weight for age z-score, height for age z-score and BMI z-score
Kuhle et al (2010) Nova Scotia, Canada (81)	n=4966, 10-11 year	HFFQ	Weight: NS
Florence et al (2008) Nova Scotia, Canada (27)	n=5200, 10-11 year	HFFQ	**Mean DQI-I score:** 62 Positive association with academic performance

Abbreviations: BMI, Body mass index; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; HEI-C, Healthy Eating Index-Canada; HFFQ, Harvard Youth/Adolescent Food Frequency Questionnaire; FFQ, Food Frequency Questionnaire; NS, not significant, WC, waist circumference. **Additional References** (3-10)

1.4 The Limitations of Diet Quality Tools

DQ tools are a relatively new method to assess overall DQ, especially in children. Several existing DQ tools have been developed for use with children; however, vast differences exist in the development of DQ tools. Several DQ tools have been used to assess overall DQ and to examine the association between DQ and nutritional Adequacy, status, and health related outcomes in healthy children, but not in children with chronic disease or those on therapeutic diets (66). As a result, the components of validated DQ tools focus on foods and nutrients of concern in healthy population (**Figure 1-1**). In addition, further components are required to be included to DQ tools to assess dietary pattern and DQ such as the consumption of wholegrain bread, green leafy vegetables, and drinking fruit juices. Furthermore, the cut-off points for good vs poor DQ need to be reliable for specific disease. Finally, the risk of obesity and cardio-metabolic dysregulation in children has increased significantly in the last decade due to changes in dietary patterns, especially increased consumption of processed foods and simple sugar (82). High consumption of simple sugar is associated with increased glycemic index (GI) and glycemic load (GL) (82).

1.5 Dietary Characteristics in the Evaluation of Diet Quality

Several nutrients and foods have been included in DQ tools, but dietary GI and GL are not currently included in DQ evaluation (3, 4). Other components, which can be considered as markers of high GI and GL foods, were assessed in DQ tools, such as *other foods*. *Other foods* consider not only added sugar, but also added fat. In addition, high GI and GL are present not only in added sugar foods, but in 100% fruit juice, rice or white bread (83). Evaluating GI and GL as additional components in DQ tools would be important due to: 1) the negative outcome of high GI and GL in healthy children and children with chronic disease, and 2) difficulty accounting for classifying GI and GL with one type of food.

1.5.1 Glycemic Index and Glycemic Load and Nutritional Status and Health-Related Outcomes

Diets characterized by high GI and GL are associated with increased postprandial blood sugar, and a subsequent increase in insulin secretion, leading to the rapid removal of glucose from the circulation. Diets rich in high GI foods have been linked with obesity, hyperglycemia, insulin resistance and hypertriglyceridemia in children and adults (84-87). Low GI diets are associated with weight reduction in female adults (85, 88). Other evidence suggests that low GI and GL diets are associated with a decrease in visceral adiposity in adults (85, 89, 90). Several prospective and interventional studies in children have reported a low GI diet decreases Body Mas Index (BMI), percentage body fat, waist-to-hip ratio, and metabolic parameters (82-84, 87, 91, 92). However, dietary intervention studies with large multi-ethnic groups of children are needed (83, 92). In addition, low GI diets are negatively associated with dyslipidemia and reduced blood glucose levels. Many studies have found that a low GI diet improved hemoglobin A1c, high density lipoproteins, triglycerides, and blood pressure (93-95).

1.5.2 Assessing Glycemic Index and Glycemic Load

GI measures the quality of carbohydrates in foods (92, 96, 97). It is defined as the incremental area under the curve of the postprandial blood glucose response of a food containing carbohydrate, compared with the same amount of glucose within a 2-hour period (92, 96, 97). Foods with GI $\geq$70, such as fruit juice, are classified as high GI; foods with GI 69-56, such as carrots and grapes, are classified as medium GI foods; and foods with GI $\leq$55, such as cucumber, are classified as low GI foods (96, 97).

GL considers both the quality and the quantity of carbohydrates in foods (96, 97). It measures the postprandial blood glucose effect of foods containing different carbohydrate types and amounts. It is calculated as the available carbohydrates (in grams), divided by 100 (96, 97).

Foods with GL ≥20 are classified as high GL foods, foods with GL 11-19 are classified as medium GL foods, while foods with GL ≤10 are classified as low GL foods (98). Diets characterized by GL ≥120, 80-119 and <80 are considered to have a high, medium and low GL (87, 98). **Table 1-4** shows an example of calculating GI and GL in an apple.

Table 1-4: Examples of Glycemic Index and Glycemic Load in Apple

	Carbohydrate (g)	Glycemic Index[1]	Glycemic Load[2]
Small Apple	13	38	5
Large Apple	26	38	10

[1]Glycemic index values were obtained from Foster-Powell et al 2002 (97) and www.glycemicindex.com.
[2]GL was calculated as GL= carbohydrate of food (g) x glycemic index/100 (97).

GI and GL have been calculated in Canadian adolescents (age 9-17 years) from Alberta (82). The mean GI and GL intake was reported to be 55 and 128 for girls and 56 and 168 for boys, respectively (82). High intakes of grains (white flour and simple sugar), and low intakes of vegetables and fruit, and milk and milk products, and meats and alternatives are components of high GI diets(82). High intakes of meats and alternatives, and milk and milk products, and low intake of grains (mostly sugar) and, vegetables and fruit are associated low GL (82).

1.5.3 Glycemic Index and Glycemic Load and Diet Quality Tools

Evaluating GI and GL of diets are not directly measured in DQ tools (3, 4). Assessing GI and GL by assessing the consumption of one food item is not valid due to two main reasons. First, high GI and GL foods are presents as *other foods* (e.g. candies), fruits and vegetables (e.g. carrot), or grains (e.g. rice) (83). Second, evidence shows that the combination of high and low GI foods "mixed meal" leads to reduce postprandial glycaemia (83, 99). Combining foods (carbohydrate [high and low GI] with protein and fat) reduces GI values and therefore reduces postprandial glycaemia (83, 99, 100). Because people consumed a combination of foods and nutrients as described earlier the "overall DQ", assessing GI and GL using a "mixed meal" method is important to evaluate overall DQ rather than a single food.

1.6 Diet Quality in Children with Liver and Gastrointestinal Disease

Malnutrition has a negative influence on growth and health status in infants, children and adolescents with many liver and gastrointestinal diseases. Children with liver and gastrointestinal disease often experience delayed growth (related to inadequate nutrition or malabsorption) or obesity (related to over nutrition), poor quality of life, and poor health status (e.g. cardio-metabolic dysregulation) (101). Consequently, evaluating overall DQ in children with liver and gastrointestinal disease is crucial to understanding the dietary patterns of this population, and providing nutritional recommendations to decrease the risk of poor health and nutrition status.

Assessing DQ through an "overall DQ" approach helps to understand dietary patterns and relate DQ to nutritional status and health-related outcomes in children with liver and gastrointestinal disease. To our knowledge, assessing overall DQ in children with liver and gastrointestinal disease has not been studied. Several studies have reported that children and adults following a GFD have high intakes of saturated fat and simple sugar and a low intake of fibre, folate, zinc, vitamin D, and vitamin K (66, 102-106). Other studies reported a high intakes of fat, saturated fat, simple sugar, GI, and GL in children and adults with Non-Alcoholic Fatty Liver Disease (NAFLD) (87, 107-109). However, no data is available to describe the dietary intake (pattern) of children post-liver transplant (LTX).

1.7 Liver and Gastrointestinal Diseases

1.7.1 Celiac Disease

CD is an autoimmune disease that is caused by an immune reaction to gluten (110). CD affects around 1% of the population (111). The Middle East and Europe have the highest prevalence of CD. The prevalence of CD increases to 20% in patients with family members affected by CD (112, 113). At the Stollery Children's Hospital, around 120 children were newly

diagnosed with CD in 2010 (114). Children with CD may have typical or atypical symptoms. Typical symptoms refer to gastrointestinal signs such as abdominal pain, chronic diarrhea, reduced appetite and impaired growth. However, many of children with CD do not complain of any symptoms. This is referred to as the "Celiac Disease Iceberg", as shown in **Figure 1-2** (115, 116).

The only treatment for children with CD is lifelong adherence to a strict GFD. Adherence to the GFD is a concern in children with CD (40%-80%) (66). Non-adherence to GFD in children with CD can lead to small intestine damage and subsequent malabsorption of essential nutrients. This leads to delayed growth and several health outcomes such as iron deficiency anemia and poor bone health (103, 110).

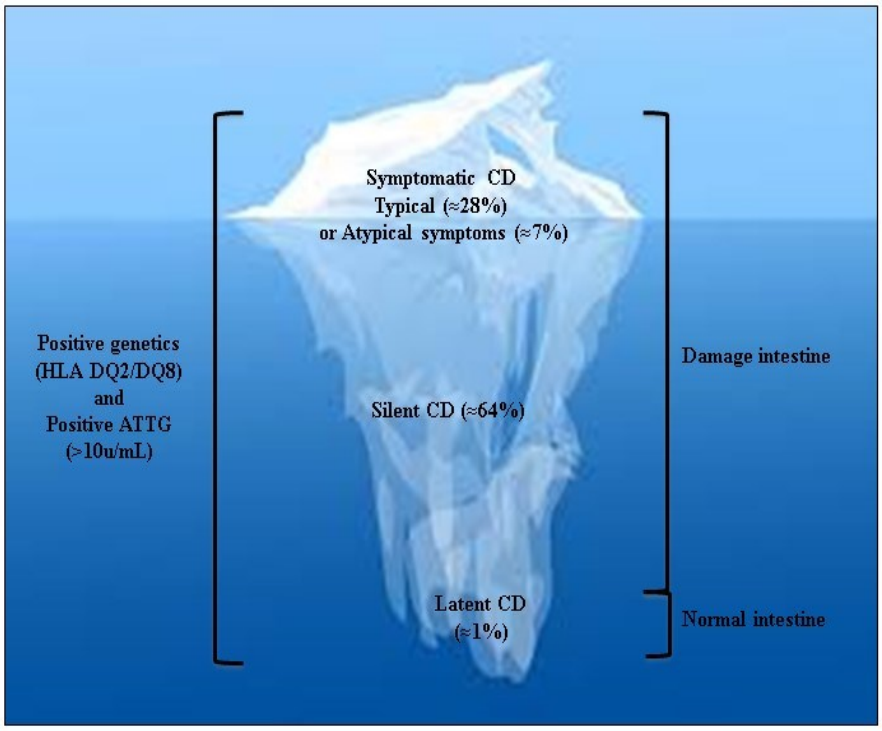


Figure 1–2: Celiac Disease Iceberg. Adapted from Rubio-Tapia et al (2013) and Nenna et al (2013) (115, 116).
Abbreviations: ATTG, Tissue Transglutaminase Antibodies; CD, Celiac Disease.

1.7.1.1 Gluten-Free Diet

GFD is a diet that excludes the protein gluten, which is found in wheat, rye, barley and

hence in a variety of packaged and processed foods (110-112). The GFD is classified to include: 1) naturally (not processed) GF foods such as fresh fruit and vegetables and 2) "gluten-free" processed foods (117). Processed "gluten-free" foods may inadvertently be contaminated with gluten (117, 118). Evidence suggests that the exposure of less than 10 mg/day is unlikely to cause pathological changes to the intestinal mucosa in patients with CD (118). In Canada, any foods not exceeding gluten more than 20 ppm (20 mg/kg) of gluten are considered "gluten-free" (117). This is based on the estimation that a contamination rate of 20 ppm is associated with usual exposure to gluten of less than 10mg/day (118).

1.7.1.2 Dietary Intake of patients with Celiac Disease and Following a Gluten-Free Diet

In addition to adherence to the diet, poor DQ is another concern in patients with CD following the GFD. Several studies have reported that children and adults with CD on GFDs, had low intakes of essential nutrients (such as fibre, folate, vitamin D, zinc, and magnesium) and high intakes of simple sugars and saturated fat (103-105, 119-121). In our previous work, children and adolescents with CD following a GFD were shown to have high intakes of saturated fat, sugar, GI and GL, and lower intakes of folate and selenium compared to healthy control children (66). More than 50% of children with CD did not meet the DRI for vitamin D, vitamin K, and folate. Moreover, we have compared DQ between children with CD and healthy controls using the HEI-C (66). Poor DQ (HEI-C ≤80) was observed in 66% of the cohort (66). Older children with CD (>10 years) had worse DQ (HEI-C ≤80) than younger children with CD (<10 years) (66). Together, these factors place the child with CD consuming a GFD at increased risk for reduced DQ. While assessment of DQ using DQ tools has not been routinely used in children with chronic GI diseases, use of such tools provide the opportunity to develop a broad understanding of the factors that affect DQ in the GFD. Understanding both the strengths and limitations of these tools is important to

minimize the potential for bias and the assessment of the overall nutritional quality in children consuming specialized therapeutic diets.

1.7.1.3 Nutritional Quality of Gluten-Free Diet

Although a GFD is the only treatment for CD, the nutritional quality of GF processed food is poor. The substitutions for grains in GF processed food are very limited e.g. rice, chickpeas, potato, or beans flour. Some GF flours are characterized by high GI and GL due to the nature of the flour (122). For example, white rice is considered to be a high GI food (GI=76). When white rice is finely milled to make white rice flour, the GI of the white rice flour becomes higher due to an increase in the absorption rate in the intestine (122). **Table 1-5** demonstrates GI values of gluten-containing and GF bread and pasta and **Table 1-6** represents the elevation of GI in processed food leading to an increase in the GL (97).

Table 1-5: The Glycemic Index in Regular (Gluten-containing) and Gluten-free Grain Products

	Regular (Gluten-containing)[1]	Gluten-free[2]
Bread	70	79-96
Pasta	45	68-78

[1] Gluten-containing bread and pasta made of white wheat.
[2]Gluten free bread made with buckwheat meal and rice flour or multigrain bread. Gluten free pasta made with corn flour, rice flour or rice and maize flour.
Adapted from Berti at el. (2004) (122), Penagini et al (2013)(123), Segura et al (2011) (124), Foster-Powell et al (2002) (97) and www.glycemicindex.com

Table 1-6: Glycemic Load in Regular (Gluten-containing) Bread and Gluten-free Bread

	Carbohydrate (g)	Glycemic Index[1]	Glycemic Load[2]
GF bread	13.5	88	12
Regular Bread	14	70	10

[1]Glycemic index of gluten-free bread was obtained from the average of Segura et al (2011) (124). Foster-Powell et al (2002) (97) and www.glycemicindex.com
[2] GL was calculated as GL= carbohydrate of food (g) x glycemic index/100 (97).

The GFD is limited in essential nutrients such as fibre, folate, iron, thiamin, riboflavin, and niacin (123, 125, 126). In Canada, fortification of GF food is not mandatory and GF foods are less

enriched with iron, folate, and vitamin B complex, compared to gluten containing foods (126-128). For example, GF pasta contains less than 8% of the daily value for iron than gluten containing pasta (127). Moreover, folate is another nutrient of concern in GF grains due to lack of mandatory fortification of GF foods (126, 129). To address these issues, policies of food fortification and enrichment may need to be re-evaluated for GF foods (125, 126). Another potential solution is to increase the consumption of GF grains that have a higher fibre, iron and folate contents (123, 125, 126). Penagini et al (2013) recommended an increase in the consumption of *pseudo-cereals* such as amaranth, quinoa and buckwheat (123). *Pseudo-cereals* are high source of protein, dietary fibre, calcium, magnesium, iron, zinc, and selenium (123). For example, quinoa (78.1 μg/100g) and amaranth (102 μg/100g) are rich sources of folic acid and teff (11-33 mg/100g) is a good source of iron (at least twice more than rice) (123).

1.7.1.4 Diet Quality in Children with Celiac Diesase and Following a Gluten-free Diet

Individuals with CD following the GFD are at risk of obesity, high blood pressure and dyslipidemia as reported in several studies (130-133). Around 30% of individuals with CD (with or without Type 1 diabetes) and following the GFD for more than 1 year are at risk for at least one criteria of cardio-metabolic dysregulation (130-133). Poor DQ and/ or poor nutritional quality of GF foods can be a potential factor contributing to risk of cardio-metabolic dysregulation in individuals with CD and on the GFD (132, 133). Several studies have concluded that GFDs are high in simple sugars and fat intake which is associated with increasing the risk of cardio-metabolic dysregulation. On the other hand, other studies reported that individuals with CD and type 1 diabetes and on the GFD have metabolic control similar to individuals with type 1 diabetes, without CD (134). There are several reasons for the discordant results of the risk of cardio-metabolic dysregulation in individuals with CD following the GFD. The first reason that explains these

differences lie in the variability for defining variation and duration of adherence to the GFD. Adherence to the GFD can be measured as normal Tissue Transglutaminase Antibodies (ATTG), self-reported dietary adherence or estimating the gluten content in the diet; each definition has its own limitations. Apparent delay in normalization of ATTG levels can be associated with both the ethnicity of the patient and with longer duration of gastrointestinal symptom recovery and with reported adherence to a GFD (135). We have reported that children and adolescents with CD of South Asian ethnicity have delayed normalization of ATTG in comparison to Caucasian children after 1 year following GFD (135). Self-reported adherence to the GFD can be challenging due to unintentional cross contamination with gluten (127). Second, the association between DQ and the risk of cardio-metabolic dysregulation in individuals with CD following GFD has not well been examined. Studies reported that the glycemic control is similar between children with CD and Type 1 Diabetes and children with Type 1 Diabetes alone. However, dosing for exogenous insulin may be significantly higher in those with Type 1 Diabetes and CD due to the high GI and GL content in GF foods (130, 134, 136). The criteria of cardio-metabolic dysregulation in children has not been determined (137). Assessing overall DQ will help to understand the effect of overall DQ on the risk of cardio-metabolic dysregulation in children with CD following GFD. Measuring DQ in children consuming the GFD through the development or adaptation of a DQ tool is important for the overall evaluation of the nutrient quality of this diet.

1.7.2 Chronic Liver Diseases

1.7.2.1 Cholestasis Liver Disease

Cholestasis is a condition resulting from impaired bile flow or bile acid uptake, conjugation, or excretion (138). Cholestasis can be caused by hepatocellular disease or biliary tract deformities (138). The etiology of cholestasis is multifactorial (**Table 1-7**) (138, 139). The most common clinical sign of neonatal cholestasis is jaundice (hyperbilirubinaemia) in infants >2 weeks of age (138, 139). Infants with cholestasis are at risk of steatorrhea, which leads to fat-soluble vitamin (A, D, E and K) malabsorption due to bile acid deficiency. Prolonged steatorrhea can result in protein energy malnutrition and a failure to thrive (139).

Table 1-7: The Etiology of Cholestasis

Etiology	Example and Disease
Toxic	Parenteral Nutrition
Metabolic disorder/ Genetic	Cystic Fibrosis Alagille Syndrome Progressive Familial Intrahepatic Cholestasis
Bile duct obstruction	Biliary Atresia Neonatal Sclerosing Cholangitis Congenital Hepatic Fibrosis
Systemic disorders	Shock, heart failure
Infection	Viral (Human Immunodeficiency Virus) Bacterial (sepsis)
Idiopathic	Idiopathic Neonatal Hepatitis

Adapted from De Bruyne et al 2011 (138), Spada 2009 (139) and Ling 2007 (140).

1.7.2.1.1 Biliary Atresia

Biliary Atresia is the main indication for LTX in infants (141, 142). Biliary Atresia is a rare disease (occurs 1 in 10,000 to 15,000 live births) and refers to an obstruction or absence of extrahepatic bile ducts, resulting in bile accumulation in the liver (139, 142). Biliary Atresia is classified based on the place of obstruction **(Figure 1-3)**. For infants with Biliary Atresia and pre-liver failure, Kasai Portoenterostomy can help to improve bile secretion. Kasai Portoenterostomy in the first 60 days can maintain the liver in up to 80% of infants (142, 143). In Canada, LTX was conducted in 60% of children with Biliary Atresia in the first two years of life and 37% of children with Biliary Atresia by the first year of life (144, 145).

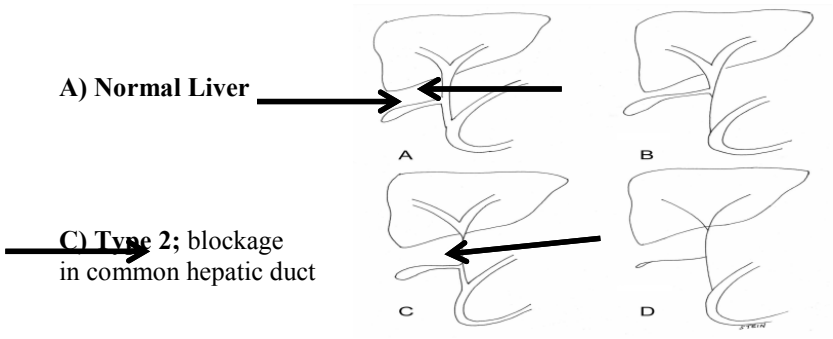


Figure 1-3: Types of Biliary Atresia.

Adapted from Ling et al (2007), Khalil et al (2010) and Hartley et al (2009) (140, 143, 146).

1.7.2.1.2 Nutritional Complications of Cholestatic Liver Diseases

Several health and nutritional co-morbidities are associated with end-stage liver disease (ESLD). Children with ESLD are at risk for anorexia, failure to thrive, protein energy malnutrition, fat-soluble vitamins deficiencies and poor bone health (142, 147-149). Failure to thrive and protein energy malnutrition are present in 60% and 90% of children with ESLD, respectively (142, 147-149). Along with the malabsorption of fat and fat-soluble vitamins, early satiety, low appetite, nausea and vomiting and abdominal distention (due to ascites) are etiological aspects of the delayed growth. In addition, a zinc and/or magnesium deficiency can contribute to changes in taste perception, thereby contributing to suboptimal food intake (147). Furthermore, children with ESLD (particularly Biliary Atresia or BA) have an increased energy expenditure and altered branched chain amino acid metabolism, leading to a significantly higher risk for protein energy malnutrition (150, 151). Although assessing DQ in children pre-LTX has not been directly measured, it has been observed that children pre-LTX have poor DQ due to increased energy and nutrients requirement, malabsorption and poor intake.

1.7.2.1.3 Liver Transplantation

Biliary Atresia is the main pediatric indication for LTX (66%) (141). The 1-year and the 5-year survival rates were reported as 92% and 85–98% in children post-LTX, respectively (152). Acute and chronic rejection is a concern in children post-LTX. The Studies of Pediatric Liver Transplantation (SPLIT) reported acute rejection in 80% of children in the first 6 months post-LTX and 60% in the first 5 years post-LTX. In addition, delayed growth occurs in up to 20-30% of infants and children post-LTX (148, 149). Linear growth is linked to pre-LTX growth, age at LTX, and the use of immunosuppressive therapy (148, 149). Accelerated growth rate (catch up growth) occurs within the first 1-2 years post-LTX (148, 149).

1.7.2.1.4 Risk for Cardio-Metabolic Dysregulation post-Liver Transplant

Evidence has reported an increased risk of cardio-metabolic dysregulation in children post-LTX (**Table 1-8**) (153, 154). The prevalence of cardio-metabolic dysregulation was reported in 14% of children post-LTX (154). The prevalence of having a symptom of cardio-metabolic dysregulation such as obesity can reach up to 67% in children post-LTX (154, 155). Obesity has been noted in the same population and this can be a factor in increasing the risk of cardio-metabolic dysregulation. The SPLIT database reports obesity in 10-19% of children (1- 10 years) post-LTX (154, 156-158). Other symptoms of cardio-metabolic dysregulation have also been examined in children post-LTX including blood pressure, lipid profile and insulin resistance (154). SPLIT research group examined the prevalence of increasing blood pressure in 815 children that received transplants between 2005-2008 (159). Elevated blood pressure was observed in around 21-24% of children after 5-12 years post-LTX (101, 154, 159). Moreover, elevated triglycerides and total cholesterol were observed in around 10-26 % and 7-20% of children 6-10 years post-LTX, respectively (154, 156, 157). Several factors for cardio-metabolic dysregulation were reported: age at LTX, ethnicity, indication of LTX, and immunosuppressant therapy (Stroid/Tacrolimus) (101,

156-160). The variation of cardio-metabolic dysregulation in children after TX was high in the literature due to: 1) the age of the cohort, 2) age at LTX, 3) duration of follow up, 4) no specific gender, 5) the effect of ethnicity, 6) the differences of immunosuppressive regime, 7) the definition of cardio-metabolic dysregulation and 8) the differences of anthropometric measurements (waist circumference) measurement or the growth chart e.g. The Centers for Disease Control (CDC) or World Health Organization (WHO) (101, 154, 156-160). On the other hand, dietary intake and DQ have a significant influence on the symptoms of cardio-metabolic dysregulation but have not been examined in this population.

Table 1-8: Cardio-Metabolic Dysregulation in Children and Adolescents After Liver Transplantation

Study (year)	Sample size (n) and Years of LTX Follow-Up (year) Age at LTX (year)	Diagnostic Criteria: Prevalence (%)	Risk Factors
Kosola et al (2014) (154)	n=66 from 1987 to 2007 Follow up: 12 (3-22)[1] Age at LTX: 4 (0.5-17)[1]	Obesity (BMI≥30 kg/m^2): 20% Hypertension: 24% Elevated TG: 9% and Low HDL: 23% HOMA-IR>2.5= 27% Impaired fasting glucose levels:14%	No associations with immunosuppressive medications
Ng et al (2012) (156)	n=167 (SPLIT) from 1995 to1999 Follow up: 10 to 11 Age at LTX: 1 (0.6-3.6)[2]	BMI > 95th percentile: 10% Height < 10th percentile: 23% Elevated TC: 40 % and Elevated TG: 26 %	At 10 years, no association with steroid use or AST/ALT At 10 years, steroid (43%) At 10 years, no association with AST/ALT
McLin et al (2012) (159)	n=815 (SPLIT) from 2005 to 2008 Follow up: 5 to 10 Age at LTX: 3.5 ± 4.0[3]	Elevated: SBP or DBP > 95th percentile or antihypertensive medication us 5 years: 20.7% and 10 years: 27.5% Borderline: SBP or DBP 90th - 95th percentile 5 years: 7.9% and 10 years: 7.3%	Age of 5-7 years (vs <1 year) at LTX Steroid use Low GFR Medication at LTX and at last follow-up: TAC (58 and 70%) and CSA (28 and 13%)
Sundaram et al (2011) (158)	n=1706 (SPLIT) from 1995 to 2007 Follow up: from1 to 5 Age at LTX: 4.6[3]	BMI > 95th percentile 1-5year: 19-11%	Overweight/obesity before LTX Age < 6 years at LTX Persistent use steroid
Hathout et al (2009) (160)	n=1611 (SPLIT) from 1995 to 2004 Age at LTX:1.9[1]	Insulin, oral hypoglycemic use, glucose intolerance or DM: 13.3%	Age > 5 years at LTX Medication: Steroid use at LTX and TAC Cholestatic disease
Ng et al (2008) (157)	n=461 (SPLIT) from1991 to 2001 Follow up: 6 (5-15)[1] Age at LTX: 1.6 (0.7-6.5)[2]	Weight > 95th percentile: 12% Height < 10th percentile: 29% Antihypertensive medication use: 9%	At 5 years, No association with steroid use At 5 years, Associated with steroid (36%) At 5 years, 49% on steroid

[1] median or median (range).
[2] median (interquartile range).
[3] mean or mean ± standard deviation.
Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; GFR, glomerular filtration rate; HDL, high-density lipoprotein; HOMA-IR, Homeostasis Model Assessment for Insulin Resistance; LTX, liver transplant; SBP, systolic blood pressure; SPLIT, Studies of Pediatric Liver Transplantation; TAC, tacrolimus; TC, total cholesterol; TG, triglyceride. **Another reference**: Rothbaum Perito et al (2012) (101).

1.7.2.1.5 Dietary Intake and Diet Quality in Children and Adolescents Post-Liver Transplant

Although cardio-metabolic dysregulation is observed in children post-LTX, the associations between dietary intake and DQ and cardio-metabolic dysregulation in children post-LTX has not been studied. The link between DQ and cardio-metabolic dysregulation has been examined in other populations, such as NAFLD, diabetes, and cardiovascular disease (87, 107-109, 161-164). High intake of fat, saturated fat, and simple sugars in children with cardio-metabolic dysregulation was associated with central obesity, high blood pressure, insulin resistance, and dyslipidemia in these populations, but assessing overall DQ was not evaluated (87, 107-109, 161-164).

Dietary intake has been evaluated in children post renal TX (RTX). A cross-sectional study compared dietary intake between stable children after RTX and control children (165). One interesting finding was that all stable children after RTX and the majority of control children had a saturated fat intake >10% of kcal and more than 60% of children post-RTX had a polyunsaturated fatty acids intake <5% of Kcal. With the exception of vitamin C and potassium intake, dietary intake was similar between children post-RTX and the control group and no association was found between dietary intake and lipid profile and insulin resistance. On the other hand, two other studies found that dyslipidemia was negatively associated with the intake polyunsaturated fatty acids and negatively associated with monounsaturated fatty acids and trans fat (166, 167). The differences in results can be due to an immunosuppressive regime, and ethnicity and related with different dietary patterns.

Siirtola et al (2008) did not observe any significant difference in the majority of micronutrient intakes between children post-renal transplant and healthy controls (165). We can speculate that dietary intake in children post-LTX was similar to healthy children but we do not have information regarding the dietary intake in children post-LTX in comparison to

the DRI. Moreover, no data is available regarding added sugar and simple sugar intake in this population. As a result, prospective studies to examine dietary intake and DQ in children post-LTX are necessary.

1.7.2.2 Nonalcoholic Fatty Liver Disease

NAFLD is one of the most common chronic liver diseases in children (162). NAFLD is defined as the accumulation of excess triglycerides in the hepatocyte (>5% of liver weight) (162). Liver dysfunction in NAFLD presents across a spectrum of simple steatosis, steatosis with inflammation and/or fibrosis (nonalcoholic steatohepatitis or NASH) to cirrhosis, and may lead to liver failure (168, 169). Obesity and cardio-metabolic dysregulation are risk factors for NAFLD. The cardio-metabolic dysregulation is a condition with several manifestations (insulin resistance, obesity, hypertension, dyslipidemia) and is associated with several clinical conditions such as cardiovascular disease and NAFLD (107).

1.7.2.2.1 Dietary Intake and Diet Quality in Children with Nonalcoholic Fatty Liver Disease

Sedentary lifestyles and poor DQ are the main causes of NAFLD and lifestyle modification (improving DQ and physical activity) the only treatment for both cardio-metabolic dysregulation and NAFLD (107, 170). Several dietary interventions reported positive health outcomes in children and adolescents with NAFLD (87, 171, 172). Dietary interventions to reduce simple sugar intake and GL and increase omega-3 intake were associated with reduced systolic blood pressure, Alanine Aminotransferase, Homeostasis Model of Assessment of Insulin Resistance, and body fat percentage in obese children with NAFLD (87, 171, 172). The main limitations of all the studies were a small sample size and a lack of liver biopsy to confirm diagnosis. The results of those studies were not consistent due to the following reasons. First, the diagnosis of NAFLD was different between the studies (elevated liver enzymes, ultrasonography, hepatic liver or biopsy). The second reason is the

variation of diets (low fat diet <30% vs 25-30%) in interventional studies. Third, adherence to the interventional diet was not well reported. Using a single 24-hour recall to evaluate the adherence to the interventional diet or the changes in DQ may not be accurate and, in particular, the underestimation of intake in obese populations has been observed. To overcome this issue, multiple methods to measure dietary intake, (>3 days of food diaries, food records or 24-hour recall) and biomarkers were used (173).

The association between a "single nutrient" (simple sugar, fat, and saturated fat) and the risk of obesity, cardio-metabolic dysregulation, and NAFLD have been reported in several studies (107-109, 170). However, limited studies have examined the association between overall DQ and the risk of NAFLD (73, 174). Two studies conducted in adults with NAFLD showed that poor DQ (using DQI-I and HEI) was associated with NAFLD (73, 174). Several studies reported an inverse association between high consumption of fruits and vegetables, legumes, calcium, vitamin D, and antioxidants and NAFLD (73, 174). Using DQ tools (in addition to other nutrients) to assess DQ may help to understand the association between diet and obesity, dyslipidemia, and hypertension in children with NAFLD. This may help clinically to evaluate the adherence to the dietary recommendation in children with NAFLD (9).

1.8 Conclusion

This thesis will evaluate "overall diet quality" using three different DQ tools (HEI-C, DGI-CA, and DQI-I), GI and GL in three different pediatric clinical tools populations: CD, post-LTX, and NAFLD (**Figure 1-1**). None of these tools has been validated for use in children with chronic gastrointestinal diseases. However, all of these tools have been validated with children for the assessment of DQ. We chose to use HEI-C, DGI-CA, and DQI-I for several reasons. First, HEI-C, DGI-CA, and DQI-I have been used and validated

in children between 4-16 years (5, 9, 10). Second, HEI-C and DQI-I have been used in Canadian children (27, 35, 66). Third, DQI-I was developed to compare DQ between two different populations that do not share the same ethnicity or diet type (16). This is important to assess given the multi-ethnic population in Canada and the differences in diet type in patients with chronic GI diseases. Finally, HEI-C, DGI-CA, and DQI-I have been examined to measure the association between DQ and nutritional status and health-related outcomes in healthy children (5, 8-10). Very limited studies assessing DQ in clinical populations (adults with Chronic Obstructive Pulmonary Disease) have been done (175).

Use of different DQ tools helps to examine some concepts (such as micronutrient intake) that are not evaluated in each tool. In addition to these three DQ tools, we will assess GI and GL in children with NAFLD and children with CD on the GFD. We have evaluated the association between DQ tools (HEI-C, DGI-CA and DQI-I), GI and GL intake, and socio-demographic, anthropometric variables, and health related outcomes such as quality of life. In children with CD, we have examined the association between HEI-C, DGI-CA, and DQI-I, GI and GL and anthropometric, socio-demographic variables, and quality of life (**Chapter 3**). In addition, we have assessed DQ and nutritional status in children post-LTX using HEI-C, DGI-CA, and DQI-I, GI and GL (**Chapter 4**). Finally, the relationships between HEI-C, DGI-CA, DQI-I, GI and GL and body composition, liver enzymes, and some markers of cardio-metabolic dysregulation were examined in children with NAFLD (**Chapter 5**).

Chapter 2 Research Plan

2.1 Rationale

The associations between health outcomes and a single specific nutrient are difficult to evaluate. Quantification of one aspect of a diet does not take into account the variety of different dietary factors and potential nutrient interactions that may impact health and disease, particularly in early childhood where effects on growth and development must also be taken into consideration. Consequently, overall diet quality (DQ) may be a better indicator of the nutritional quality of an individual's diet rather than a single nutrient. DQ tools evaluate the overall nutritional quality of an individual's dietary intake by examining the diet from a broad perspective that includes meal portion size and diversity of food group intake, as well as intake of micro and macronutrients known to be important for chronic disease prevention (4, 69). There are a variety of validated tools that have been developed to measure DQ in children. These include the Healthy Eating Diet Index-Canada (HEI-C), Revised Children's Diet Quality Index, Diet Quality Index-International (DQI-I), Healthy Diet Indicator, Dietary Guideline Index for Children and Adolescents (DGI-CA) and Diet Quality Score (4, 69). At present, very limited studies have assessed DQ in children and adolescents with chronic diseases (8, 9, 176).

Several studies have examined the association of DQ tools with nutritional adequacy of food intake and biomarkers of micronutrient status (9). For example, the HEI was correlated with plasma and red blood concentrations of α-carotene, β-carotene, vitamin C and vitamin E (177, 178). Similarly, DGI-CA was positively correlated with fibre, folic acid, vitamin D, vitamin C, vitamin E, iron and zinc intake (31). In addition, poor DQ using DQ tools (HEI and DGI) was associated with the risk of chronic diseases (e.g. cancer, cardiovascular diseases) and mortality in adults (4, 69). Finally, DQ scores were related to adiposity in children and adolescents (4, 31, 69).

There are several DQ tools that have been validated and used in children and adolescents; however, the HEI-C is the only DQ tool validated in Canadian children and adolescents (37). To date, no DQ tool has been extensively studied in children with gastrointestinal and liver diseases. Children with gastrointestinal and liver diseases may experience malabsorption of essential nutrients and poor dietary intake, which can result in growth and developmental delays (135, 156). In addition to poor growth, children with gastrointestinal and liver diseases may also experience reduced quality of life in physical (abdominal pain), emotional, and social (feeling isolated) domains. Little is known how these impact DQ of children's diets (179). Most DQ tools that have been developed focus on macronutrient consumption, particularly fat and cholesterol, with some emphasis on food variety/moderation. However, few tools assess other components of dietary intake such as simple sugar intake and/or micronutrient intake. Factors such as glycemic index and glycemic load may contribute to overall health and well being of a child, by influencing glycemic control and risk for several chronic liver diseases. Poor DQ (high glycemic index and glycemic load) is associated with several chronic diseases such as obesity, non-alcoholic fatty liver diseases (NAFLD), diabetes, and cardiovascular diseases (180, 181). Evidence from human and animal studies has demonstrated the negative influence of high glycemic index and glycemic load on adiposity and cardio-metabolic dysregulation (180, 181). High glycemic index and glycemic load diets are associated with increased postprandial blood sugar, hyperlipidemia, obesity and visceral adiposity (85, 88-90). The impact of overall DQ and other features of dietary intake (glycemic index and glycemic load) on anthropometric, body composition, markers of cardio-metabolic dysregulation, and quality of life has not been extensively examined in children with chronic gastrointestinal and liver disorders. Consequently, examining DQ using a variety of methods such as validated DQ tools, as well glycemic index and glycemic load intake, is important to ensure a

comprehensive evaluation of diet quality and its associated interrelationships with health outcomes such as quality of life is done.

2.2 Overall Thesis Objectives and Hypotheses

***Overall Thesis Objectives*:**

1. To assess overall DQ with the emphasis on dietary analysis to include examination of macronutrient intake, food groups, glycemic index and glycemic load, and validated DQ tools (HEI-C, DGI-CA, DQI-I) in children with chronic gastrointestinal (Celiac Disease [CD]) or liver disease (nonalcoholic fatty liver disease [NAFLD]) and (children post liver transplantation [LTX]) and compare intake to healthy children/disease control populations.
2. To assess the interrelationships between overall DQ and body composition, some disease risk factors (cardio-metabolic dysregulation) and health outcomes (quality of life, gastrointestinal symptomology) in children and adolescents with chronic gastrointestinal and liver diseases.

Overall Thesis Hypotheses:

1. Poor overall DQ (low DQ scores, high glycemic index, and high glycemic load) will be observed in children with chronic gastrointestinal (CD) and liver diseases (LTX and NAFLD), relative to control populations.
2. Good overall DQ (high DQ score and lower glycemic index and glycemic load) will be associated with improved health outcomes in children and adolescents with chronic gastrointestinal and liver diseases.

2.3 Chapter 3: Diet Quality of the Gluten-Free Diet and Quality Of Life in Ethnically Diverse Populations of Children and Adolescents with Celiac Disease

2.3.1 Rationale

CD is an autoimmune disease of the small intestine that affects approximately 1 in 100 individuals worldwide (110). Exposure to gluten in individuals with CD leads to damage of the small intestine and malabsorption of essential nutrients (110). Classically, the presentation of CD in children has been associated with diarrhea, abdominal pain and failure to thrive (110). However, it has become apparent that this represents only the "tip of the iceberg", where many children now present with other symptoms such as anemia, poor bone health, muscle pain, and fatigue, in the presence of normal growth (110, 135). Although treatment for CD is a gluten-free diet (GFD), adherence to the diet can be a concern in 40% to 80% of patients with CD (66). Non-adherence to a GFD in children with CD can lead to sustained small intestine damage, malabsorption of macro and micronutrients, and contribute to ongoing challenges with growth/development, and overall bone health (103, 110). In our previous pilot study, children and adolescents with CD following a GFD had nutrient intakes characterized by high intakes of saturated fat, sugar, higher glycemic index and glycemic load, and lower intakes of folate compared to healthy control children (66). More than 50% of children with CD did not meet the Dietary Reference Intake of vitamin D, vitamin K, and folate (66). In addition, older children with CD (>10 years) had worse DQ (HEI-C ≤80) than younger children with CD (<10 years) (66). Together, these components place the child with CD consuming a GFD at increased risk for reduced DQ. A recent study reported that children and adolescents with CD experienced emotional and social limitations (feeling alone and feeling different from others) related to having CD and following a GFD and fears related to the potential risk for gluten exposure during social activities (179). These were reported to diminish overall quality of life in children and adolescents with CD (179). Following a GFD with high DQ is challenging and the inability to do so may pose direct challenges to optimizing quality of life in

the child with CD. The effect of the DQ of a GFD on quality of life in children and adolescents with CD is currently unknown.

2.3.2 Study Objectives and Hypotheses

Study Objective:

1. To compare overall DQ by assessing macronutrient intakes, food groups, glycemic index, glycemic load, and DQ using validated DQ tools (HEI-C, DGI-CA, DQI-I) between children and adolescents with CD on the GFD and non-CD children with chronic gastrointestinal diseases (disease controls).
2. To determine whether the child's/parent's perception of quality of life influences dietary adherence and nutritional intake in children with CD on a GFD.

Study Hypotheses:

1. Children and adolescents with CD following the GFD have poor quality of life and DQ scores compared to children and adolescents without-CD (gastrointestinal disease controls).
2. Reduced DQ in children and adolescents with CD on the GFD will be related to poor health related quality of life by the parent perspective and child perspective.

2.4 Chapter 4: Diet Quality in Children Post Liver Transplantation

This thesis study represents a subset of a published paper with some modifications. Alzaben AS, MacDonald K, Robert C, et al. Diet quality of children post-liver transplantation does not differ from healthy children. Pediatr Transplantation. 2017;00e12944.
https://doi.org/10.1111/petr.12944, Wiley Global Permissions.

2.4.1 Rationale

Biliary atresia (BA) is the most common pediatric cholestatic liver disease requiring liver transplantation (LTX) in infancy and early childhood (156). BA is related to impairment of bile flow due to obstruction of the biliary tree, which causes severe cholestasis. Additionally, malabsorption of fat and fat-soluble vitamins and alterations in hepatic metabolism of energy and

macronutrients in the pre-LTX period can result in increased nutritional requirements and cause malnutrition (182). Due to malnutrition prior to LTX, children and adolescents with cholestatic liver disease are at risk of poor health outcomes and delayed neurodevelopment pre- and post-LTX (182, 183). It has been reported that 10 years after LTX, 23% of children and adolescents were below the 10th percentile of height for age (156). Preliminary work from our centre demonstrated that delayed height is apparent in children and adolescents up to six years post-LTX (184). Several factors may contribute to sustained poor growth post-LTX, including pre-LTX malnutrition, post-LTX organ rejection, immunosuppressive therapy (e.g. corticosteroid use) and/or hepatic vein stenosis (156, 182, 185). All of the factors described above may contribute to inadequate macro and micronutrient intake, resulting in poor growth and health outcomes for children post-LTX (such as prolonged hospitalization following LTX). In addition, obesity and cardio-metabolic dysregulation were observed in 10-20% of children five years post-LTX due to immunosuppression therapy (101, 155, 183).

2.4.2 Study Objective and Hypothesis

Study Objective: To describe and compare overall DQ by assessing macronutrient intakes, food groups, glycemic index and glycemic load, and DQ using validated DQ tools DQ tools (HEI-C, DGI-CA, DQI-I) between children post-LTX and healthy children.

Study Hypothesis: Children and adolescents post-LTX will have lower DQ score and higher glycemic index and glycemic load compared to healthy controls.

2.5 Chapter 5: Influence of Diet Quality on Anthropometric and Markers of Cardio-Metabolic and Liver Disease Function in Youth with Non-Alcoholic Fatty Liver Disease

2.5.1 Rationale

Non-alcoholic fatty liver disease (NAFLD) presents as a spectrum of liver dysfunction in overweight and obese children from simple steatosis (excessive fat accumulation) to more serious liver diseases, characterized by inflammation with or without fibrosis (nonalcoholic steatohepatitis, NASH), and leads to hepatic dysregulation (186). The etiology of NAFLD is multifactorial, but is primarily related to obesity and lifestyle factors (poor diet and physical inactivity) (187). Several studies have reported that children and adolescents with NAFLD consume a diet characterized by high energy, saturated fat, and simple sugar intake coupled with low intake of antioxidants and long chain polyunsaturated fatty acids (187). No research is currently available regarding the overall DQ in children and adolescents with NAFLD.

Understanding DQ in this population is important since the mainstay of treatment for NAFLD is lifestyle modification. Poor DQ is associated with adiposity, dyslipidemia, lipid accumulation, and/or altered fatty acid composition (87, 188, 189). A prospective study in our group found that a high fat meal is associated with postprandial hyperlipidemia, hyperinsulinemia, and increased plasma saturated fatty acids in children with NAFLD compared to lean control children (188). Several studies have proposed different dietary interventions for NAFLD including supplementation of omega-3 fatty acids or antioxidants (vitamin E) or diets low in saturated fat and added sugar (87, 170, 172, 190, 191). Recent endeavors by our group showed that youth with NAFLD consuming iso-caloric diets lower in glycemic index and glycemic load (FRAGILE study) experience improvements in markers of cardio-metabolic and liver dysfunction (87). Although several lifestyle interventions have been studied, few studies have shown sustained long-term success in the treatment of NAFLD (172, 191). Many families of children with NAFLD understand the need for dietary change, but adherence to diet therapy remains poor due to the lack of simple

tools to assist families in making key dietary changes (192). Assessing DQ in children and adolescents with NAFLD is an important step in evaluating the efficacy of changes in diet that may contribute to improvements in liver function and to assist with the development of effective interventions and simple-to-use nutrition education tools for NAFLD (193).

2.4.2 Study Objectives and Hypotheses

Study Objectives:

1. To assess and compare overall DQ in youth with NAFLD and healthy lean controls. Overall DQ was assessed by: a) macronutrient intake, b) micronutrient intake (with emphasis on antioxidants vitamin A, vitamin C, vitamin E), c) food groups, d) glycemic index and glycemic load, and e) DQ tools (HEI-C, DGI-CA, DQI-I). Assessing overall DQ using three different DQ tools was based on the total score and the components of each DQ tools.
2. The secondary objective was to examine the interrelationships between DQ and anthropometric measurements (body weight, body composition) and markers of liver dysfunction, and cardio-metabolic parameters.

Study Hypotheses:

1. Children and adolescents with NAFLD have poor overall DQ compared to lean children.
2. Poor overall DQ is associated with an increased risk for obesity, liver dysfunction (liver enzymes), and cardio-metabolic markers (markers of insulin resistance and lipid profile) in children with NAFLD.

Chapter 3 Diet Quality of The Gluten-Free Diet and Health Related Quality of Life in Ethnically Diverse Populations of Children and Adolescents with Celiac Disease

3.1 Introduction

Celiac Disease (CD) is an autoimmune disorder triggered by the consumption of gluten and is associated with enteropathy (194, 195). CD affects around 1% of the general population (194, 195). However, evidence suggests that the global prevalence of CD has been underestimated (195, 196). A cross-sectional study in the United States reported that only 17% of patients with CD (age >6 years) have been diagnosed, with the remaining 83% of patients being undiagnosed (196). The wide spectrum of clinical presentations of CD is the main reason for the under-diagnosis of CD (194). Patients with CD may experience typical symptoms (e.g. abdominal pain), atypical symptoms (such as iron deficiency anemia and poor bone health) or silent CD (no symptoms) (194, 195). Due to a better understanding of the presentation of CD, and to prevent any risk of growth impairment, serological testing for CD is recommended for children with a positive family history of CD (197, 198). Consequently, the number of newly diagnosed children with CD at the Stollery Children's Hospital has increased by 11 times between 1998 and 2007; 46% of newly diagnosed children had an absence of symptoms, but reason for screening, or had atypical symptoms (114).

The prevalence and the incidence of CD may vary between individuals of different ethnicities and geographical locations. A cross-sectional study found that the highest prevalence of CD occurred in individuals from Northern India relative to those from Southern Indians, East Asians and Hispanics countries of ancestry (199). A recent epidemiological study in Europe reported the geographical variation in the prevalence of CD in different European countries (200). Differences in CD presentation at time of diagnosis and at a one-year follow-up were also observed in children and adolescents with CD at the Stollery Children's Hospital. While children of

Southern Asian ethnicities with CD experienced poor growth and delay in the normalization of anti-tissue transglutaminase (ATTG) levels, the majority of Caucasian children reported gastrointestinal symptoms (GS) (135, 201).

A gluten-free diet (GFD) is the only treatment for children with CD. However, it is challenging to follow a nutritious GFD. Earlier studies by our group found that children and adolescents with CD had a higher intake of saturated fat, Glycemic Index (GI), and Glycemic Load (GL) and a lower intake of folate and selenium than healthy control group (66, 103). The majority of children with CD (>50%) did not meet the Dietary Reference Intake (DRI) for vitamin D, vitamin K, folate and iron and had intakes characterized by lower overall diet quality (DQ) (66). The results of our previous studies were consistent with other studies involving children and adults with CD consuming a GFD. Patients with CD following a GFD reported low intakes of fibre, vitamin D, zinc, magnesium, and high intakes of simple sugars and saturated fats (66, 104, 106). Inadequate intake of essential nutrients in children with CD is likely due to the consumption of pre-packaged GF food (such as bread and pasta), which often provides lower nutritional quality than gluten-containing equivalents. GF bread contains higher fat and lower protein levels than gluten-containing bread and GF pasta is higher in carbohydrates while being lower in fibre, iron, and folate (202) .

In addition to poor DQ of a GFD, adherence to a GFD is another concern in patients with CD. Poor compliance to a GFD has been observed in children with CD (64%) (203). The lowest rate of adherence to a GFD was reported in children with no GS, and older age at diagnosis (>13 years) (204-206). Several factors were associated with low compliance to a GFD, including reduced palatability of gluten-free options, challenges with dining outside the home, cost of a GFD, and poor availability of GF products and poor labeling of GF foods (203, 205-207). Low adherence

to a GFD in children and adolescents with CD may be associated with a delay in healing the small intestine causing malabsorption of essential nutrients, delayed growth, and may contribute to a lower overall health related quality of life (HRQOL) (206).

Adherence to a GFD was associated with improved HRQOL in adults with CD (208, 209), but not in adolescents (206, 210). Adolescents with CD reported low HRQOL related to the burden of CD (179, 209-212). Having CD and following a GFD (regardless of DQ of the GFD) can cause negative social and emotional impact upon children and adolescents with CD (179, 210). A qualitative study reported that adolescents with CD had concerns related to feeling alone, feeling different from others, and being left out of social activities (e.g. parties) that children without CD enjoy (179). Wagner et al (2008) examined the association between adherence to a GFD and HRQOL in children and adolescents with CD (210). Adherence to a GFD was associated with low HRQOL scores in domains related to social, mental and physical school function (210).

The purpose of this study was to compare overall DQ by assessing macronutrient intakes, food groups, GI, GL, and DQ using validated DQ tools between children and adolescents with CD on the GFD and non-CD children with chronic gastrointestinal diseases (disease controls) and to determine whether the child's/parent's perception of HRQOL influences dietary adherence and nutritional intake in children with CD on a GFD and vice versa. We hypothesized that 1) children and adolescents with CD following the GFD have poor HRQOL and DQ compared to children and adolescents without CD (gastrointestinal disease controls), and 2) reduced DQ in children and adolescents with CD on the GFD will be related to poor HRQOL by the parent prospective and child prospective.

3.2 Methods

3.2.1 Participants

A prospective multicenter cohort study was conducted at four sites: Stollery Children's Hospital (Edmonton), Sick Children's Hospital (Toronto), McMaster Hospital (Hamilton), and Regina Qu'Appelle Region (Regina). Children with CD, aged 3-18 years old, were recruited. All children with CD were clinically diagnosed with CD by duodenal and/or jejunal biopsy. The disease control group (CON) (3-18 years old) consisted of children with minor gastrointestinal complaints (such as abdominal pain and functional constipation) with a CD diagnosis ruled out by routine clinical blood screening. CON recruitment occurred from the Gastrointestinal Clinics at the Stollery Children's Hospital (Edmonton). Exclusion criteria included: children and adolescents with additional medical and nutritional diagnoses known to influence dietary intake (such as failure to thrive); those undergoing dietary treatment for an underlying medical issue (e.g. type 1 diabetes, food allergy); and those with other chronic diseases (e.g. inflammatory bowel disease, cystic fibrosis, short bowel syndrome). All children and their parents consented to study participation prior to enrollment. Ethics approvals were obtained from all sites. Ethical, operational approval and administrative approvals were obtained from the Human Research Ethics Board (Pro00033867), Alberta Health Services, and the Northern Alberta Clinical Trials Centre at the University of Alberta.

This thesis chapter will present *a subset of the CD/parent participants (n=30) and CON/parent participants (n=50)* recruited from the Edmonton site only; representing approximately 15-20% of the entire participants recruited for this study.

3.2.2 Socio-demographic Data

Socio-demographic data were collected from the parents of children and adolescents with

CD and CON regarding gender, date of CD diagnosis, age of the child at time of diagnosis and date, parental education, number of children in the household and income. Household income information was assessed using Statistics Canada Census "superdemographics" database for postal codes (213-215). The postal codes from parents of children with CD and CON were linked to the database to determine the average income of the neighborhood and therefore only represent information regarding general income of the residential area in which participants resided (213).

Ethnicity and country of birth for CON children and parents were not routinely available. This chapter is reporting on a subset of patients recruited into the study, which precluded the ability to perform in depth analyses related to multiple ethnicity classifications and/or country of birth. Two categories for each variable were included: *Caucasian vs other ethnicity* and *Canada vs other countries* of birth.

3.2.3 Anthropometric Data

Weight and height of children with CD and CON were obtained from medical charts at time of clinic visit. All patients attending the CD and General Gastrointestinal clinics had weight and height measurements performed by trained individuals on the same scales. Weight was measured to the nearest 0.1 kg and height to the nearest 0.1 cm according to standard methodologies (188). Body mass index (BMI, kg/m^2) was calculated as the ratio between weight (kg) divided by height squared (m^2) (188). Weight, height, and body mass index were compared to normative pediatric data using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group; http://cpeg-gcep.net/sites/default/files/plotter/index.html) (216).

3.2.4 Laboratory and Histopathology Variables

At the time of CD diagnosis, children with CD underwent duodenal and/or jejunal biopsy to confirm diagnosis, as recommended by the American Gastroenterological Association (217). Marsh scores were collected from the endoscopy report. A Marsh score refers to the severity of enteropathy and depends on three main criteria: number of intraepithelial lymphocytes, presence of crypt hyperplasia and presence/severity of villous atrophy (217). Marsh scores vary from I, II, IIIA, IIIB or IIIC; a marsh score I refers to infiltrative lesions (normal mucosa contained intraepithelial lymphocytosis) and score III refers to intestinal atrophy (217). Serum ATTG level of children with CD and CON was collected at the time of routine clinical assessment. Serum ATTG levels above 7 U/mL were considered abnormal (66, 103).

3.2.5 Dietary Intake Assessment

The emphasis of dietary analysis in this thesis will be on assessing factors related to macronutrient intake and overall DQ as assessed by GI and GL (characteristics of carbohydrate quality/quantity), saturated fat, polyunsaturated and monounsaturated fatty acid (fat quality), % acceptable macronutrient distribution, use of DQ tools and food guide servings, rather than micronutrient intake. Dietary intake was assessed using two multi-pass 24-hour recalls (one weekday, one weekend day) conducted by trained interviewers (218). Macronutrient intake was analyzed using Food Processor (SQL 10.15 ESHA® Research, Salem, OR, USA). The brand names of consumed GF foods were collected and analyzed for macro and micronutrients content. Macronutrient intake was compared to the age-and gender-specific DRI (219, 220).

Food group consumption was determined based on the age-and gender-specific Alberta Nutrition Guidelines for Children and Youth (ANGCY) (77). The 95% of confidence interval of the ratio of energy intake to Basal Metabolic Rate was calculated to assess misreporting

(under/over) of energy intake (221). Values below the 95% of confidence interval were considered under-reported energy intake and values above the 95% of confidence interval were considered over-reported energy intake (221).

3.2.6 Adherence to Gluten-Free Diet

Adherence to the GFD was assessed in three ways: 1) self-reported adherence to GFD (KINDL® test), 2) gluten intake (<10 mg/day) as estimated in 24-hour recalls, and 3) serum ATTG levels (levels <7 U/mL). One flaw with using serum ATTG levels to assess adherence is that abnormal serum ATTG levels can occur up to 2 years post-diagnosis in children and, hence, this was only done in children who had a CD where diagnosis >1 year (135, 222). In addition, ATTG levels can be normal even in the face of non-adherence to the GFD (or with gluten cross contamination) as they reflect recent gluten intake and are affected by the degree of chronic intestinal damage (135, 222). In general, practitioners assess response to the GFD and adherence by changes in ATTG levels over time for the individual patient.

3.2.6.1 Estimation of Gluten Intake

Gluten intake was assessed in both GF foods and gluten-containing food. In the US and Canada, GF processed foods should not exceed 20 ppm (20 mg per 1 kg of food) of gluten due to cross-contamination (118). Our assumption was that the GF food had 20 mg of gluten per 1 kg of food, as previously described (118). For gluten-containing grains, gluten content was calculated as reported by the *Osborne method*, which states that 80% of protein in grains is gluten. We multiplied 0.8 by the amount of protein in gluten-containing grains (223). The gluten content of "mixed foods" (foods falling into more than one food groups, as defined by ANGCY) was calculated by estimating the number of servings of grains using the Canadian Diabetes Association exchange system, with the assumption that one exchange from grains weights around 30 g (223).

For GF mixed foods, we multiplied the number of servings from grains by 30g to estimate the weight of GF foods in g and then multiplied by 20 mg and divided by 1000 g to estimated gluten content (mg) in GF foods. For gluten-containing grains, we assumed that 1 serving of grains contains 2 g of protein and then we multiplied the estimated protein in grains by 0.8 to estimate gluten content (g) in gluten-containing foods (223).

3.2.7 Glycemic Index and Glycemic Load

The GI and GL of each food was calculated using GI values from Foster-Powell 2002 and Atkinson 2008 (96, 97). The GI of each food item was calculated by multiplying the GI value of each food item by the amount of carbohydrate of that food item (g) divided by the total carbohydrates (g) (87). The GL of each food item was calculated by multiplying the GI value of each food item by the amount of carbohydrate for that food item (g), divided by 100 (87, 97). The GI and GL values of each participant's diet was calculated as the sum of the GI and GL for each food item (87). Diets with GI values ≥70, between 69-54, and ≤55 are classified as high, medium, and low GI, respectively (87, 96, 97, 224). Diets with GL ≥120, between 80-119, and <80 are classified as high, medium, and low GL, respectively (87) (**Appendix A).**

3.2.8 Diet Quality Tools: Healthy Eating Index-Canada, Dietary Guideline Index for Children and Adolescents and Diet Quality Index-International

The Healthy Eating Index-Canada (HEI-C), Dietary Guideline Index for Children and Adolescents (DGI-CA), and Diet Quality Index-International (DQI-I) are DQ tools which have been used to measure overall DQ in children and adolescents (16, 31, 35, 74, 225, 226). This thesis will focus on assessing overall DQ using DQ tools and assessing macronutrient intake (quantity and quality), food groups, GI and GL. DQ scores range from 0-100 where a score of 100 refers to the "optimal" DQ (16, 31, 35). To ensure that these DQ tools were reflective of Canadian nutrient reference intakes, and Canadian nutritional recommendations, each DQ tool was modified to

incorporate these recommendations (**Appendix A, Table A-1** to **A-3)**. This methodology has been used previously for existing DQ tools and been shown to be more reflective of individual national nutritional standards (35, 69, 77, 220, 227, 228). Bland Altman Analysis and Intra Class Correlation (ICC) were performed to determine the level of agreement between the adapted vs non-adapted DQ tools (**Appendix B, Figures B-1** to **B-3** and **Table B-1).**

The HEI-C is the Canadian version of HEI, which measures the number of servings consumed from each food group, total fat, saturated fat and cholesterol (35, 225). HEI-C scores ≤50, 51-80 and >80 refers to poor DQ, as the diet 'needs improvement' and good DQ, respectively (35, 225). We have modified the HEI-C (**Appendix A, Table A-1)** as follows:

1. Food group recommendations are based on the age- and gender-specific ANGCY (77).
2. The cut-off values for fat (30-40%), saturated fat (7-10%) and cholesterol (300-400 mg) intake were changed to reflect the recommendations of the DRI and the Food and Agriculture Organization of the United Nations (FAO) for children 3-18 years (220, 227).
3. The "variety" component was adapted to meet at least 0.5 servings from each food group: 2 scores for milk and alternatives, 2 scores for grain products, 2 scores for meat and alternative, and 4 scores for fruit and vegetables. The changes were made due to the recommended number of servings of meat and alternative in children <9 years was one serving and this would have caused duplication in the scores (4, 31).

The DGI-CA is a validated tool for children and adolescents to evaluate the adequacy (food groups and *other food*) and food choices (whole grain bread, reduced fat dairy, healthy fat, variety) in their diet (31, 74). Diets were categorized as good (DGI-CA scores >68), needs improvement

(DGI-CA scores between 55-68), and poor DQ (DGI-CA scores ≤54) (31, 74). The main adaptation of DGI-CA was that number of food group servings were based on age- and gender-specific ANGCY (77). In addition, the "beverage" score was modified as follows: maximum score (10) if there is no consumption of sweetened beverages, minimum score (0) if there is no drinking water, and a score of 5 if there is consumption of sweetened beverages. The modification of the DGI-CA is shown in **Appendix A, Table A-2** (31, 69, 77, 220, 227, 228).

The DQI-I assesses Variety (overall variety and variety within protein sources), Adequacy (fruit and vegetables, grain, percent protein, fibre, calcium, iron, sodium and vitamin C), Moderation (percent of total fat and saturated fat and cholesterol) and overall diet balance (macronutrients ratio and saturated fat, polyunsaturated fat and monounsaturated ratio) (16). Good DQ was considered as DQI-I scores ≥60 (226). DQI-I was modified (**Appendix A, Table A-3**) (16, 69, 77, 220, 226-229) as follows:

1. Food group recommendations based on age- and gender-specific ANGCY (77). Fruit and vegetables grouped as one component and the scoring system of food groups was changed to scaled-based.
2. The "overall food group variety" component was adapted to meet at least 0.5 servings of each food group.
3. The cut-off values for fat (30-40%), saturated fat (7-10%) and cholesterol (300-400 mg) and sodium (2400-3400 mg) intake were modified based on the DRI and the Food and Agriculture Organization of the United Nations (FAO) for children 3-18 years (220, 227).
4. The cut-off value of "empty calories" was altered based on the HEI-C cut-off values, the number of servings from *other foods* in the HEI-C.

3.2.9 Health Related Quality of Life Variables: Generic Tools and Celiac Disease Specific Tools

Figure 3-1 illustrates the different types of HRQOL tools (and domains) used in the current study (230-232). Both disease specific and generic HRQOL tools were used (230-232). All HRQOL tools were previously validated for assessment of HRQOL in parents and children (230-232). The use of generic tools and disease specific tools enabled a comprehensive assessment of the potential factors affecting HRQOL in children with CD. Many of these disease specific tools address the presence/absence of GS, dietary adherence to GFD, and how these factors affect psychosocial domains in a variety of environments such as school and social gatherings (230-232) **(Figure 3-1 and 3-2)**. The generic and CD specific HRQOL tools all share some components such as an evaluation of psychosocial domains of HRQOL as shown in **Figure 3-2.** These are important to ensure a comprehensive evaluation of the factors influencing HRQOL in children and adolescents with chronic gastrointestinal diseases.

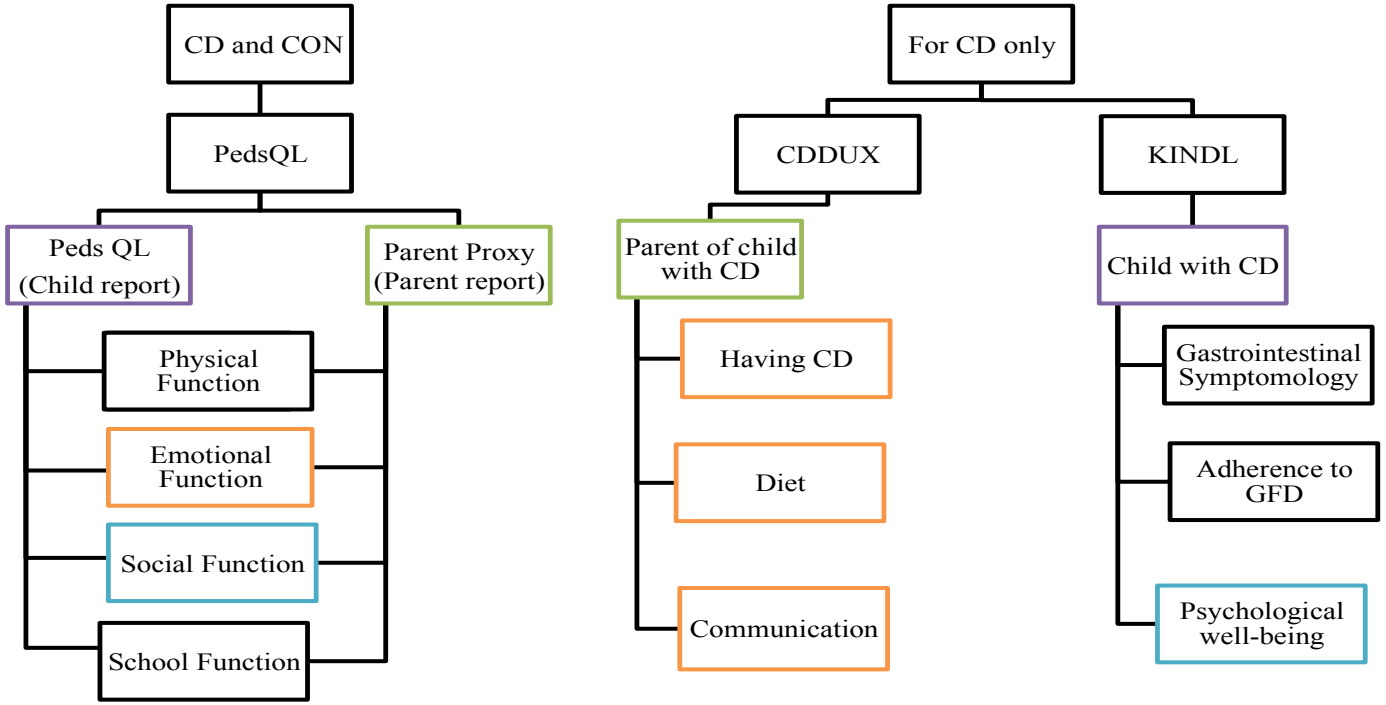


Figure 3–1: The Health Related Quality of Life Tools. The Generic [PedsQL™ 4.0 Generic Core Scales (PedsQL)] and Disease Specific [Celiac Disease DUX (CDDUX) and Celiac Disease Quality of Life Scale (KINDL)] Quality of Life Tools used in the Current (Celiac Disease) study (230-232). Boxes highlighted in the same color indicate similar concepts that are addressed within each tool.
Abbreviations: CD, Celiac Disease; CON, disease control; GFD, Gluten-free diet.

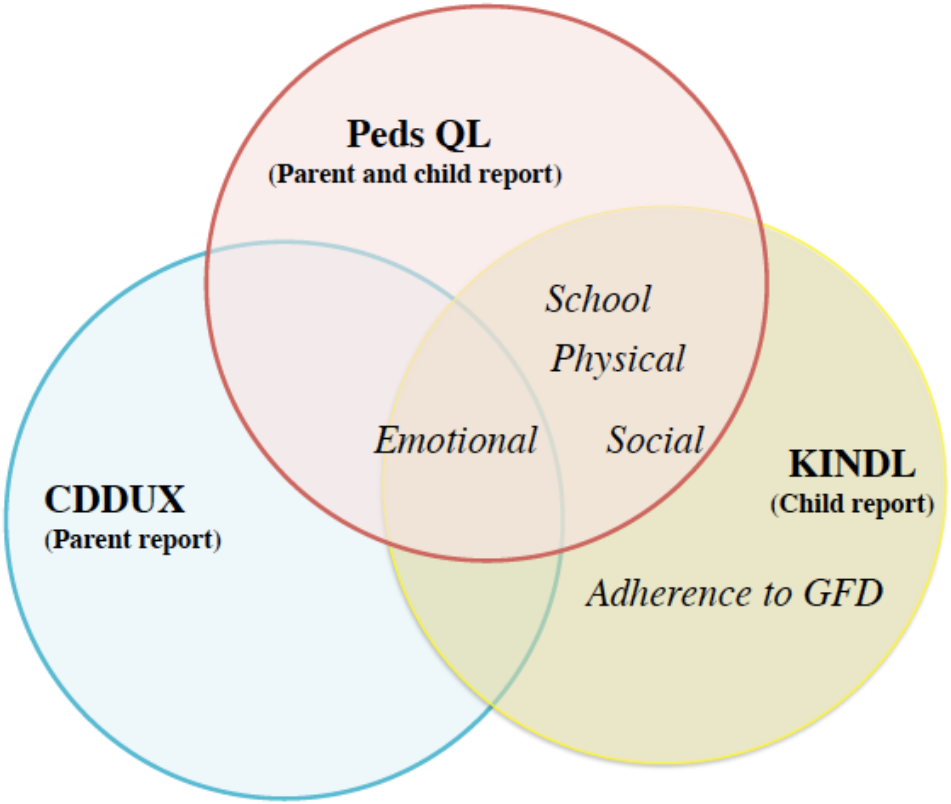


Figure 3–2: The Interrelationships between Health Related Quality of Life Tools. The Interrelationships between Generic [PedsQL™ 4.0 Generic Core Scales (PedsQL)] and Disease Specific [Celiac Disease DUX (CDDUX) and Celiac Disease Quality of Life Scale (KINDL)] Quality of Life Tools (230-232).
Abbreviations: CD, Celiac Disease; CON, disease control; GFD, Gluten-free diet.

3.2.9.1 Generic Quality Of Life Tools: PedsQL™ 4.0 Generic Core Scales and PedsQL ™ Gastrointestinal Symptom Scale

The *PedsQL ™ 4.0 Generic Core Scales* is the most common tool to assess HRQOL from both child (PedsQL™ V4.0) and parent/caregiver (Parent Proxy Report of the PedsQL) perspectives (230). It was validated in healthy children and children with chronic health conditions such as asthma and diabetes (230). This questionnaire has the same questions for children and their parents but is worded to be appropriate for the developmental stage of children based on age (5-7 years, 8-12 years, 13-18 years) (230). We chose to assess HRQOL from both toddler's, children's and adolescent's and parent's perspectives for several reasons. First, a child's perception of HRQOL may change from childhood to adolescence (233, 234). Second, it has been reported in many studies that the perception of HRQOL in parents of children with chronic disease is usually lower than children with chronic disease because the parents of children with chronic disease may experience emotional, social, and financial challenges, which results in reduced HRQOL for families in households of children with chronic diseases (233-235). Third, child age, domains investigated, and parents' own HRQOL are factors influencing the child's perspectives of HRQOL (233, 234, 236). The PedsQL questionnaire (child report and parent proxy report) does not include the toddler age (2-4 years); therefore, the PedsQL questionnaire was not collected for children younger than 5 years old (230). Scores ranged from 0-100, where a higher value indicates better HRQOL (230). The score of each domain was calculated as the average of the related questions. The psychosocial domain was calculated as the average of the social, emotional, and school domains (230). The score of each domain was compared to norms of healthy children (230, 237). Scores 1 SD below the norm of healthy children were considered at risk status for impaired HRQOL (230, 237).

The PedsQL™ Gastrointestinal Symptom Scale (GSS) is a validated tool that was completed by the parents and used to evaluate functional gastrointestinal symptoms (GS) over the past month (238, 239). The GSS contains 9 GS subcategorizations: (abdominal pain, diarrhea, constipation, nausea, vomiting, discomfort in the abdomen or stomach, passing gas, not feeling hungry, and bloating). Each GS subcategorization was scored from 0 to 100 with lower scores referring to worse GS and a score of 100 referring to no GS (238). The average score of all GS was calculated and the analysis was run to examine the average score and scores related to each individual GS subcategorization. We chose the GSS because it is a quick tool and has been used in other gastrointestinal populations. The internal consistency reliability of GSS was high (α = 0.77) and was correlated with PedsQL™ 4.0 Generic Core Scales (child report and parent proxy) (238). The internal consistency reliability measures the agreement between multiple test items referencing the same construct or idea.

3.2.9.2 Celiac Specific Quality Of Life Tools: Celiac Disease DUX and Celiac Disease Quality of Life Scale

In order to explore factors that are specific to a diagnosis of CD that influence overall HRQOL, we also used two validated disease-specific tools used to assess HRQOL for the CD group were the Celiac Disease DUX (CDDUX) questionnaire and the KINDL® Quality of Life Scale for children with CD (KINDL). The CDDUX questionnaire focuses on three main aspects of emotional HRQOL: having CD, communication and diet (240). The scores ranged from 0-100 with a higher score reflecting higher HRQOL (240). CDDUX scores were categorized as very bad HRQOL (1-20), bad HRQOL (21–40), neutral HRQOL (41–60), good HRQOL (61–80), and very good HRQOL (81–100) (240). The KINDL test is a validated tool for use in children older than 6 years who have CD and it covers different aspects of disease-related HRQOL including the concepts related to adherence to the GFD, presence of GS, and psychosocial well-being such as

social activities (232).

3.2.10 Statistical analysis

Data analysis was completed using SAS 9.0 statistical software (SAS, Version 9.4; SAS Institute Inc., Cary, NC, USA). A p-value <0.05 was considered significant. Data were expressed as mean ± standard deviation (SD) or median and interquartile range (IQ), unless otherwise specified. The Shapiro-Wilk test was conducted to assess the normality of distribution. Independent T-Tests were conducted to compare the mean between study groups. For data demonstrating skewed distributions, a Mann Whitney test was performed. Fisher's exact test was used to measure the differences in categorical data. Two statistical analyses were conducted to assess the agreement between the adapted and not adapted DQ tools: 1) Bland Altman analysis (**Appendix B, Figure B-1** to **B-3)** and 2) two-way mixed effect model (absolute agreement, single measure) ICC in both groups (**Appendix B, Table B-1)** (236, 241). The strength of the agreement between adapted vs non-adapted DQ tools was classified based on ICC scores; ICC ≤ 0.40 refers to fair agreement, 0.41–0.60 refers to moderate agreement, 0.61–0.80 refers to good agreement, and 0.81–1.00 refers to excellent agreement (241).

To assess the effect of misreporting energy intake and macronutrient intake, GI, GL, and DQ scores, one-way Anova tests followed by Bonferroni tests were conducted between adequate reporters, under and over-reporters (**Appendix C, Table C-1**). Bonferroni test p-values of <0.01 were considered significant. Comparison in HRQOL scores between CD/CON and norms of healthy children was evaluated using a one sample T-Test and one sample median (Wilcoxon sign) test for skewed variables. Agreement between child report HRQOL and parent proxy report of HRQOL was assessed using median difference testing using Wilcoxon sign test (**Appendix D, Table D-1**) (236, 241).

For primary analysis (HRQOL, DQ scores, GI and GL), two-sample independent t-tests or Mann Whitney tests were conducted to compare the statistical differences between CD and CON for normally distributed variables and variables demonstrating skewed distributions, respectively. For secondary analysis, the focus of this analysis was to examine the interrelationships within the CD group, as the smaller sample size in this thesis analysis precluded the ability to assess a group effect (**Appendix E, Table E-1** for power analysis). In addition, the analyses related to HRQOL included Peds QL and CDDUX, rather than a focus on KINDL® results. Within the CD group, an analysis examining the interrelationships between socio-demographic (age at diagnosis, CD duration, ethnicity) and HRQOL assessments was done. In the entire cohort, we assessed interrelationships between socio-demographic (gender, GSS) and anthropometric factors and HRQOL assessments.

Multivariate analysis was conducted to examine interrelationships between HRQOL and the potential confounders including age, age at diagnosis, disease duration, gender, ethnicity, parental age, parental educational level, income, and GSS. In this thesis chapter, the association of each GS within the GSS, with HRQOL and DQ was examined. The GS (abdominal pain, constipation, discomfort in abdomen or stomach) were categorized to never, almost never or sometimes, often, often always (**Appendix F, Figure F-1**). Potential confounding variables were dichotomized parents' educational level (high school and registered apprenticeship vs college and university) and by median value: age (≥ and <9 years), age at diagnosis (≥ and <7 years), disease duration (≥ and <1 year), GSS (≥ and <64) parents' age (mothers ≥ and <39 and fathers ≥ and <43), and income (≥ and < $81,836/year). Skewed variables were log10 transformed. Due to small sample size, especially in the CD group, we did not include the effect of study group in models, as there was insufficient power to justify this approach to a multivariate analysis. Hence, we grouped

all data together. To assess the effects of DQ, GI, and GL on HRQOL, dichotomized of DQ, GI and GL were based on the cut-off values for poor DQ (DGI-CA [≥ and <55] and DQI-I [≥ and <60]) and the cut-off value of high and low GI and GL (GI [≥ and <55], GL [≥ and <120]). Due to the lack of power to detect any associations between HRQOL and HEI-C, we have chosen the median value as a cut-off value HEI-C (≥ and <66).

3.3 Results

3.3.1 Recruitment

This study is an ongoing multi-site study. This thesis will present data from the first 80 participants recruited at the Stollery Children's site only. One CON child where a diagnosis of CD was ruled out using conventional testing, was excluded from overall analysis as they were following a GFD (non-prescribed). Therefore, results in this chapter represent data from n=30 CD children/parents and n=49 CON children/ parents.

3.3.2 Socio-demographic Data

Table 3-1 presents the socio-demographic data in children with CD and CON. This thesis will present data from 30 children with CD (Male=8, Female=22) and 49 CON (Male=16, Female=33; p=0.62). The main indications for clinic visit in the CON group were abdominal pain (n=12; 24%), constipation (n=6, 12%), diarrhea (n=2; 4%), gastroesophageal reflux disease (n=6, 12%), multiple reasons such as abdominal pain and diarrhea (n=9; 18%), or other conditions (n=14; 29%).

Among children with CD, the mean age at time of CD diagnosis and duration of CD was 7.8 ± 3.5 years and 1.4 ± 0.9 years, respectively. Approximately 44% of children with CD (n=8) reported a positive family history of CD. The majority of children with CD were *Caucasian* (n=19; 68%) and born in *Canada* (n=26; 96%). The majority of children from *other ethnicity* were *South*

Asian. The majority of parents (mothers and fathers) with CD were *Caucasian* (n=21; 72%) and born in *Canada* (mothers, n=19; 68% and fathers, n=21; 72%). No significant differences were found in age, age at diagnosis, or duration of CD between *Caucasian* children compared to children of *other ethnicity* (p>0.05).

Table 3-1: Socio-Demographic Data in Children with Celiac Disease and Disease Controls

	CD (n=30)	CON (n=49)	p- value[1]
Mother's Age (years)[2]	40 ± 6	39 ± 6	0.35
Mother's Education level (%)[3]			
High School	28	35	
University	60	24	0.01
College	8	42	
Registered Apprenticeship	4	0	
Father's Age (years)[4]	43 (37-45)	42 (37-47)	0.73
Father's Education level (%)[3]			
High School	4	23	
University	60	23	<0.01
College	36	32	
Registered Apprenticeship	0	23	
Number of children in household[4]	2 (2-2)	2 (1-3)	0.14
Income (CAN$/year)[4]	81,836 (77,779-103,87)	84,807 (81,592-99,979)	0.29

[1]p-values <0.05 are considered statistically significant.
[2]Normally distributed variables are presented as mean ± standard deviation. Two-sample Independent t-test was conducted to compare the statistical differences between CD and CON.
[3]Variables are frequency and are presented as percentage.
[4]Variables demonstrating skewed distributions are presented as median (interquartile range). Mann Whitney tests were preformed to measure the statistical differences between CD and CON.
Abbreviations: CD, Celiac Disease; CON, disease control.

3.3.3 Anthropometric Data

Anthropometric data for children with CD and control group are presented in **Table 3-2**. Children with CD had significantly lower wt-z, BMI and BMI-z compared to the control group (p<0.05). Among children with CD, *Caucasian* children (0.37 ± 0.92) had significantly higher BMI-z than children from *other ethnic* backgrounds (-0.65 ± 1.20); p=0.02). No significant difference was found in wt-z (*Caucasian*: 0.18 ± 0.85 vs *other ethnicity*: -0.58 ± 1.15; p= 0.06) and ht-z (*Caucasian*: -0.22 ± 0.86 vs o *other ethnicity*: -0.38 ± 1.16); p=0.69) between children from *Caucasian* ethnicity and children from *other ethnicity*.

Table 3-2: Anthropometric Data in Children with Celiac Disease and Disease Controls

	CD (n=30)	CON (n=49)	p- value[4]
Age (year) [1]	9.1 ± 3.4	10.2 ± 4.3	0.24
Weight (kg)[2]	27.9 (22.4-34.0)	33.9 (21.9 -58.5)	0.11
Weight-for-age z-score[1,3]	-0.07 ± 1.00	0.57 ± 1.16	0.02
Height (cm) [1]	131 ± 20	137 ± 24	0.21
Height-for-age z-score[1,3]	-0.29 ± 0.98	0.11 ± 1.15	0.13
BMI (kg/m^2)[2]	16.7 (15.3-17.8)	19.4 (16.1-22.4)	0.01
BMI-for-age z score[1,3]	0.05 ± 1.08	0.73 ± 1.15	0.01

[1]Normally distributed variables are presented as mean ± standard deviation. Two-sample Independent t-test was conducted to compare the statistical differences between CD and CON.
[2]Variables demonstrating skewed distributions are presented as median (interquartile range). Mann Whitney tests were preformed to measure the statistical differences between CD and CON.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (216).
[4]p-values <0.05 are considered statistically significant.
Abbreviations: BMI, body mass index; CD, Celiac Disease; CON, disease control.

3.3.4 Laboratory and Histopathology Data

The median ATTG levels were 3U/mL (IQ= 1-9 U/mL) in children with CD. All CON children had ATTG levels <1 U/mL. Only 30% (n=8) of children with CD had ATTG levels >7 U/mL; no CON children had elevated ATTG levels. In children with CD, no significant differences were found between children with CD for ≥ and <1 year and between children with CD and from *Caucasian* ethnicity and children with CD from *other ethnicity* (p>0.51). The majority of children with CD (n=21; 81%) had Marsh scores of IIIA (n=11), IIIB (n=3), or IIIC (n=7).

3.3.5 Dietary Intake: Macronutrient Intake

Table 3-3 represents macronutrients intake in children with CD and the control group. The majority of the cohort (n=42; 65%) had two days 24-hour food recall completed; the remaining had one. No significant differences were observed in energy (one day: 1512 ± 355 kcal vs two days: 1622 ± 397 kcal), protein (one day: 63 ± 19g vs two days: 65 ± 21g), carbohydrate (one day: 203 ± 53g vs two days: 214 ± 55g), and fat (one day: 52 ± 19g vs two days: 58 ± 20g) between participants with 1 (weekday) vs 2 days (weekend and weekday) 24-hour recall, respectively (p>0.05). Polyunsaturated Fatty Acid intake was significantly lower in CD group compared to the

CON (p<0.01), likely secondary to low intake of Canola oil. The energy intake to Basal Metabolic Rate ratio was significantly higher in children with CD (1.5 ± 0.3) compared to CON (1.3 ± 0.4; p=0.02). However, the rates of under-reporting (CD: 39% (n=11) vs CON: 38% (n=13)) and over-reporting (CD: 28% (n=8) vs CON: 32% (n=11)) of energy intake did not differ between groups (p>0.05). Misreporting of dietary intake had no effect on assessments of macronutrient intake as percent of kcal (p>0.05) (**Appendix C, Table C-1)**. The majority of children (n=19; 70%) were adherent to the GFD (ATTG <7) and therefore an assessment of the effects of adherence to the GFD and nutrient intake was not performed in this analysis.

Table 3-3: Dietary Intake in Children with Celiac Disease and Disease Controls

	CD (n=28)	CON (n=37)	AMDR or RDA/AI	p-value[3]
Energy (kcal)[1]	1670 ± 373	1517 ± 383	-	0.11
Protein (g)[1]	66 ± 22	62 ± 19	13-52[4]	0.43
% Protein[2]	15 (13-18)	17 (14-19)	5-30[5]	0.43
Carbohydrate (g)[1]	219 ± 48	203 ± 58	130[4]	0.25
% Carbohydrate[1]	53 ± 8	54 ± 6	45-65[5]	0.82
Fibre (g)[2]	14 (10-19)	14 (11-17)	19-38[6]	0.73
Fat (g)[1]	60 ± 22	53 ± 16	-	0.13
% Fat[2]	33 (27-37)	33 (27-37)	25-40[5]	0.32
SFA (g)[2]	19 (15-32)	19 (13-25)	-	0.35
% SFA[1]	12 ± 3	11 ± 3	10	0.69
PUFA (g)[2]	5 (3-9)	9 (6-10)	-	0.01
% PUFA[2]	3 (2-4)	5 (4-6)	10	<0.01
MUFA (g)[1]	17 ± 8	19 ± 7	-	0.38
% MUFA[1]	9 ± 3	11 ± 3	10	0.01
Cholesterol (mg)[2]	234 (122-305)	164 (114-199)	-	0.08

[1]Normally distributed variables are presented as mean ± standard deviation. Two-sample Independent t-test was conducted to compare the statistical differences between CD and CON.
[2]Variables demonstrating skewed distributions are presented as median (interquartile range). Mann Whitney tests were preformed to measure the statistical differences between CD and CON.
[3]p-values <0.05 are considered statistically significant.
[4]Recommended Daily Allowance (RDA). [5]Acceptable Macronutrient Distribution Range (AMDR). [6]Adequate Intake (AI).
Abbreviations: CD, Celiac Disease; CON, disease control; PUFA; Polyunsaturated Fatty Acid, MUFA; Monounsaturated Fatty Acid; SFA, Saturated Fatty Acid.

3.3.6 Food Groups according to the Alberta Nutrition Guidelines for Children and Youth

Data regarding the dietary intake of food group servings (ANGCY) are presented in **Table 3-4**. No significant differences were found in the number of children meeting the recommended

grain (CD=13; 46% vs CON=17; 46%) fruit and vegetables (CD=5; 18% vs CON=11; 30%), milk and alternatives (CD=9; 32% vs CON=11; 30%) and meat and alternatives (CD=22; 79% vs CON=23; 62%) servings between CD and CON, respectively ($p>0.05$). For the entire cohort, children who under-reported dietary intake (EI/BMR < lower 95th confidence interval) had significantly lower intakes of grains products (3.9 ± 1.3) compared to over-reporters (5.7 ± 1.9, $p<0.01$) (**Appendix C, Table C-1**).

Table 3-4: Food Group Intake in Children with Celiac Disease and Disease Controls based on The Alberta Nutrition Guidelines for Children and Youth

	CD (n=28)	CON (n=37)	Recommended Intake[3]	p-value[4]
Grain Products[1]	5.1 ± 2.2	4.5 ± 1.5	3-6	0.21
Fruit and Vegetables[1]	4.2 ± 2.5	4.2 ± 2.1	4-7	0.96
Milk and Alternatives[1]	2.3 ± 1.2	2.0 ± 1.2	2-4	0.28
Meats and Alternatives[2]	1.9 (1.4-2.5)	1.5 (1.1 – 2.3)	1-3	0.31

[1]Normally distributed variables are presented as mean ± standard deviation. Two-sample Independent t-test was conducted to compare the statistical differences between CD and CON.
[2]Variables demonstrating skewed distributions are presented as median (interquartile range). Mann Whitney tests were preformed to measure the statistical differences between CD and CON.
[3]Recommended intake based on the Alberta Nutrition Guidelines for Children and Youth (ANGCY) (77).
[4]p-values <0.05 are considered statistically significant.
Abbreviations: CD, Celiac Disease; CON, disease control.

3.3.7 Estimation of Gluten Intake and Adherence to the Gluten Free Diet

Self-reported adherence to GFD by KINDL test was found in 96% of children with CD (n=22) (**Figure 3-10 C**). The median intake of gluten in children with CD (median= 3, IQ= 2 - 5 mg/day) was significantly lower than the control group (median= 9034, IQ= 6100 - 1278 mg/day; $p<0.01$). No significant difference was found in gluten intake between children who misreported vs adequate reported dietary intake ($p>0.05$; **Appendix C, Table C-1**). All children with CD consumed <8 mg/day of gluten indicative of acceptable levels of gluten intake (<10 mg/day) on the GFD (**Figure 3-3)** (118). Gluten intake was not significantly different between children of different ages (≥ and <9 years) or gender ($p>0.05$). Among children with CD, there was no significant difference in gluten intake by age at diagnosis (≥ and <7 years) or duration of the disease (≥ and < 1 year) ($p>0.05$). Gluten intake was not significantly different between children with CD from *Caucasian* ethnicity (median= 3, IQ= 2-4 mg/day) and children with CD from *other*

ethnicities (median= 3, IQ= 3-3 mg/day) mg/day; p>0.05). Among children with CD, gluten intake was not significantly different between children with CD and GS (median= 3, IQ= 2-3 mg/day) and children with CD with no GS (median=3, IQ= 3-4 mg/day; p>0.05). Gluten intake was inversely correlated with ATTG levels (r^2=0.16) and GSS (r^2= 0.24) (p<0.01).

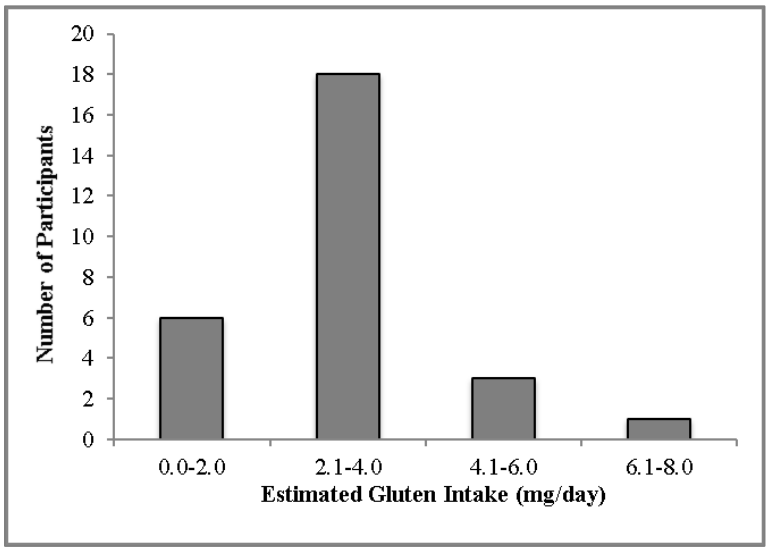


Figure 3–3: Estimated Gluten Intake (mg/day) Distribution in Children with Celiac Disease (n=28). Estimated gluten intake was calculted as described La Vieille et al (2014) (118).

3.3.8 Glycemic Index and Glycemic Load

Figure 3-4 demonstrates GI and GL intake in children with CD and CON. **Figure 3-5** displays the proportion of children with high and low GI and GL intake in children with CD and CON. No significant difference was found in GI or GL between adequate and misreporting (over and under-reporter) children (p>0.05; **Appendix C, Table C-1**).

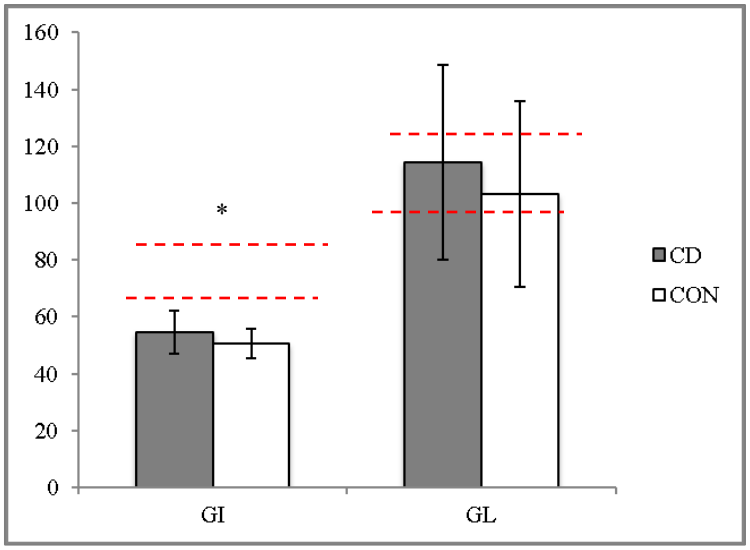


Figure 3–4: Glycemic Index and Glycemic Load Intake in Children with Celiac Disease (n=28) and Disease Controls (n=37). Data are presented as mean ± standard deviation. Dashed red lines represent the cut-off values of high, medium and low GI ≥70, between 69-56, and ≤55 and GL ≥120, between 80-119, and <80, respectively (96, 97, 224). An asterix (*) represents a significant difference between children with CD and CON (p=0.01).
Abbreviations: CD, Celiac Disease; CON, disease control; GI, Glycemic index; GL, Glycemic load.

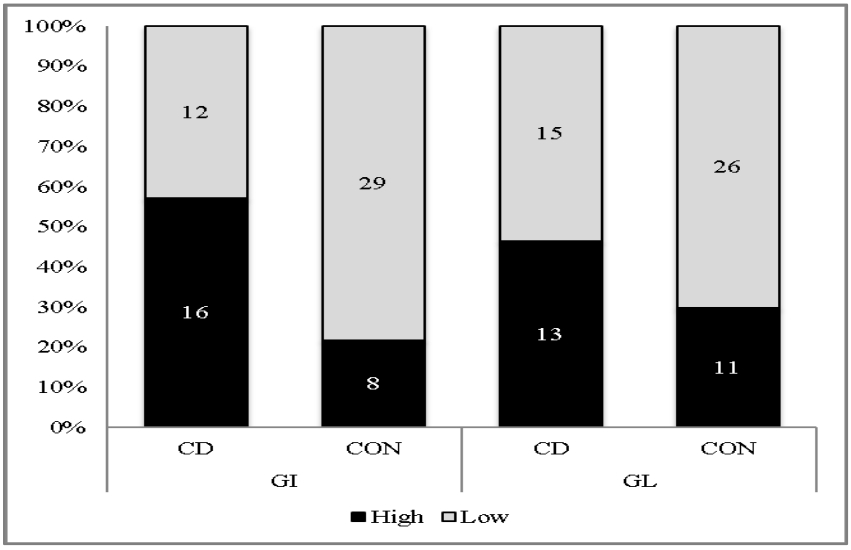


Figure 3–5: Proportion of Children with High and Low Glycemic Index and Glycemic Load Intake in Children with Celiac Disease (n=28) and Disease Controls (n=37).
Glycemic index scores (≥ vs < 55; p<0.01) and glycemic load scores (≥ vs < 120; p=0.21) (96, 97, 224).Values inside the bars are the n number of each group. Values with an asterix (*) represent significant differences between groups (p<0.05).
Abbreviations: CD, Celiac Disease; CON, disease control; GI, Glycemic index; GL, Glycemic load.

3.3.9 Diet Quality Scores: Healthy Eating Index-Canada, Dietary Guideline Index for Children and Adolescents and Diet Quality Index-International

Bland Altman analysis was conducted to assess the level of agreement between adapted and non-adapted DQ tools in both CD and CON groups, wherein the majority of values presented within 2 SD **(Appendix B, Figures B-1** to **B-3).** On average, there was a 1.5-3.6 scores difference between adapted vs non-adapted DQ tools in both CD and CON. The ICC analysis outlines that perfect agreement (ICC>0.8) between the adapted and non-adapted DQ tools in both CD and CON groups ($p<0.01$; **Appendix B, Table B-1).**

Figure 3-6 represents the HEI-C, DGI-CA, and DQI-I scores in children with CD and CON. More than 40-60% of children with CD and CON had poor DQ score (**Figure 3-7)**. No significant differences were found in the proportion of children with low vs high HEI-C and DGI-CA between children with CD and CON ($p>0.05$). Under-reporter children (61 ± 10) had significantly lower HEI-C scores than adequate reporters (70 ± 10) and over-reporter children (70 ± 8; $p<0.02$) (**Appendix C, Table C-1)**.

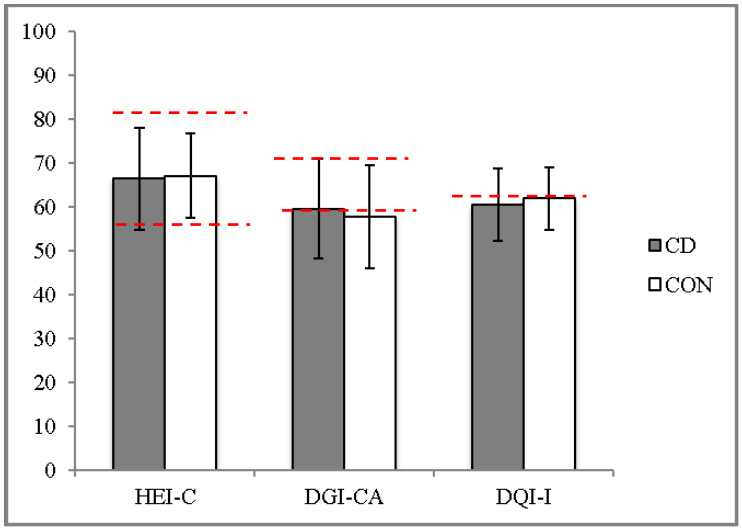


Figure 3–6: Diet Quality Scores in Children Celiac Disease (n=28) and Disease Controls (n=37). Data are presented as mean ± standard deviation. Red lines represent the cut-off values of "good", "needs improvement" or "poor" diet quality. HEI-C scores were categorized as good (>80, needs improvement (HEI-C scores 51-80), and poor diet (≤50) (35). DGI-CA scores were categorized as good (>68), needs improvement (55-68), and poor diet (<55) (31, 74). DQI-I scores were categorized as good (≥60), and poor diet (<60) (226).
Abbreviations: CD, Celiac Disease; CON, disease control; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; HEI-C, Healthy Eating Index-Canada.

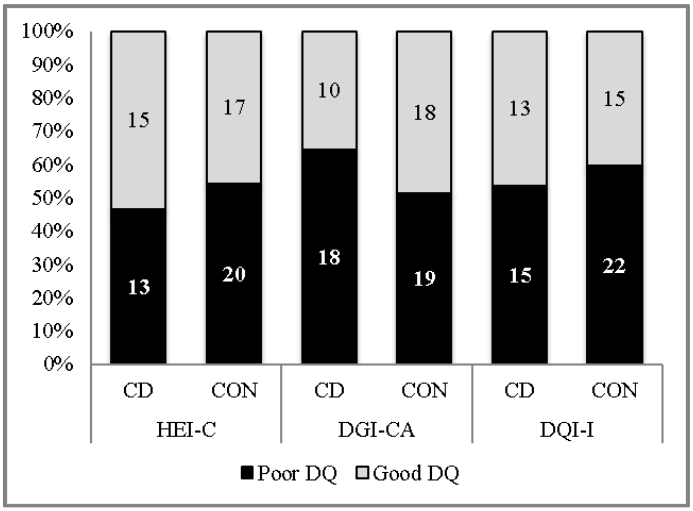


Figure 3–7: Proportion of Good vs Poor Diet Quality Scores in Children with Celiac Disease (n=28) and Disease Controls (n=37). HEI-C scores (good ≥ 66 vs poor< 66), DGI-CA scores (good ≥ 68 vs poor< 68), and DQI-I scores (good ≥ 60vs poor< 60). Values inside the bars are the n number of each group. No significant differences were found in the proportion of children with poor vs good DQ score between HEI-C, DGI—CA, and DQI-I tools (p=0.49).
Abbreviations: CD, Celiac Disease; CON, disease control; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQ, Diet quality; DQI-I, Diet Quality Index-International; HEI-C, Healthy Eating Index-Canada.

3.3.10 Interrelationships between Dietary Analysis (Macronutrient, Glycemic Index, Glycemic Load, Gluten Intake, Dietary Adherence To The Gluten-free Diet) with Socio-Demographic (Age of Diagnosis, Duration of Celiac disease, Ethnicity), and Anthropometric

A) CD and CON

No significant differences in GI and GL intakes were found based on age (≥ and < median 9 years), mother's age (≥ and < median 39 years), parents' educational level (high school and registered apprenticeship vs college and university) ($p>0.05$; **Appendix C, Table C-4, C-6 and C-7**). Father's age (≥43 year) was associated with higher GL intake ($p<0.01$; **Appendix C, Table C-5**). GI intake was significantly higher in children with lower (< $81,836/year) compared to children with higher income (≥$81,836/year) ($p=0.03$; **Appendix C, Table C-8**). Females (102 ± 30) had lower GL than males (124 ± 38; $p=0.02$). GL intake ($p=0.02$) was associated with gender ($p=0.03$) and age (≥ and <9 years) ($p=0.02$).

B) Children with CD

No significant differences were found in GI and GL between age at diagnosis above and median (≥ and <7 years). GL was significantly higher in *Caucasian* children (n=18; 124 ± 27) than children from *other ethnicities* children (n=8; 91 ± 40; $p=0.01$). Children diagnosed with CD ≥1 year (n=13; 58 ± 7) had significantly higher GI than newly diagnosed children (duration of CD <1year) (n=15; 52 ± 7; $p=0.045$).

3.3.11 Interrelationships between Diet Quality Scores (Healthy Eating Index-Canada, Dietary Guideline Index for Children and Adolescents and Diet Quality Index-International) and Socio-Demographic Factors (Gender, Age, Age of Diagnosis, Duration of Celiac Disease, Ethnicity), and Anthropometric Data

A) CD and CON

No significant differences were found between gender, mother's age (≥ and <39 years), father's age (≥ and <43 years), parents' educational level (high school and registered apprenticeship vs college and university), income (≥ and < $81,836/year) and DQ tools (HEI-C,

DGI-CA and DQI-I) (p>0.05) (**Appendix C, Table C-4** to **Table C-8**). Children ≥9 years of age had lower HEI-C (63 ± 10 vs 70 ± 10); p=0.01), and DQI-I (59 ± 7 vs 63 ± 7; p=0.04) than children <9 years. Children with poor DQ (DQI-I <60) (-0.53 ± 0.87) had lower ht-z scores than children with DQI-I ≥60 (0.15 ± 1.17; p=0.02). Significant interrelationships between DQ scores (HEI-C, DGI-CA, and DQI-I) and age above and below the median (≥ and <9 years) and gender are illustrated in **Appendix G, Table G-6**.

B) Children with CD

No significant differences were found in DQ scores (HEI-C, DGI-CA and DQI-I) between ethnic groups (*Caucasian* vs *other ethnicity*), age at diagnosis above and below the median (≥ and <7 years), or duration of CD above and below the median (≥ and <1 year) (p>0.05).

3.3.12 Quality of Life Data

3.3.12.1 Generic Quality Of Life Tool: Gastroenterology Symptom Score

Among children with CD, no significant differences in GSS between *Caucasian* children (median= 86, IQ= 78-97) and children with CD of *other ethnicities* (median= 89, IQ= 69-96; p=0.93) were noted. Children with CD reported higher GSS (less GS) than CON (p<0.01) as shown in **Figure 3-8**. Children with CD had significantly higher scores of all GS (using GSS tool) compared to CON (**Appendix F, Figure F-1**) (p<0.05). A greater proportion of CD children (n=23; 85%) than CON (n=10; 24%) reported GSS ≥64 (less abdominal pain; p<0.01). In children with CD, no differences in Marsh score by ethnic group or GSS were found (p>0.05). However, no data are available about Marsh score and ethnicity in CON.

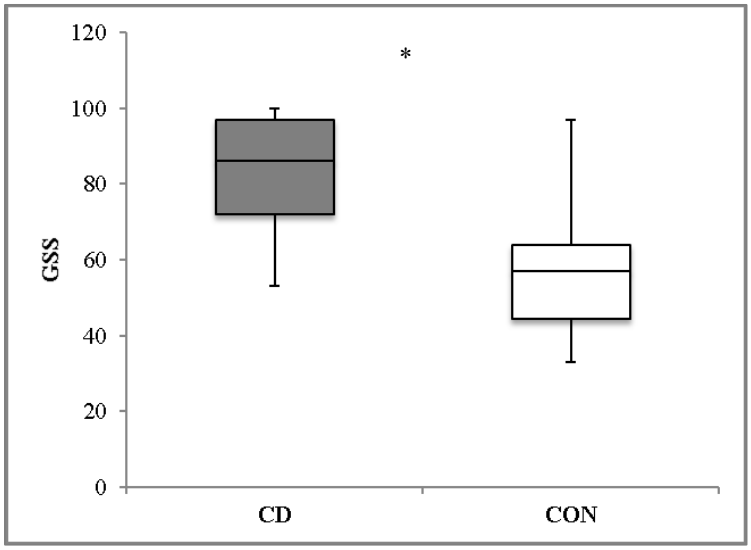


Figure 3–8: The PedsQL™ Gastrointestinal Symptom Scale in Children with Celiac Disease (n=27) and Disease Controls (n=42). The total score was calculated as the average of all GS (abdominal pain, diarrhea, constipation, nausea, vomiting, discomfort in a abdomen or stomach, passing gas, not feeling hungry, and bloating) (238). Data are presented as median (interquartile range). An asterix (*) represents as significant difference between children with CD and CON ($p<0.01$). Ten children (24%) in CON had GSS higher than the 75th percentile.
Abbreviations: CD, Celiac Disease; CON, disease control; GSS, Gastroenterology Symptoms Score.

3.3.12.2 Generic Quality Of Life Tool: PedsQL™ 4.0 Generic Core Scales

By assessing the agreement between child report and parent proxy report, no differences were found in the median scores between child report and parent proxy report in both CD and CON ($p>0.05$) (**Appendix D, Table D-1)**. **Table 3-5** presents the HRQOL scores in children with CD and CON in comparison to the HRQOL scores of healthy Canadian children (healthy norms). The number of children at risk of reduced HRQOL in the school domain (≥-1 SD below the average of norms healthy children) as reported in child report Peds QL in CON was significantly higher than CD children ($p>0.04$) (**Figure 3-9).**

Table 3-5:PedsQL™ 4.0 Generic Core Scales in Children with Celiac Disease and Disease Controls in Comparison to the Quality of Life Scores of Healthy Norms Children

	CD	CON	Healthy norms[5]	p-value CD vs CON[6]	p-value CD vs healthy[6]	p-value CON vs healthy[6]
Child Report **(CD=28 and CON=35)**						
Average[1,3]	83 ± 11	75 ± 11	84	0.01	0.66	<0.01
Physical[2]	94 (84-100)	84 (75-94)	88	<0.01	0.07	0.01
Psychological[1,4]	79 ± 14	71 ± 13	82	0.03	0.24	<0.01
Emotional[2]	75 (60-90)	65 (55-80)	79	0.09	0.32	<0.01
Social[2]	95 (80-100)	90 (70-100)	85	0.22	0.10	0.92
School[1]	74 ± 15	63 ± 18	81	0.01	0.02	<0.01
Parent Proxy Report **(CD=26 and CON=38)**						
Average[2,3]	85 (71-88)	79 (67-89)	82	0.60	0.43	0.13
Physical[2]	90 (81-97)	84 (75-94)	84	0.27	0.07	0.58
Psychological[2,4]	80 (63- 88)	77 (63-87)	81	0.86	0.14	0.04
Emotional[2]	70 (60-85)	68 (55-80)	81	0.77	<0.01	<0.01
Social[2]	90 (75-100)	90 (75-100)	83	0.71	0.66	0.43
School[2]	73 (55-90)	73 (55-83)	78	0.58	0.13	0.01

[1]Normally distributed variables are presented as mean ± standard deviation. Two-sample Independent t-test was conducted to compare the statistical differences between CD and CON. One sample t-test was preformed between the study group (CD or CON) and healthy norms.

[2]Variables demonstrating skewed distributions are presented as median (interquartile range). Mann Whitney tests were preformed to measure the statistical differences between CD and CON. Wilcoxon signed rank was preformed between the study group (CD or CON) and healthy norms.

[3]Average values were computed as the mean of four domains (physical, emotional, social and school functioning).

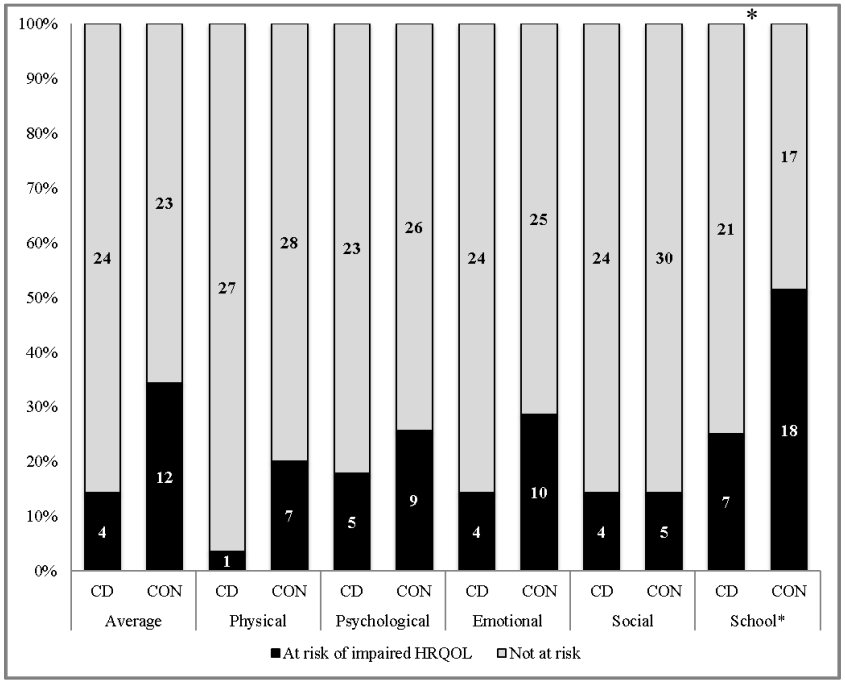
[4]Psychological values were computed as the average of three domains (emotional, social and school functioning).

[5]The mean of healthy norms was obtained from Varni et al (2003) (230).

[6]p-values <0.05 are considered statistically significant.

Abbreviations: CD, Celiac Disease; CON, disease control.

A



B

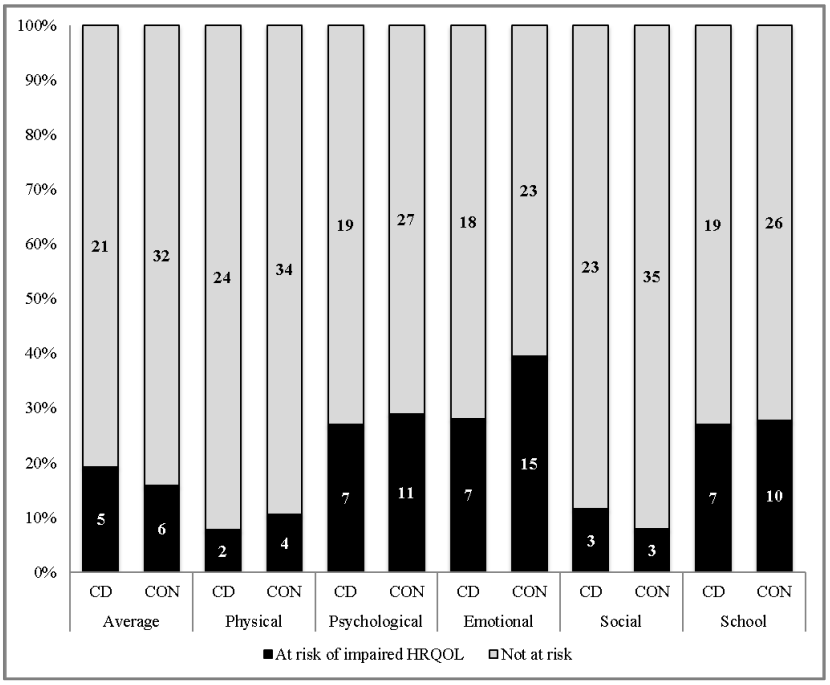


Figure 3–9: Proportion of Children with Celiac Disease and Disease Controls at Risk of Impaired Health Related Quality of Life using PedsQL™ 4.0 Generic Core Scales, (A) child report (CD=28 and CON=35) and **(B) parent proxy** (CD=26 and CON=38) (230, 237). Impaired Health Related Quality of Life defined as ≥-1 SD below healthy children norms. An asterix (*) represents significant difference between children with Celiac Disease and disease controls.
Abbreviations: CD, Celiac Disease; CON, disease control; HRQOL, Health Related Quality of Life.

3.3.12.3 Celiac Disease Specific Quality of Life Tools: Celiac Disease DUX and Celiac Disease Quality of Life Scale

Figure 3-10 shows the CDDUX scores in children with CD. Only 4% (n=1) of children with CD had good HRQOL (average CDDUX score ≥60) and 29% (n=8) of children with CD had poor HRQOL (average CDDUX score ≤40). **Figure 3-11** demonstrates the responds of KINDL test. The majority of children with CD (87%; n=21) had GS at time of study recruitment (**Figure 3-10 B**).

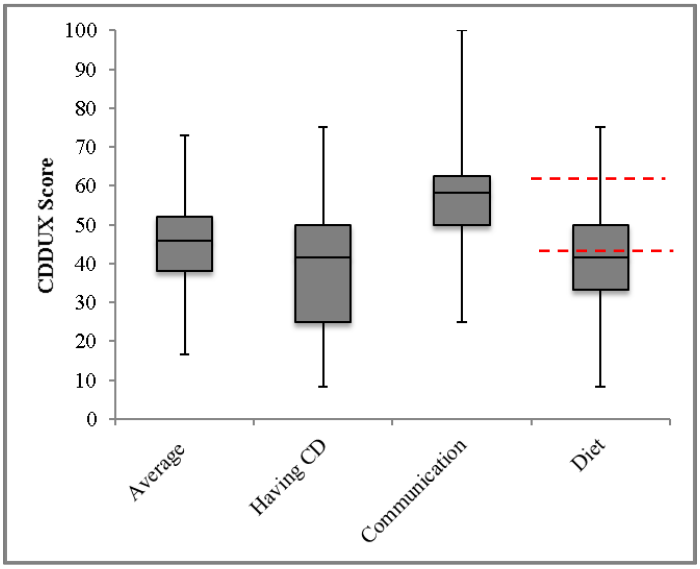


Figure 3–10: Celiac Disease DUX (CDDUX) Scores in Children with Celiac Disease (n=27). Average scores (maximum score is 100) were computed as the mean of three domains (having Celiac Disease, communication and diet (GFD)) (240). Red lines represent the cut-off values of "good" (>60), "neutral" (41–60), or "bad" (<41) health related quality of life. Data are presented as median (interquartile range).
Abbreviations: CD, Celiac Disease; CDDUX, Celiac Disease DUX.

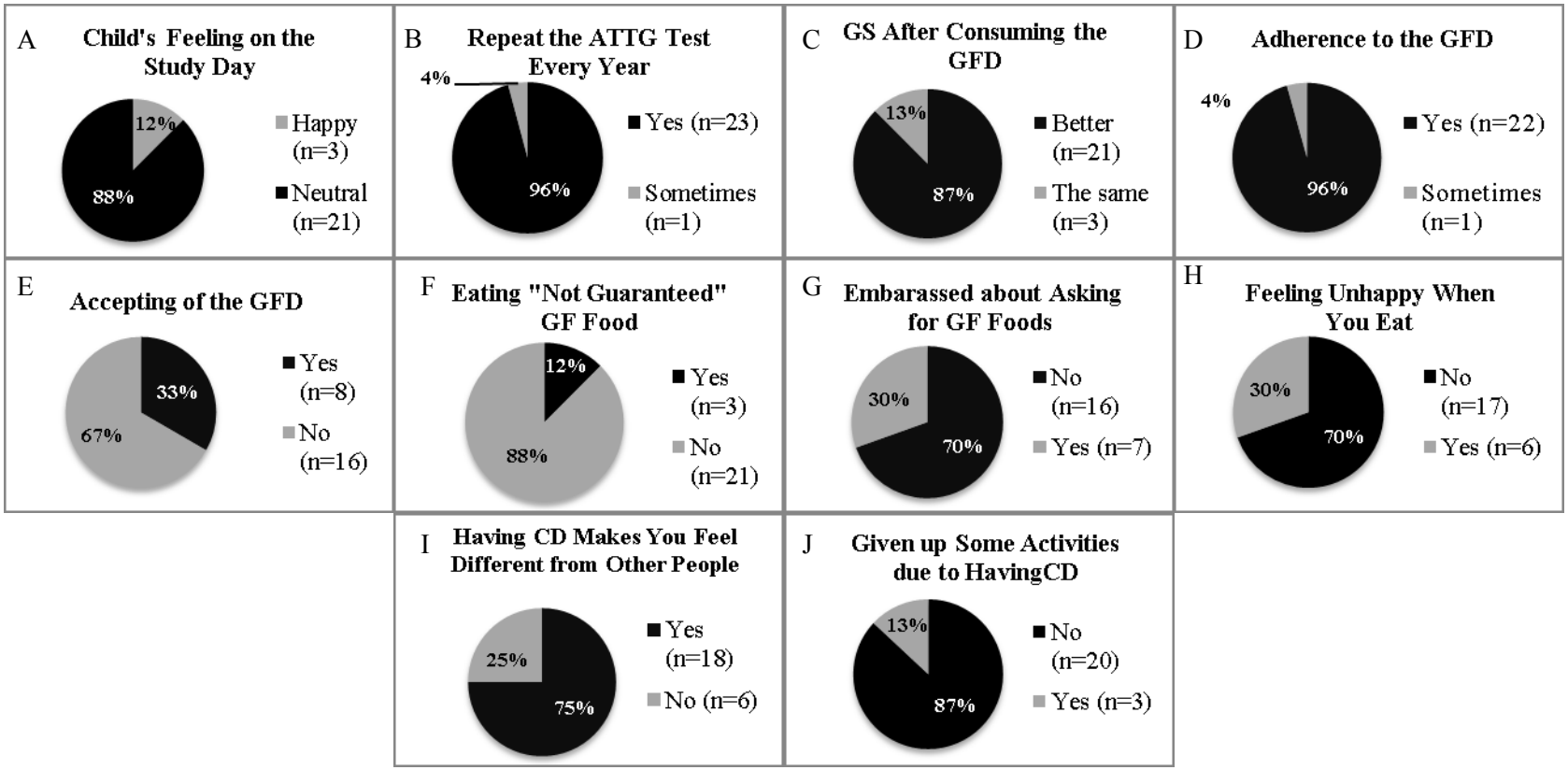


Figure 3–11: KINDL® Quality of Life Scale for Children with Celiac Disease (n=24). (A) Child feeling on the study day (Happy [happy, very happy] /Neutral). (B) Percent repeating the Anti-Tissue Transglutaminase (ATTG) testing every year (yes [regularly, occasionally]/ no). (C) Improvement in gastrointestinal symptomology (GS) after following the Gluten-Free Diet (GFD) (improved GS/ GS same [or worse]). (D) Self-reported adherence to the GFD (yes/sometimes). (E) Acceptance of the GFD (yes [a lot, quite a lot, a little]/ no [but sometimes its difficult, not at all]). (F) Eating "not-guaranted gluten free (GF) food (yes [often, rearly]/ no). (G) Feelings embarrassed asking about GF foods at a restaurant/outside activities (yes/ no). (H) Feeling unhappy when eat (yes [on social occasions, many occasions, in the cafetria]/ no). (I) Presence of CD causing the child to feel different (yes [always, often, sometimes] /no). (J) Impact of eating a GFD on daily activities (yes/ no).

3.3.13 Interrelationships between Quality of Life (Generic and Celiac Disease Specific Tools), and Socio-Demographic Factors, and Anthropometric Variables

A) CD and CON

We did not observe any significant differences between mother's age (≥ and <39 years), father's age (≥ and <43 years), and parents' educational level (high school and registered apprenticeship vs college and university) in HRQOL tools (p>0.05) (**Appendix G, Table G-1** to **Table G-5**). Children younger than median age (<9 years old) reported higher HRQOL scores in physical (<9 years: median= 94, IQ= 88-94; ≥9 years: median= 84, IQ= 75-94; p=0.03), emotional (<9 years: median= 75, IQ= 55-90; ≥9 years: median= 70, IQ= 60-80; p<0.01), and school (<9 years: 74 ± 18; ≥9 years: 63 ± 16; p<0.01) than children ≥9 years old. No significant differences in parent proxy report scores were found based on child age (≥ and < median 9 years), mother's age (≥ and < median 39 years), father's age (≥ and < median 43 years), parents' educational attainment (high school and registered apprenticeship vs college and university) or income (≥ and < median $81,836/year) (p>0.05) (**Appendix G, Table G-1** to **Table G-5**).

B) Children with CD

In children with CD, no association was found between results of parent proxy report of HRQOL ethnicity (*Caucasian* vs *other ethnicity*), age at diagnosis above and below the median (≥ and <7 years) or CD duration above and below the median (≥ and <1 year). Children diagnosed with CD for ≥1 year (median= 97, IQ= 93-100) reported higher physical scores than children diagnosed with CD <1 year (median= 93, IQ= 81-94; p=0.04). Children who were diagnosed with CD <7years of age reported higher physical (median= 97, IQ= 92-100 vs median= 92, IQ= 81 – 94), psychosocial (87 ± 11 vs 73 ± 12), emotional (median= 90, IQ= 80-98 vs median= 70, IQ= 60-75), school (82 ± 12 vs 68 ± 15) and average (90 ± 9 vs 78 ± 100) scores than children who had diagnosed with CD ≥7 years, respectively (p<0.04). Children from *Caucasian* ethnicity reported

lower physical (*Caucasian*: median=91, IQ= 81-94 vs *other ethnicity*: median=100, IQ= 94-100) and psychosocial (*Caucasian*: 77 ± 13 vs *other ethnicity*: 88 ± 8) scores than children from different ethnic group ($p<0.03$). However, children with CD and from *Caucasian* ethnicity reported higher communication CDDUX scores (median=58, IQ= 50-75) than children with CD and from different ethnic group (median=50, IQ= 42-54; $p=0.01$)). The majority of children with CD who reported GS (using KINDL test) were *Caucasian* children (n=13, 72%). We were not able to assess interrelationships between ethnicity in the CON group and these factors due to the lack of available data regarding ethnicity and the CON group. No association was found in CDDUX (average, having CD, communication, diet) and gender in children with CD ($p>0.05$).

3.3.14 Interrelationships between Gastrointestinal Symptomology Scores and Diet Quality Score, Glycemic Index and Glycemic Load

No significant differences were found in HEI-C, DGI-CA. DQI-I, GI and GL between children with GSS ≥64 (less GS) and children with GSS <64 (severe GS) ($p>0.05$; **Appendix G, Table G-6**). GSS was not an independent covariate of DQ (**Appendix G, Table G-7)**.

3.3.15 Interrelationships between Gastrointestinal Symptomology Scores and PedsQL™ 4.0 Generic Core Scales, and Celiac Disease DUX Scores

Child report and parent proxy Peds™ QL scores were significantly higher in children with GSS ≥64 (less GS) than in children with GSS <64 (more severe GS) ($p>0.05$) (**Table 3-6**). Among children with CD, children with GSS ≥64 (less GS) had significantly higher CDDUX (average and diet) than children with GSS <64 (more GS) (**Table 3-7**).

Table 3-6: Health Related Quality of Life Score (PedsQL™ 4.0 Generic Core Scales) and Gastrointestinal Symptomology Scores (Above and Below the Median Value)

	Lower GSS (GSS<64, n=36)	Higher GSS (GSS≥64, n=33)	p-value[1]
	Child Report		
Average[2,4]	73 ± 9	85 ± 11	<0.01
Physical[3]	84 (75-88)	94 (88-100)	<0.01
Psychosocial[3,5]	68 ± 11	82 ± 13	<0.01
Emotional[3]	60 (55-75)	80 (65-90)	<0.01
Social[3]	85 (70-95)	100 (90-100)	<0.01
School[2]	59 ± 15	76 ± 16	<0.01
	Parent Proxy Report		
Average[3,4]	74 (66-84)	87 (75-91)	<0.01
Physical[3]	84 (72-91)	94(84-97)	<0.01
Psychosocial[3,5]	72 (62-80)	82 (68-92)	<0.01
Emotional[3]	65 (50-70)	80 (60-90)	0.01
Social[3]	85 (65-100)	95 (80-100)	0.03
School[3]	65 (45-80)	75 (65-90)	0.01

[1]p-values <0.05 are considered statistically significant.
[2]Normally distributed variables are presented as mean ± standard deviation. Two-samples Independent t-tests were conducted to compare the statistical differences between the study groups (CD and CON). One sample t-tests were preformed between the study group (CD or CON) and healthy norms.
[3]Variables demonstrating skewed distributions are presented as median (interquartile range). Mann Whitney test were preformed to measure the statistical differences between the study groups (CD and CON). Wilcoxon signed rank was preformed between the study group (CD or CON) and healthy norms.
[4]Average values were computed as the mean of four domains (physical, emotional, social and school functioning).
[5]Psychological values were computed as the mean of three domains (emotional, social and school functioning).
Abbreviations: CD, Celiac Disease; CON, disease control.

Table 3-7:Health Realted Quality of Life Score (Celiac Disease DUX) and Gastrointestinal Symptomology Scores (Above and Below the Median Value) in Children with Celiac Disease

	Lower GSS (GSS<64)	Higher GSS (GSS≥64)	p-value[1]
Average[2,4]	31 ± 14	47 ± 10	0.01
Having CD[2]	28 ± 21	41 ± 15	0.14
Communication[3]	54 (38-63)	58 (50-67)	0.62
Diet[2]	23 ± 13	45 ± 12	<0.01

[1]p-values <0.05 are considered statistically significant.
[2]Normally distributed variables are presented as mean ± standard deviation. Two-samples Independent t-tests were conducted to compare the statistical differences between the study groups (CD and CON). One sample t-tests were preformed between the study group (CD or CON) and healthy norms.
[3]Variables demonstrating skewed distributions are presented as median (interquartile range). Mann Whitney test were preformed to measure the statistical differences between the study groups (CD and CON). Wilcoxon signed rank was preformed between the study group (CD or CON) and healthy norms.
[4]The average score values were computed as the mean of three domains (having Celiac Disease, Communication and diet (GFD)).
Abbreviations: CD, Celiac Disease; CON, disease control.

3.3.16 Interrelationships between Dietary Intake (Macronutrient Intake, Gluten Intake, Adherence To Gluten-free Diet, Food Groups) and Diet Quality (Glycemic Index, Glycemic

Load, Diet Quality Scores) and Health Related Quality of Life (Generic and Disease Specific)

A) CD and CON

Children with lower HEI-C (63 ± 15) had lower school function score than children with higher HEI-C (73 ± 17; p=0.02). Parents of children with HEI-C scores below the median (< 66) perceived that their children had had lower school (median= 65, IQ= 45-73 vs median= 85, IQ= 70-95), psychosocial (median= 68, IQ= 63-82 vs median= 83, IQ= 62-90) and average (median= 74, IQ= 67-85 vs median= 86, IQ= 77-91) functioning scores than parents of children with HEI-C scores above the median (≥66) (p<0.02). Parents of children with lower DGI-CA (<57) perceived that their children had had lower school (median= 65, IQ= 45-75 vs median= 83, IQ= 60-90), psychosocial (median= 72, IQ= 63-82; median= 82, IQ= 67-93) and average (median= 76, IQ= 67-87 vs median= 85, IQ= 75-95) functioning scores than parents of children with higher DGI-CA (≥57) (p<0.05). Parents of children with lower DQI-I (<62) perceived that their children had had lower school score (median= 65, IQ= 48-75) compared to parents of children with higher DGI-CA ≥62 (median= 80, IQ= 60-90; p=0.04). No association was found between Peds™ QL and GSS and GI and GL (p>0.05). Significant interrelationships were observed between PedsQL™ 4.0 Generic Core Scales (average, emotional, school and psychosocial domains) and GSS and DQ scores (HEI-C, DGI-CA and DQI-I) (**Appendix G, Table G-8).**

B) *Children with CD*

Significant interrelationships were found between CD specific HRQOL (average and having CD domains) and GSS and DQ scores (HEI-C, DGI-CA and DQI-I) in children with CD (**Appendix G, Table G-7).** No associations were found between CDDUX and GSS and GI and GL values (p>0.05).

3.4 Discussion

CD is a chronic gastrointestinal disease that affects around 1% of people worldwide (194, 195). The sole treatment for children with CD is a lifelong adherence to a GFD (194, 195). Numerous factors have been associated with poor adherence to GFD including GS, age of the child, palatability of GF products, cost of GF foods, and social factors such as dining outside the home (203-207). Although adherence to a GFD is important to treat small intestine damage and prevent complications such delayed growth, several studies have reported poor nutritional quality of processed GF foods, which may be associated with health complications such as obesity (66, 103, 104, 106, 135). Both adherence to and nutritional quality of the GFD are potentially associated with physical, social, and emotional impacts on overall health and potentially contributing to reduced HRQOL (206). This study is the first study to examine child and parent perspectives of HRQOL and explore the potential interrelationships between HRQOL and socio-demographic factors (age, gender, ethnicity, family history of CD, age at diagnosis, and duration of the disease), GS, dietary intake, and adherence to GFD in children with CD. The study objective was to assess and compare DQ and HRQOL in children with CD relative to children with chronic gastrointestinal disease (non-CD), and to examine the factors that affect poor HRQOL /DQ in children with CD.

We found that the majority of children with CD were adherent to a GFD. No significant differences in energy consumption, macronutrient intake, food groups, GL or DQ scores were found between groups. These results may depend upon the choice of DQ tools used for this evaluation. We utilized three different DQ tools developed by nutritional experts based on current knowledge, guidelines, and recommendations of a "healthy diet" for use in healthy populations. However, these tools were not specifically designed to address the potential limitations of food type inherent with therapeutic diets such as the GFD. In therapeutic diets (the GFD), assessing

overall DQ can be more challenging due to several concerns: 1) adherence to the therapeutic diet, 2) nature (quality) of the therapeutic diets including consideration of required food restrictions which may alter DQ, 3) food manufacturing and labeling of processed therapeutic foods, and 4) use of reliable DQ tools that can address these potential limitations. In our cohort, the majority of children with CD who adhered to a GFD had poor DQ. Poor DQ in children with CD is directly influenced by the nutritional limitations of GF foods whereas poor DQ in CON may be associated with food choices of a gluten-containing diet (124, 242, 243).

In the current study, around 33% of foods purchased in children with CD were processed and/or from the *other foods* group (data not shown) and likely the major reason for the lower observed DQ. The number and types of food servings consumed within each food group (e.g. grains) may lead to alterations in DQ and GI/GL of the diet (66, 106, 123, 244, 245). This may also potentially explain why the children with CD had higher GI and lower polyunsaturated fatty acid intakes than the CON group. These findings were comparable to previous studies (66, 105, 123, 124, 242, 245, 246). Other factors that may influence GI/GL and overall DQ include age of the child, ethnicity of the parent/child and the presence of GI symptoms. Our findings are consistent with other studies where by older age (>9 years), and ethnicity (*Caucasian*) were associated with reductions in DQ and elevations in GI and GL (66, 82, 247). Finally, GSS was not an independent predictor of DQ. This further illustrates that the presence of GS indirectly affects DQ of the foods consumed by children with chronic gastrointestinal illness.

The present study found that children with CD reported higher HRQOL scores than CON. The differences in these findings may be attributed to several factors. First, the HRQOL tools that were used in previous studies are different from our study with other studies typically using either a generic or CD specific tool, but rarely both (206, 248-251). Hence, study findings offer the

opportunity to compare and contrast HRQOL with two disease populations (CD and non-CD GI) and healthy children. Second, HRQOL in children with chronic disease should be obtained from both child and parent perspectives as several developmental factors may influence the child's perception of HRQOL (e.g. age of the child, parental influences) (179, 231, 251). Third, the factors that influence HRQOL in children with CD (e.g. family history of CD and duration of CD) have not been examined in previous studies (206). This is important since food purchases in these households may be distinctly different from households without any family history of CD. Fourth, age of child (adolescents vs children) and other socio-demographic factors such as parental place of birth/ethnicity and its interrelationships to both DQ and HRQOL in childhood CD has not been extensively studied (206, 248-251). Finally, the control group in other studies were not specifically tested to rule out CD as they may have silent or asymptomatic CD, which will affect HRQOL (206, 248, 250). This is an important point since CD is so highly prevalent in the general population and children may experience chronic symptoms that may unknowingly influence HRQOL. One important finding to this study, is that with the exception of the school domains, most children with CD in this subset analysis had HRQOL comparable to that of healthy children. This may be related to the difficulties in obtaining GF foods in the school setting and the effects on social settings whereby dietary restrictions may have adverse social sequelae (206).

In the current study, the level of agreement between child report and parent proxy-reported HRQOL was low. This is similar to findings in other studies with the presence of GS in the child being the major factor influencing reduced perceptions of HRQOL in both the child and parent (206, 252, 253). In particular, the presence of abdominal pain or discomfort in the abdomen were the main GS symptomology associated with reduced HRQOL from both child and parent perspectives (**Appendix G, Table G-9** to **G-11**). This is not surprising since the presence of pain

is often reported to be a consistent feature of lower HRQOL in other clinical populations (179, 238, 253).

We did not find any associations between GFD adherence and HRQOL. This is likely due to a high level of reported adherence to the GFD (>90%), limiting the ability to make dichotomous comparisons (adherent vs non-adherent). Furthermore, macronutrient intake was not associated with HRQOL and poor DQ was not related to lower child reported HRQOL scores. In contrast, lower DQ was related to lower parent proxy HRQOL scores. In previous studies, associations between improved DQ and HRQOL were noted in obese children and in children with neurological diseases following the ketogenic diet (254, 255).

Some study limitations exist. Insufficient power to determine differences in ethnicity and DQ between children with CD and CON and to determine differences between dietary variables is an issue. A sample size of n=150/group was determined to be sufficient to detect an average difference of 1.5 SD in HRQOL between groups (α=0.05 and β=0.8:**Appendix E, Table E-1**). The potential for selection bias exists as the majority of families were *Caucasian* with high incomes and high education level (especially in CD group) and hence findings may not be generalizable to families of lower socio-economic status. Finally, it would be ideal to have a healthy control to assess the relationship between DQ and HRQOL (without the presence of GS). In comparison to healthy children (2-18 years) from the LTX study, GI, GL and DQ scores were not significantly different between healthy children and CD or CON ($p>0.05$) **(Chapter 4 [Figure 4-1 and Figure 4-2])**.

In conclusion, children with CD following a GFD report good HRQOL compared to CON and healthy norms. The presence of GS was associated with poor HRQOL. Poor DQ was indirect related to reduced HRQOL. Age was the main factor associated with poor DQ, whereas a multitude

of factors (age, GS, ethnicity and age of diagnosis, gender and DQ) were associated with lower HRQOL scores in children with CD and strictly adherent to a GFD. Other factors influencing the assessment of the interrelationships between DQ and HRQOL include the choice of DQ and HRQOL tools. Future research should focus on the development of DQ tools that consider therapeutic restrictive diets. This would be beneficial in the assessment of how improving DQ may influence patient outcomes in clinical populations.

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Chapter 4 Diet Quality in Children Post Liver Transplantation

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4.1 Introduction

One of the most common causes of cholestatic liver disease and liver transplantation (LTX) in infancy is biliary atresia (BA) (256). Malnutrition is a significant problem in infants with cholestatic liver disease; it places a child at risk for poor clinical outcomes pre- and post-LTX (256). Malnutrition leading to growth failure has been found to be an independent risk factor for pre-transplant and post-transplant mortality and delayed neurodevelopment (256). The Pediatric End-Stage Liver Disease scoring system illustrates growth failure to be a key indicator of mortality risk (256).

Nutritional deficiencies are common in infants with cholestatic liver diseases pre-LTX (257). Protein and energy intake may be inadequate due to anorexia, nausea, vomiting, and early satiety due to impingement upon viscera by ascites or an enlarged liver or spleen (182, 257). Fat and fat-soluble vitamin malabsorption (A, D, E and K) may also occur (257-259). In addition, alterations in hepatic metabolism of energy, carbohydrate, fat and protein including branched chain amino acids can result in increased nutritional requirements (182). While much is known about the challenges for optimal dietary intake facing children in the pre-LTX period, little has been studied about overall diet intake and diet quality (DQ) in infants and children following LTX.

DQ refers to the concept of evaluating the overall nutritional quality of an individual's diet by assessing macro and micronutrient intake (including fibre, saturated fat and micronutrients such as calcium, vitamin C, iron, sodium), and overall diversity of food intake (typically including number of food servings from each food group) (3). There are validated indices to measure DQ in children such as the Healthy Eating Diet Index-Canada (HEI-C), Dietary Guideline Index for Children and Adolescents (DGI-CA) and Diet Quality Index-International (DQI-I) (9). However, these DQ tools do not include an in-depth evaluation of carbohydrate type/quality (3). Evaluating glycemic index (GI) and glycemic load (GL) intake addresses these concerns. Evaluation of these factors is particularly relevant in populations where risk of metabolic dysregulation is high (e.g. obesity, diabetes) (108). High GI and GL intakes have been associated with the onset and expression of metabolic dysregulation in chronic liver disease, such as non-alcoholic fatty liver disease in children, but no data were available for children post-LTX (87). This is important as the risk of metabolic dysregulation due to immunosuppression in children post-LTX is increased (155, 183). Little is known about dietary intake and DQ in children post-LTX. The objective of this pilot study was to describe and compare overall DQ by assessing macronutrient intakes, food groups, GI and GL, and DQ using validated DQ tools between stable, ambulatory children post-LTX and healthy children. We hypothesized that children and adolescents post-LTX have lower total DQ score and higher GI and GL, compared to healthy controls.

4.2 Methods

4.2.1 Subjects

A prospective study design was utilized to compare dietary intake in children between the ages of 2-18 years who had undergone LTX (n=27) between 1996-2012 at the Stollery Children's Hospital in Edmonton and healthy children (n=28). Healthy children with normal body weights and no known healthy conditions, were randomly recruited from the community via flyers. All children in the LTX group were at least one year post-LTX (5 ± 3) years. Children were excluded from assessment for any of the following reasons; experiencing acute rejection, prednisone treatment, hormone replacement therapy, parenteral nutrition therapy, a history of other pre-existing gastrointestinal diseases (e.g. celiac disease), and/or history of food restrictions (e.g. allergies) warranting a special diet. Ethics Approval was obtained from the Human Research Ethics Board at the University of Alberta (Pro00026331).

4.2.2 Demographic, Anthropometric and Laboratory Data

Demographic data of children post-LTX were collected from participants' medical records. Collected data included age at LTX(s), date of LTX(s), medication history, history of co-morbidities, anthropometric data at time of LTX assessment, and routine clinical blood work (electrolytes, albumin, international normalized ratio (INR), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and total bilirubin). Anthropometric data were measured by trained personnel at time of routine clinic visits for post-LTX children and in the Clinical Research Unit at the University of Alberta for healthy controls using validated methodologies (260). Weight was measured using an upright scale (Detecto, Missouri, USA) to the nearest 0.1 kg. Height was measured using a wall mounted stadiometer (Holtain Ltd, Crymych, Dyfed, UK) to the nearest 0.1 cm. Height-for-age z-score (ht-z), weight-for-age z- score (wt-z), body mass index (BMI) and BMI z-score (BMI-z) were calculated using Epi Info 3.5.1 software® (Atlanta, GA, USA) using Centre

for Disease Control growth standards (260). We did not use the World Health Organization Growth Chart standards for Canada (the Canadian Pediatric Endocrine Group) as it was not available at the time of study.

4.2.3 Dietary Intake Assessment

Intake was assessed using two methods a) two 24-hour recalls (one weekday, one weekend day) using the multi-pass technique (218, 261), and b) a validated food frequency questionnaire specific for assessment of vitamin D and calcium intake (262). Micro and macronutrient intake in the 24-hour recalls were analyzed using the Canadian database (Canadian Nutrient File CNF) of Food Processor (SQL 10.8 ESHA® Research, Salem, OR, USA). Vitamin K intake was determined using the United States Department of Agriculture database (Release 27). Macro and micronutrient intakes were compared to age- and-gender matched recommended dietary reference intakes (DRI) (219, 263). To assess for the potential for under-reporting of actual intake, energy intake (EI) was divided by an estimate of basal metabolic rate (BMR). BMR was calculated using the World Health Organization equations, which are specific for age, gender and weight (264). Accurate reporting of EI was determined by calculating the ratio of EI divided by estimated BMR with values between the upper and lower 95^{th} confidence limits as defining agreement (221). Individuals with EI/BMR <95% or >95% confidence intervals were considered as under-reporters or over-reporters, respectively (221). Dietary intake was categorized into food groups and the number of servings based on the Alberta Nutrition Guidelines for Children and Youth (ANGCY) for age and gender (77).

4.2.4 Glycemic Index and Glycemic Load

GI and GL calculation is described in **Chapter 3** (87, 97).

4.2.5 Diet Quality Tools: Healthy Eating Index-Canada, Dietary Guideline Index for Children and Adolescents, and Diet Quality Index-International

Diet quality tools are discussed in details in **Chapter 3**. DQ tools were adapted based on ANGCY and the DRI for age and gender (77, 219, 263) (**Appendix A, Table A-1 to A-3)**.

4.2.6 Statistical analysis

Data were expressed as median and interquartile range (IQ), unless otherwise specified. If the data were normally distributed, an Independent t-test was used to assess differences between groups. For data demonstrating skewed distributions, a Mann Whitney test was performed. Multivariate models and the Fisher's exact test were used to assess comparisons with age (> and ≤ median: 8.6 years), the DRI (Adequate intake: AI or Recommended Daily Allowance: RDA), ANGCY, HEI-C scores (≤and >80), DGI-CA scores (≤and >68), DQI-I scores (≤ and >60), GI (≤ and >60) and GL (≤ and >120) (35, 87). Assessment of categorical cut-offs was based on a high vs low intake (GI/GL), DQ scores reflecting good DQ vs poor/ needs improvement scores (HEI-C, DGI-CA, DQI-I), or compared to recommended ranges of intake/food servings (DRI/ANGCY). Where necessary, adjustment for potential confounding variables (gender, age, EI) known to influence primary outcome variables (macro and micronutrient intake) was performed. A Bland Altman test and Intra Class Correlations (ICC) were conducted to measure the DQ scores between the original vs the adapted version of HEI-C, DGI-CA and DQI-I in children post-LTX and healthy children (**Appendix H, Figure H-1** to **H-3**). P-values <0.05 were considered significant. Data analysis were completed using the SAS 9.0 statistical software (SAS, Version 9.4; SAS Institute Inc., Cary, NC, USA).

4.3 Results

4.3.1 Demographic, Anthropometric and Laboratory Data

The main indication for LTX was BA (n=16, 56%). The mean age at LTX was 3.5 ± 3.8 years (0.2-13.1 years) and mean time since LTX was 5 ± 3 years (1 13 years). All children post-LTX were on Tacrolimus as the primary mode of immunosuppressive therapy. **Table 4-1** represents the anthropometric data in children post-LTX compared to healthy controls. Wt-z and ht-z were not different between children with BA (wt-z: -0.2 ± 1.3; ht-z: 0.1 ± 1.4) compared to children with other indications of LTX (wt-z: -0.3 ± 1.0; ht-z: 0.9 ± 0.9) ($p>0.05$) (**Table 4-2)**. Children who had LTX at less than 2 years of age had a lower ht-z (-0.91 ± 2.09) than children ≥2 years (0.09 ± 0.30; $p=0.03$).

Table 4-1:Anthropometric Data in Children Post-Liver Transplantation and Healthy Children

	Post-LTX (14 M/13 F; n=27)[1]		Healthy Control (12M/16F; n=28)[1]		p-value[2]
	Mean ± SD (range)	Median (interquartile range)	Mean ± SD (range)	Median (interquartile range)	
Age (years)	8.8 ± 3.7(2.3-15.9)	8.4 (6.2-10.6)	8.8 ± 4.3 (2.0-16.8)	8.7 (5.2-11.6)	0.95
Weight (kg)	33.8 ± 20.6 (11.0-103.2)	28.9 (18.7-41.0)	32.7 ± 15.8 (13.8-63.5)	33.3 (18.4-39.9)	0.97
Weight-for-age z-score[3]	0.12 ± 1.29 (-2.9-2.5)	0.07 (-0.37-1.06)	0.25 ± 0.90 (-1.3-2.3)	0.30 (-0.46-0.99)	0.67
Height (cm)	129.5 ± 24.9 (83.0-178.8)	128.0 (110.7-148.6)	132.1 ± 23.8 (87.2-183.9)	134.8 (113.7-153.4)	0.56
Height-for-age z-score[3]	-0.32 ± 1.10 (-2.3-2.4)	-0.11 (-1.13-0.55)	0.55 ± 0.97 (-1.2-2.7)	0.40 (0.02-0.97)	<0.01
BMI (kg/m^2)	18.6 ± 5.2 (13.1-39.8)	17.3 (16.1-19.4)	17.2 ± 3.1 (13.2-23.8)	16.2 (14.8-19.2)	0.23
BMI-for-age z score[3]	0.44 ± 1.27 (-2.3-2.7)	0.69 (-0.26-1.30)	-0.10 ± 1.02 (-1.8-2.0)	-0.05(-0.95-0.54)	0.08

[1]Data are presented as mean ± standard deviation (range), median (interquartile range).
[2]p-values <0.05 are considered statistically significant.
[3]Z-scores were calculated using CDC Epi Info software.
Abbreviations: BMI, Body Mass Index; F, Females; LTX, Liver Transplantation; M, Males.

Table 4-2: Anthropometric Data in Children with Differening Indications for Liver Transplantation

Indication for LTX (n)	Weight (kg)[1]	Weight-for-age z-score[2]	Height (cm)[1]	Height-for-age z-score[2]	BMI (kg/m2)[1]	BMI-for-age z-score[2]
Biliary Atresia (n=15)	28.8 ± 13.8 (16.6-56.2)	-0.22 ± 1.28 (-2.91-1.72)	127.7 ± 25.4 (91.5-178.8)	-0.31 ± 1.21 (-2.31-1.61)	16.8 ± 2.4 (13.1-22.7)	0.05 ± 1.39 (-2.25-2.71)
Acute Fulminant Hepatic Failure (n=2)	22.0 ± 15.5 (11.0-32.9)	-0.31 ± 2.03 (-1.74-1.13)	107.5 ± 34.6 (83.0-131.9)	-0.77 ± 1.49 (-1.82 – 0.29)	17.4 ± 2.1 (16.0-18.9)	0.47 ± 1.13 (-0.33-1.27)
Familial Intrahepatic Cholestatsis Type 1 and 2 (n=2)	21.4 ± 4.1 (18.5-24.3)	-0.48 ± 0.57 (-0.88–(-0.07))	116.5 ± 7.7 (111.0-121.9)	-0.89 ± 0.33 (-1.12-(-0.66))	15.7 ± 0.94 (15.0-16.4)	0.10 ± 0.37 (-0.17-0.36)
Scelerosing Cholngititis (n=3)	47.1 ± 11.6 (40.0-60.4)	1.34 ± 0.35 (0.98-1.67)	144.8 ± 19.2 (133.4-167.0)	0.21 ± 0.75 (-0.42-1.04)	22.3 ± 0.56 (21.7-22.7)	1.47 ± 0.67 (0.69-1.91)
α-1-Antitrypsin Deficiency (n=1)	32.8	1.21	143.2	2.43	16.0	0.08
Hepatocellular Carcinoma (n=1)	69.6	1.66	164.7	0.89	25.7	1.51
Urea Cycle Defect (n=3)	50.3 ± 46.1 (18.8-103.2)	0.77 ± 1.51 (-0.26-2.51)	130.3 ± 28.1 (106.0-61.0)	-0.95 ± 0.94 (-1.96-(-0.11))	25.1 ± 12.8 (16.7-39.8)	1.48 ± 0.87 (0.97-2.48)
Total (n=27)	**33.8 ± 20.6 (11.0-103.2)**	**0.16 ± 1.30 (-2.91-2.51)**	**129.5 ± 24.9 (83.0-178.8)**	**-0.25 ± 1.21 (-2.31-2.43)**	**18.6 ± 5.2 (13.1-39.8)**	**0.46 ± 1.26 (-2.25-2.71)**

[1]Data are presented as mean ± standard deviation (range).
[2]Z-scores were calculated using CDC Epi Info software.
Abbreviations: BMI, Body Mass Index; LTX, Liver Transplantation.

Table 4-3 represents the laboratory data in children post-LTX. Of note, two children had elevations in ALT/AST due to coinciding infections that were resolving and were not related with any major changes in recent dietary intake.

Table 4-3: Laboratory Data in Children Post-Liver Transplantation

	Mean ± SD (range)	Median (interquartile range)	Normal Reference
ALT (U/L)[1]	35 ± 20 (15-104)	27 (25-38)	<50
AST (U/L)[1]	37 ± 13 (19-82)	35 (30-38)	<40
ALP (U/L)[1]	265 ± 62 (161-370)	266 (221-303)	130-500
Total Bilirubin (umol/L)[1]	8 ± 5 (3-20)	7 (6-8)	<20
Albumin (g/L)[1]	42 ± 3 (35-46)	41 (40-45)	35-50
Sodium (mmol/L)[1]	138 ± 3 (135-143)	138 (137-141)	133-146
Potassium (mmol/L)[1]	4.2 ± 0.4 (3.3-5.0)	4.3 (4.0-4.4)	3.3-4.8
Creatinine (umol/L)[1]	51 ± 29 (18-107)	42 (32-57)	25-110
Urea (mmol/L)[1]	5 ± 2 (3-10)	5 (4.2-5.5)	2-7
Magnesium (mmol/L)[1]	0.7 ± 0.2 (0.6-1.5)	0.7 (0.68-0.73)	0.7-1.0
Calcium (mmol/L)[1]	2.4 ± 0.1 (2.2-2.6)	2.4 (2.3-2.4)	2.2-2.7
INR[2]	1.1 ± 0.1(1.0-1.4)	1.1 (1.0-1.1)	0.8-1.2
Tacrolimus level (µmol/L)[2]	4.7± 1.9 (1.7-11.4)	4.7 (3.2-5.8)	3-5

Values are presented as mean ± standard deviation (range), median (interquartile range).
[1]n=21 for total bilirubin, AST, ALT, ALP, albumin, sodium, potassium, creatinine, urea, magnesium and calcium.
[2]n=26 for INR and Tacrolimus.
Abbreviations: AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase; ALP, Alkaline Phosphatase; INR, International Normalized Ratio; LTX, Liver Transplantation.

4.3.2 Macronutrient Intake

Table 4-4 represents dietary intake in children post-LTX compared to healthy controls. No significant differences in energy (on an absolute, or per kg and per 1000 kcal basis), carbohydrate, protein or fat intake were found between groups ($p>0.05$). Misreporting (over/under reporting) of EI as defined by EI/BMR was significantly lower in children post-LTX (n=13) compared to healthy children (n=21) ($p=0.054$). No differences were observed in under-reporting of EI (lower 95 % confidence intervals; post-LTX: n=7 vs controls: n=10) and over-reporting of EI (higher 95 % confidence intervals; post-LTX: n=6 vs controls: n=11) between children post-LTX and healthy control ($p>0.05$). Neither gender nor age (> and ≤ the median age: 8.6 years) had significant effects on energy or macronutrient intake ($p>0.05$) in either group studied.

4.3.3 Fibre, Sugar, Saturated Fat, Polyunsaturated Fat, and Monounsaturated Fat

The majority of children exceeded recommendations for saturated fatty acid intake (post-LTX: n=20 (74%) vs controls: n=19 (69%); $p>0.05$) as a percentage of EI. With the exception of total sugar intake (males: 73.7± 40.9 g/d vs females: 62.8 ± 42.5 g/d; $p=0.04$), no significant effects of gender or age (> and ≤ 8.6 years) related to fibre, sugar (simple), saturated fat, polyunsaturated fatty acid or monounsaturated fatty acid intake between and within groups were observed ($p>0.05$).

Table 4-4: Macronutrients Intake (24-hour recall) in Children Post-Liver Transplantation and Healthy Children

	Post-LTX (n=27) [1]		Healthy Control (n=28) [1]		DRI	p-value[2]
	Mean ± SD (range)	Median (interquartile range)	Mean ± SD (range)	Median (interquartile range)		
Energy (kcal)	1601 ± 627 (827-3589)	1508 (1168-1768)	1436 ± 418 (826-2802)	1323 (1160-1682)	-	0.46
Protein (g)	59 ± 28 (15-122)	52 (41-68)	62 ± 21 (35-99)	51.7 (46-86)	13-52[3]	0.63
% Protein	15 ± 4 (7-23)	15 (12-17)	17 ± 4 (12-32)	17 (14-19)	5-30[4]	0.02
Carbohydrate (g)	209 ± 79 (85-511)	203 (158-241)	189 ± 62 (114-391)	182 (147-217)	130[3]	0.24
% Carbohydrate	53 ± 9 (35-69)	51 (50-58)	53 ± 7 (35-65)	54 (47-58)	45-65[4]	0.79
Total Sugar (g)	85 ± 42 (9-213)	78 (68-93)	81± 27.8 (34-137)	75 (61- 99)	-	0.84
Fibre (g)	12.5 ± 7.6 (2.0-40.3)	11.5 (8.0-16.1)	11.0 ± 4.7 (5.0-22.8)	9.9 (8.2-13.0)	19-38[5]	0.48
Fat (g)	61 ± 32 (24-146)	59 (41-68)	51 ± 18 (26-95)	45.9 (39-56)	-	0.26
% Fat	33 ± 7 (18-45)	34 (31-38)	32 ± 6 (21-43)	31 (27-35)	25-40[4]	0.41
SFA fat (g)	22 ± 15 (4-72)	20 (12-25)	19 ± 7 (9-38)	17 (13-22)	-	0.54
% SFA fat	12 ± 4 (3-22)	12 (9-14)	12 ± 3 (8-18)	11 (10-14)	10	0.98
Trans Fat (g)	0.6 ± 0.4 (0.0-1.4)	0.50 (0.30-0.83)	0.38 ± 0.25 (0.0-0.90)	0.40 (0.17-0.53)	-	0.13
Cholesterol (mg)	163 ± 122 (34-566)	132 (91-205)	215 ± 131 (56-629)	185 (135-298)	-	0.06
PUFA (g)	9.7 ± 5.2 (1.2-25.8)	8.5(6.5-12.5)	7.6 ± 3.5 (3.6-16.6)	7.3 (5.1-8.5)	-	0.12
% PUFA	5.4 ± 2.0 (0.9-9.1)	5.2 (4.2-6.7)	4.8 ± 1.7 (2.8-9.9)	4.3 (3.8-5.0)	10	0.07
MUFA (g)	20.1 ± 11.1 (3.2-50.2)	18.5 (12.4-25.6)	19.3 ± 8.7 (7.7-37.5)	16.8 (13.2 -23.8)	-	1.00
% MUFA	11.0 ± 3.5 (2.4-17.9)	11.8 (8.2-13.0)	11.9 ± 3.4 (5.8-20.6)	11.3 (9.5 -13.4)	10	0.37
EI/BMR	1.45 ± 0.50 (0.53-2.57)	1.39 (1.22-1.64)	1.30 ± 0.35 (0.72-2.01)	1.28 (1.06-1.53)	-	0.20

[1]Values are presented as mean ± standard deviation (range), median (interquartile range).
[2]p-values <0.05 are considered statistically significant.
[3]Recommended Daily Allowance (RDA).
[4]Acceptable Macronutrient Distribution Range (AMDR): The percentage of energy derived from fat, carbohydrate and protein were all within AMDR.
[5]Adequate Intake (AI): Only one child post-LTX met the AI for fibre.
Abbreviations: BMR, Basal Metabolic Rate; DRI, Dietary Reference Intakes; EI, Energy intake; LTX, Liver Transplantation; MUFA, Monounsaturated Fatty Acid; PUFA, Polyunsaturated Fatty Acid; SD, Standard Deviation; SFA, Saturated Fatty Acid.

4.3.4 Micronutrient Intake

Micronutrient intake in children post-LTX and healthy children is shown in **Table 4-5.** Healthy children had higher dietary intake of vitamin B12 (control: 3.9 ± 1.6 mg/d vs post-LTX: 3.0 ± 1.7 mg/d; p=0.03). No other significant differences were found in macronutrient or micronutrient intake between groups (p>0.05). The majority of the cohort (71%) was on multivitamin supplementation. Multivitamin supplementation occurred in 85% of children post-LTX (n=23) and 57% of healthy children (n=16). Male children had higher intakes of thiamin (males: 1.19 ± 0.61 mg/d vs females: 0.84 ± 0.40 mg/d; p=0.01). Younger children had lower intakes of niacin (≤8.6 years: 9.3 ± 7.2 mg/d vs >8.6 years: 14.1 ± 10.4 mg/d; p=0.02), sodium (≤8.6 years: 1491 ± 594 mg/d vs >8.6 years: 2073 ± 1269 mg/day; p<0.01), and selenium (≤8.6 years: 59 ± 27 μg/day vs >8.6 years: 81 ± 37 μg/day; p=0.03) than older children.

There were no significant differences in vitamin D and calcium intake between groups using the two different measures of dietary intake assessment. Although children post-LTX were routinely prescribed vitamin D supplements (~85%) in the form of single preparations and/or multivitamin preparations (range: 400-1400 IU/d) in clinic, only n=19 children post-LTX met the RDA for vitamin D when considering the combined effects of supplementation and diet on total vitamin D intake. Even fewer healthy children met the RDA (n=6, 21%) for vitamin D when vitamin D supplementation (200-500 IU/d) was included in the overall assessment of vitamin D intake. The effect of calcium supplementation in multivitamin preparations (range: 40-1000 mg/d) resulted in 44% (n=12) of children post-LTX and 21% (n=6) of healthy children meeting the RDA for calcium. This was likely due to the low intake of multi-vitamin preparations (post-LTX: n=17 vs controls: n=3). No effects of age and/or gender on calcium and vitamin D intake were observed.

Table 4-5:Micronutrients Intake (24-hour recall) in Children Post-Liver Transplantation and Healthy Children

	Post-LTX (n=27) [1]		Healthy Control (n=28) [1]		DRI	p-value[2]
	Mean ± SD (range)	Median (interquartile range)	Mean ± SD (range)	Median (interquartile range)		
Vitamin A (RAE)	450 ± 286 (137-1346)	386 (246-456)	457 ± 356 (28-1858)	367 (248-595)	300-900[3]	0.97
Vitamin B1 (mg)	1.3 ± 0.5 (0.4-2.2)	1.2 (1.0-1.7)	1.1 ± 0.5 (0.4-3.0)	1.0 (0.8-1.2)	0.5-1.2[3]	0.09
Vitamin B2 (mg)	1.6 ± 0.6 (0.5-3.5)	1.6 (1.2-2.0)	1.6 ± 0.4 (0.6-2.7)	1.6 (1.4-1.9)	0.5-1.3[3]	0.88
Vitamin B3 (mg)	12.0 ± 6.2 (3.8-29.8)	11.4 (7.0-14.5)	14.4 ± 7.0 (4.5-32.6)	12.9 (9.1-18.8)	6-16[3]	0.17
Vitamin B6 (mg)	1.2 ± 0.5 (0.3-2.5)	1.1 (0.8-1.4)	1.1 ± 0.4 (0.4-2.0)	1.1 (0.8-1.3)	0.5-1.3[3]	0.85
Vitamin B12 (mg)	3.0 ± 1.7 (0.3-7.2)	2.8 (1.8-3.8)	3.9 ± 1.6 (1.5-8.7)	3.8 (2.7-4.4)	0.9-2.4[3]	0.03
Vitamin C (mg)	108 ± 72 (6-296)	99 (63-151)	84 ± 63 (14-293)	68 (28-118)	15-75[3]	0.18
Vitamin D (IU)	209 ± 131 (39-611)	186 (130-240)	191 ± 123 (7- 467)	189 (85-246)	600[3]	0.71
Vitamin K (μg)[3]	52 ± 58 (8-285)	38 (16-59)	51 ± 64 (4-296)	28 (12-49)	30-75[5]	0.41
Vitamin E (mg)	4.0 ± 5.1 (0.2-26.6)	2.1 (1.4-4.5)	2.8 ± 1.3 (0.8-6.7)	2.6 (2.1-3.3)	6-15[3]	0.90
Folate-DFE (μg)	209 ± 92 (67-437)	208 (143-270)	243 ± 128 (95-633)	226 (129-307)	150-400[3]	0.44
Calcium (mg)	921 ± 432 (139-2167)	912 (718-1104)	798 ± 280 (97-1314)	799 (642-951)	700-1300[3]	0.33
Iron (mg)	10.7 ± 4.5 (3.9-25.4)	10.7 (7.7-12.5)	10.0 ± 3.7 (3.9-19.3)	9.9 (7.5-12.6)	7-15[3]	0.63
Magnesium (mg)	215 ± 78 (53-462)	201 (168-266)	202 ± 73 (109-379)	177 (151-246)	80-410[3]	0.29
Selenium (μg)	63 ± 24 (18-112)	58 (50-82)	73 ± 19 (43-111)	78 (59-85)	20-55[3]	0.09
Sodium (mg)	2071 ± 1124 (506-5733)	1800 (1532-2404)	1811 ± 757 (935-4020)	1681 (1231-1991)	1000-1500[5]	0.36
Zinc (mg)	9.5 ± 7.5 (2.4-33.7)	7.3 (5.0-10.0)	8.0 ± 3.2 (4.4-17.1)	7.2 (5.5-10.0)	3-11[3]	1.00

[1]Values are presented as mean ± standard deviation (range), median (interquartile range).
[2]p-values <0.05 are considered statistically significant. [3] Vitamin K content was analyzed using the USDA online nutrient database.
[3]Recommended Daily Allowance (RDA): Children met the RDA: folate (post-LTX: n=9 (33%) vs controls: n=11 (39%); p=0.78), vitamin A (post-LTX: n=8 (30%) vs controls n=10 (36%); p=0.78), vitamin E (post-LTX: n=3 (11%) vs controls: n=0 (0%); p=0.11), calcium (post-LTX: n=7 (26%) vs healthy children: n=5 (18%), and magnesium (post-LTX n=18 (67%) vs controls n=11 (39%); p=0.06). Only one child post-LTX met the RDA for vitamin D.
[4]Acceptable Macronutrient Distribution Range (AMDR).
[5]Adequate Intake (AI): Children met the AI for vitamin K (post-LTX: n=7 (26%) vs controls: n=6 (21%); p=0.76).
Abbreviations: DRI, Dietary Reference Intakes; DFE, Dietary Folate Equivalent; RAE, Retinol Activity Equivalents; LTX, Liver Transplantation; SD, Standard Deviation.

4.3.5 Food Groups

No significant differences were found in the total number of food group servings consumed grains (post-LTX: 4.7 ± 2.8 vs controls: 4.0 ± 1.5; p=0.08), milk and alternatives (post-LTX: 2.2 ± 2.1 vs controls: 2.0 ± 2.3; p=0.85) or meat and alternatives (post-LTX: 1.3 ± 2.1 vs controls: 1.5 ± 1.3; p=0.90) between children post-LTX and healthy controls. However, children post-LTX had a significantly higher intake of fruits and vegetables (3.9 ± 2.1) compared to healthy controls (1.5 ± 1.3) (p=0.02). No significant effects of age or gender on the number of food groups servings consumed were found (p>0.05).

4.3.6 Glycemic Index and Glycemic Load

Figure 4-1 represents GI and GL intakes of children post-LTX and healthy controls. No significant differences were observed in GI and GL intakes between groups (p>0.05). Most children had GI intakes reflecting low-moderate GI (<60; post-LTX: n=27 vs controls: n=26; p>0.05) and low-moderate GL intake (post-LTX: n=21 (75%) vs controls: n=23 (86%); p=0.24).

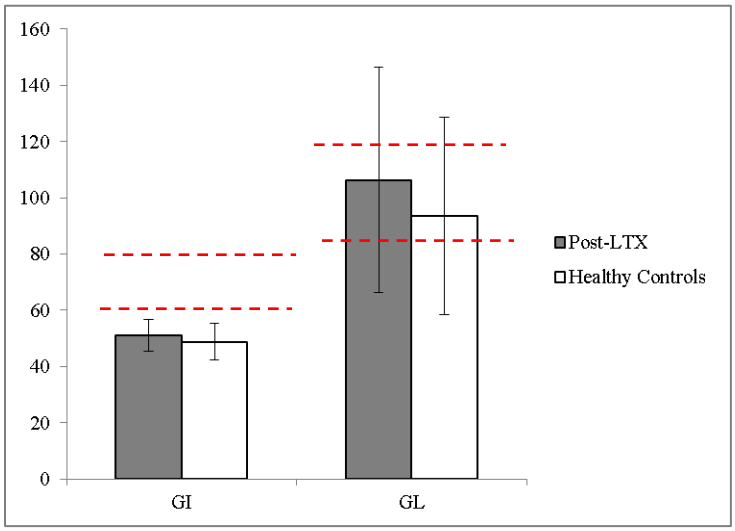


Figure 4–1: Glycemic Index and Glycemic Load in Children Post-Liver Transplant (n=27) and Healthy Controls (n= 28). Dashed red lines represent the cut-off values of high, medium and low GI ≥70, between 69-56, and ≤55 and GL ≥120, between 80-119, and <80, respectively (87, 96, 97, 224). No significant differences were observed in GI and GL intakes between groups (p>0.05).
Abbreviations: GI, Glycemic index; GL, Glycemic load; LTX, liver transplant.

4.3.7 Diet Quality Scores: Healthy Eating Index-Canada, Dietary Guideline Index for Children and Adolescents, and Diet Quality Index-International

The Bland Altman analysis to assess level of agreement between the adapted and not adapted (original) DQ tools in both children post-LTX and healthy controls and the majority of values were within 2 SD **(Appendix H, Figures H-1** to **H-3** and **Table H-1). Figure 4-2** presents the DQ scores between children post-LTX and healthy controls. Many children in the post-LTX group had low DQ. The majority of children post-LTX had a DGI-CA scores ≤68 (n=23, 85%) compared to controls (n=16, 57%) (p=0.04). No significant differences were found in the proportion of children with HEI-C scores ≤80 (post-LTX: n=24, 89%; control: n=24, 86%) and DQI-I ≤60 (post-LTX: n=12, 44%; control: n=15, 54%) between children post-LTX and controls (p>0.05).

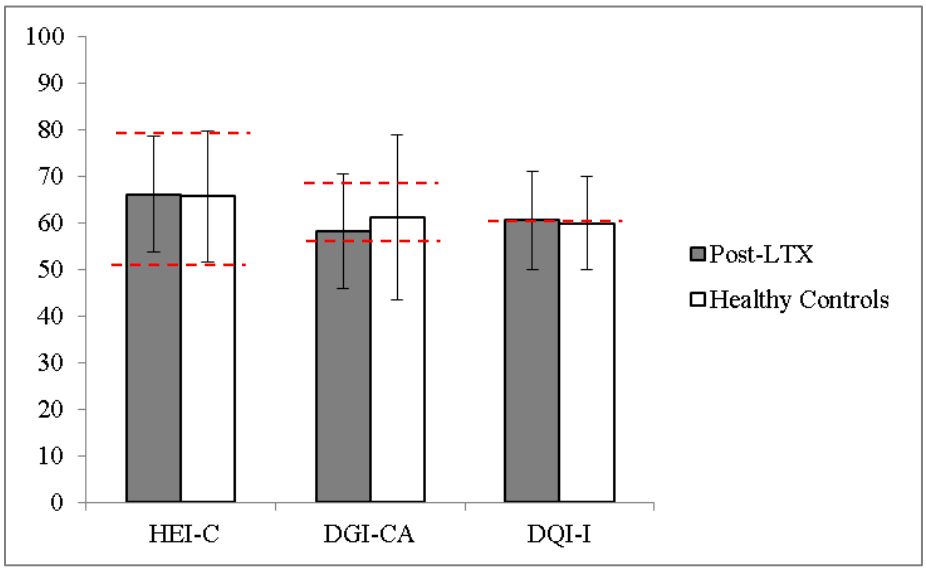


Figure 4–2: Diet Quality Scores in Children Post-Liver Transplant (n=27) and Healthy Controls (n= 28). Dashed red lines represent the cut-off values of "good", "needs improvement" or "poor" diet quality. HEI-C scores were categorized as good (>80, needs improvement (HEI-C scores 51-80), and poor diet (≤50) (35, 225). DGI-CA scores were categorized as good (>68), needs improvement (55-68), and poor diet (<55) (31, 74). DQI-I scores were categorized as good (≥60), and poor diet (<60) (226).
Abbreviations: HEI-C, Healthy Eating Index-Canada; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; LTX, liver transplant.

4.3.8 Interrelationships between Dietary Intake and Anthropometric and Demographic Variables

No significant differences were found between gender and anthropometric (wt-z, ht-z, and BMI-z), and macro and micronutrient intake, GI, GL, or DQ scores (HEI-C, DGI-CA and DQI-I) ($p>0.05$). GL was higher in children >8.6 years than children ≤8.6 years ($p=0.03$). Children older than the median age of 8.6 years had a significantly higher GL (children >8.6 years: 107 ± 45 vs children ≤8.6 years: 84 ± 36) and lower HEI-C score (children >8.6 years: 59 ±13 vs children ≤8.6 years: 72 ± 10), DGI-CA score (children >8.6 years: 52 ±15 vs children ≤8.6 years: 67 ±12), and DQI-I (children >8.6 years: 56 ± 11 vs children ≤8.6 years: 64 ± 8) scores than children younger than the median age of 8.6 years ($p<0.01$). Within the LTX group, no relationships were found between demographic variables (age at LTX, time since LTX) and macro-and-micronutrient intake, GI, GL, HEI-C, DGI-CA, and DQI-I scores ($p>0.05$).

4.4 Discussion

Adequate dietary intake in children post-LTX is important to improve growth and enhance post-transplant outcomes. This study is the first study to describe dietary intake and DQ of children who have undergone LTX. Overall, with a few exceptions, our study findings indicate that macro- and micronutrient intake of children post-LTX and healthy controls are very similar and both groups had similar limitations in DQ. These limitations included intakes characterized by lower fruit, vegetable and dairy products, lower fibre, and polyunsaturated fatty acid and higher saturated fat intake compared to recommendations of children and adolescents for age and gender.

Intakes of micronutrients consumed in inadequate amounts in the diet were also very similar between the groups. Many children had low intakes of vitamin D and calcium and marginal intakes of folate, vitamin K and vitamin A; likely due to reduced intakes of vitamin D-fortified dairy products and fruits and vegetables; particularly green leafy vegetables. Almost all children

did not meet the RDA of vitamin D from diet alone. This finding is similar to what is reported in the majority of Canadian children; where a suboptimal vitamin D status related to inadequate intakes of vitamin D fortified dairy products has been consistently reported (265, 266). Collectively, our data illustrate that children post-LTX have dietary intake patterns similar to their healthy counterparts. All of this indicates the need for routine supplementation of these nutrients and the importance of promoting improved intakes of vitamin D fortified dairy products and green leafy vegetables in children post-LTX (267, 268).

Poor DQ has been previously reported in healthy children and children with chronic disease such as non-alcoholic fatty liver disease and type-1 diabetes (31, 87, 269). A recent study found that poor DQ (HEI score) is associated with non-alcoholic fatty liver disease (174). In our study, approximately 50-75% of our entire cohort had poor DQ scores (controls and post LTX). Reduced DQs score may be due to higher intakes of fat, saturated fat and sugar and lower intakes of fruit and vegetables coupled with reduced variety in food selection. This is particularly evident in children who were over 8.6 years (median age). Children older than 8.6 years had lower DQ scores than their younger peers. This is consistent with the literature, where it had been found increasing age, intakes of dairy products and fruit and vegetables decrease and dietary intake of fat and saturated fat increase in children (270, 271).

This study measured DQ using three validated DQ tools in healthy population. We have adapted the DQ tools to be consistent with the Canadian recommendations (DRI and ANGCY) (**Appendix A, Table A-1** to **A-3).** One of the main challenges of adaptation of DQ tools was food group analysis. DGI-CA and DQI-I are based on American and Australian food guides in which fruit and vegetables are two separate food groups. We followed the Dubois et al (2000) approach by grouping fruit and vegetables into one food group (69). Another challenge was to adapt the DRI

and the AMDR to meet the recommendations for children. Bland Altman analysis was conducted between the original vs the adapted version of DQ tools in both children post-LTX and healthy children (**Appendix H, Figure H-1** to **H-3**). The difference in scores between the original vs the adapted DQ tools ranged from 1-3 scores and the majority of scores were within 2 SD of the difference between DQ original vs adapted DQ tool.

The development or modification an existing DQ tool to measure nutrients at risk in healthy children and children post-LTX is necessary. We have measured DQ using three different DQ tools to capture the majority of nutrients of concern in children and adolescents post-LTX. While children and adolescents post-LTX are at risk for poor bone health, obesity, and cardio-metabolic dysregulation, there are no validated DQ tools designed to capture all the nutrients and foods of concern in this vulnerable population such as the quality of protein (amino acids), fat (omega-3 to omega-6 fatty acids), carbohydrate (fibre, fructose, GI, and GL) and the major micronutrients such as sodium and vitamin K (due to high risk of poor bone health and cardio-metabolic dysregulation). In regard to foods and food variety, assessing the intake of fruit and vegetables compared to the recommendations does not give a clear picture of food variety. For example, it is important to assess the intake of green leafy vegetables, fruit as whole or juice, beans and nuts. Finally, the cut-off values of the components for the DQ tools may need to be modified. The cut-off values of the current DQ tools are based on healthy children. However, youth post-LTX are at particularly high risk of cardio-metabolic dysregulation due to chronic effects of immunosuppressant therapy on metabolic pathways. These medications place the child post-LTX at a higher risk for cardio-metabolic dysregulation than healthy children of comparable body weights. Therefore, the cut-off scores should be established based on the risk for the development of cardio-metabolic dysregulation in children.

Children post-LTX are at high risk of cardio-metabolic dysregulation due to immunosuppression regime and obesity (155, 183). Obesity after transplantation has been observed in adults and pediatrics (155, 183). In our study, two children post-LTX were obese (BMI-z >2) and 26% of children post-LTX were classified overweight (BMI-z >1). This may be due to poor DQ (overall DQ, fat, GI, and GL). Poor DQ is highly related to cardio-metabolic dysregulation (elevated liver enzymes, dyslipidemia) (87, 272). Complications can influence both graft survival and long-term survival rate (158, 273). Body composition (body fat and central adiposity) is another factor influencing long-term survival rates. Some evidence has shown that long-term survivors of childhood LTX have reduced body cell mass and increased fat mass with an increasing potential for the development of cardio-metabolic dysregulation (274). These are important considerations because although dietary intake may not differ between post-LTX children and healthy controls, reduced body cell mass and increased fat mass observed in children following LTX could result in an increased risk for cardio-metabolic dysregulation; all of which may have important influences on long-term graft survival (158, 273, 274).

This study is unique due to limited information about dietary intake and DQ in children post-LTX especially in Canada. The Stollery Children's Hospital in Edmonton and Sick Children Hospital in Toronto are the only centres in Canada that preform LTX in infants and children. Around 40% of the study participants live out of Edmonton or Alberta; hence collecting a one day 24-hour recall may not represent the usual intake. This is important as 24-hour recalls might have included the day that was spent travelling to attend clinic. To minimize this potential bias, our study included two 24-hour recalls to assess dietary intake (50). In the current study, both children post-LTX and healthy controls equally misreported intake (EI/ BMR) and this did not change the overall assessment of DQ since under/over-reporting did not affect the assessment of macro-and-

micronutrient intake (% kcal), GI, DQ scores (HEI-C, DGI-CA and DQI-I) in either groups (**Appendix I, Table I-1**). In addition, the overall coefficient of variation in each group approximated 20%, which is similar to what has been reported in other diet studies in children and adults (221, 275, 276). Hence, it is unlikely that a systematic bias related to under/over-reporting of dietary intake influenced overall study findings.

The main limitation of the current study was the small sample size (Post Hoc Power Analysis, **Appendix I, Table I-3**). Other limitations within the study design include the inability to form definitive conclusions regarding multiple factors (e.g. health related outcomes post-LTX, quality of life, socio-economic and cultural factors) influencing dietary intake in children who have undergone LTX. Finally, it is not possible to relate dietary intake with the risk of cardio-metabolic dysregulation, as we did not collect biochemical variables (such as fasting insulin, lipid profile) in this study design.

In conclusion, our results demonstrate that the diets of children five years post-LTX are very similar to their healthy peers and was low in comparison to current nutritional guidelines; with all the same limitations in DQ (77, 219, 263). This included higher intakes of fat, saturated fat and lower intakes of several micronutrients important to long-term growth and development including bone health. Understanding the long-term implications of suboptimal nutritional intake on improving graft survival and overall risk of cardio-metabolic dysregulation is important in children post-LTX.

Chapter 5 Influence of Diet Quality on Anthropometric and Markers of Cardio-Metabolic and Liver Disease Function in Youth with Non-Alcoholic Fatty Liver Disease

5.1 Introduction

The prevalence of childhood obesity and risk for cardio-metabolic dysregulation in childhood have both been increasing rapidly worldwide. Almost 50% of overweight and obese children and adolescents are at risk for cardio-metabolic dysregulation (107). Cardio-metabolic dysregulation can manifest in several ways (obesity, hypertension, dyslipidemia) and is associated with a variety of clinical conditions (cardiovascular disease, non-alcoholic fatty liver disease [NAFLD]) (107). NAFLD includes a spectrum of liver disorders ranging from a simple steatosis (SS), to more advanced liver disease encompassing inflammation (non-alcoholic steatohepatitis (NASH)), to cirrhosis (107). SS is defined by fat accumulation in the liver (>5% of liver weight), whereas NASH is characterized by fat infiltration, inflammation, and hepatic cellular damage with or without fibrosis (107, 277).

Sedentary lifestyle and imbalanced dietary intake are risk factors for NAFLD (170). Several dietary factors have been associated with NAFLD including diets with high energy (kcal) densities and/or unbalanced macronutrient intakes that are high in saturated fat, and simple sugars, and low in omega-3 fatty acids, fibre, and antioxidants (vitamin A, vitamin C, vitamin E) (73, 87, 170, 174, 187, 188). Excessive kcal and macronutrient intakes are associated with increased risk of cellular oxidation and cause liver damage, fibrosis, and inflammation (278)**.** Antioxidants play an important biological role through scavenging free radicals and reducing fat accumulation in liver. A study conducted in adults with NASH reported low plasma levels of antioxidants relative to the control group (279, 280). Low antioxidant levels in patients with NAFLD may be related to poor diet quality (DQ) (73, 174, 279, 280).

In general, lifestyle modification (dietary intake, physical activity) is the mainstay treatment for NAFLD (107). However, there is no specific dietary prescription for NAFLD (281, 282). Several dietary intervention studies have been conducted in children and adults with NAFLD focusing on dietary reduction of total fat, saturated fat, glycemic index (GI), and glycemic load (GL), while optimizing omega-3 fatty acid and antioxidant intake (vitamin C and vitamin E) (87, 108, 109, 171, 172, 283). Some studies in children with NAFLD following low GI and GL diets for 6 months have illustrated reductions in liver steatosis, alanine aminotransferase (ALT) levels, systolic blood pressure, apo-lipoprotein B100 levels, and HOMA-IR scores. Other studies performed in adults with NAFLD, have reported that increasing omega-3 fatty acid consumption improved lipid profiles (triglyceride [TG], high-density lipoprotein [HDL], low-density lipoprotein [LDL]) (108, 284, 285). Supplementation with vitamin C (1 g/day) and vitamin E (1000 IU/day) for 4 years was associated with a 71% reduction in hepatic steatosis in adults with NAFLD. However, evidence is lacking regarding the efficacy of antioxidant therapy (286). Most of these dietary approaches have also included an emphasis on low energy consumption to promote weight loss. Long-term adherence to these dietary interventions is suggesting that other approaches may be needed to elicit lasting improvements in overall liver function in NAFLD. No prior dietary interventions have investigated overall DQ; a concept that focuses on improving overall nutritional quality of diet in youth with NAFLD.

Recent novel work by our group has demonstrated that consumption of an iso-caloric, low GI/GL/fructose diet was associated with significant improvements in liver enzymes, the markers of insulin sensitivity, and apo-lipoprotein B100 in youth with NAFLD (87). This therapeutic approach included a focus on optimizing DQ by promoting intake of fresh fruits and vegetables, rather than processed forms of these foods (e.g. sugar sweetened beverages). However, direct

measures of DQ were not included in the overall analysis of this study. Dietary intervention studies for children with NAFLD that focus on overall DQ to ensure: 1) overall dietary balance rather than single nutrient intake and 2) adherence to a balance dietary pattern, as there are no specific diet therapy for children with NAFLD (3, 4, 9, 73, 174).

The main study objectives are to assess and compare overall DQ in youth with NAFLD and healthy lean controls. Overall DQ are assessed by: 1) macronutrient intake, 2) antioxidants (vitamin A, vitamin C, vitamin E), 3) food groups, 4) GI and GL, and 5) DQ tools (Healthy Eating Index-Canada [HEI-C], Dietary Guideline Index for Children and Adolescents [DGI-CA], Diet Quality Index-International [DQI-I]). Assessing overall DQ using three different DQ tools is based on the total score and the components of each DQ tools. The secondary objective of this chapter is to examine the interrelationships between DQ and anthropometric measurements (body weight, body composition) and markers of liver dysfunction, and cardio-metabolic parameters. We hypothesized that children and adolescents with NAFLD have poor overall DQ compared to lean children. Poor overall DQ is associated with an increased risk for liver dysfunction and cardio-metabolic markers in children with NAFLD.

5.2 Material and Methods

This thesis chapter presents a secondary analysis of data from an earlier prospective study examining the interrelationships between dietary intake and markers of lipid metabolism in obese children (± NAFLD) and healthy lean children (188, 189). This chapter will evaluate macronutrient intakes, antioxidants (vitamin A, vitamin C, vitamin E), food groups, GI and GL, and DQ tools (HEI-C, DGI-CA, and DQI-I score, as well as specific components of the tools: Adequacy, Moderation and Variety) that are important to the overall assessment of DQ. (87).

5.2.1 Subjects

A prospective study was conducted in n=37 (n=18, NAFLD; n=19, lean control) children and adolescents (8-18 years old) (188, 189). Children and adolescents with NAFLD were recruited from the Liver Clinics (NAFLD) at the Stollery Children's Hospital, Edmonton, Alberta, Canada between 2010-2014. Lean controls with body weights within normal reference ranges and not known any healthy conditions were recruited from the general community using advertisements. Children and adolescents with NAFLD underwent comprehensive medical history, abdominal ultrasound, and serological workup to rule out other liver diseases, such as chronic hepatitis B and C, autoimmune hepatitis, alpha 1-antityrpsin deficiency, and Wilson disease (188, 189). All patients with NAFLD were tested to exclude presence of competing liver diseases (e.g. viral hepatitis).

Several methods for NAFLD diagnosis have been reported: liver biopsy, ultrasonography, computerized tomography, magnetic resonance imaging, and fibroscans (287). Liver biopsy is considered the gold standard for diagnosis as it is able to distinguish between SS and NASH (87, 188, 189, 287). A diagnosis of NAFLD was confirmed with Ultasound (n=7) or liver biopsy (n=9) in addition to elevated liver enzymes. The stage of NAFLD (SS vs NASH) was determined in patients with liver biopsy (87, 188, 189). Ethics approval was obtained from the University of Alberta Human Research Ethics Board (Ethics File # Pro00000512).

5.2.2 Anthropometrics, Body Composition and Biochemical Variables

Elaborating from previous analysis from our lab, anthropometrics (weight and height, waist and hip circumference) skinfold measurement and body composition were measured (87, 188). Weight-for-age z-score (wt-z), height-for-age z-score (ht-z), body mass index (BMI), and BMI-for-age z-score (BMI-z) were calculated using the 2014 World Health Organization (WHO) Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-

gcep.net/sites/default/files/plotter/index.html) (216).

Routine blood work (liver enzymes, metabolic parameters) was analyzed by Laboratory Services, Alberta Health Services including: liver enzymes (ALT, Aspartate Aminotransferase [AST], γ-Glutamyltransferase [γGT]), fasting glucose, insulin, lipid profile (TG, total cholesterol, HDL, LDL), and C-Reactive Protein [CRP] concentrations were investigated (87, 188).

5.2.3 Dietary Intake Assessment

Dietary Intake was assessed using three day food records (2 weekdays and 1 weekend day) and analyzed with Food Processor software (SQL 10.8.0 ESHA® Research, Salem, OR, USA, 2011). Basal metabolic rate (BMR) was calculated using the WHO equations for age and gender (288). Ideal body weight was used to calculate BMR for participants with actual body weights above 120% or below 90% of ideal body weight. To assess the potential of misreporting actual food intake, the ratio of energy intake (EI) to estimated BMR was calculated. Misreporting of energy intake (over or under reporting) was defined as EI/BMR values outside the 95% confidence intervals for each group (276). Food groups were categorized based on age- and gender-specific Alberta Nutrition Guidelines for Children and Youth (ANGCY) (77). Macronutrient intakes were compared to age- and gender-specific Acceptable Macronutrient Distribution Range (AMDR), Recommended Dietary Allowance (RDA), or Adequate Intake (AI) (219, 263). We assessed the intake of vitamins A, C, and E between children with NAFLD and lean controls and compared micronutrient intakes to age-and gender-specific RDAs (219, 263).

5.2.4 Glycemic Index, Glycemic Load

GI and GL intakes were calculated as described in **Chapter 3** and **Appendix A.** Diets with GI values ≥70, between 69-54, and ≤55 are classified as high, medium, and low GI, respectively

(96, 97, 224). Diets with GL ≥120, between 80-119, and <80 are classified as high, medium, and low GL, respectively (87).

5.2.5 Diet Quality Tools: Healthy Eating Index-Canada, Dietary Guideline Index for Children and Adolescents, and Diet Quality Index-International

Three validated DQ tools were used to assess overall diet quality: Healthy Eating Index-Canada (HEI-C), Dietary Guideline Index for Children and Adolescents (DGI-CA), and DQI-I. DQ scores range from 0-100, with 100 points referring to the "optimal level" of DQ and lower results indicating "lower level" or poorer DQ (16, 31, 35). Details about DQ tools are described in **Chapter 3** and **Appendix A (Table A-1** to **A-3)**. For this thesis chapter only, we have assessed DQ in three different ways: **A)** total DQ Scores (HEI-C, DGI-CA and DQI-I), **B**) components of DQ scores (Adequacy, Moderation, Variety), and **C**) DQ Models.

B) The Components of DQ Scores (**Figure 5-1**) were measures as follows:

1. Adequacy

- HEI-C: the sum score of fruit and vegetables, grains, milk and alternatives, and meat and alternatives (Maximum score is 50).
- DGI-CA: the sum score of fruit and vegetables, grains, milk and alternatives, and meat and alternatives (Maximum score is 40).
- DQI-I: the sum score of fruit and vegetables, grains, fibre, protein, iron, calcium, and vitamin C (Maximum score is 40).

2. Moderation

- HEI-C: the sum score of fat, saturated fat, cholesterol, and *other foods* group (Maximum score is 40).

- DGI-CA: the sum score of *other foods* group, beverage and food choice (saturated fat) (Maximum score is 40).
- DQI-I: the sum score of fat, saturated fat, cholesterol, sodium, and *other foods* group (Maximum score is 30).

3. Variety or Diversity (Overall food groups and within food groups)

- HEI-C (variety): the score of variety (Maximum score is 10). We did not assess the interrelationships between HEI-C (variety) score and anthropometric and biochemical markers because the majority of our cohort had 100% of the maximum score of Variety score.
- DGI-CA (Foods): the sum score of whole grains, and low fat milk (Maximum score is 10).
- DGI-CA (Grain): the sum score of total grains and whole grains (Maximum score is 10).
- DGI-CA (Milk): the sum score of milk and alternatives and low fat milk (Maximum score is 10).
- DQI-I (overall food groups and within protein sources): the sum score of overall food groups and within food groups (Maximum score is 20).

4. Overall Balance

We did not analyze in one specific DQ tool: DQI-I (overall balance; Maximum score is 10) which includes macronutrient ratios as %Kcal (carbohydrate: protein: total fat) and fatty acid ratios (saturated fatty acid: monounsaturated fatty acid: polyunsaturated fatty acid), since 97% of our cohort had <30% of the maximum score.

C) Diet Quality Models for Assessment of Adequacy and Moderation

DQ models for Assessment of Adequacy and Moderation were calculated based on the sum of Adequacy and Moderations within and between DQ tools (**Figure 5-1**). This thesis chapter will present DQ models within DQ tools only.

1. **Within Diet Quality Tool**

   a. **HEI-C:** the sum of Adequacy (food groups) and Moderation (fat, saturated fat, cholesterol, and *other foods* group), maximum score is 90.

   b. **DGI-CA:** the sum of Adequacy (food groups) and Moderation (saturated fat, beverage, and *other foods*), maximum score is 80.

   c. **DQI-I:** the sum of Adequacy (fruit and vegetables, grains, fibre, protein, iron, calcium, and vitamin C) and Moderation (fat, saturated fat, cholesterol, sodium and *other foods* group), maximum score is 70.

2. **Between Diet Quality Tools:** This data are presented in **(Appendix J, Tables J-51** to **J-56).**

   a. **DQ Model 1:** the sum of Adequacy (DQI-I) and Moderation (HEI-C) scores (Maximum score is 80).

   b. **DQ Model 2:** the sum of Adequacy (DQI-I) and milk and alternatives and meat and alternatives scores from DGI) and Moderation (HEI-C) scores (Maximum score is 95). Due to lack of assessing milk and alternatives meat and alternatives in DQI-I, we added DGI-CA (milk and alternatives and meat and alternatives) scores.

   c. **DQ Model 3:** the sum of Adequacy (DQI-I and meat and alternatives score from DGI-CA) and Moderation (HEI-C) scores (Maximum score is 90). We have included meat and alternatives only because milk and alternatives was correlated with DQI-I calcium score ($r=0.7$, $p<0.01$) and was the main source of calcium (**Appendix J, Figure J-1)**.

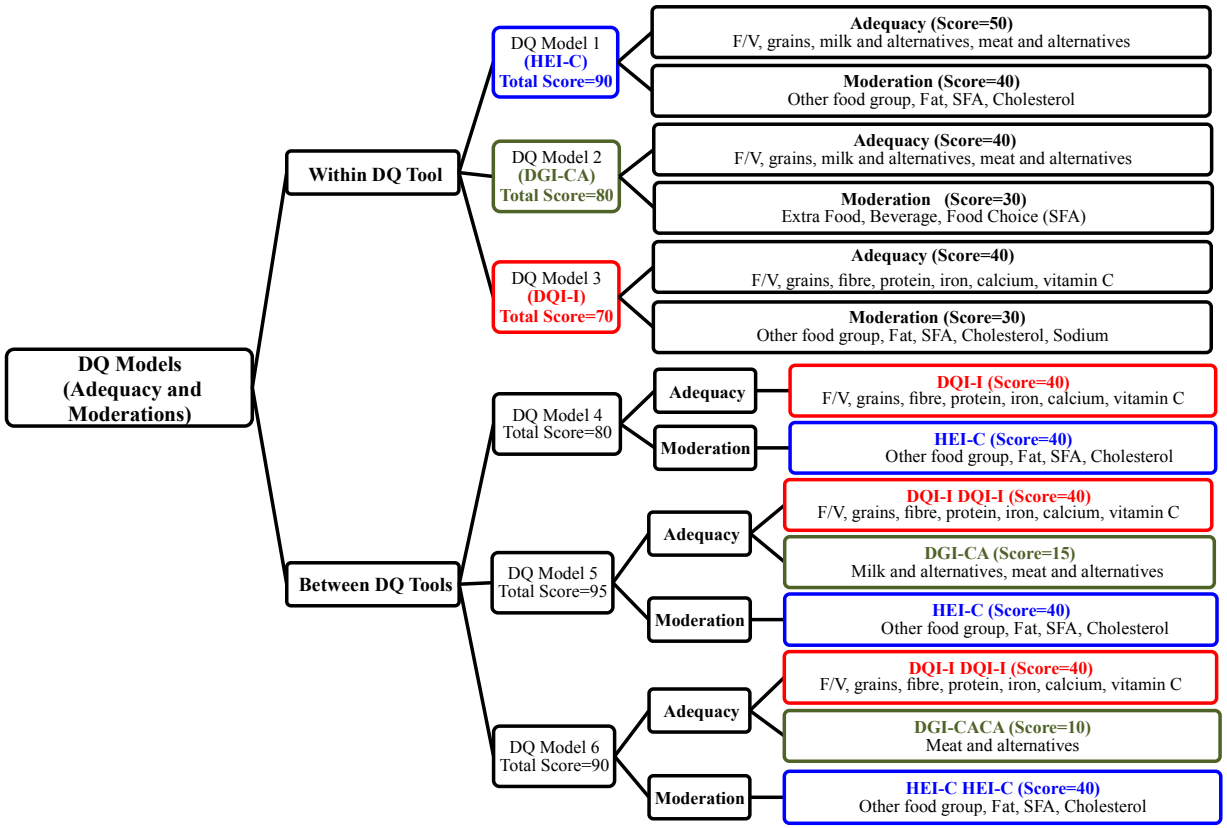


Figure 5–1: The Components Diet Quality Models for Assessment of Adequacy and Moderation.

Each Model is the sum of Adequacy and Moderation scores within (Model 1 to Model 3) Diet Quality tools and between Diet Quality tools (Model 4 to Model 6). Boxes highlighted in the same color indicate similar Diet Quality tool.
Abbreviations: DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; HEI-C, Healthy Eating Index-Canada; F/V, Fruit and Vegetables; SFA, Saturated Fatty Acid.

5.2.6 Statistical analysis

Statistical analyses were performed using SAS 9.0 statistical software (SAS, Version 9.4; SAS Institute Inc., Cary, NC, USA). Data were expressed as mean ± standard deviation (for parametric variables) or as median and interquartile range (IQ) for non-parametric variables. A p-value <0.05 was considered statistically significant.

For primary analysis (anthropometric, body composition, biochemical, DQ scores, GI and GL), two-sample independent t-tests or Mann Whitney tests were conducted to compare the statistical differences between NAFLD and lean control in normally distributed variables and variables demonstrating skewed distributions, respectively. Fisher exact tests were conducted to analyze categorical data. For secondary analysis (examine the interrelationships within the NAFLD group), all data were grouped together (NAFLD and lean control) due to insufficient power to detect group effects in multivariate analysis. Multivariate analysis was used to examine interrelationships between food groups, GI, GL, and DQ (total and components) and potential confounders including gender and age (< and ≥ median age 14 years). To assess the interrelationships between DQ (total and components), GI, GL and wt-z, BMI-z, body composition, liver dysfunction, cardio-metabolic parameter, DGI-CA and DQI-I were dichotomized based on cut-off values of "good DQ" for DQ (DGI-CA ≥ and <68; DQI-I (≥ and <60). Conversely, we used median as cut-off values: HEI-C scores (< and ≥70), GI (< and ≥48), GL (< and ≥108), HEI-C Adequacy (< and ≥34), DGI-CA Adequacy (< and ≥27), DQI-I Adequacy (< and ≥26), HEI-C Moderation (< and ≥30), DGI-CA Moderation (< and ≥28), DQI-I Moderation (< and ≥21), DGI-CA Foods (< and ≥5.2), DGI-CA Grains (< and ≥6), DGI-CA Milk (< and ≥7), DQI-I Variety (< and ≥18), and DQ Models for Assessment of Adequacy and Moderation within

HEI-C (< and ≥60), DGI-CA (< and ≥54), and DQI-I (< and ≥45). Skewed variables (body composition, liver dysfunction, and cardio-metabolic parameters) were log transformed.

5.3 Results

5.3.1 Participants, Demographic Data

A total of n=37 children and adolescents with NAFLD (n=18 (3F:15M)) and lean controls (n=19 (10F:9M)) were reviewed. No significant difference was found in age between NAFLD (14 ± 2 years) and lean control (14 ± 2 years; p=0.99).

5.3.2 Anthropometric and Body Composition Data

Table 5-1 demonstrates anthropometric and body composition between children with NAFLD and lean controls. No significant differences in wt-z, ht-z, and BMI-z between children ≥14 and <14 years old or by gender were noted (p>0.05; **Appendix J, Table J-2** and **J-3).** Children ≥14 years had significantly higher fat mass (kg) and fat free mass (kg) compared to children <14 years old (p<0.05; **Appendix J, Table J-2).** Male children had significantly higher waist circumference and fat free mass relative to females (p<0.05; **Appendix J, Table J-3).**

Table 5-1: Anthropometric and Body Composition Data in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	NAFLD (n=18)	Lean Control (n=19)	p-value[1]
Weight (kg)[2]	91 (71-106)	49 (42-51)	<0.01
Weight for age z-score[2,4]	2.58 ± 0.51	-0.23 ± 1.00	<0.01
Height (m)[3]	1.64 ± 0.13	1.59 ± 0.13	0.18
Height for age z-score[3,4]	0.70 ± 1.36	-0.01 ± 0.83	0.07
BMI (kg/m^2)[2]	32.0 (29.3-36.2)	18.4 (17.7-19.9)	<0.01
BMI for age z-score[2,4]	2.74 ± 0.39	-0.30 ± 0.99	<0.01
Waist circumference (cm)[2,5]	96 (89-111)	63 (61-66)	<0.01
Hip circumference (cm)[3,5]	109 ± 14	84 ± 9	<0.01
Waist to hip[3,5]	0.91 ± 0.07	0.75 ± 0.05	<0.01
Waist to height[2,5]	0.57 (0.55-0.65)	0.40 (0.38-0.42)	<0.01
%Fat free mass [2,5]	65.9 (56.1-69.8)	87.1 (82.9-89.8)	<0.01
Fat free mass (kg)[3,5]	59.3 ± 12.2	41.5 ± 9.9	<0.01
%Body Fat [2,5]	34.1 (30.3-43.9)	12.9 (10.2-17.1)	<0.01
Fat mass (kg)[2,5]	30.7 (20.6-51.5)	6.7 (4.4-8.6)	<0.01

Data were used with the permission of SAGE: Mager et al (2012) Nutrition in Clinical Practice and Mager et al (2013) Journal of Parenteral and Enteral Nutrition.
[1]p-values <0.05 are considered statistically significant.
[2]Variables demonstrating skewed distributions are presented as median (interquartile range). Mann Whitney tests were conducted.
[3]Normally distributed variables are presented as mean ± standard deviation. Independent *t*-tests were conducted.
[4]Weight-for-age z-score, height-for-age z-score, and BMI for-age z-score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (216).
[5]NAFLD: n=13, lean control: n=17.
Abbreviations: BMI, body mass index; NAFLD, Non-Alcoholic Fatty Liver Disease.

5.3.3 Biochemical Data

Table 5-2 illustrates biochemical variables: fasting liver enzymes (AST, ALT, γGT), cardio-metabolic parameters (markers of insulin resistance, and lipid profile) levels in children with NAFLD and lean controls. Liver enzymes (ALT, AST, γGT), HOMA-IR, and lipid panel (TG, total cholesterol, LDL, HDL) were not significantly different between children ≥ and <14 years (p>0.05; **Appendix J, Table J-4).** Males had significantly higher ALT, AST, γGT, glucose, insulin, and HOMA-IR and lower HDL values than females (p<0.05; **Appendix J, Table J-5)**.

Table 5-2: Biochemical Variables in Children with Non-Alcoholic Fatty Liver Disease and

Lean Controls

	NAFLD	Lean Control	Reference Range	p-value[1]
		Liver Enzymes		
ALT (U/L)[2,5]	55 (33-94)	15 (13-19)	<20 (289)	<0.01
AST (U/L)[2,6]	34 (32-60)	21 (19-26)	2-9 years: <50 ≥10 years: <40	<0.01
γGT (U/L)[2,5]	16 (11-31)	5 (5-5)	Male: <70 Female: <55	<0.01
		Markers of Insulin Resistance		
Glucose (mmol/L)[3,5]	5.1 ± 0.6	4.6 ± 0.4	3.3 - 6.1	<0.01
Insulin (mU/L)[2,6]	23 (15-44)	8 (5-10)	5 - 20	<0.01
HOMA-IR[2,4,6]	5.9 (2.9-11.7)	1.7 (1.0-2.1)	<3.0	<0.01
		Lipid Profile		
Triglyceride (mmol/L)[2,5]	1.2 (1.0-1.7)	0.6 (0.5-0.9)	<1.5	<0.01
Total Cholesterol (mmol/L)[3,5]	3.7 (3.1-4.3)	3.7 (3.5-4.4)	<4.4	0.74
HDL (mmol/L)[2,5]	0.95 (0.83-1.02)	1.37 (1.18-1.54)	>1.00	<0.01
LDL (mmol/L)[3,5]	2.5 (1.8-3.4)	2.3 (1.9-2.5)	<2.80	0.34

Data were used with the permission of SAGE: Mager et al (2012) Nutrition in Clinical Practice and Mager et al (2013) Journal of Parenteral and Enteral Nutrition.

[1]p-values <0.05 are considered statistically significant.

[2]Variables demonstrating skewed distribution are presented as median (interquartile range). Mann Whitney tests were conducted.

[3]Normally distributed variables are presented as mean ± standard deviation. Independent *t*-tests were conducted.

[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x glucose (mmol/L).

[5]NAFLD: n=17-19, lean control: n=19.

[6]NAFLD: n=12-16, lean control: n=18-19.

Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; LDL, Low Density Lipoprotein; NAFLD, Non-Alcoholic Fatty Liver Disease.

5.3.4 Dietary Intake

5.3.4.1 Macronutrient Intake

Dietary intake is presented in **Table 5-3**. No significant differences in energy intake between children with NAFLD and lean controls were observed (p>0.05). Misreporting of energy intake was calculated in n=9 (60%) children with NAFLD and n=11 (69%) lean children. No significant differences in macronutrient consumption between participants with adequate and misreported energy intakes were found (p>0.05; **Appendix J, Table J-6).**

Table 5-3: Dietary Intake in Children with Non-Alcoholic Fatty Liver Disease and Lean

Controls

	NAFLD (n=15)	Lean Control (n=16)	AMDR or RDA/AI	p-value[1]
Energy (Kcal/d)[2]	1560 ± 427	1691 ± 345	-	0.36
Protein (g/d)[2]	78 ± 21	71 ± 19	19-52[4]	0.37
Protein (%)[3]	20 (16-24)	17 (13-19)	10-30[5]	0.09
Carbohydrate (g/d)[2]	194 ± 65	249 ± 60	130[4]	0.02
Carbohydrate (%)[2]	49 ± 8	59 ± 7	45-65[5]	<0.01
Fibre (g/d)[3]	16 (13-17)	19 (13-21)	25-38[6]	0.13
Fat (g/d)[2]	55 ± 20	50 ± 18	-	0.48
Fat (%)[2]	31 ± 5	26 ± 7	25-35[5]	0.04
SFA (g/d)[2]	19 ± 7	18 ± 7	-	0.83
SFA (%)[2]	10 ± 2	9 ± 3	10	0.29
Trans fat (g/d)[3]	0.29 (0.18-0.62)	0.19 (0.04-0.29)	-	0.06
MUFA (g/d)[3]	17 (12-24)	16 (11-20)	-	0.27
MUFA (%)[2]	11 ± 3	8 ± 3	10	0.03
PUFA (g/d)[2]	10.8 ± 5.2	8.2 ± 4.2	-	0.14
PUFA (%)[3]	6 (4-7)	4 (3-5)	10	0.02
Cholesterol (g/d)[2]	204 ± 72	166 ± 54	-	0.99
EI/BMR[2]	1.1 ± 0.3	1.2 ± 0.3	-	0.47

[1]p-values <0.05 are considered statistically significant.
[2]Normally distributed variables are presented as mean ± standard deviation. Independent *t*-tests were conducted.
[3]Variables demonstrating skewed distribution are presented as median (interquartile range). Mann Whitney tests were conducted.
[4]Recommended Dietary Allowance (RDA).
[5]Acceptable Macronutrient Distribution Range (AMDR).
[6]Adequate Intake (AI).
Abbreviations: BMR, Basal metabolic rate; EI, Energy intake; MUFA, Monounsaturated Fatty Acid; NAFLD, Non-Alcoholic Fatty Liver Disease; PUFA, Polyunsaturated Fatty Acid; SFA, Saturated Fatty Acid.

5.3.4.2 Vitamin A, Vitamin C, and Vitamin E Intake

No significant differences in vitamin A and vitamin E intakes between children with NAFLD and lean controls were found (p>0.05; **Appendix J, Table J-7).** Only n=3 (20%) children with NAFLD and n=6 (38%) lean controls met the RDA of vitamin A and none of our cohort met the RDA of vitamin E (p>0.05). Children with NAFLD (55 (32-82) mg/day) had significantly lower intakes of vitamin C than lean controls (124 (71-180) mg/day; p=0.02; **Appendix J, Table J-7).** The proportion of children meeting the RDA for vitamin C was significantly lower in the NAFLD group (n=4; 26%) than lean controls (n=11; 69%; p=0.03).

5.3.5 Food Groups according to the Alberta Nutrition Guidelines

Table 5-4 demonstrates food group intake in children with NAFLD and lean controls according to ANGCY. The majority of our cohort (>30%) did not meet food group recommendations (**Figure 5-2**). No significant difference in food group intake between participants with adequate and misreported energy consumption was found (p>0.05; **Appendix J, Table J-6).** Children ≥14 years old had significantly higher intakes of meat and alternatives (p>0.05; **Appendix J, Table J-8)** than children <14 years old. No significant difference in food group intake was observed between males and females (p>0.05; **Appendix J, Table J-9)**.

Table 5-4:Food Group Intake in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls according to the Alberta Nutrition Guidelines

	NAFLD (n=15)	Lean Control (n=16)	Recommended Intake[4]	p-value[3]
Grain Products[1]	3.9 ± 1.6	5.8 ± 1.3	4-6	0.08
Fruit and Vegetables[1]	3.0 (2.9-3.7)	5.0 (3.9-7.0)	5-7	0.01
Milk and Alternatives[1]	1.7 ± 1.1	2.3 ± 1.1	2-4	0.10
Meats and Alternatives[2]	2.0 (1.4-3.2)	1.7 (1.2- 2.1)	1-3	0.10

[1]Normally distributed variables are presented as mean ± standard deviation. Independent *t*-tests were conducted.
[2]Variables demonstrating skewed distribution are presented as median (interquartile range). Mann Whitney tests were conducted.
[3]p-values <0.05 are considered statistically significant.
[4]Recommended intake based on the Alberta Nutrition Guidelines (ANGCY) (77).
Abbreviations: NAFLD, Non-Alcoholic Fatty Liver Disease.

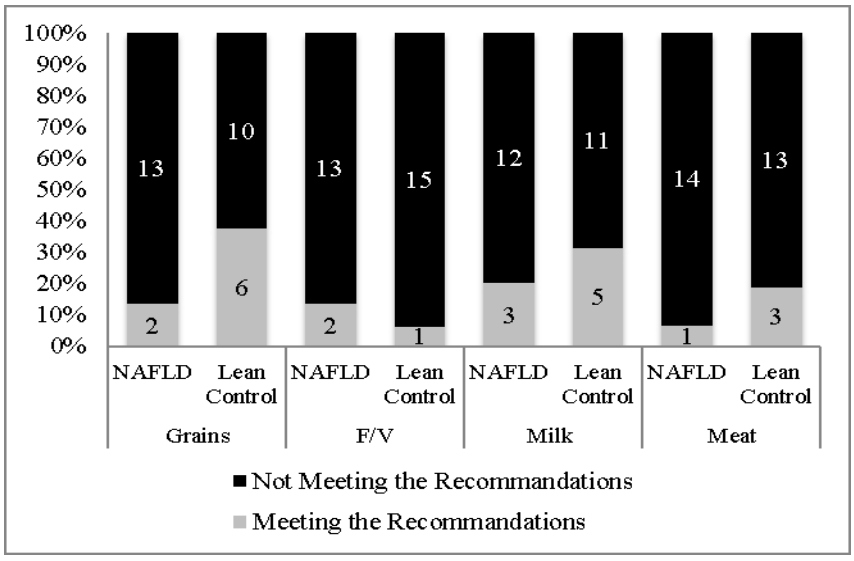


Figure 5–2: Percentage of Children who Met Food Groups Recommendation in Children with Non-Alcoholic Fatty Liver Disease (n=15) and Lean Control Children (n=16).
Abbreviations: F/V, Fruit and vegetables; NAFLD, Non-Alcoholic Fatty Liver Disease.

5.3.6 Glycemic Index and Glycemic Load

No significant differences were observed in GI and GL between children with NAFLD and lean controls ($p>0.05$**; Figure 5-3**). No significant differences in GI above (NAFLD, n=8; lean control, n=8) and below the median (NAFLD, n=7; lean control, n=8; p=1.00) or GL above (NAFLD, n=7; lean control, n=9) and below the median (NAFLD, n=8; lean control, n=7; p=0.72) were observed. No significant differences in GI and GL between participants with adequate and misreported energy intakes, children ≥ and <14 years old, or by gender were found ($p>0.05$**; Appendix J, Table J-6, Table J-8,** and **Table J-9).**

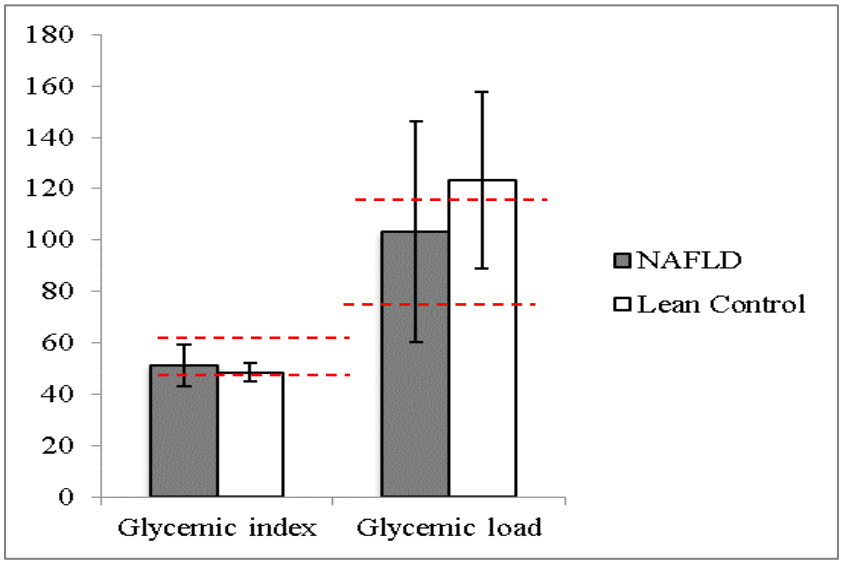


Figure 5–3:Glycemic Index and Glycemic Load in Children with Non-Alcoholic Fatty Liver Disease (n=15) and Lean Controls (n=16). Data are presented as mean ± standard deviation. Dashed red lines represent the cutoff values of high, medium and low GI ≥70, between 69-56, and ≤55 and GL ≥120, between 80-119, and <80, respectively (96, 97, 224). No significant differences were observed in GI and GL between the groups ($p>0.05$). The majority of the cohort had GI scores <55 (NAFLD, n=10 vs lean control, n=15) and GL scores >80 (NAFLD, n=11 vs lean control, n=15) ($p>0.05$).
Abbreviations: NAFLD, Non-Alcoholic Fatty Liver Disease.

5.3.7 Diet Quality Scores: Healthy Eating Index-Canada, Dietary Guideline Index for Children and Adolescents, and Diet Quality Index-International

5.3.7.1 Total Diet Quality Scores

Children with NAFLD had significantly lower HEI-C, DGI-CA, and DQI-I scores than lean controls ($p<0.04$**; Figure 5-4**). The majority of children with NAFLD (>50%) had poor DQ (**Figure 5-5)**. No significant differences in HEI-C, and DGI-CA, scores between participants with adequate and misreported energy intakes or between gender were found ($p>0.05$; **Appendix J, Table J-6** and **Table J-9).** Children ≥14 years old had significantly lower DQI-I scores than children <14 ($p=0.04$**; Appendix J, Table J-8).**

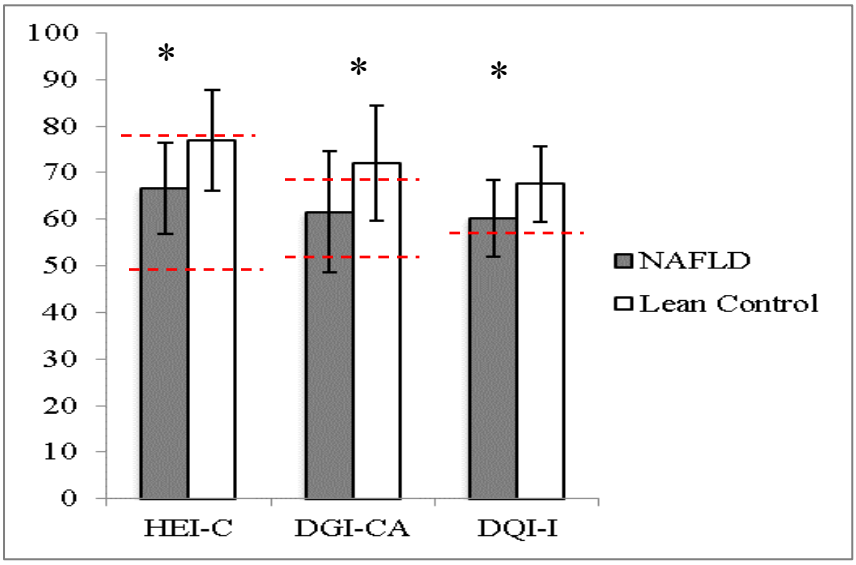


Figure 5–4: Diet Quality Scores in Children with Non-Alcoholic Fatty Liver Disease (n=15) and Lean Controls (n=16). Data are presented as mean ± standard deviation. Dashed red lines represent the cutoff values of "good", "needs improvement" or "poor" diet quality. HEI-C scores were categorized as good (>80, needs improvement (HEI-C scores 51-80), and poor diet (≤50) (35, 225). DGI-CA scores were categorized as good (>68), needs improvement (55-68), and poor diet (<55) (31, 74). DQI-I scores were categorized as good (≥60), and poor diet (<60) (226). Variables with an asterix (*) indicate significant differences between children with Non-Alcoholic Fatty Liver Disease and Lean Controls ($p<0.03$).

Abbreviations: DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; HEI-C, Healthy Eating Index-Canada; NAFLD, Non-Alcoholic Fatty Liver Disease.

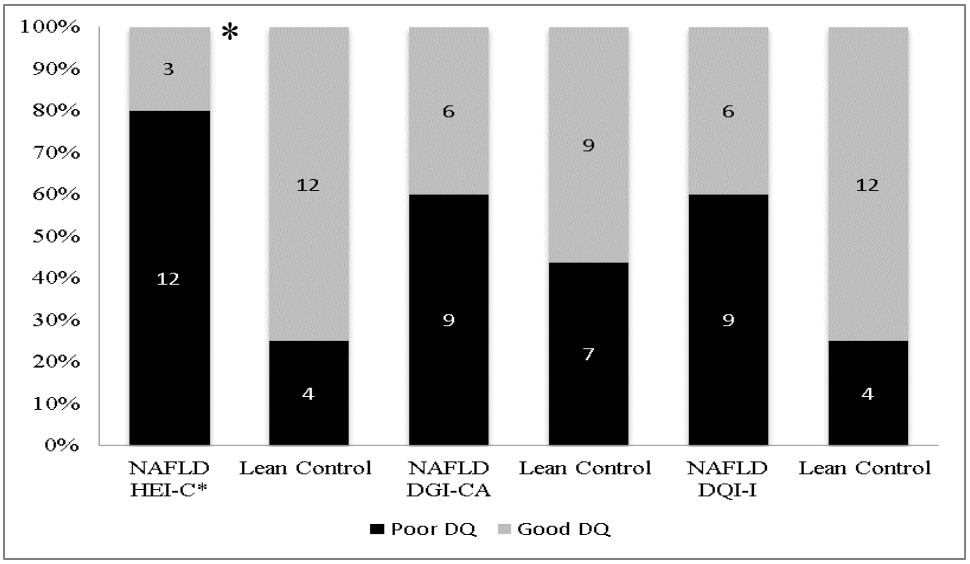


Figure 5–5: Percentage of Participants with Good and Poor DQ between Children with Non-Alcoholic Fatty Liver Disease (n=15) and Lean Controls (n=16).

HEI-C scores (≥ vs < median of 70; p<0.01), DGI-CA scores (poor <68 vs good ≥68; p=0.48), and DQI-I scores (poor <60 vs good ≥60; p=0.07). Values inside the bars are the n number of each group. Values with asterix (*) represent significant differences between groups (p<0.05).
Abbreviations: DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; HEI-C, Healthy Eating Index-Canada; NAFLD, Non-Alcoholic Fatty Liver Disease.

5.3.7.2 The Components of Diet Quality Scores: Diet Adequacy, Moderation and Variety in the Diet

Table 5-5 presents the components of DQ Scores in children with NAFLD and lean controls. No significant differences were observed in Adequacy (HEI-C, DGI-CA, DQI-I), Moderation (HEI-C, DQI-I), Variety (DGI-CA Food, DGI-CA Grains, DGI-CA Milk, DQI-I), and DQ Model between children ≥ and <14 years (p>0.5**; Appendix J, Table J-8).** Females had higher Adequacy scores of all DQ tools (HEI-C, DGI-CA, DQI-I) and DQ Model score (the sum of Adequacy of DQI-I and Moderation of HEI-C) than males (p<0.5**; Appendix J, Table J-9).**

Table 5-5:The Components of Diet Quality Scores in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	NAFLD (n=15)	Lean Control (n=16)	Maximum Score	p-value[1]
		Adequacy		
HEI-C[2,3]	31 ± 6	38 ± 7	50	0.01
DGI-CA[2,4]	25 ± 6	30 ± 6	40	0.03
DQI-I[2,5]	23 ± 6	30 ± 4	40	<0.01
		Moderation		
HEI-C[2,6]	26 ± 7	31 ± 5	40	0.04
DGI-CA[2,7]	23 ± 11	26 ± 8	40	0.30
DQI-I[2,8]	18 ± 5	20 ± 4	30	0.24
		Variety		
HEI-C[2,9]	9.4 ± 0.8	9.8 ± 0.3	10	0.08
DGI-CA (Food)[2,10]	4 ± 3	6 ± 3	10	0.02
DGI-CA (Grains)[2,11]	5 ± 2	6 ± 2	10	0.06
DGI-CA (Milk)[2,12]	5 ± 3	8 ± 2	10	0.01
DQI-I[2,13]	18 ± 2	18 ± 1	20	0.43

[1]p-values <0.05 are considered statistically significant.
[2]Normally distributed variables are presented as mean ± standard deviation. Independent *t*-tests were conducted.
[3]HEI-C (Adequacy): sum score of fruit and vegetables, grain products, milk and alternatives, and meat and alternatives.
[4]DGI-CA (Adequacy): sum score of fruit and vegetables, grain products, milk and alternatives, and meat and alternatives.
[5]DQI-I (Adequacy): sum score of fruit and vegetables, grain products, fibre, protein, iron, calcium, and vitamin C.
[6]HEI-C (Moderation): sum score of fat, saturated fat, cholesterol, and *other foods* group.
[7]DGI-CA (Moderation): sum score of *other foods* group, beverage, and food choice (saturated fat).
[8]DQI-I (Moderation): sum score of fat, saturated fat, cholesterol, sodium, and *other foods* group.
[9]HEI-C (Variety): The score of the Variety.
[10]DGI-CA (Foods): sum score of whole grains and low fat milk.
[11]DGI-CA (Grains): sum score of the total grains and whole grains.
[12]DGI-CA (Milk): sum score of total milk and alternatives and low fat milk.
[13]DQI-I (Variety): sum score of the variety of food groups and within milk and meat products.
Abbreviations: DGI-CA; Dietary Guideline Index for Children and Adolescents; DQ, Diet Quality; DQI-I, Diet Quality Index-International; HEI-C, Healthy Eating Index-Canada; NAFLD, Non-Alcoholic Fatty Liver Disease.

5.3.7.3 Diet Quality Models Combined Adequacy and Moderation Within Diet Quality Tools

Table 5-6 shows the DQ Models of Adequacy and Moderation within DQ Tools in Children with NAFLD and lean controls. Children ≥14 years old had significantly lower DQ model of Adequacy and Moderation within DQI-I tool than children <14 (p=0.04; **Appendix J, Table J-8**). Females had higher DQ model of Adequacy and Moderation within HEI-C and DQI-I than males (p=0.4**; Appendix J, Table J-9).**

Table 5-6:The Diet Quality Models of Adequacy and Moderation within Diet Quality Tools

in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	NAFLD (n=15)	Lean Control (n=16)	Maximum Score	p-value[1]
HEI-C[2,3]	57 ± 10	69 ± 10	90	<0.01
DGI-CA[2,4]	48 ± 13	56 ± 10	80	0.06
DQI-I[2,5]	42 ± 8	50 ± 5	70	<0.01

[1]p-values <0.05 are considered statistically significant.
[2]Normally distributed variables are presented as mean ± standard deviation. Independent *t*-tests were conducted.
[3]HEI-C: sum score of fruit and vegetables, grain products, milk and alternatives, meat and alternatives, fat, saturated fat, cholesterol, and *other foods* group.
[4]DGI-CA: sum score of fruit and vegetables, grain products, milk and alternatives, meat and alternatives, beverage, "*other foods* group, and food choice (saturated fat).
[5]DQI-I: sum score of fruit and vegetables, grain products, fibre, protein, iron, calcium, vitamin c, fat, saturated fat, cholesterol, sodium, and *other foods* group.
Abbreviations: DGI-CA; Dietary Guideline Index for Children and Adolescents; DQ, Diet Quality; DQI-I, Diet Quality Index-International; HEI-C, Healthy Eating Index-Canada; NAFLD, Non-Alcoholic Fatty Liver Disease.

5.3.8 Interrelationships between Glycemic Index, Glycemic Load and Anthropometrics, and Body Composition

Children with GL ≥108 had higher %fat free mass and lower %fat mass compared to children with GL <108 (p<0.05; **Appendix J, Table J-11**). No significant differences were found between GI (< and ≥48) and GL (< and ≥108) and wt-z, ht-z, BMI-z, waist and hip circumferences (p>0.05; **Appendix J, Table J-10** and **J-11**).

5.3.9 Interrelationships between Diet Quality and Anthropometrics, and Body Composition

On average, the effect size of anthropometrics, and body composition between NAFLD and lean control is 1.5 and between children with DQ HEI-C (Total) ≥ 70, HEI-C (Adequacy) ≥34, DQI-I (Adequacy) ≥26 and HEI-C (Moderation) ≥30 and children with DQ HEI-C (Total) <70, HEI-C (Adequacy) <34, DQI-I (Adequacy) <26 and HEI-C (Moderation) <30 is 0.8.

A) Total Diet Quality Scores

Children with HEI-C scores ≥70 had lower wt-z, BMI-z, hip and waist circumferences and fat mass (%) and higher fat free mass (%) compared to children with HEI-C scores <70 (p<0.05; **Appendix J, Table J-12**). No significant differences were found between DGI-CA (≥ and <68) or

DQI-I (≥ and <60) and wt-z, BMI-z, and waist and hip circumferences (p>0.05; **Appendix J, Table J-13** and **Table J-14**).

B) The Components of Diet Quality

Diet Adequacy Scoring

Children with high Adequacy scores (HEI-C ≥34, DQI-I ≥26) had significantly higher fat free mass (%) coupled with lower wt-z, BMI-z, waist and hip circumferences, and fat mass (%) than children with low Adequacy scores (HEI-C <34, DQI-I <26) (p<0.05; **Appendix J, Table J-15** and **Table J-17**). Children with DGI-CA Adequacy scores ≥26 had significantly higher fat free mass (%) and lower waist and hip circumferences, and fat mass (%), than children with DGI-CA Adequacy scores <26 (p<0.05; **Appendix J, Table J-16**).

Diet Moderation Scoring

Children with HEI-C Moderation scores ≥30 had significantly lower hip circumference than children with HEI-C Moderation scores <30 (p<0.05; **Appendix J, Table J-18**). No significant differences in anthropometrics, fat mass, or fat free mass between children with DGI-CA Moderation scores (≥ and <28) and DQI-I Moderation scores (≥ and <21) and were noted (p>0.05; **Appendix J, Table J-19** and **Table J-20**).

Diet Variety Scoring

No significant differences in anthropometrics, fat mass and fat free mass in children with DGI-CA Food scores ≥ and <5.2, DGI-CA Grains scores ≥ and <6, and DQI-I Variety scores ≥ and <18 were observed (p>0.05; **Appendix K, Table J-21, Table J-22,** and **Table J-24**). Children with DGI-CA Milk scores ≥7 had significantly lower wt-z, BMI-z, hip circumference and body fat mass (kg) than children with DGI-CA Milk scores <7 (p<0.04; **Appendix J, Table J-23**).

C) Diet Quality Models for Assessment Adequacy and Moderation within Diet Quality Scores

Children with DQ model scores for HEI-C ≥60 and DQI-I ≥45 has significantly wt-z, BMI-z, waist and hip circumference and fat mass (%) and higher fat free mass (%) compared to children with DQ model scores for HEI-C<60 and DQI-I <45 ($p<0.05$; **Appendix K, Table J-25,** and **Table J-27**). No association was found in wt-z, BMI-z, waist and hip circumference, fat mass and fat free mass between children DQ model scores for DGI-CA ≥54 than children with DGI-CA <54 ($p>0.05$; **Appendix K, Table J-26**).

5.3.10 Interrelationships between Glycemic Index, Glycemic Load, and Total Diet Quality Scores and Anthropometrics, and Body Composition

Several interrelationships were observed between GL, and total DQ scores (HEI-C, DQI-I) and BMI-z, fat mass and fat free mass **(**$p<0.05$**; Appendix J, Table J-28)**.

5.3.11 Interrelationships between Glycemic Index and Glycemic Load and Biochemical Variables

Total cholesterol was significantly lower in children with GI <48 (3.6 (3.2-3.9) mmol/L) compared to children with GI ≥48 (4.2 (3.6-4.5) mmol/L; $p=0.02$). No significant differences between GI/GL and liver enzymes concentrations were found ($p>0.05$**; Appendix J, Table J-29** and **J-30).**

5.3.12 Interrelationships between Diet Quality and Biochemical Variables

A) Total Diet Quality Scores

Children with HEI-C scores ≥70 had significantly lower ALT, γGT, glucose, insulin, and HOMA-IR concentrations ($p<0.05$; **Appendix J, Table J-31**). Children with DQI-I scores ≥60 had significantly lower insulin level compared to children with DQI-I scores <60 ($p<0.05$; **Appendix J, Table J-33).** No association was found in biochemical markers between children with DGI-CA scores ≥68 and children with DGI-CA scores <68 ($p<0.05$; **Appendix J, Table J-32).**

B) The Components of Diet Quality

Diet Adequacy Scoring

High Adequacy scores (HEI-C ≥34, DGI-CA ≥26 and DQI-I ≥26) were associated with lower liver enzymes (ALT, γGT), HOMA-IR, insulin, and glucose levels ($p<0.05$; **Appendix J, Table J-34** to **Table J-36**). HDL levels were significantly higher in children with HEI-C Adequacy scores ≥34 and DGI-CA Adequacy scores ≥26 than children with HEI-C Adequacy scores <34 and DGI-CA Adequacy scores <26 ($p<0.05$; **Appendix J, Table J-34** and **Table J-35**).

Diet Moderation Scoring

No associations were found between Moderation scores (HEI-C ≥30, DGI-CA ≥28, DQI-I ≥21) and liver enzymes, insulin, glucose, or HOMA-IR values ($p>0.05$; **Appendix J, Table J-37** to **Table J-39**). Higher Moderation scores (HEI-C ≥30, DQI-I ≥21) were associated with lower total cholesterol and LDL levels ($p<0.05$; **Appendix J, Table J-37** and **Table J-39**).

Diet Variety Scoring

No associations were found between DGI-CA Food scores ≥5.2 or DGI-CA Grains scores ≥6 and liver enzymes ($p>0.05$; **Appendix J, Table J-40** and **Table J-41**). Children with DGI-CA Milk scores ≥6 and DQI-I Variety scores ≥18 had lower γGT levels compared to children with DGI-CA Milk scores <6 and DQI-I Variety scores <18 ($p<0.05$; **Appendix J, Table J-42** and **Table J-43**). Children with DGI-CA Grains scores ≥6 and DGI-CA Milk scores ≥7 had lower glucose and HOMA-IR compared to children with DGI-CA Grains <6 and DGI-CA Milk scores <7 ($p<0.05$; **Appendix J, Table J-41** and **Table J-42**). DGI-CA Milk scores ≥7 were related to lower TG concentrations ($p<0.05$; **Appendix J, Table J-42**).

C) Diet Quality Models for Assessment Adequacy and Moderation within Diet Quality Tools

Children with DQ model for Assessment Adequacy and Moderation within (HEI-C ≥60 and DQI-I ≥45) had lower ALT, γGT, glucose, insulin, and HOMAR-IR concentrations compared to children with DQ model for Assessment Adequacy and Moderation within (HEI-C <60 and DQI-I <45) ($p<0.05$; **Appendix J, Table J-44** and **Table J-46**). No associations were found between children with DQ model for Assessment Adequacy and Moderation within DGI-CA <54 and liver enzymes, insulin, glucose, HOMA-IR, and lipid panel and children with DQ model for Assessment Adequacy and Moderation within DGI-CA ≥54 ($p>0.05$; **Appendix J, Table J-45).**

5.4 Discussion

Suboptimal dietary intakes and sedentary lifestyle are risk factors for obesity and may lead to NAFLD (170). Several dietary interventions have been reported to treat NAFLD (87, 108, 109, 170-172, 283). Recently, researchers focused on studying the relationship between overall DQ and the cause or the treatment of obesity and/or NAFLD (4, 9). The aims of the current study were to compare overall DQ (macronutrients, antioxidants, food groups, GI, GL and DQ scores) between children with NAFLD and lean control children and to examine the interrelationships between overall DQ, anthropometric variables, liver enzymes and cardio-metabolic parameters. We hypothesized that children and adolescents with NAFLD have poor overall DQ compared to lean children. We further hypothesized that poor overall DQ is associated with an increased risk for increased serum concentrations of liver biochemistries and serum markers of cardio-metabolic dysfunction in youth with NAFLD.

The current study found that children with NAFLD had higher intakes of fat and lower intakes of carbohydrate, and fruit and vegetables. Although no significant differences were found in the consumption of milk and alternatives, the consumption of "low fat milk" was significantly lower in children with NAFLD. Children with NAFLD had lower DQ scores (HEI-C, DGI-CA,

and DQ-I) especially related to the concepts of Adequacy and Moderation when compared to healthy children and all study populations examined within this doctoral thesis. High Adequacy and Moderation scores were associated with reduced adiposity, fat mass, liver enzymes and cardio-metabolic parameters. These findings are similar to previous studies conducted in children and adults with NAFLD (62, 73, 79, 87, 174, 188). In addition, children with NAFLD had lower intakes of fruit and vegetables than lean controls which may be a surrogate marker for low vitamin C intake in NAFLD group. The majority of the cohort did not meet the RDA for vitamin A or vitamin E, likely due to low consumption of green leafy vegetables and nuts. Due to insufficient power (<50%) of vitamin A and vitamin E analysis (**Appendix J-47)**, we were unable to investigate the impact of vitamin A and vitamin E intake on anthropometrics, body composition, liver enzymes, or cardio-metabolic markers.

In the current study, we did not find any differences in GI or GL intake between children with NAFLD and lean controls due to lower intake of carbohydrate in NAFLD children. Four children with NAFLD (27%) had GL intake (<50) potentially due to lower intake of carbohydrate (<45% Kcal) in NAFLD children compare to lean controls. Low carbohydrate intake (<40% Kcal) was associated with GL (<50) as previously reported (290). In addition, high GL was associated with higher fat free mass and lower fat mass. This result is inconsistent with other previous findings (87). Due to lower carbohydrate intake in NAFLD group compared to control group, GL was adjusted for carbohydrate intake and no association was found between GL and fat mass and fat-free mass (data not shown). The current study did not examine the variables that are associated with the variation of GI and GL intake. Previous studies reported that under-reporting dietary intake, individual dietary patterns, and variation in intake between weekend and weekdays are all associated with differences in GI and GL (290, 291).

Although we did not find any significant differences in energy intake between children with NAFLD and lean controls, children with NAFLD had lower DQ scores (HEI-C, DGI-CA and DQI-I) compared to lean controls primarily driven by the limited scores in the DQ sub-scores categories related to the concepts of Adequacy and Moderation. This was likely due to the low intake of fruit and vegetables and high consumption of fat, saturated fat and *other foods* groups such as sweetened beverages, particularly in the children with NAFLD. We observed that children with NAFLD had lower scores (by 5-10 points) related DQ scores (especially in Adequacy and Moderation) compared to children with CD, post-LTX and lean controls. In the current study, we have adapted the definition of diet Adequacy and Moderation based on existing DQ tools. Adequacy is the intake of food groups, protein, iron, vitamin C, fibre, and calcium and Moderation as the intake of *other foods,* fat, saturated fat and cholesterol. However, we did not include the intake of vitamin A and E and added sugar and fructose to the assessment of Adequacy and Moderation. This study and other studies found that individuals with NAFLD had higher intake of added sugar and fructose and low intake of vitamin A and E than the control group (73, 87, 174). Including those nutrients into the definitions of adequacy and moderation may be important to ensure a comprehensive definition of dietary Adequacy and Moderation in this population is performed. However, more work needs to be done to establish these definitions in children's diets and developing a DQ tool to assess Adequacy and Moderation; particularly in reference to children with chronic liver diseases such as NAFLD.

Evaluating dietary patterns is an important aspect in the provision of specific nutritional therapy for children with liver diseases. For example, diet therapy for children with low moderation scores may need to focus on reducing *other foods* group consumption or substituting a healthier food choice. Evaluation of these subset scores pinpoints dietary concepts that should

be included in the development of specific therapeutic dietary interventions in youth with NAFLD. Recent studies have shown that adults with NAFLD have diets characterized by lower Adequacy scores and higher "dietary dense energy" scores (indicating lower moderation scores) compared to healthy adult (73, 174).

The present study found that DQ score (especially HEI-C) is associated with an elevation of liver enzymes and markers of cardio-metabolic dysfunction. This finding has been previously reported in both healthy and obese children and adults, but not in children with NAFLD (62, 79, 87). Previous studies reported the association between Adequacy and Moderation scores and outcomes such as risk for adiposity, cardio-metabolic and liver dysregulation (4, 9, 174). In the current study, the principles of Adequacy and Moderation used in the DQ tools address the main principles of a Mediterranean diet (high fruit and vegetables legumes, and olive oil consumption and lower fat, saturated fat, high GI foods, and simple sugar intake). A study conducted in children found that adherence to the Mediterranean diet was associated with Adequacy of micronutrient intake (vitamin A, vitamin B6, vitamin C, vitamin, folate, calcium, and iron) (292). A Mediterranean dietary pattern reduces the risk of obesity, NAFLD, diabetes and cardiovascular disease (281, 282, 293-296). The adequate intake of antioxidants, omega-3 fatty acid and fibre and the moderate intake of saturated fat and simple sugar promoted by a Mediterranean diet has been associated with reduced fatty liver and improved liver enzymes and markers of insulin resistance (HOMA-IR) in adults with NAFLD (281, 282, 293-296). Therefore, the American Association of Clinical Endocrinologists and the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition recommend a Mediterranean diet as the nutritional therapy for NAFLD in adults and children (281, 282).

Several studies have reported an association between dietary diversity and risk of obesity

(297). The current study found association between Variety (DGI-CA Milk and DQI-I) scores and both adiposity and cardio-metabolic dysregulation, which indicates that the variety within food groups may be associated with better overall DQ. In the current study, we focused on the variety of food groups and within foods (protein sources and grains). Increased dietary Diversity is likely associated with increased micronutrients Adequacy in the diet. Therefore increasing dietary Diversity and Adequacy may reduce the risk of obesity and cardio-metabolic dysregulation (298). Further studies are required to assess the impact of overall food group and within food group variety on and obesity and cardio-metabolic dysregulation in children with NAFLD.

There is no specific diet therapy for children with NAFLD (281, 282, 293, 294), although the goal has historically been focused on weight loss as this has been associated with significant improvements in risk for cardio-metabolic dysregulation and liver dysfunction. Hence, lifestyle therapy has typically been focused on weight loss via dietary modification (± physical activity). More recently, isocaloric approaches have been developed due to the lack of long term weight loss maintenance success (87, 281, 282, 293, 294). Recent clinical studies have reported several dietary management strategies including low carbohydrate, fat, GI, GL, fructose, and/or high fructose corn syrup diets, as well as high antioxidant and/or omega-3 fatty acid diets; all of which emphasize modifying intakes to better approximate a Mediterranean diet pattern (87, 281, 282, 293, 294). However, the adherence (defined as the meeting ≥80% of the recommendations) to diet therapy in obese adolescents was observed to be poor in both long and short-term dietary interventions (30-80%) (294, 299). One of the reasons for poor adherence to a healthy diet in adolescence was the lack of a practical nutritional tool or practical nutritional recommendations (192). Specific nutritional recommendations to enhance the intake of food groups, fibre, micronutrients and

antioxidants, while moderating intake of *other foods* group, fat and simple sugar are required for children with NAFLD and their parents.

The sample size of the current study was determined based on the primary outcomes (postprandial insulin, lipid, and lipoprotein expression) (188). In this thesis chapter, we have sufficient power (>0.8) to assess the effect of study group on HEI-C and some components of DQ. However, we did not have sufficient power (<0.5) to assess the intake of GI and GL between the study groups (**Appendix J, Table J-47**). The influence of added sugar, and high fructose corn syrup on overall DQ was reported in several studies (300); however, the current study does not assess these variables. High intakes of simple sugars and added sugars, such as HFCS, have been shown to be associated with an upregulation of denovo lipogenesis in adults with NAFLD (87). High intakes of added sugar would have a definite impact on lowering overall DQ. In addition, gender differences between NAFLD and control group may evoke different effects on markers of cardio-metabolic dysregulation. Although we have measured body composition (fat mass and fat free mass), measuring visceral and subcutaneous fat in the body may help to understand the effect of diet on the location of fat deposition in the body.

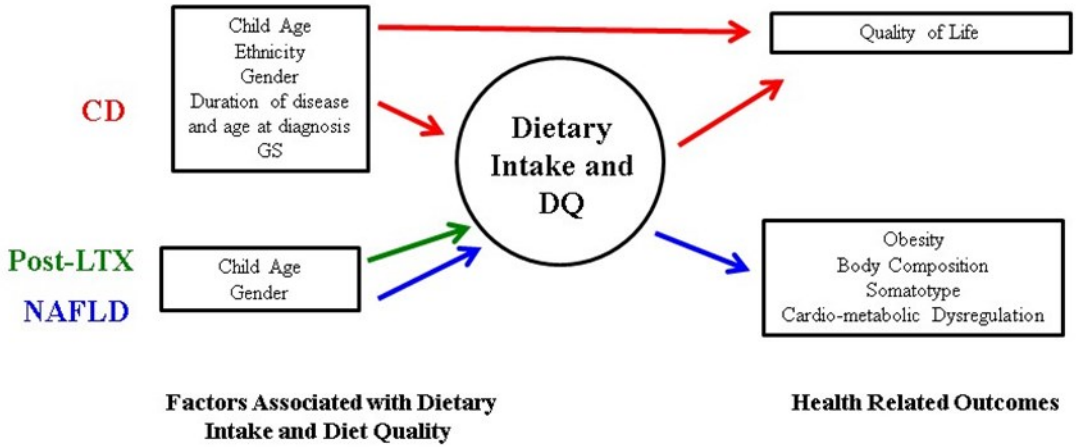
In conclusion, children with NAFLD consume a diet characterized by poor overall DQ, Adequacy and Moderation scores. Higher Adequacy and Moderation scores are associated with lower wt-z, BMI-z, waist and hip circumferences, fat mass, liver enzymes levels, and cardio-metabolic dysregulation. A dietary intervention study designed with consideration of overall DQ to focus on Adequacy and Moderation (GI, GL, added sugar, fructose, and high fructose corn syrup food) is needed to examine the long-term effects of improved DQ on overall health. Evaluating overall DQ (especially overall food groups, fibre, micronutrients and antioxidants, fat and simple sugar) is important to enhance Adequacy and Moderation. This has a clinical implication to assess

and design diet therapy for children with NAFLD and to develop practical dietary intervention tools.

Chapter 6 Conclusions and General Discussion

6.1 Introduction

Diet Quality (DQ) tools are used to assess overall nutritional quality including Adequacy, Moderation, and Variety of foods in an individual's dietary intake (3, 4, 9). Associations between overall DQ, nutritional status, and health related outcomes have been previously reported using a variety of methodologies in healthy children and adolescents (3, 4, 9). The majority of DQ tools lack evaluative components for key characteristics of dietary intake that are known to influence chronic disease risk, such as glycemic index (GI) and glycemic load (GL) (3, 4, 9). Relationships between GI/GL and nutritional status, obesity, and health related outcomes such as cardio-metabolic dysregulation have been studied in several populations such as obesity (87, 97). In addition, tools for the assessment of DQ that focus on specialized therapeutic diets needed for treatment of chronic disease (such as the gluten free diet (GFD)) have not been developed, and the associations between DQ and health outcomes in children and adults with many chronic diseases have not been evaluated. Currently there is limited data regarding the associations between overall DQ, nutritional status, and health related outcomes in children and adolescents with gastrointestinal and liver disease (66). A comprehensive analysis of the factors influencing DQ (e.g. socio-demographic features, disease duration) and its associations with patient focused outcomes such as health related quality of life (HRQOL), obesity, and cardio-metabolic dysregulation, has not been extensively conducted. This thesis reports on the above listed factors in children with gastrointestinal and liver diseases (**Figure 6.1**).



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6.2 Summary of Studies Objectives and Results

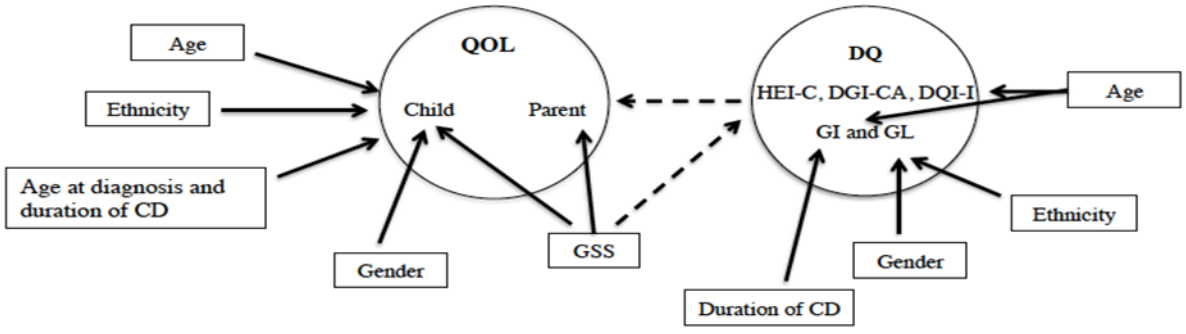
The thesis objectives were to assess and compare GI and GL intake and DQ scores between children with chronic gastrointestinal (Celiac Disease [CD]) or liver diseases (Non-Alcoholic Fatty Liver Disease [NAFLD], Post-Liver Transplantation [LTX]) to healthy children/disease control populations of similar age. Interrelationships between DQ and some health related outcomes (body composition, quality of life, cardio-metabolic dysregulation) in children/adolescents with chronic gastrointestinal and liver diseases were also assessed. This thesis has demonstrated that children with gastrointestinal and liver disease have poor to moderate DQ which negatively impacts important patient care outcomes such as risk for adiposity, cardio-metabolic dysregulation, and reduced HRQOL in comparison to healthy children of similar age. This has potential implications

for overall dietary and clinical management for children with chronic gastrointestinal and liver diseases. A comprehensive analysis of the factors influencing DQ (socio-demographic features of the child and family, disease duration) and its associations with patient focused outcomes such as HRQOL has not been extensively examined.

6.2.1 Celiac Disease (Chapter 3)

A gluten-free diet (GFD) is the only known therapy for individuals with CD; however, GFDs have significant nutritional challenges, such as higher fat, saturated fat, and simple sugar intake, coupled with lower fibre and folate consumption. We hypothesized that children/adolescents with CD following a GFD have reduced HRQOL and DQ scores and higher GI/GL intakes compared to children/adolescents with chronic gastrointestinal concerns such as constipation (gastrointestinal disease controls) (**Chapter 3**). With the exception of GI, the study null hypothesis was accepted. In fact, both children with CD and gastrointestinal disease controls had poor DQ. Poor DQ was also observed in a study by our research group that assessed DQ between children with CD and healthy controls (66). The finding of the current study (**Chapter 3**) was consistent with Tsiountsioura et al (2014) (246). Children with CD and children with chronic gastrointestinal disease (no CD) had dietary patterns characterized by high consumption of sweetened beverages, chips and sweets, such as chocolate, which resulted in a higher proportion of children with CD not meeting the recommendations for B2, B6, and calcium compared to healthy controls (246). These findings suggested that children with CD may have poor diet Adequacy and Moderation compared to healthy children. Our study elaborates on these observations by examining the association between the presence of gastrointestinal symptomology and poor DQ. The finding of our study needs to be interpreted with caution as it is not known whether poor DQ is the cause or consequence of gastrointestinal symptomology.

The second hypothesis of the current study was that reduced DQ scores and higher GI/GL will be related to perceptions of HRQOL, from both the parent and child perspectives, in children with CD on GFD. This study hypothesis was confirmed. **Chapter 3** shows that demographic variables (e.g. child age at diagnosis, child ethnicity and gender), low DQ scores, and GS were associated with poor HRQOL (**Figure 6-2**). Several studies have reported associations between GFD adherence, gastrointestinal symptomology control, and improved HRQOL in individuals with CD (301-304). However, relationships between nutritional quality and HRQOL in individuals with CD who adhered strictly to a GFD have not been previously examined. An Austrian study reported improved DQ associated with enhancements in HRQOL for elderly individuals, particularly in physical emotional and wellbeing domains (305). The World Health Organization (WHO) has defined health as a "state of complete physical, mental, and social well-being" which has important implications for individuals who score poorly in any HRQOL domains. Children/adolescents adherent to a GFD may be physically healthy according to clinical measures,



but further investigation and intervention in instances of diminished HRQOL may be necessary.

Figure 6-2: Interrelationships between Demographic Variables, Gastrointestinal Symptomology, Health Related Quality of Life, and Overall Diet Quality. Demographic variables (age, gender, ethnicity, age at diagnosis, and CD duration), Diet Quality Scores (Healthy Eating Index-Canada, Dietary Guideline Index for Children and Adolescents, and Diet Quality Index-International) and health related quality of life (PedsQL^{TM} 4.0 Generic Core Scales [parent proxy and child report]).
Abbreviations: CD, Celiac Disease; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQ, Diet Quality; DQI-I, Diet Quality Index-International; GI, Glycemic Index; GL, Glycemic Load; GSS, Gastrointestinal Symptomology Score, HEI-C, Healthy Eating Index-Canada; HRQOL, Health Related Quality of Life.

6.2.2 Post-Liver Transplantation (Chapter 4) and Non-Alcoholic Fatty Liver Disease (Chapter 5)

Diet is thought to be a main contributor to the etiology and treatment of childhood NAFLD. If NAFLD is left untreated, it may progress to non-alcoholic steatohepatitis (NASH), cirrhosis, and liver failure. Diet is an important adjuvant therapy in children post-LTX and is the main treatment modality for children with NAFLD. Hence, this thesis focused on DQ and its associations with specific patients characteristics (anthropometric, markers of cardio-metabolic dysregulation) that are a concern in children and adolescents with NAFLD and in children and adolescents post-LTX. We did not examine cardio-metabolic risk for youth post-LTX in this thesis.

We hypothesized children post-LTX have poor DQ compared to healthy controls (**Chapter 4**). The null hypothesis was accepted. In addition, we hypothesized that children with NAFLD had poor DQ compared to healthy children (**Chapter 5**). This hypothesis was proven. Children with NAFLD had DQ scores 5-10-points below all the other groups (healthy children, children with CD, children post-LTX, and gastrointestinal diseases control children without CD). This has important implications in terms of the risk for cardio-metabolic dysregulation

In **Chapter 5**, we hypothesized that poor DQ would be associated with obesity and cardio-metabolic dysregulation in children with NAFLD. The hypothesis was proven. This thesis

illustrated the association between poor DQ (Adequacy and Moderation) and cardio-metabolic dysregulation (central obesity, increased body fat mass, elevated liver enzymes, and markers of insulin resistance) in children with NAFLD. We have adapted the definitions of Adequacy and Moderation from existing DQ tools which includes food groups, vitamin C, calcium, iron, fibre, fat, saturated fat, cholesterol and *other foods* group. The concepts of Adequacy and Moderation, functions of DQ, are principles inherent to a Mediterranean diet (292, 295). Evidence has further highlighted the potential of the Mediterranean diet in reducing the risk of and/or providing treatment for cardio-metabolic dysregulation in adults with NAFLD (296). Other studies have demonstrated associations between obesity/cardio-metabolic dysregulation and dietary patterns characterized by high intakes of energy-dense foods, high fructose corn syrup, GI/GL, and meat coupled with low intakes of antioxidants and fibre (87, 188). We observed higher intake of fat and lower intakes of fruit and vegetables, vitamin C and vitamin E in children with NAFLD which may increase the severity/risk of cardio-metabolic dysregulation.

6.3 Contribution to the Literature

To the best of our knowledge, this thesis contains the first studies evaluating overall DQ using a variety of DQ tools, GI, and GL in children with gastrointestinal or liver disease. This thesis evaluated dietary intake and overall DQ in three different clinical populations with high risk of cardio-metabolic dysregulation; children with CD who in general have normal body weight, children who have previously experienced under-nutrition and are now at risk of obesity post-LTX, and obese children with NAFLD, but prescribed diets that could predispose to cardio-metabolic dysregulation.

A) Celiac Disease

The factors associated with poor HRQOL in children with CD have been examined and previously reported in the literature (179, 206, 208-212). The majority of this research focused on comparing HRQOL between individuals with CD vs CD and other comorbidities (diabetes) or healthy controls. The main factors associated with poor HRQOL in this vulnerable population are GFD adherence and presence of comorbidities such as diabetes (179, 206, 208-212). Limited data have been published discussing the impact of socioeconomic factors and overall DQ on HRQOL in children or adults with CD on a GFD. **Chapter 4** illustrates novel results assessing associations between socio-demographic factors, gluten intake (GFD adherence), overall DQ (using three different DQ tools, GI, and GL), and HRQOL in children/adolescents with CD. We were not able to examine the relationship between the economic burden of GF foods and DQ, and HRQOL due to the small sample size. Nevertheless, data from **Chapter 4** represents a subset of a larger national data pool that will consider the effect of socioeconomic variables on GFD adherence, overall DQ, and HRQOL.

B) Liver Transplantation

Several studies have shown that up to 20-30% of children five years post-LTX experience an increase in body weight and/or cardio-metabolic dysregulation due to immunosuppressive regimes (101, 154, 156-158). However, there is very limited data exploring dietary intakes of children post-LTX. **Chapter 4** demonstrates the nutritional habits of stable children post-LTX. This was assessed via (1) overall DQ (using three DQ tools, GI, and GL), (2) comparisons of macro/micronutrient and food group intake with Dietary Reference Intakes and Alberta Nutrition Guidelines for Children and Youth, and (3) comparisons of overall DQ between children post-LTX and healthy controls.

C) Non-Alcoholic Fatty Liver Disease

Obesity is a major public health concern which has been associated with numerous chronic diseases, such as NAFLD. Current literature mainly addresses the relationship between foods (e.g. meat) and/or macro and micronutrient (kcal, fat, antioxidants, GI, GL) intake and the risk of NAFLD (87, 108, 188). Only two studies have reported the impact of overall DQ and the risk of NAFLD in adults using DQ tools (HEI and DQI-I). No data was published to assess overall DQ using different tools and components of Adequacy and Moderation in children with NAFLD. **Chapter 5** evaluates the association between overall DQ using three DQ tools (Total DQ, Adequacy and Moderation Scores), GI, and GL, markers of adiposity, and cardio-metabolic parameters.

6.4 Clinical and Public Health Implications

A) Celiac Disease

This thesis provides useful information for those that counsel on the GFD. In therapeutic diets, registered dietitians (RDs) in particular, play a critical role in providing credible information about the GFD to children with CD and their families (306). A qualitative study from our research group determined that parents of children with CD feel RDs are reliable GFD counselors (307). In addition to basic GFD education for individuals and families, it is necessary to emphasize associated nutritional limitations (especially of GF processed foods), provide suggestions for improving nutritional quality of the GFD, and provide information to help people understand food labels and identify "healthy" and "unhealthy" foods. Evidence has shown that individuals with CD are at risk for obesity, hyperglycemia, and insulin resistance (308, 309). One of the potential reasons for the enhanced comorbidity risk is poor nutritional quality of processed GF foods. Nutritional education may take into consideration in: 1) adequate consumption of essential nutrients such as vitamin D, folate, and fibre, including by recommending vitamins/multivitamins,

2) increasing consumption of key food sources, and 3) moderating consumption of *other foods* group, such as sweetened beverages and candies. RDs play an invaluable role in helping children/adolescents with CD improve GFD nutritional quality to reduce the risk of cardio-metabolic dysregulation and enhance overall HRQOL.

Adherence to the GFD (self-reported, serology, interview, food records) in individuals with CD has increased from ≤60% to >70-75%, likely due to increased awareness of CD, improved nutritional education of the GFD, better labeling, reduced cross contamination of processed food and/or the increased availability of GF foods (310-313). A number of studies have focused on novel methods to improve adherence to the GFD, for example, text messages. An intervention study examined the effect of a text message intervention tool (2-3 messages/week for 3 months) on HRQOL in youth and young adults (ages 12-24 years) with CD and on a GFD for 2-10 years (314). The text messages contained information about GF recipes, restaurant search tools, CD organization websites, and reminders to stay GF. At baseline, the majority of the participants (>90%) strictly adhered to the GFD. The study found that the text messaging intervention had a positive impact on physical and mental HRQOL scores in youth and young adults with CD and adherence to the GFD. Another study found that psychological support for 6 months had a positive impact on adherence to the GFD and reduce the risk of anxiety in adults with CD (315). Therefore, clinical practitioners (physicians, RDs and nurses) would benefit from frequently assessing the adherence to the GFD and HRQOL (including psychological assessments) in children with CD. Several tools may help to improve HRQOL and anxiety. Clinical practitioners may need to establish or recommend support groups for children with CD and their families.

HRQOL assessment often includes a multi-domain approach to capturing physical and psychosocial well-being. Evaluating HRQOL is subjective and challenging to adequately capture,

especially in children and youth. The assessment of HRQOL in pediatrics can be based on child/adolescent and/or parent perspectives. For younger children, perceptions of HRQOL do not differ between child and parent report, as shown in this thesis and previous studies. This relationship is not maintained with adolescents (206, 248-251). This potentially may be due to the hormonal, physical, psychological, and social changes that occur during puberty and affect, sleep pattern, appetite, and motivation (316, 317). In pediatrics, it is necessary to assess HRQOL from both child/adolescent and parent perspectives.

Education regarding nutritional limitations of a GFD is crucial to implement. This could be achieved through a variety of channels including the Canadian Celiac Association (CCA), schools, stakeholders, and changes in governmental food policies. Children with CD on a GFD have previously reported that educational institutions lack GF food choices (312, 318). School communities could be educated about GFDs and ensure provision of nutritious GF meals/foods and/or prevention of gluten cross contamination in lunch rooms (e.g. microwaves for GF meals only). Several approaches could be utilized including with the participation of government and charitable organizations such as CCA. These strategies could include a focus on 1) individuals, families, schools, and universities about GFDs and how to reduce cross contamination and 2) educating restaurants on ways to develop a "GF kitchen". However, education could also focus on healthier GF meal options with the help of health professionals in particular RDs. In addition, the development of public policies that include: 1) mandatory folate fortification for GF flour, 2) presence of added sugar and at risk nutrients (folate) on food labels, and 3) specific nutritional recommendations for individuals following a GFD, would be beneficial and may contribute to the production of healthier food GF food choices for the Canadian public.

B) Liver Transplantation and Non-Alcoholic Fatty Liver Disease

Obesity remains an international epidemic. One of the main factors for this pandemic is related to an unhealthy lifestyle (poor DQ, sedentary) which leads to cardio-metabolic dysregulation. Poor DQ has been reported among children/adolescents due to increased consumption of dietary patterns characterized by high fat and simple sugar (319-321). Improving DQ and increasing physical activity as part of a healthy lifestyle are the main treatments for cardio-metabolic dysregulation in children. Health professionals have a significant responsibility to educate individuals and families on these healthy lifestyle components. However, adherence to "healthier" dietary patterns is low in obese children. To address these concerns, a qualitative study was conducted in youth with NAFLD and their parents at Stollery Children's Hospital (192). The parents of youth with NAFLD highlighted a need for: 1) practical dietary recommendations, 2) healthy recipes and snacks, and 3) practical and easy to follow tools for healthy diet preparation/consumption. To enhance adherence to a "healthier" dietary pattern, nutritional recommendations and programming should be developed focusing on the concept of overall DQ including a strong focus on dietary adequacy, moderation and diversity in consumption of different food groups. Overall DQ can be enhanced through meeting food group intake recommendations by the Canadian Food Guide and reducing consumption of *other foods* group. RDs may consider to design a simple and effective diet therapy regime or program for obese children addressing these areas of concern.

Health educators may consider the need to develop nutritional programs to facilitate understanding of healthier dietary choices in youth with gastrointestinal and liver disease. Collaboration between schools, families, media, governmental food policies, and other stakeholders, like food manufacturers and retailerss, is necessary to promote healthier lifestyles. Schools could expand a focus on educating children about healthy food choices and provide

adequate meal programs with a family focus to ensure overall dietary changes can be sustained. A continued focused on government food policies including examination of media advertisements of unhealthy food choices to vulnerable sectors, and the development of food policies that could improve access to quality diets is necessary. Government supported research, policy and regulations should: 1) establish upper intake limits for added sugar and fat based on food type, 2) develop a clear definition of "healthy" vs "unhealthy" foods, 3) update food labels to be more readily understood by the general public and include "healthy" or "unhealthy" labelling, which may result in changes to individual/family food choices, 4) reduce healthy food prices, and 5) tax junk food/sweetened beverages (322). A study applied an 8% tax on sweetened beverages in Mexico; the study found reducing purchases by 5% two years post-implementation (323). Finally, it is important for an evaluation of the information that is introduced on food labels with regard to information related to added sugar and high fructose corn syrup amounts and clear identification of "healthy" vs "unhealthy" products so the consumer can be more informed about the nutrient content of food product choices. Ideally, this could be translated to restaurant menus and the incorporation of healthier restaurant meal options.

6.5 Strength and Limitations

A) Participants and Study Design

We comprehensively assessed dietary intake (using multiple tools and methods to assess DQ) in three pediatric populations which chronic GI and liver diseases wherein diet plays a significant role in both the etiology and treatment. Nutritional quality investigations included dietary intake assessment (24-hour recalls, 3 day food records), validated DQ tools (HEI-C, DGI-CA, and DQI-I), and additional analyses (GI, GL). This enabled a comprehensive assessment of nutritional intake in both healthy children and children with chronic gastrointestinal (CD) and liver

diseases (NAFLD and post-LTX) across a spectrum of body habitus and ages. Furthermore, these nutritional parameters were then related to relevant patient outcomes (HRQOL, risk for metabolic dysregulation).

One limitation of this thesis was smaller sample sizes for some analyses which may have resulted in insufficient power to determine interrelationships between primary outcomes (DQ scores, GI and GL) with effect of the study group (case vs control). For example, we have grouped NAFLD and NASH etiologies due small patient numbers and lack of liver biopsies necessary to diagnose NASH (**Chapter 5**). Several additional factors affecting dietary intake and DQ including food availability, security, and acceptability in individuals with CD on a GFD were not evaluated in the presented studies. Other cofounding variables (such as socio-demographics and ethnicity) that may affect food intake were not evaluated in children with NAFLD and post-LTX. We have described the dietary intake and DQ in children post-LTX; however, associations between overall DQ and health related outcomes need to be examined further.

B) Dietary Intake and Diet Quality

One of main strengths of this thesis involved the use of three tools to evaluate DQ. These tools are either food or nutrient based and focus on different DQ components. We have adapted the DQ tools (HEI-C, DGI-CA, and DQI-I) based on Canadian nutritional recommendations and Alberta Nutrition Guidelines for Children and Youth (AGNCY). We found high agreement between non-adapted and adapted scores in children consuming therapeutic diets and those with no food restrictions.

DQ tools have been validated for use in healthy populations. We did not find differences in scores between children with CD on the GFD and disease controls due to: 1) insufficient power to observe differences between the two diets, 2) lack of GFD nutritional limitation assessment via

DQ tools, and/or 3) disease control group already presenting with poor DQ. Another general limitation with DQ is the lack of definitions and cut-off points for components of Adequacy, Moderation, or Variety. The adequate intake of micronutrients can be assessed based on Recommended Dietary Allowance (RDA) or Estimated Average Requirement (EARs). The Variety among food groups can be assessed based on meeting the recommendations or meeting 50% of the recommendations. With the exception of NAFLD, we did not assess and compare components of DQ in children with CD and post-LTX. Finally, analysis of added sugar and high fructose corn syrup would have conferred considerable additional strength to the study design, as these factors are known to influence obesity development/progression and cardio-metabolic dysregulation risk.

C) Study Outcomes

A strength of this study was the analysis of several factors influencing overall dietary intake and patient care outcomes from both child and parent perspectives (HRQOL, socio-demographic factors). A recent study demonstrated discrepancies between self and physician reported HRQOL in children with CD, related to gender and disease duration (324). Comparing HRQOL from self-reported, parent and physician perspectives would be ideal because physician's perceptions of a patient's HRQOL may influence the treatment plan (324, 325). Research in this area is limited. Poor HRQOL has been observed in children post-LTX and obese children with NAFLD (326). Interrelationships between overall DQ and HRQOL in children post-LTX need to be assessed duet to reduced HRQOL in children post-LTX (326, 327). Improved overall DQ may positively influence HRQOL with or without weight reduction. Furthermore, dietary intake is affected by several demographical factors such as cultural factors, ethnic variables, economic elements, and education level.

6.6 Further Directions

Several studies should be conducted to improve current definitions and develop specific recommendations (cut-off points) for dietary intakes in children with gastrointestinal and liver diseases (with and without therapeutic diets). First, a specific definition of a healthy diet and the criteria for distinguishing between healthy and unhealthy diets would be beneficial. Second, it is important to establish sub-categorizations of food groups and develop specific food and nutritional guidelines for adequate intake within each sub-categorizations (green leafy vegetable, low vs high fat cheese, legume consumption). Third, re-evaluation of nutrient recommendations for *other foods* may be taken into consideration by Health Canada due to a remarkable increase in the national prevalence of obesity. For example, Health Canada recommends that added sugar should not exceeded 25% of Kcal intake whereas the World Health Organization uses a limit of 10% of Kcal intake (328). Health Canada states that following the Canadian Food Guide recommendations reduces the risk of inadequate nutrient intake and cannot be used to assess the Adequacy of nutrient intakes (328). With the above recommendations, the Canadian Food Guide can be more sensitive to assess nutritional Adequacy and Moderation.

The Canadian Food Guide recommendations may be a useful tool for reducing risk of inadequate nutrient intake in healthy Canadians, but not in individuals following a GFD because it does not address key nutritional limitations. It is important to design a "Gluten-Free Food Guide" to provide accurate nutritional recommendations of a healthier GFD. In addition, a "GF DQ tool" should be developed to assess the nutritional quality of GFD. The GF DQ tool should include three main components: Adequacy, Moderation, and Variety (within food groups) (**Appendix K, Figure K-1**).

In general, it is important to design a DQ tool that assesses Adequacy, Moderation, and Variety (within food groups). This tool should examine foods/nutrients at risk in the designated clinical populations. DQ assessment should also include added sugar, GI, GL, and high fructose corn syrup as components of Moderation. The tool should be easy to use for families and children. Finally, the DQ tool should be sensitive to assess overall DQ (good, needs improvement and poor) and identify individuals with very poor DQ related to negative health outcomes such as cardio-metabolic dysregulation. Intervention studies should be conducted to assess the adherence to "healthy" dietary patterns using the DQ tool.

Studies should be conducted to assess the associations between DQ and cardio-metabolic markers in children post-LTX and children with CD following a GFD. Recent research has focused on studying the effect of sarcopenia (rather than body weight or fat mass) on morbidity, mortality, and health related outcomes due to a high prevalence in underweight children and adults. Sarcopenia has also been observed in obese individuals with and without NAFLD and post organ transplant (329-331). Poor DQ (low protein, vitamin D, and antioxidant intakes) has been related to the risk of sarcopenia (332). Future studies are needed to assess the effect of DQ on the risk and treatment of sarcopenia in children with CD, NAFLD (with increased fat mass), and post-LTX. Finally, interventional studies should be conducted to assess the relationships between overall DQ and health related outcomes in children with CD, post-LTX, and NAFLD. **Figure 6-3** summarizes the proposed future studies needed to examine factors that affect dietary intake/DQ and associations with health related outcomes in children with chronic disease (with or without a therapeutic diet).

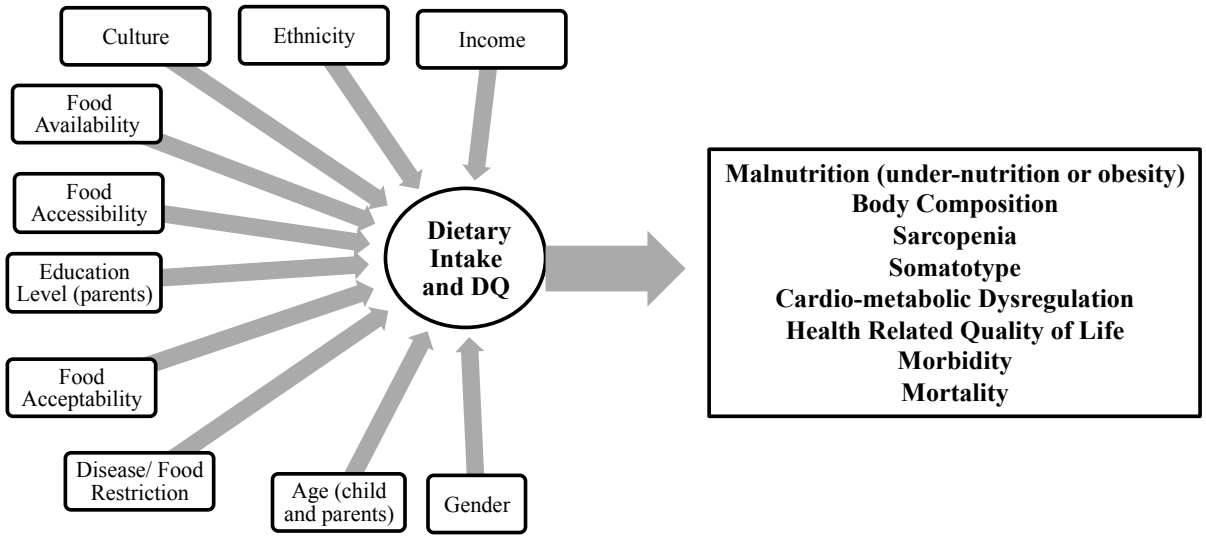


Figure 6–3: Future Studies to Be Conducted in Children with Gastrointestinal and Liver Disease. Future studies should examine the factors affecting dietary intake and DQ and associations with health related outcomes in Children with Gastrointestinal (Celiac Disease) and Liver Disease (Non-Alcoholic Fatty Liver Disease, Post Liver Transplantation).
Abbreviations: DQ, Diet Quality.

6.7 Conclusions

Children with gastrointestinal (CD) and liver diseases (NAFLD and post-LTX) have poor DQ. While poor DQ is indirectly related to reduced HRQOL in children with CD, poor DQ increases the risk of obesity and cardio-metabolic dysregulation in children with NAFLD. This has clinical implications to ensure maintenance of improved DQ (ensure adequate intake of healthy food and moderate intake of unhealthy foods) in children with chronic disease, particularly those consuming therapeutic diets, to improve HRQOL and reduce obesity/cardio-metabolic dysregulation risks. Intervention studies should focus on the impact of overall DQ on health related outcomes and disease risk. Future studies are needed to determine other factors associated with poor DQ in children with chronic disease and measure the influence of DQ on health related outcomes (**Figure 6-3)**.

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APPENDICES

Appendix A : The Standard of Operation Procedures (SOP) for Dietary Intake Analysis, Estimation Dietary Gluten, Glycemic Index, Glycemic Load and Calculations Diet Quality Tools

A-1 Dietary Intake Analysis: Food Processor

The Basics: How to use Food Pro

1. Creating a new person

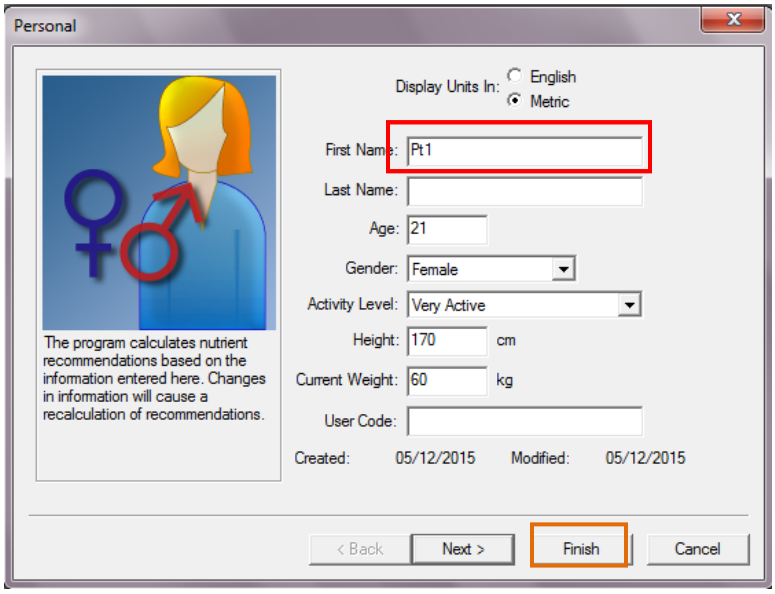
There are two ways to create a new person.

1) Go to file > new > person

OR

2) Under the task panel on the right hand side click person (you may have to click OK if there are over 400 people saved in the database), the "open person" dialog will open, on the bottom right click "New"

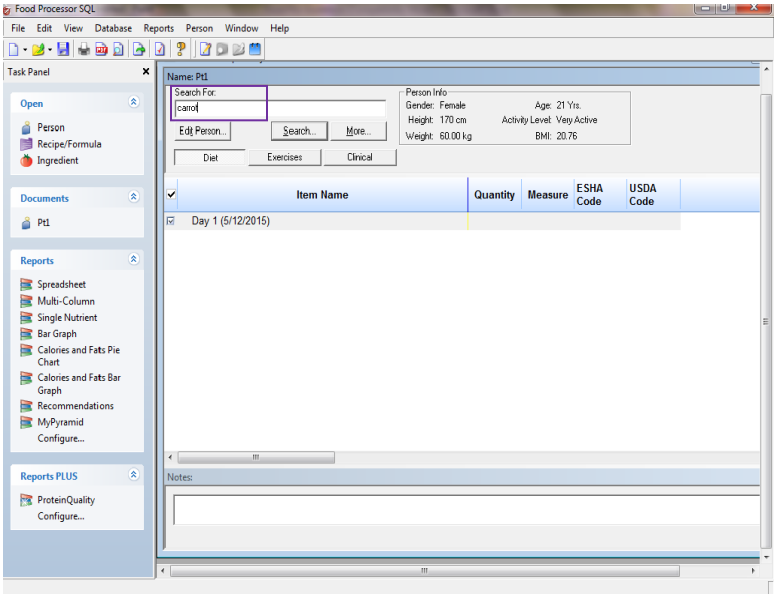
This window will pop up



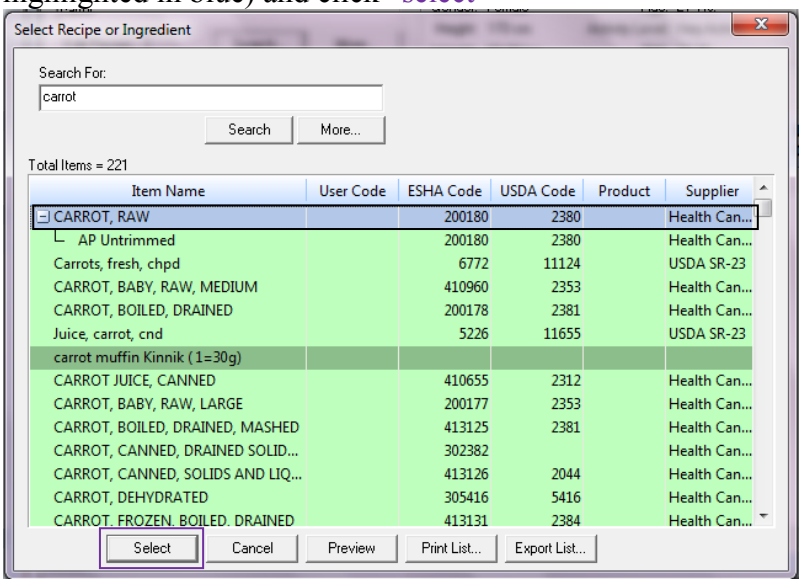
The ONLY information you need to enter here is the patient code (Example Pt1).
DO NOT input the patient's actual name. You do not need to enter the actual age, gender, height or weight, however it does require you to enter something into these fields to click "finish" (so just make up some numbers). Do not click next, you do not need to enter any information about the patients address, physician etc.
Click "Finish"

2A. How to search for and enter food items

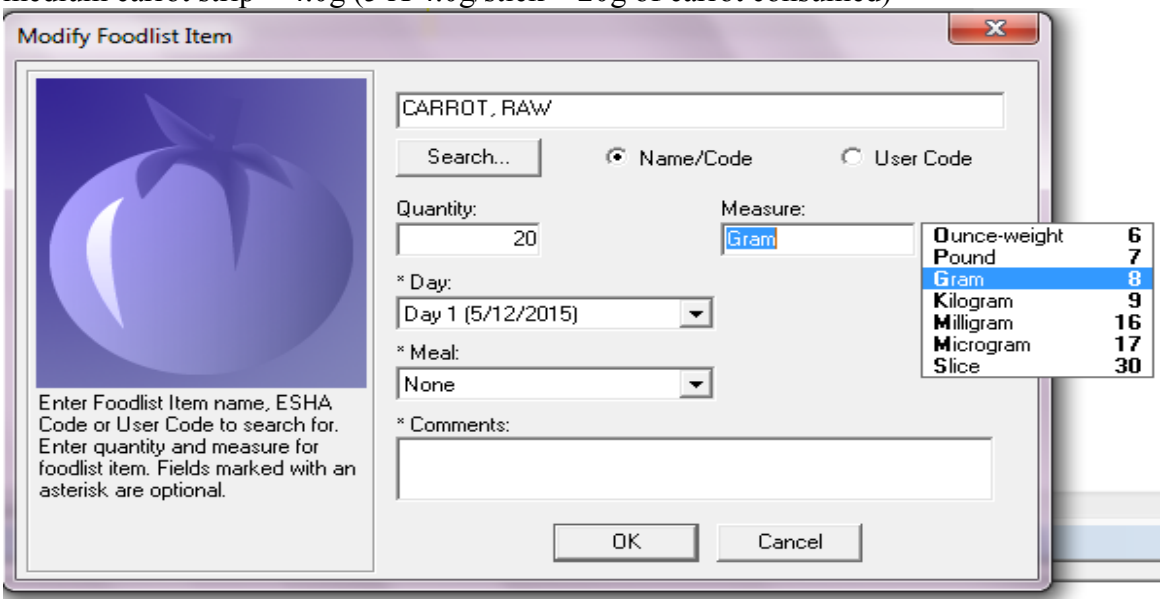
Step 1: In the search box "Search for:" under the patients name enter the food item you wish to search. For example if the food record said "5 carrot sticks" enter "carrot" into the search box and click "Search…"



Step 2: This window will pop up, click the item that applies (when an item is selected it will be highlighted in blue) and click "select"

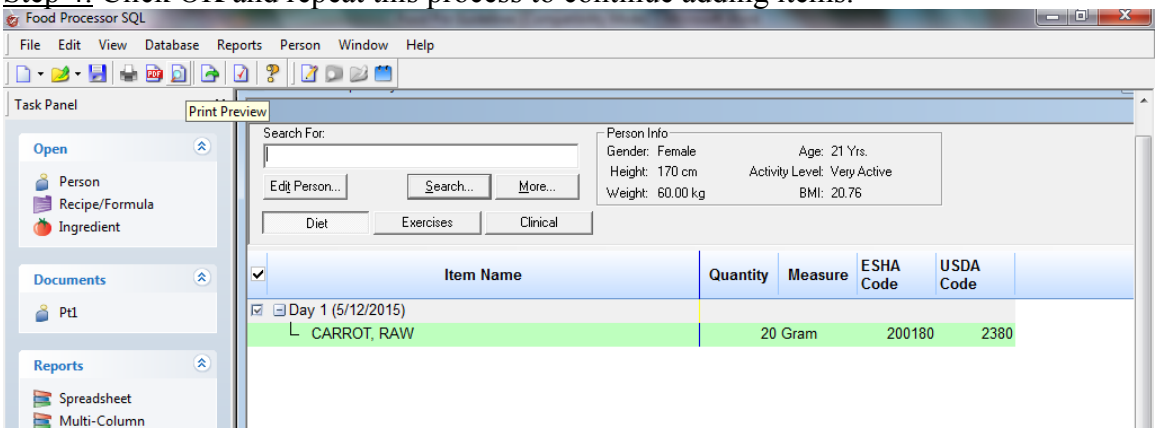


Step 3: Next you need to choose the amount of carrot consumed. In our Food Pro SOP, 1 medium carrot strip = 4.0g (5 X 4.0g/stick = 20g of carrot consumed)



1. Try to avoid using pre-selected serving sizes such as "slice" or "piece", sometimes these can get you into trouble depending on who determines how many grams of carrot constitutes as a "slice".
2. There is the option to organize the food into "meals"; however we do not do this. Leave the drop down menu for meal as "none" and input the items in the order they were eaten based on the food record as one continuous list
3. Depending on the item the options for "Measure" can change, some items will additionally include cup, teaspoon, tablespoon etc.
4. If the item in the food record is written as a fraction such as ¼ cup or ½ banana please enter this in decimal form i.e. 0.25 cup or 0.5 banana

Step 4: Click OK and repeat this process to continue adding items.

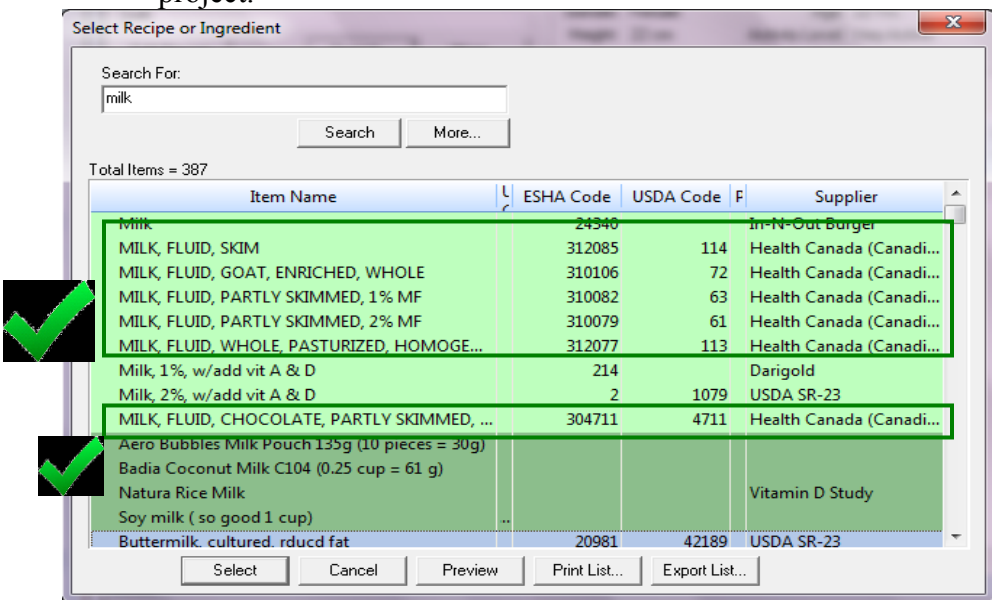


1. If you accidently input the wrong item/amount, right click on the item and you can either modify or delete the item
2. If the patient has more than one day, right click on the screen and click "add day"
3. To move a food item, left click and hold down the mouse button and you can drag the item to a new position

Step 5: How to save
Go to file > save to file > save in the appropriate file folder (use the patient ID code as file name i.e. Pt1)
SAVE OFTEN while you are working. Food Pro does crash on occasion and you will lose everything you were working on if you did not save.

2B. Which supplier do I choose from?

1. **ALWAYS choose Canadian (Health Canada) items first!!!** This will work for about 95% of the foods you encounter
2. Sometimes <4% of the time you may need to choose a United States item (USDA). However this is unlikely only choose an USDA item if this is indicated in the Food Pro SOP and/or after you have talked to the graduate student in charge of the project
3. There is a small small possibility <1% that you need to choose a name brand item (i.e Mcdonalds, Nestle, Kraft, Campbell's, etc.). This is extremely unlikely. Please only choose a name brand item after you have talked to the graduate student in charge of the project.



Why is choosing Health Canada items so important?
This is because enrichment and fortification processes differ between countries (Canada vs. United States). Unless stated otherwise assume that foods were purchased and consumed in Canada. We do not choose name brand items because we cannot be sure that the nutrition information is specific to Canada. For example the nutritional information entered for Campbell's Chicken Noodle Soup" may not reflect the nutritional content of "Campbell's Chicken Noodle Soup" that you buy from Canadian grocery stores.
Note: When searching for items, Health Canada can be tricky
-Health Canada does not like "s", for example if the patient eats "boiled carrots" or "scrambled eggs", you need to search these as "carrot" and "egg" or health Canada items will not show up in the search results
-Health Canada uses different terms to describe items than what you would expect. For example pop or soda is entered as "carbonated"
-Add stuff that Ruby found ie banana and oranges

Creating a Recipe

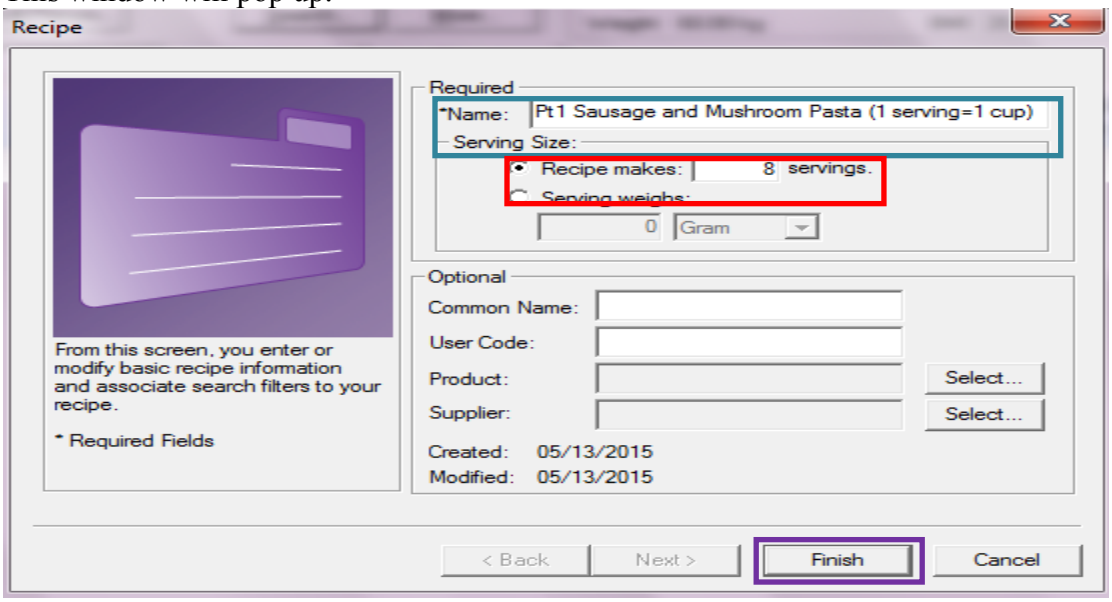
There are two ways to create a new recipe.

1) Go to file > new > recipe

OR

2) Under the task panel on the right hand side click recipe/formula the "open recipe" dialog will open, on the bottom right click "New"

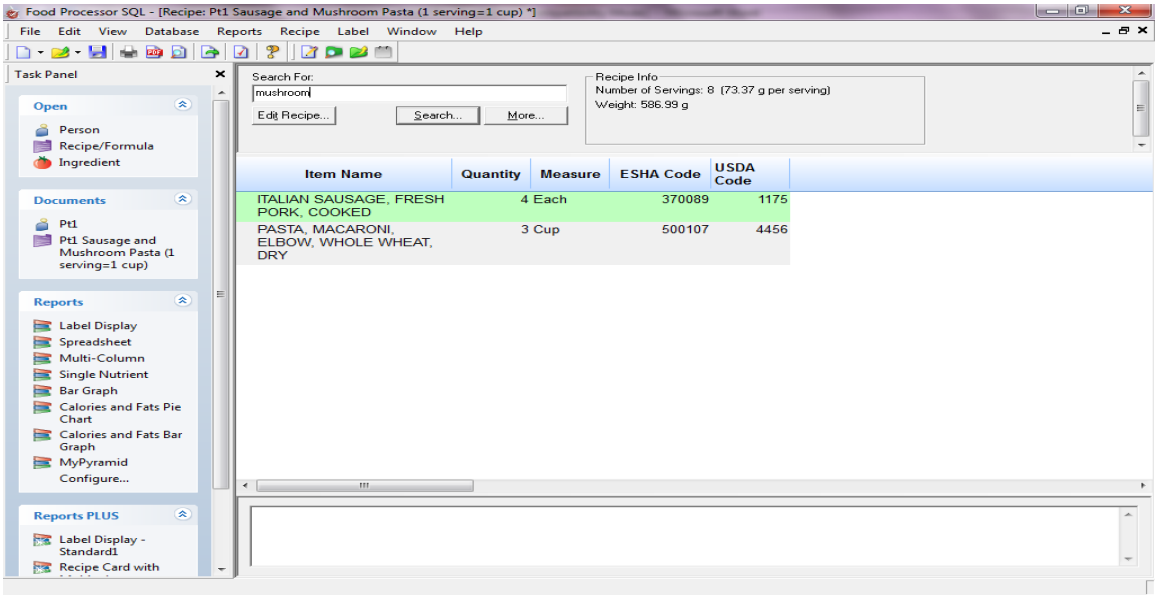
This window will pop up.



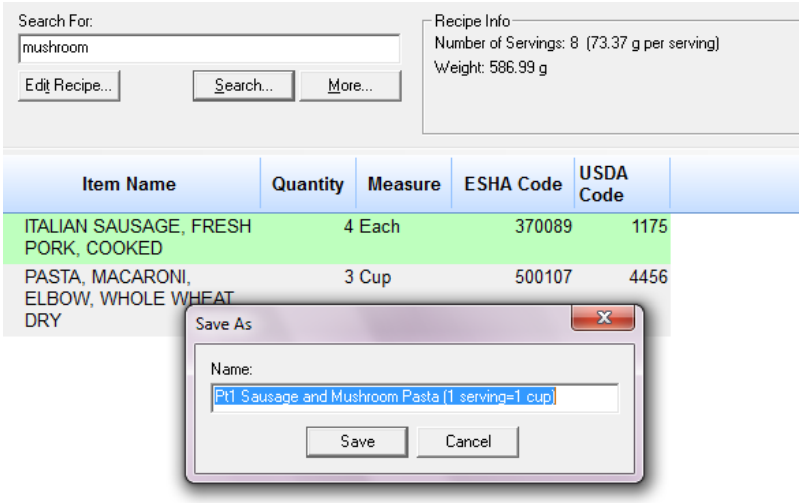
Food record example: *"1 cup of Homemade Sausage and Mushroom Pasta Recipe: 4 pork Italian sausages pan fried chopped, 3 cups of whole wheat pasta dry, 1 cup of mushrooms pan fried….etc*

1) Type the name in the Name box (include the patient ID before the recipe name), if applicable you can indicate what a "serving" means.
2) Include how many servings the recipe makes. There is the option to select serving by weight however this is more complicated and often this information is not given by the patient.
3) Click Finish

You can then start entering recipe items using the search bar

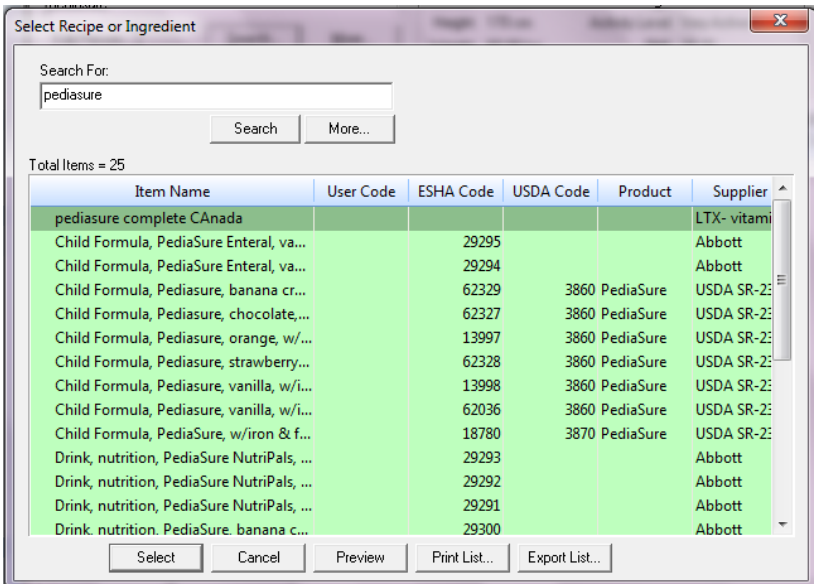


4) To save a Recipe: Choose file > save as and (make sure the recipe name is correct) and save

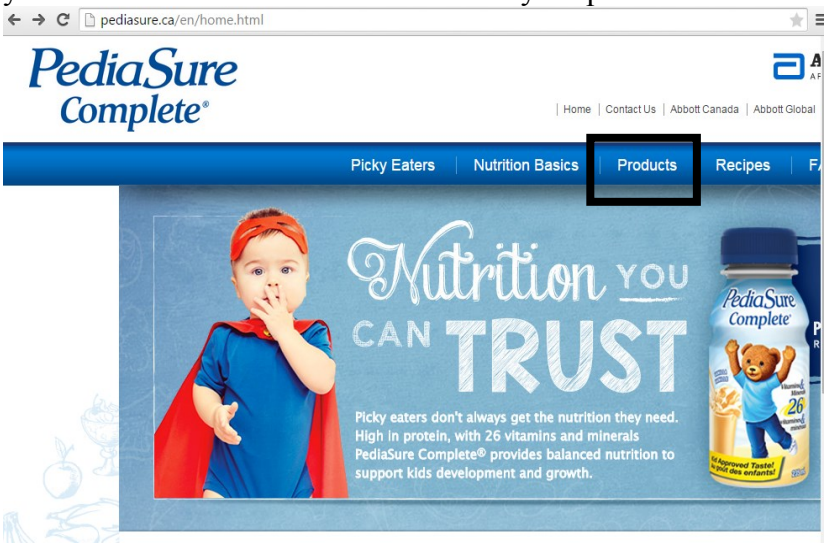


Creating a new ingredient
If you cannot find the exact food item you need/cannot find a reasonable substitution there may be times when you need to create your own ingredient

For example a nutritional supplement such as Pediasure. There was no Health Canada Pediasure so "pediasure complete Canada" was entered into our database by a student. "Ingredient/Items" which we have entered show up as a darker green in the search results



You need to find the nutritional information for the given product online. Make sure you go to a **CANADIAN (.ca)** official product website for the nutritional information i.e http://pediasure.ca/en/home.html. Websites such as pediasure often have a product tab where you can find the nutrition facts table for your product of interest



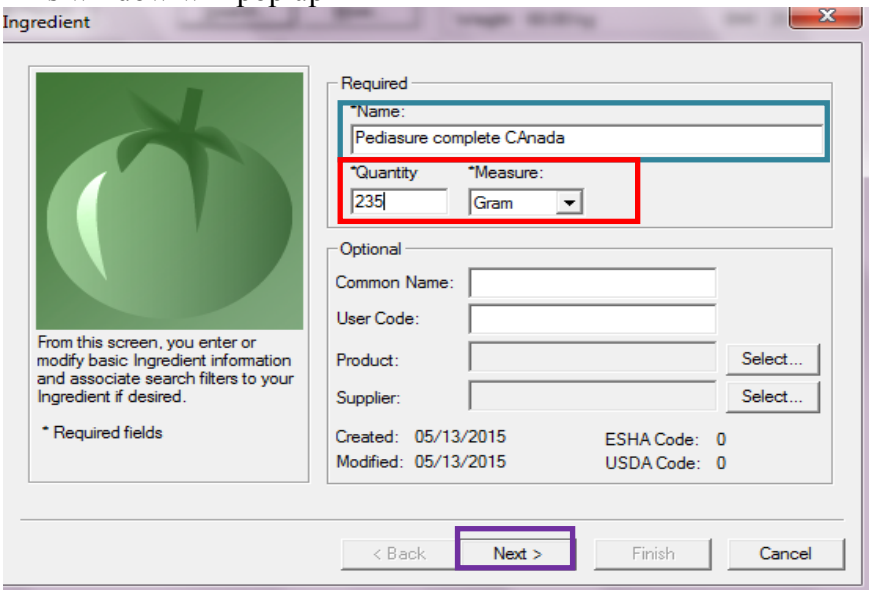
There are two ways to create a new ingredient.

1) Go to file > new > ingredient

OR

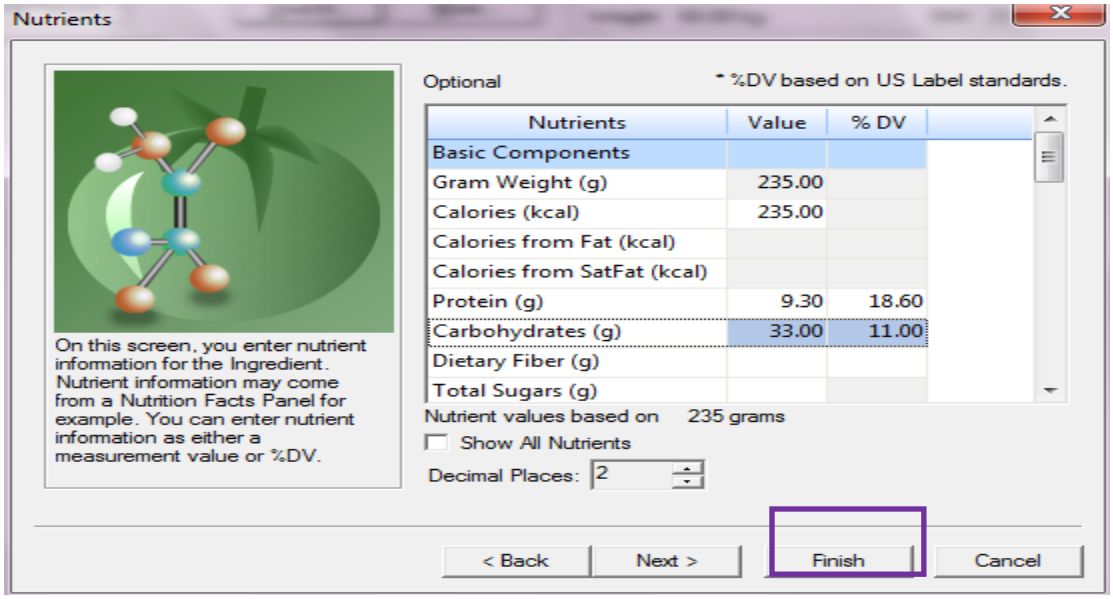
2) Under the task panel on the right hand side click ingredient the "open ingredient" dialog will open, on the bottom right click "New"

This window will pop up



1) Type the ingredient name in the Name box
2) Include the quantity and measure
3) Include which study this product was entered for "
4) Click Next

Now you need to enter the nutrient information for the product



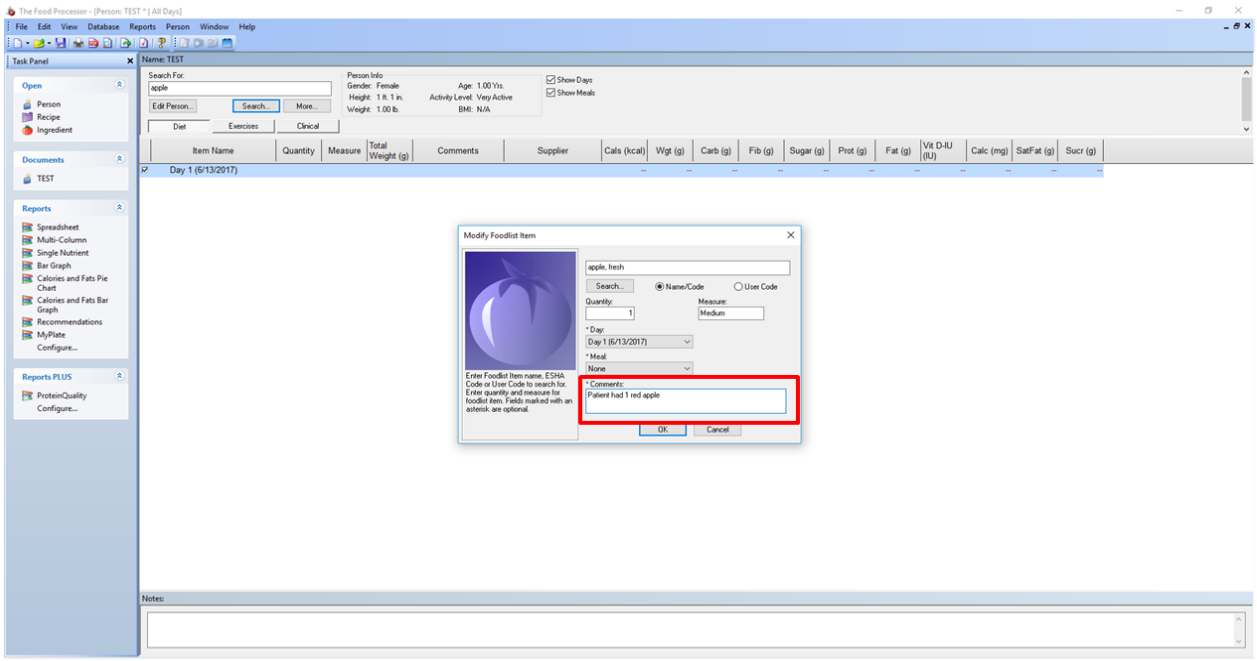
5) Click Finish

*It is best to avoid making an ingredient if you can find an option <u>already</u> found in Food Pro. Substitutions are also welcomed instead of making a new ingredient.

- For example if it was a certain brand of ice cream such as “cookies and cream”, you may use the Health Canada option for “chocolate ice cream” **IF** the macronutrients (carbs, protein, fats, sugars) are close to exactly the same. Go to the **CANADIAN** website for the cookies and cream ice cream and compare the nutrition facts with the option in Food Pro for the same number of servings.

*It is also HIGHLY recommended that you include **comments** next to the items you enter in Food Pro or why you made that food selection.

- Why is it this food choice?
- Why did you choose that number of servings?
- Why was that substitution selected?
- Where is this recipe or ingredient from (website)?
- <u>**ANY** information that will assist someone who looks back at this file later</u>



* Follow along the **Food Pro SOP's** to help you make food selections (ask your graduate student supervisor which version of the SOP to use depending on what study you are working on).

For example if the size of a fruit is not specified you choose medium. Some standard weights for items are also found on this SOP (example: size of a beef patty).

*Make sure to take a screenshot of brand name products and save recipes that are used for Food Pro entries. Save with the patients ID number, date it was accessed from Internet and add the website link.

- Over time website links change and this is not a reliable way of going back to look at a food item for its ingredients or nutrition facts. It is best to take a picture of the website information and save separately.

A-2 Glycemic Index and Glycemic Load

Glycemic Index - the ranking of carbohydrates according to the extent they raise blood glucose levels after eating (based on the total amount of carbohydrates in that day).
Glycemic Load - estimation of how much a food will raise a person's blood glucose levels after consumption, approximates the effect of consuming 1 gram of glucose (GI weighted measurement).

- Have 1 column for each: Item Name, Quantity, Measure, Weight(g), GI glucose, Serving Size, Available carb, Carb in Food, GI mix meal, GL sum, substitution.
- Copy and paste the information of the "Item Name, Quantity, Measure, Weight(g) and Carb in Food" from the Food Pro spreadsheet of the participant
- Information about the "GI glucose, Serving Size, Available carb" is obtained from: **GIGL SOP** and **Foster et al. 2008**
  - If no information can be found for the specific food or product, use the website: http://www.glycemicindex.com/
  - If no information can be found in the sources above, search through the University of Alberta library search to see if there are any journals
  - If a substitution needs to be made indicate the food item in the "substitution" column
- To calculate GI mix meal: **(GI Glucose*Carb in food) / Sum of Carb in food**
  - Note: Make sure to sum all of the carbs in food before calculating the GI mix meal
  - **Cell formula: =(E#*H#)/H# of sum Carb in food**
  - replace with the appropriate cell number
- To calculate GL sum: **(GI Glucose*Carb in food) / 100**
  - Note: the first part of the formula is the same as the one used for GI mix meal
  - **Cell formula: =(E#*H#)/100**
  - replace with the appropriate cell number

Example of Glycemic Index and Glycemic Load

	Carbohydrate (g)[1]	Glycemic Index of foods[2]	Glycemic Index	Glycemic Load[3]
Apple	26	38	=38*26/53.5= 18.5	=38*26/100=9.9
GF bread	13.5	72	=72*13.5/53.5= 18.2	=72*13.5/100=9.7
Regular Bread	14	50	=50*14/53.5= 13.1	=50*14/100=7
	Total = 53.5		49.8	26.6

[1] Data obtained from Food processor.
[2]Glycemic index values were obtained from Foster-Powell et al 2002 (97) and www.glycemicindex.com.
[3]GL was calculated. GL= carbohydrate of food (g) x glycemic index/100 (97).

Table A-1: The Adaptation of Healthy Eating Index-Canada

Components (not Adapted)	Maximum-Minimum	Adaptations and Calculations	Rational/ Source	Continuous (CONT) or Category (CAT)
Grain: Meet the recommended intakes of based on CFG	0-10	= n serving consumed/ recommended serving x10	Based on ANGCY	CONT
F/V: Meet the recommended intakes of F/V based on CFG	0-20	= n serving consumed/ recommended serving x20	Based on ANGCY	CONT
Milk: Meet the recommended intakes of milk based on CFG	0-10	= n serving consumed/ recommended serving x10	Based on ANGCY	CONT
Meat: Meet the recommended intakes of meat based on CFG	0-10	= n serving consumed/ recommended serving x10	Based on ANGCY	CONT
Other foods	0-10	≤ 1600Kcal= ≤ 4 >8 servings 1600-2200Kcal= ≤ 6 >11 servings ≥ 2200Kcal= ≤8 >14 servings	Servings in between the min and max = 5	CAT
Fat[1,4] ≤ 30% energy to <45% energy	0-10	≥ 40% =0 >30%- <40%= 5 ≤ 30% =10	Based on Health Canada recommendations	CAT
Saturated fat[2,4] ≤ 15% energy to 10 % energy	0-10	>10% =0 >7-10 = 5 ≤ 7% =10	Based on the DRI	CAT
Cholesterol[3,4] 300 mg to 450 mg	0-10	> 400% =0 >300-400 = 5 ≤ 300 =10	Based on the DRI	CAT
Variety[5]: At least one serving from each food group	0-10	At least ½ serving of each food group (2 score for meat, 2 score of milk, 2 scores grains and 4 scores for F/V)	-	CAT

[1]The original paper (Not Adapted) scored this component as proportional and the cut-off point was 30-45% (35).
[2]The original paper (Not Adapted) scored this component as proportional and the cut-off point was 10-15% (35).
[3]The original paper (Not Adapted) scored this component as proportional and the cut-off point was 300-450 mg (35).
[4]Dietary Reference Intakes for Energy, Carbohydrate, Fibre, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids (2002); Interim Summary of Conclusions (220). Dietary Recommendations on Total Fat & Fatty Acids From the Joint FAO/WHO Expert Consultation on Fats and Fatty Acids in Human Nutrition, 10-14. November, 2008, WHO, Geneva (227). Garriguet, D. Diet quality in Canada. Health Reports, 2009 Sep;20(3):41-52 (333).
[5]The original paper (Not Adapted) scores at least 1 serving from each food group to max score or min score for no serving of at least 1 food group (35).
Abbreviations: ANGCY, Alberta Nutrition Guideline for Children and Youth; CFG, Canadian Food Guide; F/V, Fruits and Vegetables.

Table A-2: The Adaptation of Dietary Guideline Index for Children and Adolescents

Components (not Adapted)	Maximum-Minimum	Adaptations and Calculations	Rational/ Source	Continuous (CONT) or Category (CAT)
F /V: Meet the recommended intakes[1,2,3]	0-20	= scores from HEI-C (F/V)	Based on ANGCY	CONT
Bread and Cereal the recommended intakes[1]	0-5	=scores from HEI-C (grains)/2	Based on ANGCY	CONT
Wholegrain: Intake of wholegrain[4]	0-5	0: No wholegrain or no bread 5: 100% wholegrain bread. 2.5: consumption both wholegrain and white bread on the same day[3]	This includes breads only: buns, pita, roti, tortilla	CAT
Meat: Meet the recommended intakes[1]	0-10	=scores from HEI-C (meat)	Based on ANGCY	CONT
Dairy: Meet the recommended intakes[1]	0-5	=scores from HEI-C (milk)/2	Based on ANGCY	CONT
Reduced-fat milk (drinking)	0-5	5: 100% low fat (≤2%), skim milk or lacto-free 0: no low fat milk or no milk (whole milk, almond milk, rice milk)	-	CAT
Beverage: Grams of water as a beverage as a proportion of total grams of beverages	0-10	10=no beverages (water only) 5=with beverages (hot chocolate, juice, pop, tea) 0=no fluid consumed	Does not include milk or chocolate milk	CAT
Extra food[1]	0-20	= scores from HEI-C "others"*2	-	CONT
Variety: Sum of food types within core food[5]	0-10	At least ½ serving of each food group (2 score for meat, 2 score of milk, 2 scores grains and 4 scores for F/V) = scores from HEI-C "variety"	-	CAT
Food Choice: % Saturated fat[6]	0-10	=scores from HEI-C (Saturated fat)	Based on the DRI	CAT

[1]The original paper (Not Adapted) used the recommended servings of food groups based on the Australian recommendations (31).
[2]The original paper (Not Adapted) has fruit and vegetables in two food groups (31).
[3] F/V were in two different food groups in the original tool (Not Adapted) (31). We grouped F/V in one food group based on the ANGCY.
[4]The original paper (Not Adapted) does not have score of 2.5 (31).
[5]The original paper (Not Adapted) used 2 scores of each food groups (fruit, vegetables, milk, meat and grains) (31).
[6]Dietary Reference Intakes for Energy, Carbohydrate, Fibre, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids (2002) (227).
Abbreviations: ANGCY, Alberta Nutrition Guideline for Children and Youth; F/V, Fruits and Vegetables.

Table A-3: The Adaptation of Diet Quality Index-International

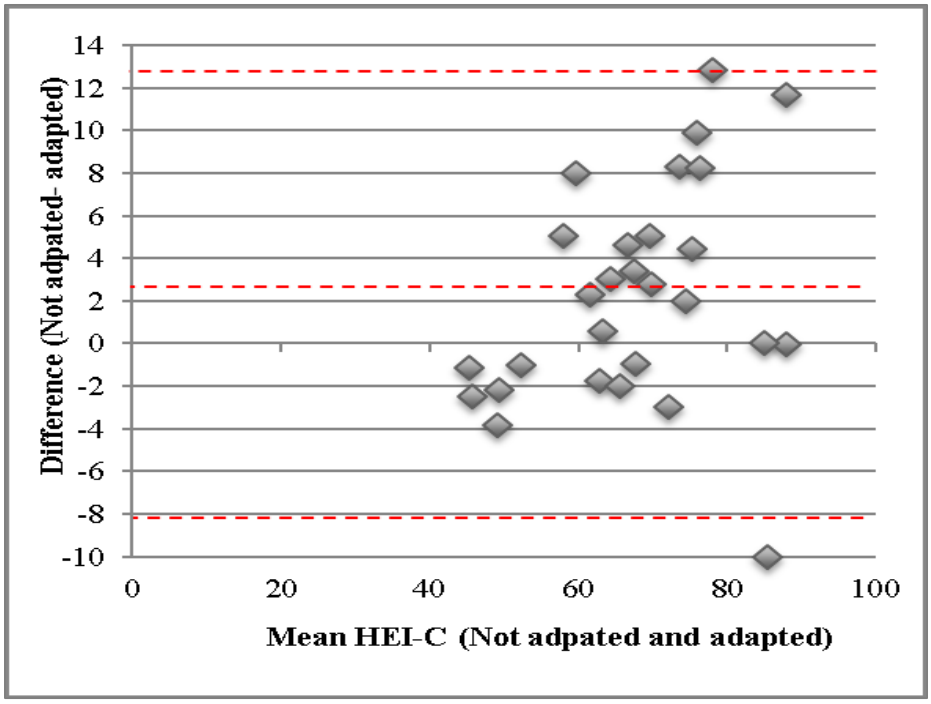
Components (not Adapted)	Maximum-Minimum	Adaptations and Calculations	Rational/ Source	Continuous (CONT) or Category (CAT)
		Variety		
Overall food group variety (meat/poultry/fish/eggs; dairy/beans; grain; fruit; vegetable)[1]	0-15	≥ 0.5 serving from each food group/d =15 Any 1 food group missing/d = 12 Any 2 food groups missing/d= 9 Any 3 food groups missing/d=6 ≥ 4 food groups missing/d=3	Change the food groups to include beans and diary as 1 food group	CAT
Within food group variety (meat, poultry, fish, dairy, beans, eggs)[1]	0-5	≥ 3 different sources/d =5 2 different sources/d =3 1 source/d =1 None=0	**Food listed** is separate food items except: Meat= beef, lamb, pork (NOT bacon) Dairy= milk, yogurt and cheese	CAT
		Adequacy		
F/V[2,3]	0-10	= scores from HEI-C (F/V)/2	Based on ANGCY	
Grain[2]	0-5	= scores from HEI-C (grains)/2	Based on ANGCY	
Fibre	0-5	Meet the RDA , 100% RDA=5 50-100% RDA=2.5 <50% RDA =0	-	CAT
Protein ≥ 10% of energy	0-5	≥ 10% = 5 <10-5% =3 <5% =0	Based on the DRI	CAT
Iron	0-5	Meet the RDA , 100% RDA=5 50-100% RDA=2.5 <50% RDA =0	-	CAT
Calcium	0-5	Meet the RDA , 100% RDA=5 50-100% RDA=2.5 <50% RDA =0	-	CAT
Vitamin C	0-5	Meet the RDA, 100% RDA=5 50-100% RDA=2.5 <50% RDA =0	-	CAT
		Moderation		

Total Fat[4,5]	0-6	≥ 40% =0 >30%- <40%= 3 ≤ 30% =6	Based on the recommendations from Health Canada	CAT
Saturated fat[5]	0-6	≥ 10% =0 >7%- <10%= 3 ≤ 7% =6	Based on the DRI*#	CAT
Cholesterol[5]	0-6	≤ 300=6 300-400 =3 ≥ 400=0	Based on the DRI*	CAT
Sodium[6] 2400 to ≤3400mg	0-6	≤ AI=6 AI-UL=3 ≥ UL=0	-	CAT
Empty Calories[7] ≤ 3% of kcal=6 >3 to 10% of kcal =3 > 10% of kcal =0	0-6	= HEI-C "Other"/10*6 ≤ min recommendations=6 within the max and min =3 > the recommendation=0	≤1600Kcal= ≤4 to >8 servings 1600-2200Kcal= ≤6 to >11 servings ≥ 2200Kcal= ≤8 to >14 servings	CAT
Overall Balance				
Macronutrient ratio (carbohydrate:protein:fat)	0-6	55-65:10-15:15-25 =6 52-68:9-16:13-27 =4 50-70:8-17:12-30= 2 Otherwise=0	If % fat>30% give 0	CAT
Fatty acid ratio (PUFA:MUFA:SFA)	0-4	P/S 1-1.5 and M/S 1-1.5=4 Else if P/S 0.8 -1.7 and M/S 0.8- 1.7=2 Otherwise =0	Calculated as PUFA (g)/ SFA (g) or PUFA(%)/ PUFA (g) If any of the proportion <0.8give 0	CAT

[1]The original paper (Not Adapted) reported max score for ≥ 1 serving from each food group/day (16).
[2]The original paper (Not Adapted) used the recommended servings of food groups based on the Australian recommendations (16).
[3] F/V were in two different food groups in the original tool (Not Adapted) (16). We grouped F/V in one food group based on the ANGCY.
[4]The original paper (Not Adapted) cut-off for total fat was 20-30% (16).
[5] Dietary Reference Intakes for Energy, Carbohydrate, Fibre, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids (2002); Interim Summary of Conclusions (220). Dietary Recommendations on Total Fat & Fatty Acids From the Joint FAO/WHO Expert Consultation on Fats and Fatty Acids in Human Nutrition, 10-14. November, 2008, WHO, Geneva (227). Garriguet, D. Diet quality in Canada. Health Reports, 2009 Sep;20(3):41-52 (333).
[6]The original paper (Not Adapted) cut-off for SFA was 2400-3400 (16).
[7]Then original paper (Not Adapted) used the 3-10% of "empty group" or "other group" as the cut-off point (16).
Abbreviations: ANGCY, Alberta Nutrition Guideline for Children and Youth; F/V, Fruits and Vegetables. MUFA, Monounsaturated Fatty Acids; PUFA, Polyunsaturated Fatty Acids; SFA, Saturated Fatty Acids.

Appendix B : The Agreement Analysis between the Adapted and Not Adapted Diet Quality Tools

A



B

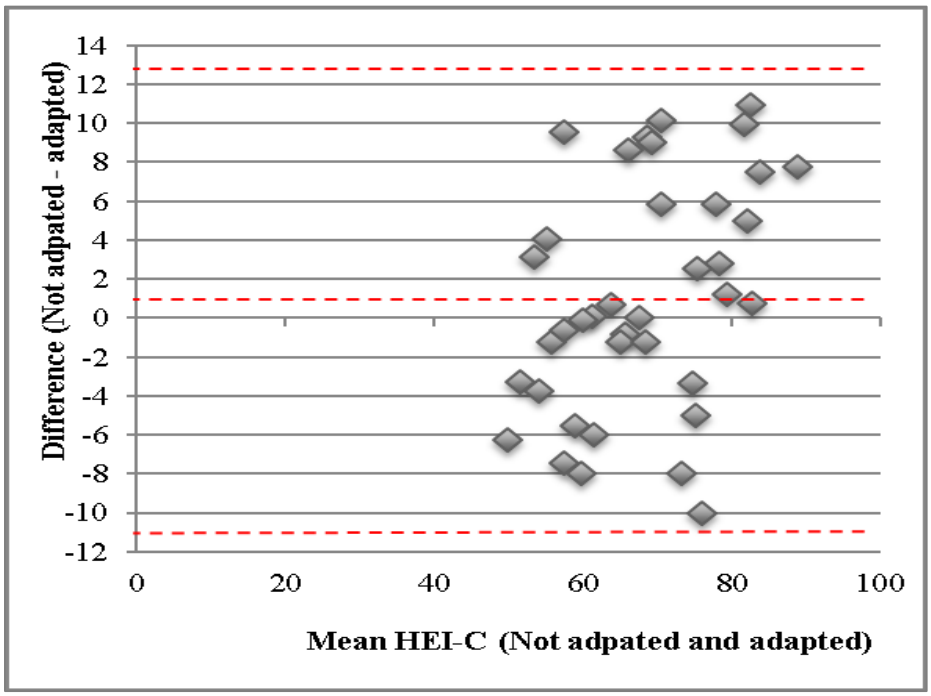
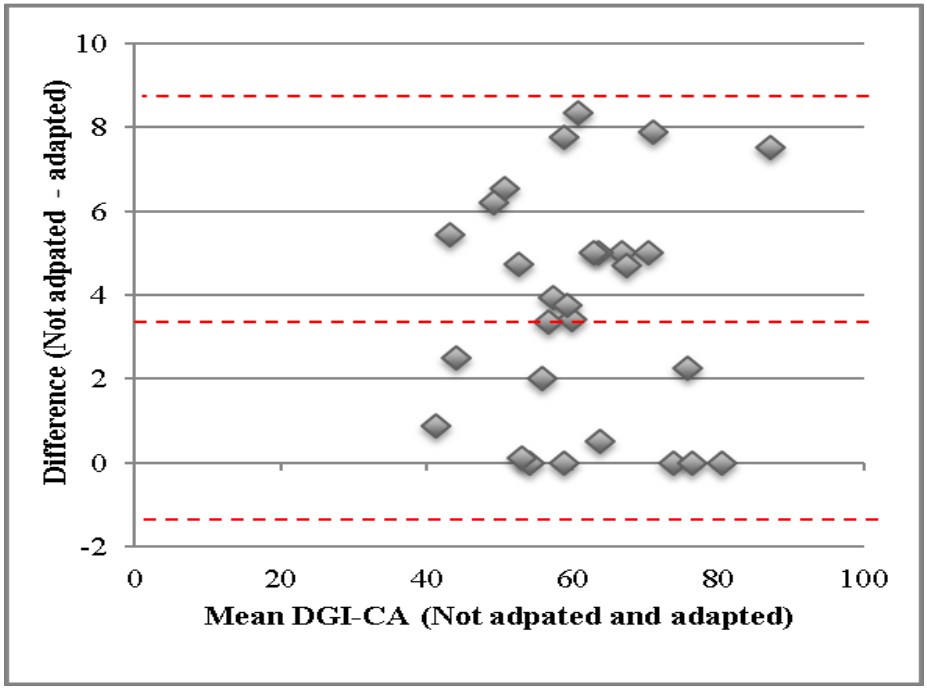


Figure B–1: Bland Altman Analysis between Adapted and Not Adapted Healthy Earing Index-Canada in children with Celiac Disease (n=27) (A) and Disease Controls (n=37) (B) (35). The adaptation of Healthy Earing Index-Canada (HEI-C) is described in **Appendix A, Table A-1.**

A



B

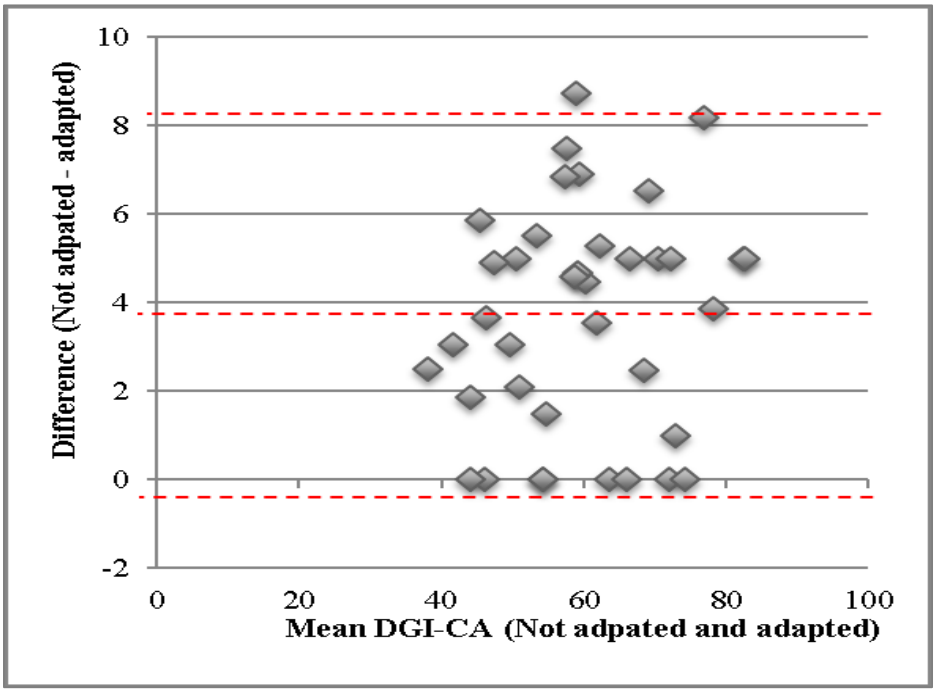
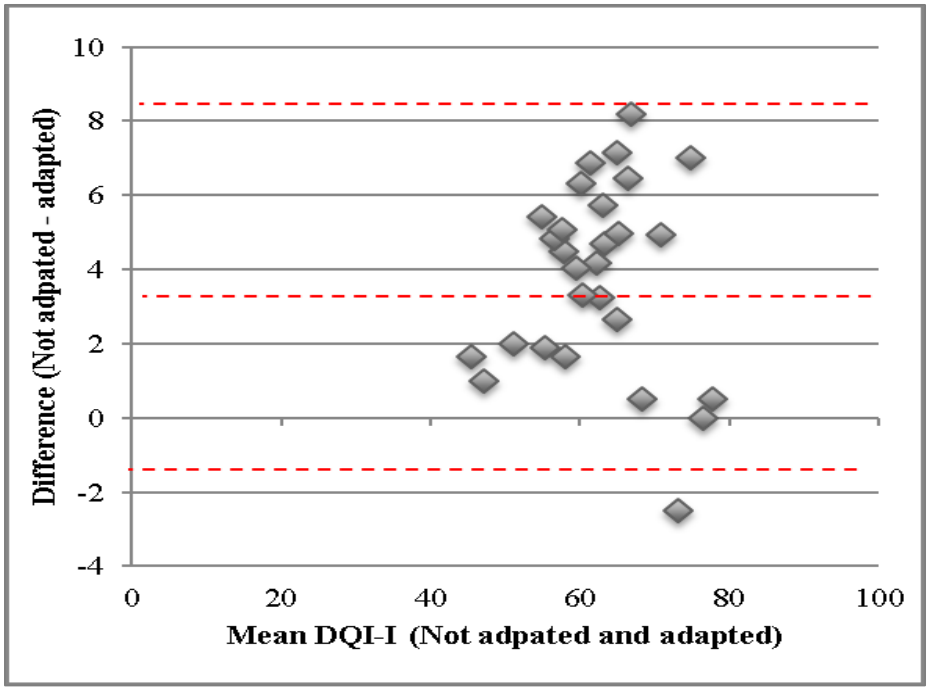


Figure B–2: Bland Altman Analysis between Adapted and Not Adapted Dietary Guideline Index for Children and Adolescents in Children with Celiac Disease (n=27) (A) and Disease Controls (n=37) (B) (31). The adaptation of Dietary Guideline Index for Children and Adolescents (DGI-CA) is described in **Appendix A, Table A-2**.

A



B

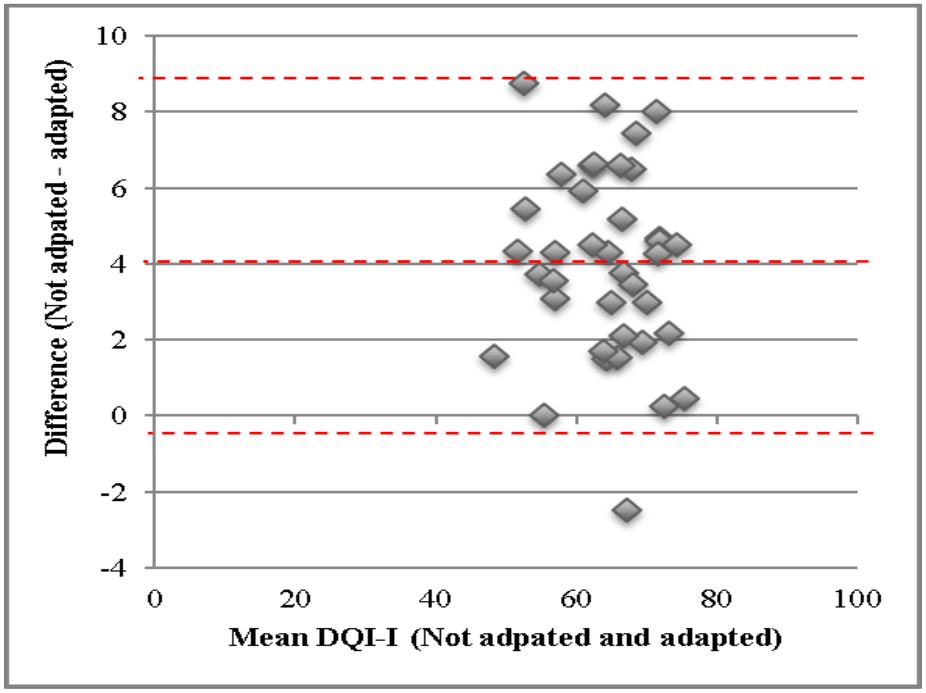


Figure B–3: Bland Altman Analysis between Adapted and Not Adapted Diet Quality Index-International in Children with Celiac Disease (n=27) (A) and Disease Controls (n=37) (B) (16). The adaptation of Diet Quality Index-International (DQI-I) is described in **Appendix A, Table A-3**.

Table B-1: Correlational Consistency Between the Adapted vs Not Adapted Diet Quality Tools in Children with Celiac Disease and Disease Controls

	CD		CON	
	ICC	**p-value**	**ICC**	**p-value**
HEI-C	0.901	<0.01	0.858	<0.01
DGI-CA	0.925	<0.01	0.933	<0.01
DQI-I	0.858	<0.01	0.804	<0.01

Two-way mixed model (absolute agreement, single measure) used SPSS 17:0. ICC ≤ 0.40 refers to poor to fair agreement, 0.41– 0.60 refers moderate agreement, 0.61–0.80 refers to good agreement and >0.8-1.0 refers to perfect agreement (230, 237, 241).
Abbreviations: CD, Celiac Disease; CON, disease control; ICC, Intra Class Correlations.

Table B-2: Correlational Consistency Between the Diet Quality Tools in Children with Celiac Disease and Disease Controls

	CD		CON	
	ICC	**p-value**	**ICC**	**p-value**
HEI-C and DGI-CA	0.814	<0.01	0.781	<0.01
DGI-CA and DQI-I	0.809	<0.01	0.578	<0.01
HEI-C and DQI-I	0.773	<0.01	0.685	<0.01

Two-way mixed model (absolute agreement, single measure) used SPSS 17:0. ICC ≤ 0.40 refers to poor to fair agreement, 0.41– 0.60 refers moderate agreement, 0.61–0.80 refers to good agreement and >0.8-1.0 refers to perfect agreement (230, 237, 241).
Abbreviations: ICC, Intra Class Correlations; LTX, liver transplant.

Appendix C : Dietary Intake Data in Children with Celiac Disease and Disease Control Children

Table C-1: Comparison in Micro and Macronutrients, Glycemic Index, Glycemic Load, Food Groups and Diet Quality Scores between Acceptable, Under- and Over-Reporting in Children with Celiac Disease and Disease Controls

	Acceptable reporting (n=19) [1]			Under-reporting (n=24) [1]			Over-reporting (n=19) [1]			p-value
	Median	IQ	Mean±SD	Median	IQ	Mean±SD	Median	IQ	Mean±SD	
Protein (g)	61	(45-87)	66±24	60	(46-67)	60±19	69	(56-78)	68±15	0.38
% Protein	16.7	(13.0-18.2)	16.5±3.7	15.6	(13.5-19.9)	16.9±4.3	14.8	(12.0-18.2)	15.3±3.3	0.57
Carbohydrate (g)	206	(160-255)	211±50[ab]	182	(153-214)	186±43 [a]	234	(198-274)	242±53 [b]	<0.01
% Carbohydrate	52.9	(48.6-58.6)	53.8±9.1	52.3	(48.1-57.1)	52.5±6.2	50.6	(48.9-59.6)	53.6±6.6	0.82
Total Sugar (g)	79	(65-115)	87±29	86	(53-105)	82±28	100	(82-123)	103±33	0.12
Fibre (g)	13.2	(10.4-17.3)	13.6±4.4	12.1	(8.5-16.9)	14.0±9.2	15.8	(13.8-19.1)	16.9±4.6	0.26
Fat (g)	62	(39-73)	54±20	50	(39-58)	51±17	63	(51-81)	66±18	0.03
% Fat	31.0	(28.3-34.1)	30.4±7.5	30.9	(28.4-34.7)	31.9±4.9	33.2	(28.0-36.4)	32.7±4.9	0.59
SFA (g)	19.4	(12.8-26.6)	21.2±9.6	18.4	(14.8-20.3)	18.7±7.4	21.9	(14.9-28.8)	24.0±10.0	0.23
% SFA	11.4	(9.7-14.3)	11.7±3.6	11.5	(9.8-13.2)	11.6±2.9	11.0	(8.7-15.5)	11.9±4.1	0.96
Trans Fat (g)	0.29	(0.16-0.68)[a]	0.37±0.27	0.53	(0.27-0.68)[ab]	0.52±0.33	0.97	(0.36-1.69) [b]	1.16±1.06	0.01
Cholesterol (mg)	167	(114-229)	185±109	170	(113-272)	204±101	189	(130-236)	211±110	0.67
PUFA (g)	5.8	(3.0-8.6)	6.6±4.9	6.73	(4.6-9.8)	7.2±3.2	8.6	(5.4-16.4)	10.8±5.8	0.04
% PUFA	3.2	(1.8-5.3)	3.8±3.1	4.2	(3.0-5.8)	4.3±2.0	5.0	(3.0-6.8)	5.3±2.5	0.05
MUFA (g)	14.6	(9.2-23.5)	16.5±8.4	14.0	(11.3-21.6)	16.6±7.0	20.4	(16.1-24.2)	20.9±5.5	0.09
% MUFA	8.9	(5.8-10.9)	9.1±3.8	9.8	(8.0-12.3)	10.1±3.2	10.5	(8.8-11.4)	10.4±2.0	0.37
Vitamin A (RAE)	394	(192-730)	515±337	397	(312-598)	460±240	614	(404-803)	626±298	0.23
Vitamin B1 (mg)	1.31	(0.71-1.52)	1.17±0.49	0.89	(0.74-1.2)	0.97±0.37	1.45	(0.77-1.66)	1.31±0.52	0.07
Vitamin B2 (mg)	1.57	(1.21-1.98)	1.58±0.48	1.26	(1.00-1.61)	1.33±0.42	1.81	(1.2-2.07)	1.70±0.43	0.03
Vitamin B12 (mg)	3.89	(2.05-4.99)	3.74±0.48	3.27	(2.14-4.21)	3.87±3.27	3.59	(2.57-4.39)	3.46±1.21	0.80
Vitamin C (mg)	89	(60-137)	109±68	88	(62-127)	103±66	85	(52-150)	103±64	0.86
Vitamin D (IU)	112	(55-210)	139±103	112	(85-152)	124±64	195	(105-224)	181±99	0.16
Folate-DFE (mg)	227	(105-397)	246±167	169	(134-222)	205±114	244	(167-315)	253±112	0.26
Calcium (mg)	795	(569-1247	914±362	678	(450-867)	717±313	1029	(833-1254)	1070±357	<0.01
Copper (mg)	0.75	(0.68-1.11)	0.81±0.33	0.715	(0.51-1.05)	0.82±0.41	0.94	(0.77-1.16)	1.02±0.37	0.11
Iron (mg)	10.3	(8.5-12.1)	10.2±2.5	8.7	(7.4-10.9)	9.2±2.9	11.6	(9.6-15.0)	12.1±3.7	0.02
Selenium (mg)	61	(34-99)	63±35	57	(40-70)	58±26	72	(44-98)	75±32	0.20
Sodium (mg)	1926	(1383-2564)	1881±729	1486	(1215-2289)	1793±713	2065	(1564-2976)	2414±1214	0.17
Zinc (mg)	8	(6.1-11.1)	9.0±4.1	8.2	(5.8-9.3)	8.0±2.5	7.8	(6.51-11.13)	8.9±3.5	0.85
Grains	5.5	(3.6-6.6)	5.2±1.9 [ab]	3.9	(2.8-4.6)	3.9±1.4 [a]	5.4	(4.8-6.9)	5.7±1.9 [b]	<0.01
Milk	2.4	(1.7-2.8)	2.4±1.0	1.5	(0.9-2.4)	1.7±1.1	2.6	(1.9-3.4)	2.7±1.2	0.02

Meat	1.4	(0.9-2.3)	2.0±1.6	2.0	(1.4-2.5)	2.1±1.2	1.5	(1.2-2.3)	1.6±0.9	0.32
F/V	4	(2-5)	3.9±2.0	3.8	(2.0-5.8)	4.1±2.3	4.5	(2.7-2.3)	4.7±2.6	0.53
HEI-C	68	(64-77)	69±10 [ab]	62	(53-68)	61±10 [b]	69	(63-77)	70±89 [a]	0.01
DGI-CA	60	(54-67)	61±10	53	(43-65)	54±12	58	(54-72)	61±10	0.07
DQI-I	61	(57-68)	62±7	58	(51-64)	58±8	63	(60-70)	64±7	0.04
GI	53	(44-58)	53±8	50	(47-57)	51±6	53	(47-57)	53±6	0.70
GL	105	(86-134)	107±32	94	(83-109)	97±22	125	(93-143)	124±41	0.03
Gluten (mg)	3612	(3-11756)	5664±6361	2169	(3-7448)	3732±4281	6340	(3-14073)	6931±6975	0.13

[1] Under-reporting (<95% of energy intake/ Basel Metabolic Rate) and over-reporting (>95% of energy intake/ Basel Metabolic Rate). Values with different Superscript are significant different. [2]p-values <0.05 are considered statistically significant.

Abbreviations: CD, Celiac Disease; CON, disease control; DFE, Dietary Folate Equivalent; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; F/V, F/V, Fruits and Vegetables; GI, Glycemic index; GL, Glycemic load; HEI-C, Healthy Eating Index-Canada; IQ, Interquartile Range; MUFA, Monounsaturated Fatty Acid; PUFA, Polyunsaturated Fatty Acid; RAE, Retinol Activity Equivalent; SD, Standard Deviation; SFA, Saturated Fatty Acid.

Table C-2: The 95% Confidence Interval and Coefficient of Variation in Children with Celiac Disease and Disease Controls

	CD (n=27)				CON (n=37)			
	CI	Mean+CI (>95% CI)	Mean-CI (<95% CI)	CV	CI	Mean+CI (>95% CI)	Mean-CI (<95% CI)	CV
Energy (kcal)	138.18	1808.32	1531.96	0.22	123.56	1640.54	1393.43	0.25
Protein (g)	8.19	74.60	58.23	0.33	6.07	68.42	56.28	0.30
% Protein	1.34	17.14	14.47	0.23	1.33	17.98	15.33	0.25
Carbohydrate (g)	17.81	236.65	201.03	0.22	18.63	221.71	184.45	0.28
% Carbohydrate	3.11	56.25	50.04	0.16	2.08	55.64	51.48	0.12
Total Sugar (g)	2.29	17.15	12.58	0.42	2.32	16.86	12.21	0.5
Fibre (g)	10.97	105.04	83.09	0.31	10.83	99.08	77.42	0.38
Fat (g)	8.22	68.58	52.14	0.37	5.18	58.26	47.89	0.30
% Fat	2.71	34.53	29.11	0.23	1.38	32.63	29.87	0.14
SFA (g)	3.7	26.08	18.68	0.45	2.75	22.40	16.90	0.43
% SFA	1.28	13.07	10.51	0.29	1.12	12.57	10.32	0.30
Trans Fat (g)	0.20	0.86	0.46	0.82	0.28	1.00	0.44	1.20
Cholesterol (mg)	44.2	271.23	182.8	0.53	27.52	202.52	147.49	0.49
PUFA (g)	2.04	8.93	4.86	0.8	1.32	10.21	7.58	0.46
% PUFA	0.83	4.29	2.63	0.65	0.79	6.02	4.44	0.47
MUFA (g)	2.91	19.81	13.98	0.47	2.26	20.79	16.27	0.38
% MUFA	1.14	9.93	7.65	0.35	0.89	11.59	9.81	0.26
Vitamin A (RAE)	127.53	687.66	432.6	0.61	76.42	578.28	425.43	0.47
Vitamin B1 (mg)	0.19	1.12	0.75	0.54	0.12	1.40	1.16	0.30
Vitamin B2 (mg)	0.17	1.68	1.34	0.3	0.15	1.67	1.36	0.32
Vitamin B3 (mg)	2.23	14.38	9.93	0.5	2.64	26.96	21.68	0.34
Vitamin B12 (mg)	1.12	5.45	3.21	0.7	0.44	3.59	2.70	0.44
Vitamin C (mg)	21.8	114.12	70.52	0.64	21.54	136.18	93.09	0.58
Vitamin D (IU)	35	196.03	126.02	0.59	27.42	158.53	103.68	0.64
Folate-DFE (mg)	25.97	175.71	123.77	0.47	42.59	336.78	251.59	0.45
Calcium (mg)	132.64	1038.57	773.28	0.4	121.56	966.64	723.53	0.45
Copper (mg)	1.29	10.95	8.38	0.36	0.99	11.92	9.93	0.28
Iron (mg)	17.81	236.65	201.03	0.22	18.63	221.71	184.45	0.28
Magnesium (mg)	29.53	212.50	153.45	0.44	23.20	252.58	206.18	0.31
Potassium (mg)	262.62	2319.70	1794.47	0.34	227.56	2315.38	1860.27	0.33
Selenium (mg)	10.51	60.74	39.73	0.56	9.30	84.19	65.59	0.39
Sodium (mg)	302.38	2184.45	1579.70	0.43	315.96	2394.23	1762.31	0.47

Zinc (mg)	1.16	9.42	7.09	0.38	1.21	10.06	7.64	0.43
EI/BMR	0.10	1.57	1.38	0.18	0.12	1.40	1.17	0.27
Grains	0.81	5.90	4.28	0.43	0.50	5.00	4.01	0.34
Milk	0.45	2.78	1.88	0.52	0.37	2.39	1.64	0.58
Meat	0.45	2.48	1.58	0.60	0.38	2.23	1.47	0.64
F/V	0.92	5.16	3.31	0.59	0.66	4.87	3.55	0.49
Gluten (mg)	0.54	3.50	2.41	0.49	1448.61	10941.34	8044.13	0.47
GI	2.76	57.40	51.87	0.14	1.66	52.11	48.80	0.10
GL	12.70	127.02	101.63	0.30	10.52	113.73	92.70	0.32
HEI-C	4.32	70.69	62.06	0.18	3.08	70.09	63.93	0.14
DGI-CA	4.22	63.70	55.27	0.19	3.79	61.53	53.94	0.20
DQI-I	3.03	63.47	57.42	0.14	2.30	64.19	59.59	0.12

Abbreviations: BMR, Basal Metabolic Rate; CD, Celiac Disease; CI, Confidence interval; CON, disease control; CV, Coefficient of variation; DFE, Dietary Folate Equivalent; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; EI, Energy Intake; F/V, Fruits and Vegetables; GI, Glycemic index; GL, Glycemic load; HEI-C, Healthy Eating Index-Canada; MUFA, Monounsaturated Fatty Acid; PUFA, Polyunsaturated Fatty Acid; RAE, Retinol Activity Equivalent; SFA, Saturated Fatty Acid.

Table C-3: Micronutrient Intake in Children with Celiac Disease and Disease Controls

	CD (n=28)					CON (n=37)				p-value[1]
	Median	Interquartile range		Mean	SD	Median	Interquartile range		Mean	SD	
Trans Fat (g)	0.58	0.33	0.72	0.66	0.54	0.43	0.20	0.93	0.72	0.862	0.65
Vitamin A (RAE)	507.	246	840	560	344	459	332	638	502	237	0.70
Vitamin B1 (mg)	0.75	0.61	1.27	0.94	0.51	1.29	0.99	1.57	1.28	0.38	<0.01
Vitamin B2 (mg)	1.48	1.18	1.86	1.51	0.46	1.47	1.10	2.01	1.5	0.48	0.93
Vitamin B12 (mg)	3.94	2.755	4.825	4.33	3.02	3.28	1.98	4.1	3.15	1.38	0.05
Vitamin C (mg)	81	58	129	92	59	101	72	150	115	67	0.18
Vitamin D (IU)	140	101	223	161	95	110	83	189	131	84	0.16
Folate-DFE (mg)	154	102.	190	150	70	288	199	397	294	132	<0.01
Calcium (mg)	906	601	1157	906	358	779	569	1029	845	377.	0.51
Copper (mg)	0.66	0.48	0.77	0.70	0.37	1.04	0.77	1.2	1.02	0.34	<0.01
Iron (mg)	8.8	7.4	11.1	9.7	3.45	11.0	8.9	12.6	10.9	3.1	0.13
Selenium (mg)	43.8	31.27	60.6	50.2	28.4	70.8	57.4	97.6	74.9	28.9	<0.01
Sodium (mg)	1825	1287	2298	1882	816	1943	1312	2564	2078	981	0.57
Zinc (mg)	7.82	5.97	9.60	8.26	3.14	8.07	6.50	10.88	8.85	3.76	0.61

[1]p-values <0.05 are considered statistically significant.

Abbreviations: CD, Celiac Disease; CON, disease control; DFE, Dietary Folate Equivalent; RAE, Retinol Activity Equivalent; SD, Standard Deviation.

Table C-4: The Association between Glycemic Index, Glycemic Load, and Diet Quality and Mother's Age in Celiac Disease and Disease Controls

	Mother's age <39 (n=31)[1]	Mother's age ≥39 (n=25)[1]	p-value[2]
	Mean ± Standard Deviation	Mean ± Standard Deviation	
GI	54 ± 6	51 ± 6	0.15
GL	105 ± 35	118 ± 22	0.11
HEI-C	65 ± 11	67 ± 10	0.58
DGI-CA	56 ± 12	60 ± 11	0.25
DQI-I	60 ± 7	62 ±8	0.55

[1]Data are presented as mean ± standard deviation.
[2] p-values <0.05 are considered significant difference.
Abbreviations: DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; GI, Glycemic index; GL, Glycemic load; HEI-C, Healthy Eating Index-Canada.

Table C-5: The Association between Glycemic Index, Glycemic Load, and Diet Quality and Father's Age in Children with Celiac Disease and Disease Controls

	Father's age <43 (n=30)[1]	Father's age ≥43 (n=24)[1]	p-value[2]
	Mean ± Standard Deviation	Mean ± Standard Deviation	
GI	53 ± 7	52 ± 6	0.49
GL	98 ± 27	127 ± 27	<0.01
HEI-C	65 ± 11	67 ± 9	0.47
DGI-CA	57 ± 12	58 ± 11	0.58
DQI-I	60 ± 8	62 ±7	0.55

[1]Data are presented as mean ± standard deviation.
[2]p-values <0.05 are considered significant difference.
Abbreviations: DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; GI, Glycemic index; GL, Glycemic load; HEI-C, Healthy Eating Index-Canada.

Table C-6: The Association between Glycemic Index, Glycemic Load, and Diet Quality and Mother's Education Level in Children with Celiac Disease and Disease Controls

	Mother's Education Level (College and University) (n=13)[1]	Mother's Education Level (High School and Registered Apprenticeship) (n=40)[1]	p-value[2]
	Mean ± Standard Deviation	Mean ± Standard Deviation	
GI	54 ± 5	52 ± 7	0.22
GL	99 ± 27	116 ± 31	0.05
HEI-C	65 ± 13	66 ± 9	0.60
DGI-CA	57 ± 14	58 ± 10	0.78
DQI-I	60 ± 9	61 ±7	0.67

[1]Data are presented as mean ± standard deviation.
[2]p-values <0.05 are considered significant difference.
Abbreviations: DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; GI, Glycemic index; GL, Glycemic load; HEI-C, Healthy Eating Index-Canada.

Table C-7: The Association between Glycemic Index, Glycemic Load, and Diet Quality and Father's Education Level in Children with Celiac Disease and Disease Controls

	Father's Education Level (College and University) (n=18)[1]	Father's Education Level (High School and Registered Apprenticeship) (n=37)[1]	p-value[2]
	Mean ± Standard Deviation	Mean ± Standard Deviation	
GI	50 ± 4	54 ± 7	0.07
GL	103 ± 24	114 ± 33	0.31
HEI-C	68 ± 10	65 ± 11	0.46
DGI-CA	59 ± 14	57 ± 11	0.68
DQI-I	63 ± 7	60 ±8	0.29

[1]Data are presented as mean ± standard deviation.
[2]p-values <0.05 are considered significant difference.
Abbreviations: DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; GI, Glycemic index; GL, Glycemic load; HEI-C, Healthy Eating Index-Canada.

Table C-8: The Association between Glycemic Index, Glycemic Load, and Diet Quality and Income in Children with Celiac Disease and Disease Controls

	Income <81,836 (n=31)[1]	Income ≥81,836 (n=25)[1]	p-value[2]
	Mean ± Standard Deviation	Mean ± Standard Deviation	
GI	54 ± 6	51 ± 6	0.03
GL	112 ± 34	99 ± 31	0.15
HEI-C	66 ± 10	68 ± 11	0.61
DGI-CA	57 ± 10	61 ± 13	0.25
DQI-I	61 ± 7	61 ±8	0.97

[1]Data are presented as mean ± standard deviation.
[2]p-values <0.05 are considered significant difference.
Abbreviations: DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; GI, Glycemic index; GL, Glycemic load; HEI-C, Healthy Eating Index-Canada.

Appendix D : Assessment of Agreement in Peds QL™ 4.0 Generic Core Scales between Self-Reported Peds QL and Parent Proxy Reported

Table D-1: Agreement (in Median Score) between Self-reported Peds QL and Parent Proxy PedsQL™ 4.0 Generic Core Scales in Children with Celiac Disease and Disease Controls

	CD Median (IQ)	p-value[1]	CON Median (IQ)	p-value [1]
Average[2]		0.24		0.20
Self Report	87 (75-91)		74 (67-80)	
Parent Proxy	85 (71-88)		79 (67-89)	
Physical		0.31		0.57
Self Report	94 (84-100)		84 (75-94)	
Parent Proxy	90 (81-97)		84 (75-94)	
Psychosocial[3]		0.41		0.22
Self Report	83 (69-88)		70 (65-78)	
Parent Proxy	80 (63- 88)		77 (63-87)	
Emotional		0.35		0.74
Self Report	75 (60-90)		65 (55-80)	
Parent Proxy	70 (60-85)		68 (55-80)	
Social		0.32		0.58
Self Report	95 (80-100)		90 (70-100)	
Parent Proxy	90 (75-100)		90 (75-100)	
School		0.80		0.17
Self Report	78 (63-85)		60 (50-75)	
Parent Proxy	73 (55-90)		73 (55-83)	

[1]Wilcoxon signed rank was preformed between self-report and parent proxy report. p-values <0.05 are considered statistically significant.
[2]Average values were computed as the average of 4 domains (physical, emotional, social and school function).
[3]Psychosocial values were computed as the average of 3 domains (emotional, social and school function).
Abbreviations: CD, Celiac Disease; CON, disease control, IQ, Interquartile Range.

Appendix E : The Post Hoc Power Test

Table E-1: The Post Hoc Power Test of Glycemic Index, Glycemic Load, Diet Quality Scores, Gastroenterology Symptoms Score, and PedsQL™ 4.0 Generic Core Scales between Children With Celiac Disease and Disease Controls

	Power (%)
Ethnicity[1]	10
Dietry Intake (CD=28 and CON=37)	
Glycemic Index	72
Glycemic Load	26
Healthy Eating Index-Canada (HEI-C)	5
Dietary Guideline Index for Children and Adolescents (DGI-CA)	9
Diet Quality Index-International (DQI-I)	12
PedsQL ™ Gastrointestinal Symptom Scale(CD=27 and CON=42)	100
PedsQL™ 4.0 Generic Core Scales	
PedsQL™ V4.0 (CD=28 and CON=35)	
Average[2]	82
Physical	90
Psychological[3]	64
Emotional	48
Social	28
School	46
Parent Proxy (CD=26 and CON=38)	
Average[2]	42
Physical	5
Psychological[3]	3
Emotional	3
Social	8
School	10

[1]Post hoc power test was conducted to detect an average value of 1.5 SD differences in Healthy Eating Index-Canada.
[2]Average values were computed as the average of 4 domains (physical, emotional, social and school function).
[3]Psychological values were computed as the average of 3 domains (emotional, social and school function).
Abbreviations: CD, Celiac Disease; CON, Disease Control.

Appendix F : Gastroenterology Symptoms Score

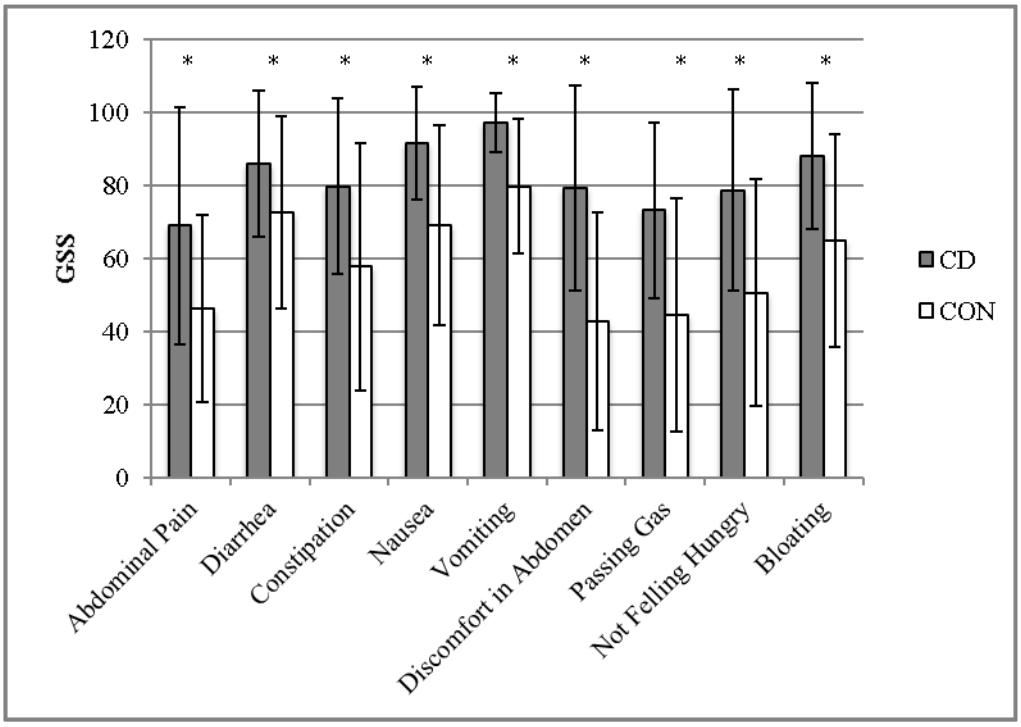


Figure F–1: Gastroenterology Symptoms Score of Each Gastrointestinal Symptomology in Children with Celiac Disease (n=27) and Disease Controls (n=42).
Data are presented as mean ± standard deviation. Asterix (*) represents as significant difference between children with CD and CON ($p<0.01$).
Abbreviations: CD, Celiac Disease; CON, disease control; GSS, Gastroenterology Symptoms score.

Appendix G : The Interrelationship between Peds QLTM 4.0 Generic Core Scales, Parent Proxy Reported Child and Gastroenterology Symptoms Score and Gastroenterology Symptoms Score and Demographic Variables

Table G-1: The Association between *PedsQL™ 4.0 Generic Core Scales* and Gastrointestinal Symptoms Scale and Mother's Age in Children with Celiac Disease and Disease Controls

	Mother's age <43 year					Mother's age ≥43 year					p-value[1]
	Median	Lower Interquartile	Upper Interquartile	Mean	Standard Deviation	Median	Lower Interquartile	Upper Interquartile	Mean	Standard Deviation	
Child Report (n=27 vs n=26)											
Average[2]	76	89	68	79	13	80	89	72	79	11	0.90
Physical	88	94	81	86	14	88	94	79	86	11	0.83
Psychosocial[3]	73	87	67	75	15	75	83	68	76	11	0.91
Emotional	75	90	55	74	20	73	80	60	70	14	0.43
Social	90	100	70	85	14	93	100	80	88	15	0.39
School	70	80	50	67	19	68	80	60	70	15	0.59
Parent Proxy report (n=28 vs n=25)											
Average[2]	83	88	67	76	18	79	88	70	79	12	0.83
Physical	86	94	75	80	21	84	97	81	88	9	0.29
Psychosocial[3]	80	87	65	74	19	75	87	63	74	15	0.74
Emotional	70	80	60	67	23	65	80	60	69	16	0.60
Social	95	100	75	86	19	85	100	75	85	16	0.61
School	70	85	58	68	22	70	85	55	69	20	0.94
GSS (n=32 vs n=26)											
GSS[4]	63	89	51	67	21	69	86	58	71	18	0.44

[1]p-values <0.05 are considered statistically significant.
[2]Average values were computed as the average of 4 domains (physical, emotional, social and school function).
[3] Psychosocial values were computed as the average of 3 domains (emotional, social and school function).
[4]GSS: the average score of 9 GS symptomologies: abdominal pain, diarrhea, nausea, vomiting, discomfort in abdomen or stomach, passing gas, not feeling hungry and bloating.
Abbreviations: CD, Celiac Disease; CON, disease control; GSS, Gastroenterology Symptoms Score.

Table G-2: The Association between *PedsQL™ 4.0 Generic Core Scales* and Gastrointestinal Symptoms Scale and Father's Age in Children with Celiac Disease and Disease Controls

	Father's age <43 year					Father's age ≥43 year					p-value[1]
	Median	Lower Interquartile	Upper Interquartile	Mean	Standard Deviation	Median	Lower Interquartile	Upper Interquartile	Mean	Standard Deviation	
Child Report (n=28 vs n=25)											
Average[2]	77	89	70	79	12	77	87	72	79	11	0.88
Physical	89	94	81	87	13	84	94	75	85	11	0.37
Psychosocial[3]	74	88	67	76	14	73	83	68	76	12	0.94
Emotional	75	90	60	73	18	75	80	60	72	16	0.91
Social	90	100	78	86	14	90	100	80	87	15	0.69
School	70	80	55	67.5	18	65	80	60	68	15	0.92
Parent Proxy report (n=31 vs n=24)											
Average[2]	85	89	71	78	17	75	86	68	76	13	0.41
Physical	84	94	78	83	17	84	98	75	84	17	0.73
Psychosocial[3]	80	92	65	75	19	71	82	63	72	15	0.21
Emotional	70	85	60	67	23	68	78	60	69	15	0.84
Social	95	100	75	87	18	85	100	65	81	17	0.15
School	75	85	60	70	22	65	83	55	66	19	0.36
GSS (n=33 vs n=25)											
GSS[4]	65	89	50	69	21	64	86	53	69	19	0.91

[1]p-values <0.05 are considered statistically significant.
[2]Average values were computed as the average of 4 domains (physical, emotional, social and school function).
[3]Psychosocial values were computed as the average of 3 domains (emotional, social and school function).
[4]GSS: the average score of 9 GS symptomologies: abdominal pain, diarrhea, nausea, vomiting, discomfort in abdomen or stomach, passing gas, not feeling hungry and bloating.
Abbreviations: CD, Celiac Disease; CON, disease control; GSS, Gastroenterology Symptoms Score.

Table G-3: The Association between *PedsQL™ 4.0 Generic Core Scales* and Gastrointestinal Symptoms Scale and Moher's Education Level in Children with Celiac Disease and Disease Controls

	Mother's Education Level (College and University)					Mother's Education Level (High School and Registered Apprenticeship)					p-value[1]
	Median	Lower Interquartile	Upper Interquartile	Mean	Standard Deviation	Median	Lower Interquartile	Upper Interquartile	Mean	Standard Deviation	
Child Report (n=18 vs n=36)											
Average[2]	75	83	68	78	12	82	89	72	80	11	0.50
Physical	83	91	75	82	12	92	94	81	87	12	0.09
Psychosocial[3]	71	77	68	75	13	79	87	67	76	13	0.83
Emotional	75	80	60	73	18	75	85	60	72	17	1.00
Social	90	95	80	86	13	90	100	73	87	15	0.45
School	65	80	50	67	20	70	80	60	69	16	0.66
Parent Proxy Report (n=18 vs n=36)											
Average[2]	74	88	67	75	17	84	88	71	78	15	0.49
Physical	73	912	63	72	20	78	87	63	75	16	0.29
Psychosocial[3]	84	97	75	82	14	91	94	81	84	18	0.62
Emotional	68	85	55	69	22	70	80	60	68	20	0.85
Social	85	100	65	82	20	95	100	75	86	17	0.50
School	68	80	55	65	23	73	88	55	70	20	0.43
GSS (n=20 vs n=39)											
GSS[4]	61	90	52	69	21	67	86	53	69	19	0.94

[1]p-values <0.05 are considered statistically significant.
[2]Average values were computed as the average of 4 domains (physical, emotional, social and school function).
[3]Psychosocial values were computed as the average of 3 domains (emotional, social and school function).
[4]GSS: the average score of 9 GS symptomologies: abdominal pain, diarrhea, nausea, vomiting, discomfort in abdomen or stomach, passing gas, not feeling hungry and bloating.
Abbreviations: CD, Celiac Disease; CON, disease control; GSS, Gastroenterology Symptoms Score.

Table G-4: The Association between *PedsQL™ 4.0 Generic Core Scales* and and Gastrointestinal Symptoms Scale Faher's

Education Level in Children with Celiac Disease and Disease Controls

	Father's Education Level (College and University)					Father's Education Level (High School and Registered Apprenticeship)					p-value[1]
	Median	Lower Interquartile	Upper Interquartile	Mean	Standard Deviation	Median	Lower Interquartile	Upper Interquartile	Mean	Standard Deviation	
Child Report (n=14 vs n=37)											
Average[2]	74	87	71	77	13	78	89	74	81	10	0.33
Physical	81	94	75	81	14	91	94	81	88	10	0.08
Psychosocial[3]	71	90	67	75	14	75	87	70	77	12	0.64
Emotional	75	90	60	73	18	75	80	60	23	17	1
Social	90	100	90	89	12	90	100	80	87	15	0.93
School	65	75	50	64	19	70	80	60	71	15	0.18
Parent Proxy report (n=15 vs n=38)											
Average[2]	78	88	67	76	16	84	88	71	78	15	0.51
Physical	84	94	75	83	14	88	97	78	85	17	0.38
Psychosocial[3]	72	85	63	72	18	79	87	65	75	17	0.51
Emotional	70	80	50	67	22	70	80	60	69	20	0.51
Social	90	100	75	86	17	93	100	70	84	19	0.79
School	70	75	45	62	20	75	90	60	72	20	0.17
GSS (n=15 vs n=51)											
GSS[4]	58	81	50	63	19	72	89	56	72	20	0.14

[1]p-values <0.05 are considered statistically significant.
[2]Average values were computed as the average of 4 domains (physical, emotional, social and school function).
[3]Psychosocial values were computed as the average of 3 domains (emotional, social and school function).
[4]GSS: the average score of 9 GS symptomologies: abdominal pain, diarrhea, nausea, vomiting, discomfort in abdomen or stomach, passing gas, not feeling hungry and bloating.
Abbreviations: CD, Celiac Disease; CON, disease control; GSS, Gastroenterology Symptoms Score.

Table G-5: The Interrelationship between Demographic variables and Gastrointestinal Symptomology Score and Quality of Life Score (PedsQL™ 4.0 Generic Core Scales and Celiac Disease Specific Quality of Life) in Children with Celiac Disease and Disease Controls

Dependent variable	Independent*	p-value independent #	R^2	P-value model#
	Peds QL (Child Report)			
Psychosocial	GSS	0.05	0.13	0.04
	Gender	0.46		
	GSS* Gender	0.05		
Psychosocial	GSS	<0.01	0.3	<0.01
	Age	0.45		
	GSS*Age	0.10		
Psychosocial	GSS	0.05	0.13	0.04
	Gender	0.46		
	GSS* Gender	0.05		
School	GSS	<0.01	0.28	<0.01
	Age	0.06		
Psychosocial	GSS	<0.01	0.31	<0.01
	Gender	0.06		
Log Emotional	Gender	0.01	0.2	<0.01
	Age	0.14		
	Age * Gender	<0.01		
Log Emotional	Age	0.63	0.19	0.01
	GSS	<0.01		
	GSS* age	0.02		
	Parent Proxy Report			
Log School	Gender	0.09	0.16	0.02
	GSS	0.02		
	GSS* Gender	0.64		
Log Average	Age	0.04	0.22	<0.01
	GSS	0.01		
	GSS* Age	0.12		
Log School	Age	<0.01	0.29	<0.01
	GSS	0.02		
	GSS* Age	0.16		
Log Psychosocial	Age	0.01	0.24	<0.01
	GSS	0.01		
	GSS* Age	0.19		
CDDUX-diet	GSS	0.05	0.39	0.01
	Gender	0.42		
	GSS*Gender	0.09		

*All independent variables are category variables: GSS above and below the median (≥ and < 64) and age above and below the median (≥ and < 9 years).
#p-value<0.05 are considered statistically significant.
Abbreviations: GSS, Gastroenterology Symptoms Score.

Table G-6: The Interrelationship between Glycemic Index, Glycemic Load and Diet Quality

Scores and Gastroenterology Symptoms Score Scores (Above and Below the Median Value) in Children with Celiac Disease and Disease Controls

	Lower GSS (GSS<64, n=32) [1]	Higher GSS (GSS≥64, n=29)[1]	p-value[2]
GI	51 ± 5	54 ± 8	0.05
GL	107 ± 35	110 ± 34	0.72
HEI-C	67 ± 10	66 ± 11	0.83
DGI-CA	58 ± 13	58 ± 11	0.95
DQI-I	62 ± 8	61 ± 8	0.66

[1]Data are presented as mean ± standard deviation.
[2]p-values <0.05 are considered statistically significant.
Abbreviations: CD, Celiac Disease; CON, disease control; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQ, Diet quality; DQI-I, Diet Quality Index-International; GI, Glycemic Index; GL, Glycemic Load; HEI-C, Healthy Eating Index-Canada.

Table G-7: The Interrelationship between Demographic and Gastroenterology Symptoms Score and Glycemic Index, Glycemic Load and Diet Quality Scores in Children with Celiac Disease and Disease Controls

Dependent variable	Independent*	p-value independent #	R^2	p-value model#
DQI-I	GSS	0.40	0.16	0.02
	Age	0.05		
	GSS *Age	0.01		
DGI-CA	GSS	0.67	0.22	<0.01
	Age	0.07		
	GSS*Age	<0.01		
HEI-C	GSS	0.48	0.16	0.03
	Age	0.01		
DGI-CA	Gender	0.27	0.15	0.02
	Age	0.01		
	Age * Gender	0.03		

*All independent variables are category variables: GSS above and below the median (≥ and < 64) and age above and below the median (≥ and < 9 years).
#p-value<0.05 are considered statistically significant.
Abbreviations: DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; GSS, Gastroenterology Symptoms Score; HEI-C, Healthy Eating Index-Canada.

Table G-8: The Interrelationship between Diet Quality Scores and Gastroenterology Symptoms Score and Quality of Life in Children with Celiac Disease and Disease Controls

Dependent variable	Independent*	p-value independent #	R^2	P-value model#
		Peds QL (Child Report)		
Average	HEI-C	0.07	0.29	<0.01
	GSS	<0.01		
		Parent Proxy Report		
Log Psychosocial	HEI-C	0.01	0.26	<0.01
	GSS	0.01		
	GSS *HEI-C	0.08		
Log School	HEI-C	<0.01	0.36	<0.01
	GSS	0.01		
	GSS *HEI-C	0.05		
Log Average	HEI-C	0.02	0.24	<0.01
	GSS	0.02		
	GSS *HEI-C	0.05		
Log Emotional	DQI-I	0.047	0.15	0.04
	GSS	0.02		
	GSS *DQI-I	0.28		
Log Psychosocial	DQI-I	0.03	0.24	<0.01
	GSS	<0.01		
	GSS *DQI-I	0.03		
Log School	DQI-I	0.02	0.26	<0.01
	GSS	<0.01		
	GSS *DQI-I	0.03		
Log Average	DQI-I	0.04	0.24	<0.01
	GSS	<0.01		
	GSS *DQI-I	0.02		
Log School	DGI-CA	0.03	0.18	0.01
	GSS	0.02		
		CDDUX		
Average	DGI-CA	0.02	0.41	0.01
	GSS	<0.01		
	GSS * DGI-CA	0.08		
Having CD	DGI-CA	0.09	0.30	0.04
	GSS	0.14		
	GSS * DGI-CA	0.01		

*All independent variables are category variables: GSS above and below the median (≥ and < 64) ; HEI-C above and below the median (≥ and < 66); DGI-C above and below the cut-off for poor DQ (≥ and < 55); and DQI-I above and below the cut-off for poor DQ (≥ and < 60).

#p-value<0.05 are considered statistically significant.

Abbreviations: DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; GSS, Gastroenterology Symptoms Score; HEI-C, Healthy Eating Index-Canada.

Table G-9: The Association between Abdominal Pain Score from Gastrointestinal Symptoms Scale and *PedsQL™ 4.0 Generic Core Scales* in in Children with Celiac Disease and Disease Controls

	Abdominal pain: almost always and always					Abdominal pain: never, almost never and sometimes					p-value[1]
	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	Mean	SD	
Child Report (n=40 vs n=20)											
Average[2]	75	68	82	75	11	89	82	93	86	11	<0.01
Physical	84	78	94	84	12	94	89	100	92	10	<0.01
Psychosocial[3]	70	63	78	71	13	86	78	91	83	12	<0.01
Emotional	70	55	80	67	20	80	68	90	78	17	0.03
Social	90	70	100	83	15	100	90	100	93	11	0.01
School	60	50	73	62	17	80	68	90	78	14	<0.01
Parent Proxy (n=41 vs n=22)											
Average[2]	74	67	85	74	16	88	78	91	84	13	0.01
Physical	8	75	91	82	15	94	84	100	88	18	0.02
Psychosocial[3]	72	63	85	70	18	82	75	92	81	13	0.01
Emotional	65	50	75	62	21	80	65	90	77	16	0.01
Social	85	70	100	81	18	93	90	100	90	13	0.08
School	65	48	80	65	21	75	70	95	76	18	0.04

[1]p-values <0.05 are considered statistically significant.
[2]Average values were computed as the average of 4 domains (physical, emotional, social and school function).
[3]Psychosocial values were computed as the average of 3 domains (emotional, social and school function).
Abbreviations: IQ, Interquartile Range; SD, Standard Deviation.

Table G-10: The Association between Constipation Score from Gastrointestinal Symptoms Scale and and *PedsQL™ 4.0 Generic Core Scale* in Children with Celiac Disease and Disease Controls

	Constipation: almost always and always					Constipation: never, almost never and sometimes					p-value[1]
	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	Mean	SD	
Child Report (n=27 vs n=33)											
Average[2]	73	67	80	74	11	85	75	92	83	12	<0.01
Physical	88	75	94	84	13	91	84	100	89	11	0.13
Psychosocial[3]	68	60	78	69	13	80	70	90	79	13	<0.01
Emotional	70	50	75	64	20	80	60	90	76	16	0.02
Social	85	70	100	82	16	95	85	100	90	13	0.03
School	60	50	70	62	17	75	60	85	72	17	0.03
Parent Proxy Report (n=31 vs n=23)											
Average[2]	75	66	88	74	16	84	72	89	81	14	0.10
Physical	84	72	94	82	16	89	80	97	86	16	0.14
Psychosocial[3]	73	62	87	70	19	81	65	92	77	15	0.12
Emotional	65	50	80	63	21	70	60	88	72	19	0.06
Social	85	65	100	81	19	95	75	100	88	14	0.10
School	65	55	85	66	22	75	63	85	72	19	0.34

[1]p-values <0.05 are considered statistically significant.
[2]Average values were computed as the average of 4 domains (physical, emotional, social and school function).
[3]Psychosocial values were computed as the average of 3 domains (emotional, social and school function).
Abbreviations: IQ, Interquartile Range; SD, Standard Deviation.

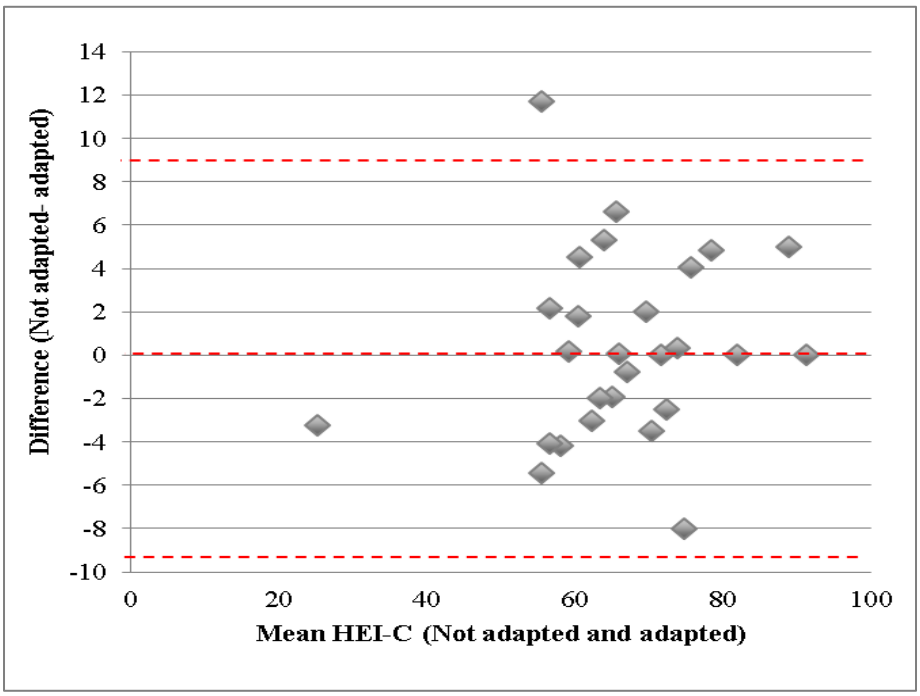
Table G-11: The Association between Discomfort in Abdomen or Stomach Score from Gastrointestinal Symptoms Scale and *PedsQL™ 4.0 Generic Core Scale* in Children with Celiac Disease and Disease Controls

	Discomfort in Abdomen or Stomach: almost always and always					Discomfort in Abdomen or Stomach: never, almost never and sometimes					p-value[1]
	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	Mean	SD	
					Child Report (n=36 vs n=24)						
Average[2]	75	68	82	74	10	89	76	96	85	12	<0.01
Physical	84	75	94	82	12	94	88	100	92	9	<0.01
Psychosocial[3]	70	64	78	70	11	83	70	95	81	15	<0.01
Emotional	68	58	78	66	18	80	65	95	78	21	0.01
Social	90	70	100	84	15	100	80	100	90	13	0.06
School	60	50	73	62	16	80	65	90	75	18	<0.01
					Parent Proxy Report (n=37 vs n=25)						
Average[2]	76	67	85	75	13	85	74	945	80	18	0.04
Physical	84	75	94	83	13	91	84	97	85	20	0.19
Psychosocial[3]	72	63	82	71	15	82	67	92	77	19	0.05
Emotional	65	55	70	64	17	80	60	90	72	25	0.06
Social	85	70	100	83	17	90	75	100	86	18	0.42
School	65	55	80	65	20	75	60	95	74	22	0.08

[1]p-values <0.05 are considered statistically significant.
[2]Average values were computed as the average of 4 domains (physical, emotional, social and school function).
[3]Psychosocial values were computed as the average of 3 domains (emotional, social and school function).
Abbreviations: IQ, Interquartile Range; SD, Standard Deviation.

Appendix H : Assessment of Agreement between the Adapted and Not Adapted Diet Quality Tool in Children Post Liver Transplant and Healthy Controls

A



B

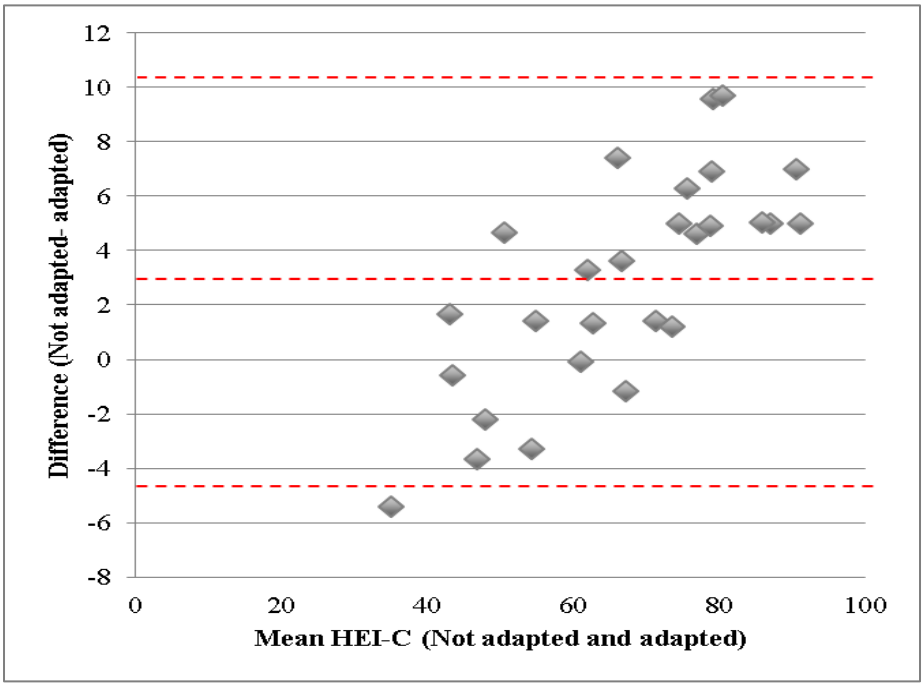
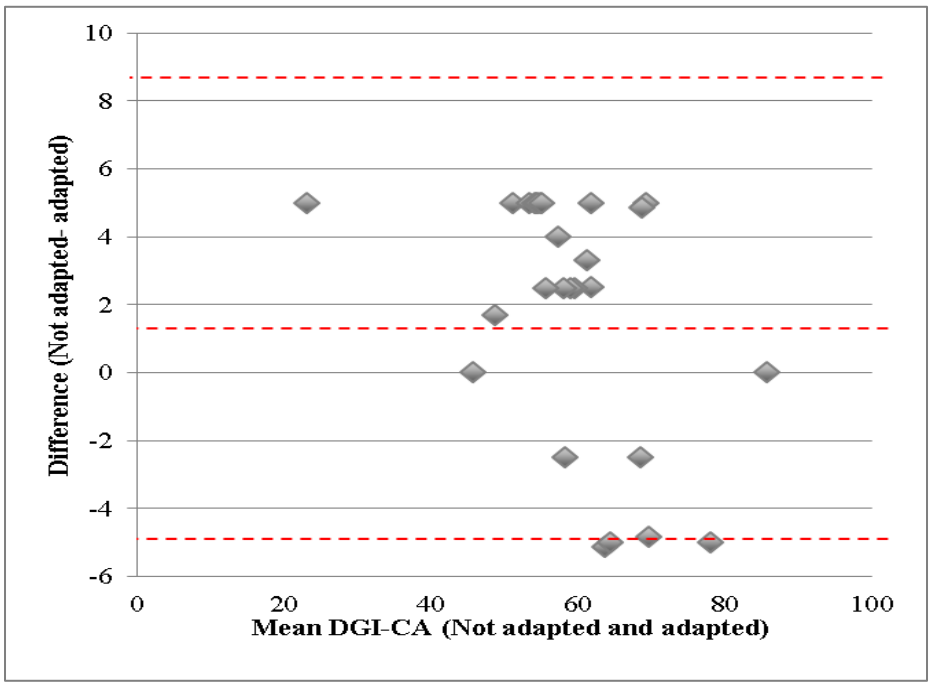


Figure H–1: Bland Altman Analysis between Adapted and Not Adapted Healthy Eating Index-Canada in Children Post-Liver Transplant (n=27) (A) and Healthy Controls (n=28) (B) (35). The adaptation of Healthy Eating Index-Canada (HEI-C) is described in **Appendix A, Table A-3.**

A



B

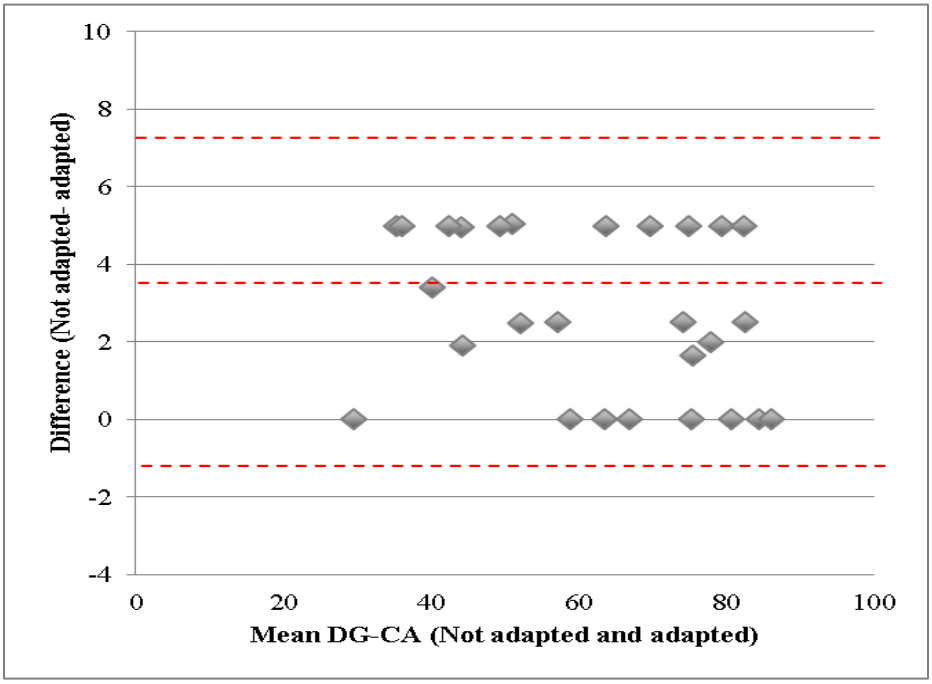
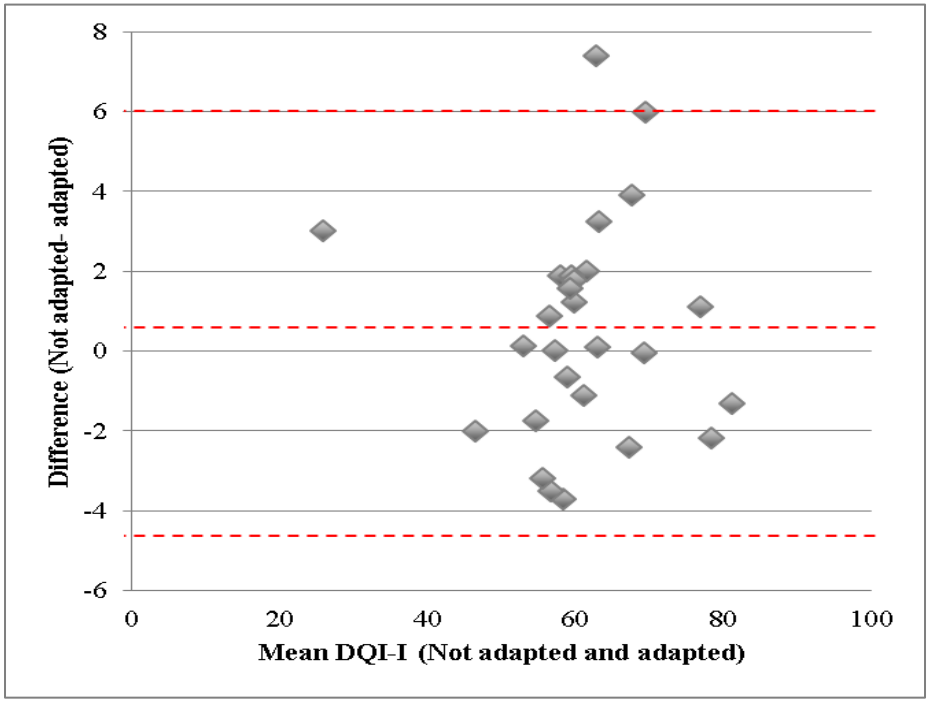


Figure H–2: Bland Altman Analysis between Adapted and Not Adapted Dietary Guideline Index for Children and Adolescents in Children Post-Liver Transplant (n=27) (A) and Healthy Controls (n=28) (B) (31). The adaptation of Dietary Guideline Index for Children and Adolescents (DGI-CA) is described in **Appendix A, Table A-2.**

A



B

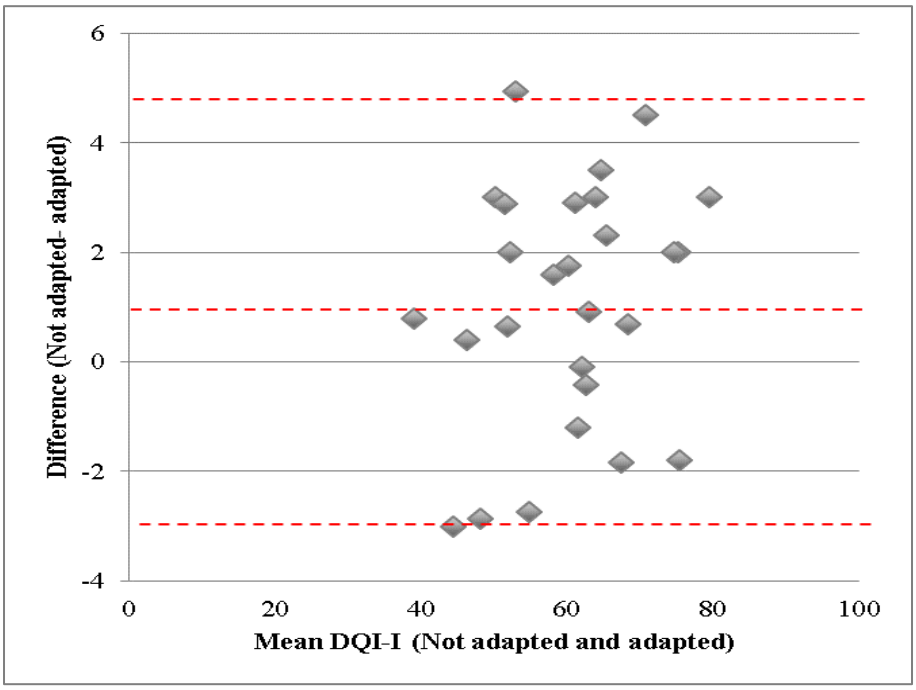


Figure H–3:Bland Altman Analysis between adapted and not adapted Diet Quality Index-International in Children Post-Liver Transplant (n=27) (A) and Healthy Controls (n=28) (B) (16). The adaptation of Diet Quality Index-International is described in **Appendix A, Table A-3.**

Table H-1: Correlational Consistency Between the Adapted vs Not Adapted Diet Quality Tools in Children Post-Liver Transplant and Healthy Controls

	Post-LTX		Healthy Controls	
	ICC	**p-value**	**ICC**	**p-value**
HEI-C	0.946	<0.01	0.953	<0.01
DGI-CA	0.938	<0.01	0.979	<0.01
DQI-I	0.966	<0.01	0.973	<0.01

Two-way mixed model (absolute agreement, single measure) used SPSS 17:0. ICC ≤ 0.40 refers to poor to fair agreement, 0.41– 0.60 refers moderate agreement, 0.61–0.80 refers to good agreement and >0.8-1.0 refers to perfect agreement (230, 237, 241).
Abbreviations: ICC, Intra Class Correlations; LTX, liver transplant.

Table H-2: Correlational Consistency Between the Diet Quality Tools in Children Post-Liver Transplant and Healthy Controls

	Post-LTX		Healthy Controls	
	ICC	**p-value**	**ICC**	**p-value**
HEI-C and DGI-CA	0.752	<0.01	0.872	<0.01
DGI-CA and DQI-I	0.777	<0.01	0.723	<0.01
HEI-C and DQI-I	0.821	<0.01	0.814	<0.01

Two-way mixed model (absolute agreement, single measure) used SPSS 17:0. ICC ≤ 0.40 refers to poor to fair agreement, 0.41– 0.60 refers moderate agreement, 0.61–0.80 refers to good agreement and >0.8-1.0 refers to perfect agreement (230, 237, 241).
Abbreviations: ICC, Intra Class Correlations; LTX, liver transplant.

Appendix I : Dietary Intake in Children Post Liver Transplant

Table I-1: Comparison in Macro and Micronutrients Intake between Misreports (Under and Over-Reporter) and Acceptable Reporters in Children Post-Liver Transplant and Healthy Controls

	Misreporting (n=21) [1]					Acceptable reporting (n=34) [1]					p-value[2]
	Mean	SD	Median	Interquartile Range		Mean	SD	Median	Interquartile Range		
Protein (g)	65	25	55	47	86	58	24	50	44	62.4	0.37
% Protein	15.5	3.5	15.0	12.8	18.2	16.3	4.8	15.6	13. 5	18.2	0.66
Carbohydrate (g)	212	41	208	189	251	190	84	172	137.1	218	0.03
% Carbohydrate	52.6	8.9	52.3	47.6	58.4	52.9	7.5	52.6	49	57	0.93
Total Sugar (g)	79	31	72	58	98	77	37	68	51	95	0.65
Fibre (g)	11.4	5.6	11.0	6.2	15.6	12.0	6.7	10.1	8.3	14.6	0.99
Fat (g)	61	22	59	50	66	53	28	44	36	56	0.03
% Fat	32.6	6.3	33.6	31.2	34.9	32.3	6.5	32.2	27.4	37.2	0.68
SFA (g)	21.7	9.6	21.3	17.9	25.6	19.5	13.2	15.5	12.5	21.9	0.08
% SFA	11.5	3.91	11.8	10.3	13.1	11.8	3.5	10.9	8.7	14.2	0.82
Trans Fat (g)	0.45	0.31	0.43	0.28	0.55	0.50	0.36	0.42	0.25	0.64	0.80
Cholesterol (mg)	219	168	157	92	300	171	94	151	91	235	0.58
PUFA (g)	9.1	5.2	8.3	7.4	10.6	8.3	4.1	6.9	5.3	11.6	0.41
% PUFA	4.8	2.0	4.3	3.9	5.9	5.2	1.8	4.9	3.9	6.1	0.52
MUFA (g)	20.8	10.1	19.3	13.5	24.7	19.0	9.8	14.9	12.3	26.5	0.34
% MUFA	11.0	3.6	11.8	8.8	12.6	11.7	3.4	11.5	9.1	13.4	0.72
Vitamin A (RAE)	501	382	418	320	453	424	278	355	225	594	0.45
Vitamin B1 (mg)	1.35	0.44	1.22	1.02	1.71	1.06	0.53	0.97	0.71	1.18	0.001
Vitamin B2 (mg)	1.70	0.44	1.63	1.38	2.00	1.60	0.61	1.54	1.20	1.87	0.44
Vitamin B3 (mg)	14.4	7.5	12.3	8.0	19.0	12.5	6.1	11.4	7.8	16.6	0.42
Vitamin B6 (mg)	1.16	0.48	1.10	0.84	1.42	1.09	0.44	0.96	0.78	1.34	0.45
Vitamin B12 (mg)	3.61	1.80	3.44	2.78	4.05	3.39	1.70	2.99	2.46	4.10	0.62
Vitamin C (mg)	104	56	100	67	146	90	75	70	28	122	0.21
Vitamin D (IU)	192	109	182	114	223	204	136	191	95	257	0.84
Vitamin K (mg)	46.7	37.3	37.9	17.7	50.5	54.7	71.9	29.1	12.2	56.1	0.33
Vitamin E (mg)	3.8	5.5	2.1	1.4	4.5	3.1	2.1	2.6	1.8	3.7	0.63
Folate-DFE (mg)	226	90	221	159	289	233	121	213	132	281	0.88

Calcium (mg)	870	227.	904	720	955	851	431	831	554	1012	0.58
Iron (mg)	11.3	3.1	10.9	9.9	13.5	9.8	4.5	9.1	7.1	12.2	0.08
Magnesium (mg)	211	489	200	177	253	207	89	193	146	273	0.04
Selenium (mg)	74.4	23.4	78.2	58.1	91.0	63.7	19.9	60.0	47.4	80.9	0.04
Sodium (mg)	1932	733	180	1606	2186	1943	1080	1627	1208	2298	0.39
Zinc (mg)	10.5	7.9	7.7	5.7	11.2	7.7	3.5	7.2	5.0	9.9	0.28
HEI-C	64	11	62	58	72	67	14	71	59	76	0.19
DGI-CA	56	12	55	49	61	62	17	65	52	75	0.10
DQI-I	60	9	59	57	62	60	11	62	56	66.526	0.37
GI	51	5	51	49	53	49	7	50	46	52	0.18
GL	108	26	109	3	127	95	43	88	73	108	0.03

[1]Misreporting includes under-reporting (<95% of energy intake/ Basel Metabolic Rate) and over-reporting (>95% of energy intake/ Basel Metabolic Rate). [2]p-values <0.05 are considered statistically significant.

Abbreviations: DFE, Dietary Folate Equivalent; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; GI, Glycemic index; GL, Glycemic load; HEI-C, Healthy Eating Index-Canada; LTX, liver transplant; MUFA, Monounsaturated Fatty Acid; PUFA, Polyunsaturated Fatty Acid; RAE, Retinol Activity Equivalent; SD, Standard Deviation.

Table I-2: The 95% Confidence Interval and Coefficient of Variation in Children Post-Liver Transplant and Healthy Controls

	Post-LTX (n=27)				Healthy Controls (n=28)			
	CI	Mean+CI (>95% CI)	Mean-CI (<95% CI)	CV	CI	Mean+CI (>95% CI)	Mean-CI (<95% CI)	CV
Energy (kcal)	236.58	1837.58	1364.42	0.39	154.71	1590.56	1281.14	0.29
Protein (g)	10.49	69.41	48.42	0.47	7.72	69.34	53.90	0.34
% Protein	1.40	15.96	13.15	0.26	1.64	19.00	15.72	0.25
Carbohydrate (g)	29.73	238.43	178.96	0.38	22.91	211.58	165.76	0.33
% Carbohydrate	3.34	56.45	49.77	0.17	2.68	55.22	49.85	0.14
Total Sugar (g)	12.96	89.20	63.28	0.45	13.14	93.10	66.81	0.44
Fibre (g)	2.86	15.38	9.66	0.61	1.73	12.77	9.31	0.42
Fat (g)	12.03	73.36	49.30	0.52	6.70	57.33	43.94	0.36
% Fat	2.68	35.83	30.47	0.21	2.09	33.80	29.62	0.18
SAF (g)	5.72	27.91	16.48	0.68	2.74	21.29	15.82	0.40
% SAF	1.58	13.25	10.10	0.36	1.15	12.78	10.47	0.27
Trans Fat (g)	0.16	0.75	0.43	0.68	0.09	0.48	0.29	0.64
Cholesterol (mg)	46.09	209.39	117.21	0.75	48.42	262.94	166.11	0.61
PUFA (g)	1.97	11.64	7.70	0.54	1.31	8.96	6.33	0.46
% PUFA	0.75	6.17	4.67	0.37	0.61	5.37	4.14	0.35
MUFA (g)	4.19	24.32	15.95	0.55	3.21	22.50	16.09	0.45
% MUFA	1.34	12.36	9.68	0.32	1.27	13.15	10.61	0.29
Vitamin A (RAE)	107.75	557.34	341.85	0.64	131.95	589.12	325.23	0.78
Vitamin B1 (mg)	0.18	1.43	1.07	0.39	0.20	1.29	0.89	0.49
Vitamin B2 (mg)	0.24	1.89	1.41	0.39	0.17	1.79	1.46	0.28
Vitamin B3 (mg)	2.33	14.34	9.67	0.52	2.59	17.01	11.84	0.48
Vitamin B6 (mg)	0.19	1.35	0.96	0.44	0.14	1.22	0.94	0.36
Vitamin B12 (mg)	0.64	3.62	2.34	0.57	0.61	4.56	3.34	0.42
Vitamin C (mg)	27.20	134.92	80.53	0.67	23.22	106.79	60.35	0.75
Vitamin D (IU)	49.24	258.48	160.01	0.62	45.53	236.27	145.22	0.64
Vitamin K (mg)	21.96	74.39	30.47	1.11	23.73	74.59	27.12	1.26
Vitamin E (mg)	1.93	5.90	2.05	1.29	0.48	3.30	2.35	0.46
Folate-DFE (mg)	34.57	243.45	174.31	0.44	45.15	296.27	205.96	0.49
Calcium (mg)	163.12	1083.65	757.42	0.47	103.63	901.64	694.37	0.35
Iron (mg)	1.68	12.42	9.06	0.41	1.38	11.38	8.61	0.37
Magnesium (mg)	29.55	244.06	184.96	0.37	27.18	229.62	175.26	0.36

Zinc (mg)	2.83	12.33	6.67	0.79	1.17	9.21	6.87	0.39
Selenium (mg)	9.01	71.72	53.70	0.38	6.86	79.46	65.74	0.26
Sodium (mg)	423.78	2494.70	1647.13	0.54	280.41	2091.60	1530.78	0.42
GI	2.10	53.15	48.95	0.11	2.42	51.14	46.29	0.13
GL	15.14	121.45	91.17	0.38	13.02	106.50	80.47	0.38
HEI-C	4.72	70.80	61.37	0.19	5.20	70.88	60.48	0.21
DGI-CA	4.62	62.74	53.50	0.21	6.51	67.59	54.57	0.29
DQI-I	3.99	64.50	56.53	0.17	3.70	63.55	56.15	0.17

Abbreviations: CI, Confidence interval; CV, Coefficient of variation; DFE, Dietary Folate Equivalent; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; GI, Glycemic index; GL, Glycemic load; HEI-C, Healthy Eating Index-Canada; LTX, liver transplant; MUFA, Monounsaturated Fatty Acid; PUFA, Polyunsaturated Fatty Acid; RAE, Retinol Activity Equivalent; SFA, Saturated Fatty Acid.

Table I-3: The Post Hoc Power analysis of Dietary Intake, Glycemic Index, Glycemic Load and Diet Quality Tools in Children Post-Liver Transplant and Healthy Controls

	Power (%)
Glycemic Index	29
Glycemic Load	23
Total Diet Quality Score	
Healthy Eating Index-Canada	10
Dietary Guideline Index for Children and Adolescents	11
Diet Quality Index-International	6

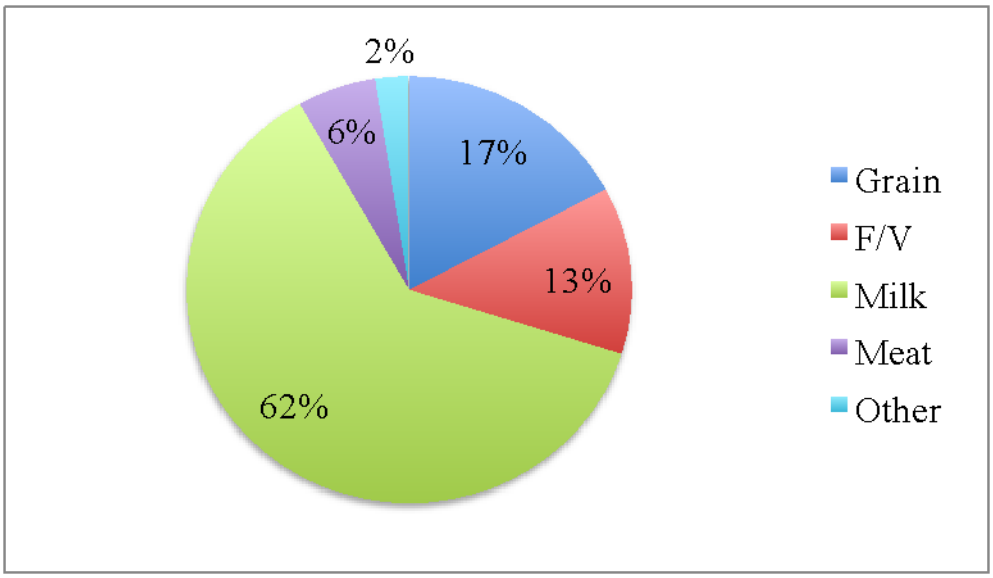
Appendix J : Dietary Intake in Children with Non-Alcoholic Fatty Liver Disease and Lean Control Children

Table J-1:The Diet Quality Models of Adequacy and Moderation between Diet Quality Tools in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	NAFLD (n=15)	Lean Control (n=16)	Maximum Score	p-value[1]
DQ Model (DQI-I and HEI-C)[2,3]	49 ± 10	60 ± 7	80	<0.01
DQ Model (DQI-I, HEI-C and DGI-CA milk and Meat)[2,4]	59 ± 10	71 ± 9	95	<0.01
DQ Model (DQI-I, HEI-C and DGI-CA Meat)[2,5]	57 ± 10	68 ± 8	90	<0.01

[1]p-values <0.05 are considered statistically significant.
[2]Normally distributed variables are presented as mean ± standard deviation. Independent *t*-tests were conducted.
[3]DQ Model is the sum score of Diet Quality Index-International (Adequacy), Healthy Eating Index-Canada (Moderation).
[4]DQ Model is the sum score of Diet Quality Index-International (Adequacy), Healthy Eating Index-Canada (Moderation) and Dietary Guideline Index for Children and Adolescents (Milk) and (Meat).
[5]DQ Model is the sum score of Diet Quality Index-International (Adequacy), Healthy Eating Index-Canada (Moderation) and Dietary Guideline Index for Children and Adolescents (Meat).
Abbreviations: DGI-CA; Dietary Guideline Index for Children and Adolescents; DQ, Diet Quality; DQI-I, Diet Quality Index-International; HEI-C, Healthy Eating Index-Canada; NAFLD, Non-Alcoholic Fatty Liver Disease.

A



B

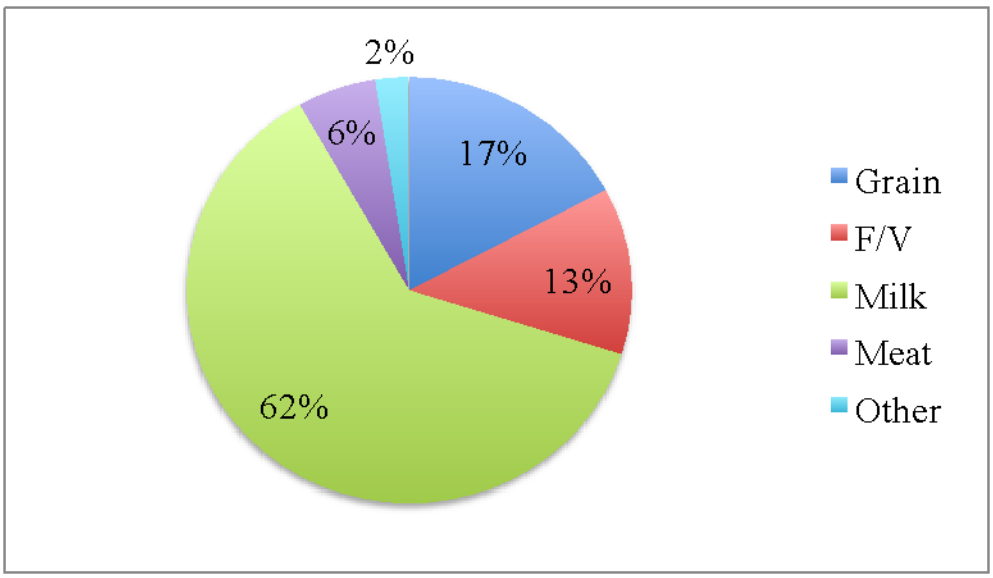


Figure J–1: Food Source of Calcium (A) and Protein (B) in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls. Food sources grain products, fruit and vegetables, milk and alternative, meat and alternatives, and other (sauce, gelatin. oil, sugar).
Abbreviations: F/V, fruit and vegetables.

Table J-2: The Interrelationship between Age (Above and Below the Median) and Anthropometric and Body Composition Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	Age <14					Age ≥14					p-value[1]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Weight for age z-score[2,3]	1.13	1.44	1.13	0.18	2.23	1.07	1.82	1.32	-0.86	2.73	0.92
Height for age z-score[2,3]	0.43	1.43	0.43	-0.36	1.17	0.23	0.86	0.24	-0.46	0.70	0.61
BMI for age z-score[2,3]	1.20	1.71	1.17	-0.17	2.89	1.08	1.77	1.22	-0.54	2.88	0.84
Waist circumference (cm)[4]	77	18	74	63	85	82	22	74	63	104	0.58
Hip circumference (cm)[4]	89	15	86	82	97	101	17	96	88	116	0.07
Waist to hip[4]	0.86	0.09	0.83	0.80	0.95	0.81	0.10	0.78	0.72	0.90	0.20
Waist to height[4]	0.50	0.12	0.44	0.41	0.57	0.47	0.11	0.41	0.38	0.56	0.47
%Fat free mass[5]	79.7	13.4	77.5	73.9	89.8	74.7	13.9	82.8	65.9	84.2	0.29
Fat free mass (kg)[5]	42.0	10.0	44.0	37.0	48.0	54.8	15.7	53.0	41.12	67.2	0.02
%Body Fat	20.3	13.4	22.5	10.2	26.1	25.3	13.9	17.2	15.8	34.1	0.29
Fat mass (kg)[5]	12.73	12.6	6.65	4.03	16.8	27.0	22.5	14.116	8.48	45.1	0.04

[1]p-values <0.05 are considered statistically significant.
[2]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[3]N= 17 in children <14 years and n=19 in children ≥14 years.
[4]N= 12-13 in children <14 years and n=16 in children ≥14 years.
[5]N= 13 in children <14 years and n=17 in children ≥14 years.
Abbreviations: BMI, Body Mass Index; IQ, Interquartile range; SD, Standard Deviation.

Table J-3: The Interrelationship between Gender and Anthropometric and Body Composition Children with Non-Alcoholic Fatty Liver

Disease and Lean Controls

	Male					Female					p-value[1]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Weight for age z-score[2,3]	1.47	1.72	2.26	0.11	2.96	0.36	1.19	0.10	-0.67	1.23	0.05
Height for age z-score[2,3]	0.56	1.29	0.5	0.17	1.48	-0.16	0.58	-0.16	-0.60	0.24	0.08
BMI for age z-score[2,3]	1.42	1.87	2.50	-0.26	3.00	0.58	1.23	0.48	-0.44	1.20	0.17
Waist circumference (cm)[4]	87	21	85	64	110	67	11	63	62	67	0.01
Hip circumference (cm)[4]	98	18	98	83	110	90	14	90	86	91	0.21
Waist to hip[4]	0.87	0.09	0.88	0.80	0.93	0.74	0.06	0.721	0.7	0.78	<0.01
Waist to height[4]	0.51	0.12	0.54	0.38	0.61	0.43	0.06	0.41	0.39	0.43	0.06
%Fat free mass[5]	75.1	15.3	74.2	61.8	89.4	80.6	9.3	82.85	77.5	83.7	0.54
Fat free mass (kg)[5]	53.4	15.7	49.2	41. 8	64.9	41.0	8.3	42.0	37.0	45.1	0.03
%Body Fat	25.0	15.3	25.8	10.6	38.3	19.4	9.3	17.2	16.3	22.5	0.72
Fat mass (kg)[5]	22.9	21.2	16.2	4.6	35.1	16.7	17. 3	8.5	7.2	14.2	0.54

[1]p-values <0.05 are considered statistically significant.
[2]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[3]N= 24 Male and n=12 Female.
[4]N= 19 Male and n=9-10 Female.
[5]N= 20 Male and n=10 Female.
Abbreviations: BMI, Body Mass Index; IQ, Interquartile range; SD, Standard Deviation.

Table J-4: The Interrelationship between Age (Above and Below the Median) and Liver Enzymes, and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	Age <14					Age ≥14					p-value[1]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)[2]	44	44	21	17	57	44	50	23	14	52	0.60
AST (U/L)[2]	37	27	32	21	34	31	21	25	19	32	0.16
γGT (U/L)[2]	31	66	9	5	15	13	11	5	5	16	0.80
Glucose (mmol/L)[2]	5.0	0.5	5.0	4.5	5.3	4.71	0.5	4.7	4.5	5.1	0.07
Insulin (mU/L)[3]	16	13	12	7	21	19	18	12	8	24	0.94
HOMA-IR[3,4]	3.8	3.7	2.8	1.6	4.4	4.5	4.4	2.7	1.7	8.8	0.97
Triglyceride (mmol/L)[2]	1.1	0.7	0.9	0.6	1.5	0.9	0.4	0.9	0.6	1.2	0.79
Total cholesterol (mmol/L)[2]	3.9	1.4	3.6	3.2	4.4	3.9	0.7	3.7	3.3	4.3	0.94
HDL (mmol/L)[2]	1.19	0.25	1.19	0.99	1.37	1.15	0.35	1.02	0.88	1.45	0.41
LDL (mmol/L)[3]	2. 4	1.0	2.6	1.9	2.8	2.4	0.9	2.3	1.8	2.52	0.72

[1]p-values <0.05 are considered statistically significant.
[2]N= 17 in children <14 years and n=17-20 in children ≥14 years.
[3]N= 14-15in children <14 years and n=16-19 in children ≥14 years.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT; Alanine aminotransferase, AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-5: The Interrelationship between Gender and Liver Enzymes, and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	Male					Female					p-value[1]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)[2]	54	53	33	19	58	25	27	15	13	17	0.01
AST (U/L)[2]	39	27	33	26	35	245	12	20	18	26	<0.01
γGT (U/L)[2]	23	52	10	5	19	18	37	5	5	11	0.19
Glucose (mmol/L)[2]	5.1	0.5	5.1	4.7	5.4	4.4	0.5	4.5	4.2	4.8	<0.01
Insulin (mU/L)[3]	22	17	13	10	30	9	7	7	5	15	0.01
HOMA-IR[3,4]	5.3	4.4	2.9	2.1	8.8	1.8	1.6	1.3	0.8	2.8	<0.01
Triglyceride (mmol/L)[2]	1.1	0.6	0.9	0.6	1.5	0.8	0.4	0.9	0.4	1.0	0.20
Total cholesterol (mmol/L)[2]	3.9	1.2	3.8	3.4	4.4	3.7	0.5	3.7	3.3	4.1	0.64
HDL (mmol/L)[2]	1.10	0.30	1.02	0.87	1.31	1.31	0.27	1.40	1.06	1.55	0.03
LDL (mmol/L)[2]	2.6	1.0	2.5	1.9	2.9	2.1	0.5	2.2	1.6	2.5	0.14

[1]p-values <0.05 are considered statistically significant.
[2]N= 22-24 Male and n=12-13 Female.
[3]N= 20-23 Male and n=11-12 Female.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation; TNF-α, Tumor Necrosis Factor-α.

Table J-6: Comparison in Micro and Macronutrients, Glycemic Index, Glycemic Load, Food Groups and Diet Quality Scores between Acceptable and Misreporting in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	Adequate Reporter (n=11)[1]					Misreporter (n=20)[1]					p-value[2]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Energy (kcal)	1563	234	1481	1423	1709	1663	451	1623	1364	2046	0.50
Protein (g)	67	13	68	58	75	78	22	72	62	95	0.15
% Protein	17.4	3.4	17.5	16.2	18.8	19.8	6.7	18.9	13.9	23.0	0.51
Carbohydrate (g)	214	47	232	163	257	228	77	224	168	279	0.59
% Carbohydrate	54.5	8.5	54.8	50.4	60.1	54.3	9.7	54.5	47.1	62.1	0.94
Total Sugar (g)	79	35	80	50	104	98	49	94	61	123	0.25
Fibre (g)	17.4	3.4	17.1	14.4	20.3	17.0	6.6	16.5	12.2	19.9	0.51
Fat (g)	52	15	50	41	62	52	21	54	34	65	0.10
% Fat	29.8	6.7	29.2	24.0	37.2	27.7	6.7	29.2	23.8	33.3	0.40
SFA (g)	17.0	4.5	17.9	12.8	19.7	18.9	8.0	20.3	12.2	25.9	0.48
% SFA	9.7	1.9	9.8	8.9	10.5	10.0	3.0	10.1	7.7	12.0	0.77
Trans Fat (g)	0.35	0.27	0.28	0.18	0.62	0.27	0.27	0.20	0.05	0.40	0.31
Cholesterol (mg)	173	72	169	144	182	191	61	189	152	224	0.36
PUFA (g)	11.12	5.0	9.6	6.3	15.9	8.6	4.6	8.1	5.0	11.5	0.17
% PUFA	6.4	2.8	6.4	3.7	8.2	4.6	1.9	3.9	3.3	6.1	0.07
MUFA (g)	18.7	7.5	17.5	12.3	22.2	17.4	9.9	15.8	10.3	21.8	0.48
% MUFA	10.6	3.3	10.1	7.5	14.1	9.1	3.4	8.9	6.4	10.7	0.23
Vitamin A (RAE)	604	327	476	466	954	492	275	396	325	604	0.19
Vitamin B1 (mg)	1.53	0.45	1.46	1.11	1.76	1.65	0.54	1.64	1.26	2.03	0.53
Vitamin B2 (mg)	1.67	0.54	1.54	1.29	1.96	1.74	0.62	1.67	1.35	2.06	0.76
Vitamin B6 (mg)	1.39	0.36	1.35	0.99	1.75	1.54	0.48	1.46	1.15	1.99	0.37
Vitamin B12 (mg)	4.4	2.8	3.4	2.3	5.6	4.0	2.5	3.3	3.0	3.9	0.90
Vitamin C (mg)	128	86	135	44	183	103	96	63	41	129	0.32
Vitamin D (IU)	223	126	247	108	274	182	166	130	102	236	0.25
Folate-DFE (mg)	277	131	243	190	400	261	69	260	203	300	0.84
Calcium (mg)	833	293	729	558	997	816	328	762	644	953	0.88
Copper (mg)	1.05	0.30	1.11	0.79	1.32	1.20	0.43	1.31	0.82	1.49	0.30
Iron (mg)	12.7	3.6	12.4	10.7	14.3	13.3	4.4	12.7	9.6	15.2	0.74
Magnesium (mg)	245	556	244	222	295	262	90	255	198	292	0.57
Potassium (mg)	2399	664	2200	2056	2992	2448	788	2286	1940	3009	0.86
Selenium (mg)	84	21	87	67	95	81	28	79	65	97	0.81
Sodium (mg)	2056	513	1815	1661	2429	2294	638	2238	1848	2485	0.30

Zinc (mg)	8.8	2.3	9.4	7.1	10.4	9.9	4.3	8.9	7.6	10.4	0.87
Grains	5.3	1.9	4.8	3.7	6.7	5.2	1.5	5.2	3.9	6.4	0.91
F/V	5.1	3.2	4.7	2.6	7.7	4.9	2.7	3.9	3.1	5.5	0.98
Milk	1.9	1.1	1.9	1.0	2.8	2.2	1.1	2.0	1.3	3.2	0.51
Meat	1.7	0.8	1.4	1.0	2.0	2.3	1.1	2.0	1.7	2.8	0.08
GI	48	6	47	46	53	51	6	49	47	53	0.18
GL	105	29	113	86	132	117	46	107	83	154	0.44
HEI-C	69	11	71	58	81	73	12	69	65	83	0.42
DGI-CA	65	14	65	53	72	68	14	69	60	77	0.49
DQI-I	65	10	65	58	74	63	9	62	57	69	0.55

[1]Under-reporting (<95% of energy intake/ Basel Metabolic Rate) and over-reporting (>95% of energy intake/ Basel Metabolic Rate).

[2]p-values <0.05 are considered statistically significant.

Abbreviations: DFE, Dietary Folate Equivalent; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; F/V, Fruits and Vegetables; GI, Glycemic index; GL, Glycemic load; HEI-C, Healthy Eating Index-Canada; IQ, Interquartile range; MUFA, Monounsaturated Fatty Acid; PUFA, Polyunsaturated Fatty Acid; RAE, Retinol Activity Equivalent; SD, Standard Deviation; SFA, Saturated Fat.

Table J-7: Micronutrient Intake in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	NAFLD (n=15)					Lean Control (n=16)					RDA/AI	p-value[1]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3		
Vitamin A (RAE)[2]	450	265	412	289	532	608	307	475	361	941	400-900[4]	0.22
Vitamin B1 (mg)	1.53	0.50	1.46	1.11	1.76	1.68	0.51	1.68	1.26	1.89	0.6-1.2[4]	0.43
Vitamin B2 (mg)	1.55	0.49	1.48	1.10	1.85	1.88	0.63	1.73	1.46	2.06	0.6-1.3[4]	0.11
Vitamin B6 (mg)	1.42	0.33	1.40	1.18	1.60	1.55	0.53	1.49	1.09	2.03	0.6-1.3[4]	0.42
Vitamin B12 (mg)[2]	4.07	2.61	3.31	2.32	5.46	4.15	2.56	3.37	2.87	4.82	1.2-2.4[4]	0.68
Vitamin C (mg)[2]	80	79	55	32	82	140	96	124	71	180	25-75[4]	0.02
Vitamin D (IU)[2]	125	69	108	99	152	263	179	253	130	283	600[4]	<0.01
Vitmin E α-Tocopherol (mg)[2]	3.7	2.3	2.7	2	6.3	4.5	2.7	3.8	2.4	6.2	7-15[4]	0.32
Folate-DFE (mg)[3]	267	118	250	175	320	252	68	267	227	297	200-400[4]	0.72
Calcium (mg)[3]	716	265	729	526	925	922	325	822	676	1033	1000-1300[4]	0.06
Iron (mg)[3]	12.6	4.8	12.0	8.56	14.66	13.54	3.43	13.54	11.18	15.55	10-15[4]	0.52
Copper (mg)[3]	0.99	0.35	1.04	0.75	1.26	1.30	0.37	1.38	1.04	1.50	440-890[4]	0.02
Magnesium (mg)[3]	230	65	225	187	261	280	85	272	227	307	130-410[4]	0.08
Potassium (mg)[3]	2145	590	2152	1829	2444	2699	774	2657	2011	3451	3800-4700[5]	0.03
Selenium (mg)[3]	84	21	87	65	96	80	29	81	62	92	30-55[4]	0.68
Sodium (mg)[3]	2095	621	1976	1699	2505	2317	576	2303	1848	2449	1200-1500[4]	0.31
Zinc (mg)[2]	10.1	5.0	9.4	7.4	10.8	9.0	1.9	8.9	7.4	10.2	5-11[4]	0.72

[1]p-values <0.05 are considered statistically significant.
[2]Variables demonstrating skewed distributions are presented as median (25th–75th percentile). Mann Whitney test was conducted to compare between groups.
[3]Normally distributed variables are presented as mean ± standard deviation. Independent *t*-test was conducted to compare between groups.
[4]Recommended Daily Allowance (RDA).
[5]Adequate Intake (AI).
Abbreviations: DFE, Dietary Folate Equivalent; IQ, Interquartile range; NAFLD, Non-Alcoholic Fatty Liver Disease; RAE, Retinol Activity Equivalent; SD, Standard Deviation.

J-1 Assessing the Intake of Vitamin A, Vitamin C, and Vitamin E Intake in comparison to the Recommendations

The intake of vitamins A, C, and E was treated as categorical variable. Children were assigned scores of 5, 2.5, or 0 for meeting 100% of the RDA, 50 to <100% of RDA, or <50% of the RDA, respectively. This approach was considered similar to the DQI-I Adequacy and Moderation approach (16). No significant differences were found in vitamin A (NAFLD: 2.5 [0-2.5] vs lean control: 2.5 [2.5-5]) and vitamin E [NAFLD: 0 [0-0] vs lean control: 0 [0-0]) scores between groups ($p>0.05$); indicating that the majority of out cohort met 50 to <100% of RDA of vitamin A and <50 % of RDA of vitamin E. Children with NAFLD (2.5 (0.8-5) mg/day) had significantly lower scores of vitamin C compared to lean control children (5.0 (3.8-5) mg/day) ($p<0.01$).

Table J-8: The Interrelationship between Age (Above and Below the Median) and Glycemic Index, Glycemic Load and Diet Quality Scores in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	Age <14 (n=14)	Age ≥14 (n=17)	p-value[1]
Grain Products[2]	5.9 ± 1.5	4.9 ± 1.4	0.07
Fruit and Vegetables[3]	3.9 (3.0-5.0)	3.5 (3.0-6.2)	0.95
Milk and Alternatives[2]	2.0 ± 1.1	2.1 ± 1.2	0.97
Meats and Alternatives[3]	1.4 (1.3-2.0)	2.3 (1.9- 3.0)	<0.1
GI[2]	50 ± 5	50 ± 7	1.00
GL[2]	121 ± 40	105 ± 41	0.28
Total Diet Quality Scores			
HEI-C[2]	76 ± 12	69 ± 11	0.12
DGI-CA[2]	68 ± 12	66 ± 15	0.59
DQI-I[2]	68 ± 8	61 ± 8	0.04
The Component of Diet Quality: Adequacy			
HEI-C[2,4]	36 ± 7	34 ± 8	062
DGI-CA[2,5]	28 ± 6	28 ± 6	0.97
DQI-I[2,6]	28 ± 5	25 ± 7	0.23
The Component of Diet Quality: Moderation			
HEI-C[2,7]	30 ± 6	26 ± 7	0.10
DGI-CA[2,8]	26 ± 8	24 ± 10	0.57
DQI-I[2,9]	21 ± 4	18 ± 4	0.05
The Component of Diet Quality: Variety			
HEI-C (Variety)[2,10]	9.6 ± 0.6	9.6 ± 0.7	0.92
DGI-CA Food[2,11]	13 ± 3	11 ± 4	0.21
DGI-CA Grains[2,12]	6 ± 2	5 ± 2	0.30
DGI-CA Milk[2,13]	8 ± 3	6 ± 3	0.07
DQI-I[2,14]	18 ± 2	18 ± 1	0.34
Diet Quality Models for Adequacy and Moderation within Diet Quality Tool [15]			
HEI-C[2]	66 ± 11	61 ± 12	0.20
DGI-CA[2]	53 ± 11	52 ± 13	0.69
DQI-I[2]	49 ± 6	43 ± 8	0.04

[1]p-values <0.05 are considered statistically significant.
[2]Normally distributed variables are presented as mean ± standard deviation. Independent *t*-test was conducted.
[3]Variables demonstrating skewed distributions are presented as median (interquartile range). Mann Whitney test was conducted.
[4]HEI-C (Adequacy): sum score of fruit and vegetables, grains, milk and alternatives and meat and alternatives.
[5]DGI-CA (Adequacy): sum score of fruit and vegetables, grains, milk and alternatives and meat and alternatives.
[6]DQI-I (Adequacy): sum score of fruit and vegetables, grains, fibre, protein, iron, calcium, vitamin C.
[7]HEI-C (Moderation): sum score of fat, saturated fat, cholesterol, and *other foods* group.
[8]DGI-CA (Moderation): sum score of *other foods* group, beverage, and food choice (saturated fat).
[9]DQI-I (Moderation): sum score of fat, saturated fat, cholesterol, sodium and *other foods* group.
[10]HEI-C (Variety): The score of Variety score.
[11]DGI-CA (Foods): sum score of whole grains, low fat milk, beverage and *other foods* group.
[12]DGI-CA (Grains): sum score of the total grains and whole grains.
[13]DGI-CA (Milk): sum score of milk and alternatives and low fat milk.
[14]DQI-I (Variety): sum score of the variety of food groups and within milk and meat products.
[15] Model is the sum score Adequacy and Moderation within DQ tool (HEI-C, DGI-CA and DQI-I).
Abbreviations: DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; GI, Glycemic index; GL, Glycemic load; HEI-C, Healthy Eating Index-Canada; SD, Standard Deviation.

Table J-9: The Interrelationship between Gender and Glycemic Index, Glycemic Load and

Diet Quality Scores in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	Male (n=20)	Female (n=11)	p-value[1]
Grain Products[2]	5.2 ± 1.6	5.2 ± 1.8	0.81
Fruit and Vegetables[3]	3.2 (2.9-5.0)	5.2 (4.4-7.7)	0.01
Milk and Alternatives[2]	2.2 ± 1.1	1.8 ± 1.1	0.24
Meats and Alternatives[3]	2.0 (1.3-2.7)	2.0 (1.4-2.6)	0.87
GI[2]	51 ± 7	48 ± 5	0.35
GL[2]	117 ± 45	108 ± 27	0.59
Total Diet Quality Scores			
HEI-C[2]	70 ± 11	76± 11	0.11
DGI-CA[2]	64 ± 13	72 ± 13	0.13
DQI-I[2]	62 ± 9	68 ± 8	0.04
The Component of Diet Quality: Adequacy			
HEI-C[2,4]	33 ± 7	39 ± 6	0.03
DGI-CA[2,5]	26 ± 6	32 ± 4	0.01
DQI-I[2,6]	25 ± 6	30 ± 4	0.01
The Component of Diet Quality: Moderation			
HEI-C[2,7]	27 ± 7	30 ± 6	0.27
DGI-CA[2,8]	24 ± 10	26 ± 8	0.63
DQI-I[2,9]	19 ± 5	20 ± 4	0.78
The Component of Diet Quality: Variety			
HEI-C (Variety)[2,10]	9.7 ± 0.6	9.5 ± 0.8	0.44
DGI-CA Food[2,11]	12 ± 3	11 ± 4	0.34
DGI-CA Grains[2,12]	6 ± 2	6 ± 2	0.54
DGI-CA Milk[2,13]	7 ± 3	6 ± 4	0.37
DQI-I[2,14]	18 ± 1	17 ± 2	0.15
Diet Quality Models for Adequacy and Moderation within Diet Quality Tool [15]			
HEI-C[2]	60 ± 11	69 ± 11	0.04
DGI-CA[2]	50 ± 13	57 ± 11	0.09
DQI-I[2]	44 ± 8	50 ± 7	0.04

[1]p-values <0.05 are considered statistically significant.
[2]Normally distributed variables are presented as mean ± standard deviation. Independent *t*-test was conducted.
[3]Variables demonstrating skewed distributions are presented as median (interquartile range). Mann Whitney test was conducted.
[4]HEI-C (Adequacy): sum score of fruit and vegetables, grains, milk and alternatives and meat and alternatives.
[5]DGI-CA (Adequacy): sum score of fruit and vegetables, grains, milk and alternatives and meat and alternatives.
[6]DQI-I (Adequacy): sum score of fruit and vegetables, grains, fibre, protein, iron, calcium, vitamin C.
[7]HEI-C (Moderation): sum score of fat, saturated fat, cholesterol, and *other foods* group.
[8]DGI-CA (Moderation): sum score of *other foods* group, beverage, and food choice (saturated fat).
[9]DQI-I (Moderation): sum score of fat, saturated fat, cholesterol, sodium and *other foods* group.
[10]HEI-C (Variety): The score of Variety score.
[11]DGI-CA (Foods): sum score of whole grains, low fat milk, beverage and *other foods* group.
[12]DGI-CA (Grains): sum score of the total grains and whole grains.
[13]DGI-CA (Milk): sum score of milk and alternatives and low fat milk.
[14]DQI-I (Variety): sum score of the variety of food groups and within milk and meat products.
[15]Model is the sum score Adequacy and Moderation within DQ tool (HEI-C, DGI-CA and DQI-I).
Abbreviations: DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; GI, Glycemic index; GL, Glycemic load; HEI-C, Healthy Eating Index-Canada; SD, Standard Deviation.

Table J-10: The Interrelationship between Glycemic Index and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	GI<48					GI≥48					p-value[1]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Weight for age z-score[2,3]	1.28	1.49	1.23	-0.12	2.38	1.04	1.49	1.02	-0.22	2.30	0.66
Height for age z-score[2,3]	0.85	0.99	0.74	0.04	1.44	0.07	1.12	0.23	-0.53	0.60	0.05
BMI for age z-score[2,3]	0.97	1.35	1.05	-0.37	2.24	0.98	1.47	1.54	-0.26	2.21	0.10
Waist circumference (cm)[4]	78	16	79	62	90	81	21	67	63	98	0.57
Hip circumference (cm)[4]	95	17	93	86	100	96	16	91	83	109	0.86
Waist to hip[4]	0.82	0.09	0.81	0.74	0.88	0.83	0.11	0.81	0.72	0.91	0.80
Waist to height[4]	0.48	0.09	0.46	0.39	0.57	0.48	0.11	0.41	0.39	0.56	0.87
%Fat free mass[5]	74.8	13.6	77.0	65.9	84.2	78.4	14.1	82.9	68.4	87.1	0.56
Fat free mass (kg)[5]	49.0	17.4	48.9	37.1	53.0	51.7	12.9	46.9	42.9	61.9	0.66
%Body Fat[5]	25.2	13.6	23.0	15.8	34.1	21.6	14.1	17.1	12.9	31.6	0.56
Fat mass (kg)[5]	24.9	21.9	16.8	7.2	39.5	18.3	18.5	8.7	6.4	28.5	0.37

[1]p-values <0.05 are considered statistically significant.
[2]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[3]N= 14 in children with GI <48 and n=16 in children with GI ≥48.
[4]N= 10-11 in children with GI <48 and n=15 in children with GI ≥48.
[5]N= 13 in children with GI <48 and n=13 in children with GI ≥48.
Abbreviations: BMI, Body Mass Index; GI, Glycemic Index; IQ, Interquartile range; SD, Standard Deviation.

Table J-11: The Interrelationship between Glycemic Load and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	GL<108					GL≥108					p-value[1]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Weight for age z-score[2,3]	1.63	1.51	1.78	0.72	2.55	0.74	1.35	0.31	-0.48	1.84	0.10
Height for age z-score[2,3]	0.76	1.04	0.61	-0.13	1.44	0.16	1.13	0.23	-0.51	0.88	0.14
BMI for age z-score[2,3]	1.34	1.35	1.54	0.99	2.25	0.66	1.39	-0.13	-0.38	2.07	0.18
Waist circumference (cm)[4]	82	19	82	63	96	78	20	66	63	89	0.72
Hip circumference (cm)[4]	98	20	98	86	122	94	13	91	83	106	0.57
Waist to hip[4]	0.84	0.09	0.85	0.78	0.90	0.82	0.11	0.80	0.73	0.91	0.57
Waist to height[4]	0.48	0.09	0.45	0.39	0.57	0.48	0.11	0.41	0.39	0.56	0.70
%Fat free mass[5]	69.3	12.6	68.5	57.6	80.5	82.9	11.6	84.1	74.5	92.1	0.01
Fat free mass (kg)[5]	52.8	17.1	51.0	43.0	64.9	48.2	13.4	46.0	39.6	49.4	0.72
%Body Fat[5]	30.7	12.6	31.6	19.6	42.4	17.1	11.6	16.0	7.9	25.5	0.01
Fat mass (kg)[5]	28.5	22.0	22.0	10.6	45.5	15.6	16.9	8.6	4.0	16.8	0.11

[1]p-values <0.05 are considered statistically significant.
[2]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[3]N= 15 in children with GL <108 and n=16 in children with GL ≥108.
[4]N= 11-12 in children with GL <108 and n=14 in children with GL ≥108.
[5]N= 12 in children with GL <108 and n=14 in children with GL ≥108.
Abbreviations: BMI, Body Mass Index; GL, Glycemic Load; IQ, Interquartile range; SD, Standard Deviation.

Table J-12: The Interrelationship between Healthy Eating Index-Canada and Anthropometrics and Body Composition in

Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	HEI-C <70					HEI-C ≥70					p-value[1]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Weight for age z-score[2,3]	1.80	1.52	2.05	1.17	2.77	0.51	1.13	0.27	-0.36	1.29	0.01
Height for age z-score[2,3]	0.44	1.25	0.52	-0.03	1.50	0.44	1.00	0.15	-0.43	1.22	0.99
BMI for age z-score[2,3]	1.56	1.43	2.04	1.13	2.49	0.39	1.10	-0.06	-0.37	1.07	0.02
Waist circumference (cm)[4]	90	20	92	79	110	68	10	64	63	71	0.01
Hip circumference (cm)[4]	104	16	106	91	122	85	8	86	82	91	<0.01
Waist to hip[4]	0.85	0.10	0.86	0.80	0.91	0.79	0.10	0.76	0.71	0.85	0.10
Waist to height[4]	0.52	0.11	0.54	0.42	0.61	0.43	0.07	0.40	0.39	0.45	0.07
%Fat free mass[5]	70.5	13.89	68.4	57.6	84.2	82.7	10.8	83.4	77.5	89.8	0.04
Fat free mass (kg)[5]	60.6	13.1	61.9	49.1	71.3	40.0	8.6	41.1	36.1	47.7	<0.01
%Body Fat[5]	29.5	13.9	31.6	15.8	42.4	17.3	10.8	16.6	10.2	22.5	0.04
Fat mass (kg)[5]	34.3	21.1	30.8	15.5	51.5	8.8	6.8	7.2	4.0	8.7	<0.01

[1]p-values <0.05 are considered statistically significant.
[2]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[3]N= 15 in children with HEI-C <70 and n=16 in children with HEI-C≥70.
[4]N= 14 in children with HEI-C <70 and n=11-12 in children with HEI-C≥70.
[5]N= 13 in children with HEI-C <70 and n=13 in children with HEI-C≥70.
Abbreviations: BMI, Body Mass Index; HEI-C, Healthy Eating Index-Canada; IQ, Interquartile range; SD, Standard Deviation.

Table J-13: The Interrelationship between Dietary Guideline Index for Children and Adolescents and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DGI-CA<68	DGI-CA ≥68	p-value[1]

	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Weight for age z-score[2,3]	1.20	1.52	1.62	-0.14	2.48	1.16	1.64	1.13	-0.28	2.84	0.94
Height for age z-score[2,3]	0.21	1.29	0.38	-0.42	0.87	0.54	0.98	0.32	-0.01	1.07	0.22
BMI for age z-score[2,3]	1.26	1.73	1.94	-0.25	2.73	1.16	1.63	1.10	-0.35	2.89	0.87
Waist circumference (cm)[4]	83	19	83	64	96	76	19	66	63	87	0.27
Hip circumference (cm)[4]	100	17	98	88	109	91	15	86	83	98	0.18
Waist to hip[4]	0.83	0.09	0.81	0.78	0.90	0.83	0.11	0.81	0.73	0.92	0.97
Waist to height[4]	0.48	0.10	0.44	0.41	0.56	0.47	0.11	0.40	0.39	0.57	0.70
%Fat free mass[5]	76.6	14.4	82.9	67.1	87.1	76.6	13.6	77.5	68.4	83.7	0.80
Fat free mass (kg)[5]	52.2	14.1	49.1	42.9	62.6	48.4	16.4	47.7	37.0	49.4	0.54
%Body Fat[5]	23.4	14.4	17.1	12.9	32.9	23.4	13.6	22.5	16.3	31.6	0.80
Fat mass (kg)[5]	24.4	20.4	15.5	8.5	45.1	18.7	20.3	8.7	6.7	23.4	0.46

[1]p-values <0.05 are considered statistically significant.
[2]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[3]N= 16 in children with DGI-CA <68 and n=15 in children with DGI-CA ≥68.
[4]N= 14 in children with DGI-CA <68 and n=11-12 in children with DGI-CA ≥68.
[5]N= 13 in children with DGI-CA <68 and n=13 in children with DGI-CA ≥68.
Abbreviations: BMI, Body Mass Index; DGI-CA, Dietary Guideline Index for Children and Adolescents; IQ, Interquartile range; SD, Standard Deviation.

Table J-14: The Interrelationship between Diet Quality Index–International and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQI-I <60					DQI-I ≥60					p-value[1]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Weight for age z-score[2,3]	1.59	1.81	2.28	0.48	3.00	0.95	1.39	1.02	-0.37	2.19	0.29
Height for age z-score[2,3]	0.00	1.32	0.37	-0.58	0.75	0.57	1.01	0.36	-0.04	1.12	0.41

BMI for age z-score[2,3]	1.77	1.91	2.70	1.17	3.00	0.90	1.46	0.69	-0.34	2.56	0.10
Waist circumference (cm)[4]	88	20	92	64	98	74	17	66	63	82	0.10
Hip circumference (cm)[4]	102	19	106	86	122	91	13	91	83	98	0.10
Waist to hip[4]	0.85	0.09	0.87	0.78	0.91	0.81	0.11	0.80	0.71	0.88	0.33
Waist to height[4]	0.51	0.11	0.54	0.38	0.58	0.46	0.09	0.41	0.39	0.57	0.62
%Fat free mass[5]	68.8	15.4	67.1	55.4	84.4	80.7	11.1	82.9	74.5	89.8	0.07
Fat free mass (kg)[5]	59.7	13.8	57.6	49.4	71.3	45.3	13.6	45.1	37.0	48.9	0.02
%Body Fat[5]	31.2	15.4	32.9	15.6	44.6	19.3	11.1	17.1	10.2	25.5	0.07
Fat mass (kg)[5]	34.4	25.5	30.7	14.1	53.0	14.8	12.9	8.7	6.7	20.6	0.06

[1]p-values <0.05 are considered statistically significant.
[2]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[3]N= 11 in children with DQI-I<60 and n=20 in children with DQI-I ≥60.
[4]N= 10 in children with DQI-I<60 and n=15-16 in children with DQI-I ≥60.
[5]N= 9 in children with DQI-I<60 and n=17 in children with DQI-I ≥60.
Abbreviations: BMI, Body Mass Index; DQI-I, Diet Quality Index-International; IQ, Interquartile range; SD, Standard Deviation.

Table J-15: The Interrelationship between Healthy Eating Index-Canada (Adequacy) and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	HEI-C (Adequacy) <34[1]					HEI-C (Adequacy) ≥34[1]					p-value[2]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Weight for age z-score[3,4]	1.95	1.47	2.67	1.52	3.00	0.45	1.28	0.33	-0.47	1.23	0.01
Height for age z-score[3,4]	0.53	1.34	0.39	0.24	1.79	0.22	0.95	0.14	-0.51	0.60	0.46
BMI for age z-score[3,4]	1.97	1.65	2.75	1.54	3.00	0.50	1.34	-0.05	-0.45	1.20	0.01
Waist circumference (cm)[5]	92	18	93	80	109.5	66	7	64	63	66	<0.01
Hip circumference (cm)[5]	105	16	106	96	122	84	7	86	82	90	<0.01
Waist to hip[5]	0.87	0.09	0.89	0.8	0.92	0.77	0.09	0.74	0.71	0.81	0.01
Waist to height[5]	0.53	0.11	0.55	0.42	0.61	0.42	0.05	0.40	0.39	0.42	0.03
%Fat free mass[6]	69.1	12.9	68.4	57.6	74.5	84.1	10.1	83.7	80.6	89.8	0.01
Fat free mass (kg)[6]	60.9	12.6	61.9	49.1	71.3	39.7	8.3	41.1	36.1	46.9	<0.01
%Body Fat[6]	30.9	12.9	31.6	25.5	42.4	16.0	10.1	16.3	10.2	19.4	0.01
Fat mass (kg)[6]	35.4	19.9	30.7	16.8	51.5	7.71	5.78	6.65	4.03	8.57	<0.01

[1]HEI-C (Adequacy) is the sum score of fruit and vegetables, grains, milk and alternatives and meat and alternatives (Maximum score is 50).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group) (http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 15 in children with HEI-C (Adequacy) <34 and n=16 in children with HEI-C (Adequacy) ≥34.
[5]N= 14 in children with HEI-C (Adequacy) <34 and n=11-12 in children with HEI-C (Adequacy) ≥34.
[6]N= 13 in children with HEI-C (Adequacy) <34 and n=13 in children with HEI-C (Adequacy) ≥34.
Abbreviations: BMI, Body Mass Index; IQ, Interquartile range; HEI-C, Healthy Eating Index-Canada; SD, Standard Deviation.

Table J-16: The Interrelationship between Dietary Guideline Index for Children and Adolescents (Adequacy) and

Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DGI-CA (Adequacy) <26[1]					DGI-CA (Adequacy) ≥26[1]					p-value[2]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Weight for age z-score[3,4]	1.93	1.45	2.48	1.52	3.00	0.56	1.38	0.48	-0.48	1.32	0.05
Height for age z-score[3,4]	0.55	1.38	0.55	0.24	1.79	0.22	0.92	0.16	-0.46	0.57	0.38
BMI for age z-score[3,4]	1.93	1.68	2.79	1.54	3.00	0.63	1.42	0.07	-0.35	1.22	0.10
Waist circumference (cm)[5]	94	17	93	83	110	67	10	64	62	67	0.01
Hip circumference (cm)[5]	105	16	106	97	117	88	12	86	83	91	0.01
Waist to hip[5]	0.89	0.07	0.90	0.83	0.93	0.76	0.08	0.74	0.71	0.80	0.01
Waist to height[5]	0.54	0.11	0.55	0.44	0.63	0.43	0.07	0.40	0.39	0.42	0.08
%Fat free mass[6]	69.8	12.5	69.1	60.7	79.4	82.4	12.2	83.6	77.5	92.1	0.02
Fat free mass (kg)[6]	60.2	15.5	62.3	48.4	73.8	41.8	8.1	43.0	37.0	48.0	<0.01
%Body Fat[6]	30.2	12.5	30.9	20.7	39.4	17.6	12.2	16.5	7.9	22.5	0.02
Fat mass (kg)[6]	30.5	21.5	24.6	14.8	45.5	13.9	15.9	7.8	5.8	14.2	0.01

[1]DGI-CA (Adequacy) is the sum score of fruit and vegetables, grains, milk and alternatives and meat and alternatives (Maximum score is 40).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group) (http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 14 in children with DGI-CA (Adequacy) <27 and n=17 in children with DGI-CA (Adequacy) ≥27.
[5]N= 12 in children with DGI-CA (Adequacy) <27 and n=13-14 in children with DGI-CA (Adequacy) ≥27.
[6]N= 12 in children with DGI-CA (Adequacy) <27 and n=14 in children with DGI-CA (Adequacy) ≥27.
Abbreviations: BMI, Body Mass Index; DGI-CA, Dietary Guideline Index for Children and Adolescents; IQ, Interquartile range; SD, Standard Deviation.

Table J-17: The Interrelationship between Diet Quality Index-International (Adequacy) and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQI-I (Adequacy) <26[1]	DQI-I (Adequacy) ≥26[1]	p-value[2]

	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	
Weight for age z-score[3,4]	2.07	1.32	2.68	1.52	3.00	0.44	1.35	0.18	-0.48	1.32	<0.01
Height for age z-score[3,4]	0.62	1.38	0.73	0.38	1.79	0.16	0.90	0.12	-0.46	0.37	0.27
BMI for age z-score[3,4]	2.06	1.52	2.82	1.54	3.00	0.52	1.45	-0.17	-0.54	1.22	0.01
Waist circumference (cm)[5]	93	17	95	80	110	66	9	63	62	65	<0.01
Hip circumference (cm)[5]	106	17	107	97	123	87	9	86	83	91	<0.01
Waist to hip[5]	0.89	0.08	0.90	0.81	0.93	0.77	0.09	0.74	0.71	0.81	<0.01
Waist to height[5]	0.54	0.11	0.56	0.44	0.63	0.42	0.06	0.40	0.39	0.42	0.01
%Fat free mass[6]	67.9	11.1	68.4	57.6	74.5	85.3	10.2	87.1	82.9	92.1	<0.01
Fat free mass (kg)[6]	61.2	12.3	61.9	49.1	71.3	39.4	8.0	41.1	36.1	45.1	<0.01
% Body Fat[6]	32.1	11.1	31.6	25.5	42.4	14.7	10.2	12.9	7.9	17.1	<0.01
Fat mass (kg)[6]	33.1	20.5	28.5	15.5	51.5	10.1	11.8	6.7	4.0	8.6	<0.01

[1]DQI-I (Adequacy) is the sum score of Fruit and Vegetables, Grains, Fibre, Protein, Iron, Calcium, Vitamin C (Maximum score is 40).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 14 in children with DQI-I (Adequacy) <26 and n=17 in children with DQI-I (Adequacy) ≥26.
[5]N= 12-13 in children with DQI-I (Adequacy) <26 and n=13 in children with DQI-I (Adequacy) ≥26.
[6]N= 13 in children with DQI-I (Adequacy) <26and n=13 in children with DQI-I (Adequacy) ≥26.
Abbreviations: BMI, Body Mass Index; DQI-I, Diet Quality Index- International; IQ, Interquartile range; SD, Standard Deviation.

Table J-18: The Interrelationship between Healthy Eating Index-Canada (Moderation) and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	HEI-C (Moderation) <30[1]					**HEI-C (Moderation) ≥30[1]**					**p-value[2]**
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	

Weight for age z-score[3,4]	1.62	1.62	2.28	0.48	2.73	0.86	1.46	1.02	-0.45	1.74	0.19
Height for age z-score[3,4]	0.10	1.21	0.38	-0.06	0.57	0.56	1.09	0.28	-0.26	1.17	0.27
BMI for age z-score[3,4]	1.73	1.77	2.6	1.17	3.00	0.84	1.50	0.69	-0.35	2.51	0.14
Waist circumference (cm)[5]	87	21	92	63.5	104	73	15	66	63	80	0.10
Hip circumference (cm)[5]	103	19	106	87	123	90	10	90	83	96	0.04
Waist to hip[5]	0.84	0.09	0.86	0.79	0.90	0.81	0.11	0.8	0.73	0.85	0.41
Waist to height[5]	0.51	0.11	0.54	0.40	0.59	0.45	0.09	0.41	0.39	0.46	0.33
%Fat free mass[6]	73.1	15.6	70.5	57.6	87.1	78.8	12.4	81.8	72.2	86.9	0.44
Fat free mass (kg)[6]	56.9	14.2	55.3	44.0	71.3	46.2	14.5	47.3	36.6	49.3	0.08
% Body Fat[6]	26.9	15.6	29.5	12.9	42.4	21.2	12.4	18.25	13.2	27.9	0.44
Fat mass (kg)[6]	31.6	20.5	35.1	14.1	51.5	15.3	17.7	8.6	6.2	18.7	0.06

[1]HEI-C (Moderation) is the sum score of Fat, Saturated Fat, Cholesterol, and *other foods* Groups (Maximum score is 40).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 13 in children with HEI-C (Moderation) <30 and n=18 in children with HEI-C (Moderation) ≥30.
[5]N= 12 in children with HEI-C (Moderation) <30 and n=13-14 in children with HEI-C (Moderation) ≥30.
[6]N= 10 in children with HEI-C (Moderation) <30 and n=16 in children with HEI-C (Moderation) ≥30.
Abbreviations: BMI, Body Mass Index; HEI-C, Healthy Eating Index-Canada; IQ, Interquartile range; SD, Standard Deviation.

Table J-19: The Interrelationship between Ditary Guideline Index for Childern and Adolescents (Moderation) and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DGI-CA (Moderation) <28[1]					DGI-CA (Moderation) ≥28[1]					p-value[2]
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	
Weight for age z-score[3,4]	1.35	1.35	1.71	0.18	2.63	1.02	1.75	1.02	-0.37	2.92	0.56

Height for age z-score[3,4]	0.21	1.28	0.37	-0.56	0.75	0.53	1.02	0.36	0.06	1.03	0.45
BMI for age z-score[3,4]	1.48	1.45	2.33	-0.17	2.70	0.96	1.83	1.05	-0.45	2.95	0.39
Waist circumference (cm)[5]	81	18	80	64	95	78	21	67	63	90	0.47
Hip circumference (cm)[5]	99	14	96	91	107	92	18	86	83	104	0.26
Waist to hip[5]	0.81	0.10	0.80	0.72	0.90	0.84	0.10	0.83	0.75	0.91	0.47
Waist to height[5]	0.49	0.10	0.46	0.41	0.56	0.46	0.11	0.40	0.38	0.57	0.23
%Fat free mass[6]	77.9	12.6	81.8	70.5	85.8	75.5	15.0	77.3	65.9	89.5	0.66
Fat free mass (kg)[6]	52.4	13.6	47.1	42.0	64.9	48.5	16.5	47.8	37.0	57.6	0.53
% Body Fat[6]	22.2	12.6	18.3	14.3	29.5	24.5	15.0	22.8	10.5	34.1	0.66
Fat mass (kg)[6]	22.6	19.1	14.8	8.6	37.9	20.7	21.7	11.4	5.8	28.5	0.53

[1]DGI-CA (Foods) is the sum score of *other foods* group, beverage and food choice (saturated fat) (Maximum score is 40).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 15 in children with DGI-CA (Foods)<28 and n=16 in children with DGI-CA (Foods) ≥28.
[5]N= 13 in children with DGI-CA (Foods)<28 and n=12-13 in children with DGI-CA (Foods) ≥28.
[6]N= 12 in children with DGI-CA (Foods)<28 and n=14 in children with DGI-CA (Foods) ≥28.
Abbreviations: BMI, Body Mass Index; DGI-CA, Dietary Guideline Index for Children and Adolescents; IQ, Interquartile range; SD, Standard Deviation.

Table J-20: The Interrelationship between Diet Quality Index-International (Moderation) and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQI-I (Moderation) <21[1]					DQI-I (Moderation) ≥21[1]					p-value[2]
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	
Weight for age z-score[3,4]	1.11	1.66	1.52	-0.48	2.68	1.25	1.50	1.32	0.29	2.76	0.80
Height for age z-score[3,4]	0.01	1.07	0.21	-0.46	0.39	0.71	1.14	0.66	0.14	1.48	0.09
BMI for age z-score[3,4]	1.27	1.70	2.33	-0.33	2.75	1.16	1.66	1.16	-0.14	2.89	0.85
Waist circumference (cm)[5]	81	20	75	63	96	78	19	77	62	87	0.57

Hip circumference (cm)[5]	100	16	92	88	109	91	16	86	82	100	0.18
Waist to hip[5]	0.80	0.10	0.79	0.71	0.89	0.85	0.09	0.83	0.80	0.92	0.21
Waist to height[5]	0.49	0.11	0.48	0.40	0.58	0.46	0.10	0.42	0.38	0.57	0.51
%Fat free mass[6]	78.0	12.9	82.9	67.1	87.1	75.2	14.9	77.0	68.4	84.2	0.64
Fat free mass (kg)[6]	52.4	14.4	45.1	42.9	62.6	48.2	16.1	48.0	37.0	57.6	0.49
%Body Fat[6]	21.98	12.9	17.1	12.9	32.9	24.8	14.9	23.0	15.8	31.6	0.64
Fat mass (kg)[6]	22.78	19.7	14.1	8.5	39.5	20.4	21.3	14.2	6.7	23.4	0.70

[1]DQI-I (Moderation) is the sum score of fat, saturated fat, cholesterol, sodium and *other foods* groups (Maximum score is 30).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 15 in children with DQI-I (Moderation) <21 and n=16 in children with DQI-I (Moderation) ≥21.
[5]N= 14 in children with DQI-I (Moderation) <21 and n=11-2 in children with DQI-I (Moderation) ≥21.
[6]N= 13 in children with DQI-I (Moderation) <21 and n=13 in children with DQI-I (Moderation) ≥21.
Abbreviations: BMI, Body Mass Index; DQI-I, Diet Quality Index- International; IQ, Interquartile range; SD, Standard Deviation.

Table J-21: The Interrelationship between Dietary Guideline Index for Children and Adolescents (Foods) and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DGI-CA (Foods) <5.2[1]					DGI-CA (Foods) ≥5.2[1]					p-value[2]
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	
Weight for age z-score[3,4]	1.33	1.59	1.74	-0.28	2.73	0.97	1.59	1.23	0.18	2.23	0.57
Height for age z-score[3,4]	0.52	0.77	0.39	-0.01	0.75	0.40	1.50	0.38	-0.46	1.17	0.80
BMI for age z-score[3,4]	1.31	1.63	1.54	-0.33	2.88	0.99	1.77	1.05	-0.17	2.89	0.63
Waist circumference (cm)[5]	84	23	79	63	111	76	16	74	64	85	0.37
Hip circumference (cm)[5]	103	16	96	90	122	89	16	86	81	99	0.05
Waist to hip[5]	0.81	0.11	0.78	0.71	0.90	0.85	0.08	0.82	0.80	0.90	0.42

Waist to height[5]	0.48	0.11	0.42	0.38	0.58	0.48	0.10	0.44	0.40	0.57	0.95
%Fat free mass[6]	74.0	16.3	74.5	57.6	87.1	78.6	11.3	77.5	69.8	89.5	0.49
Fat free mass (kg)[6]	52.6	13.8	49.1	43.0	61.9	46.5	15.1	46.9	37.0	49.4	0.31
% Body Fat[6]	26.0	16.3	25.5	12.9	42.4	21.4	11.3	22.5	10.5	30.2	0.49
Fat mass (kg)[6]	29.7	24.6	28.5	8.5	51.5	13.9	10.9	12.6	5.8	20.6	0.14

[1]DGI-CA (Foods) is the sum score of whole grains, and low fat milk (Maximum score is 10).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 13 in children with DGI-CA (Foods)<5.2 and n=14 in children with DGI-CA (Foods) ≥5.2.
[5]N= 11 in children with DGI-CA (Foods) <5.2 and n=12-13 in children with DGI-CA (Foods) ≥5.2.
[6]N= 13 in children with DGI-CA (Foods)< 5.2 and n=11 in children with DGI-CA (Foods) ≥5.2.
Abbreviations: BMI, Body Mass Index; DGI-CA, Dietary Guideline Index for Children and Adolescents; IQ, Interquartile range; SD, Standard Deviation.

Table J-22: The Interrelationship between Dietary Guideline Index for Children and Adolescents (Grains) and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DGI-CA (Grains) <6[1]					DGI-CA (Grains) ≥6[1]					p-value[2]
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	
Weight for age z-score[3,4]	1.51	1.35	1.73	0.26	2.70	0.83	1.72	0.91	-0.86	2.68	0.23
Height for age z-score[3,4]	0.36	1.28	0.50	-0.29	1.03	0.38	1.02	0.32	-0.26	0.57	0.95
BMI for age z-score[3,4]	1.64	1.44	2.36	0.36	2.89	0.76	1.79	0.38	-0.54	2.75	0.14
Waist circumference (cm)[5]	86	20	85	63	98	73	17	65	62	85	0.11
Hip circumference (cm)[5]	100	14	97	89	109	92	17	86	82	100	0.23
Waist to hip[5]	0.85	0.11	0.90	0.74	0.93	0.80	0.08	0.80	0.74	0.84	0.18
Waist to height[5]	0.50	0.11	0.50	0.39	0.61	0.46	0.09	0.41	0.39	0.56	0.30
%Fat free mass[6]	75.9	12.7	76.0	68.4	84.4	77.4	15.3	83.3	61.8	90.8	0.64

Fat free mass (kg)[6]	51.3	13.3	48.5	43.0	61.9	49.2	17.5	46.0	38.3	60.1	0.73
% Body Fat[6]	24.1	12.7	24.0	15.6	31.6	22.6	15.3	16.7	9.2	38.3	0.64
Fat mass (kg)[6]	19.8	17.0	14.9	8.6	28.5	23.7	23.9	10.5	6.2	42.3	0.84

[1]DGI-CA (Grains) is the sum score of the total grains and whole grains (Maximum score is 10).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 16 in children with DQI-I (Grains) <6 and n=15 in children with DQI-I (Grains) ≥6.
[5]N= 12-13 in children with DQI-I (Grains) <6 and n=13 in children with DQI-I (Grains) ≥6.
[6]N= 14 in children with DQI-I (Grains) <6 and n=12 in children with DQI-I (Grains) ≥6.
Abbreviations: BMI, Body Mass Index; DGI-CA, Dietary Guideline Index for Children and Adolescents; IQ, Interquartile range; SD, Standard Deviation.

Table J-23: The Interrelationship between Dietary Guideline Index for Children and Adolescents (Milk) and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DGI-CA (Milk) <7[1]					DGI-CA (Milk) ≥7[1]					p-value[2]
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	
Weight for age z-score[3,4]	1.80	1.44	2.63	0.54	2.84	0.43	1.37	0.55	-0.45	1.32	0.01
Height for age z-score[3,4]	0.56	1.04	0.38	-0.06	0.99	0.14	1.26	0.24	-0.46	0.75	0.31
BMI for age z-score[3,4]	1.90	1.44	2.60	1.17	2.89	0.38	1.55	0.11	-0.54	1.22	0.01
Waist circumference (cm)[5]	86	19	99	65	98	72	17	64	62	80	0.05
Hip circumference (cm)[5]	102	14	102	91	110	88	16	86	80	96	0.03
Waist to hip[5]	0.84	0.11	0.86	0.72	0.91	0.81	0.09	0.80	0.74	0.85	0.55
Waist to height[5]	0.50	0.10	0.54	0.40	0.57	0.45	0.10	0.41	0.38	0.46	0.25
%Fat free mass[6]	72.2	14.5	69.1	57.6	84.4	81.7	11.3	83.5	75.8	89.7	0.11
Fat free mass (kg)[6]	54.23	15.4	50.4	42.9	62.6	45.7	13.9	46.0	38.3	49.3	0.15
% Body Fat[6]	27.8	14.5	30.9	15.6	42.4	18.3	11.3	16.5	10.4	24.3	0.11

Fat mass (kg)[6]	29.2	21.3	26.0	8. 7	45.1	12.6	15.0	7.9	4.5	14.9	0.02

[1]DGI-CA (Milk) is the sum score of milk and alternatives and low fat milk (Maximum score is 10).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 17 in children with DQI-I (Milk) <7 and n=14 in children with DQI-I (Milk) ≥7.
[5]N= 14 in children with DQI-I (Milk) <7 and n=11-12 in children with DQI-I (Milk) ≥7.
[6]N= 14 in children with DQI-I (Milk) <7 and n=12 in children with DQI-I (Milk) ≥7.
Abbreviations: BMI, body mass index; DGI-CA, Dietary Guideline Index for Children and Adolescents; IQ, Interquartile range; SD, Standard Deviation.

Table J-24: The Interrelationship between Diet Quality Index-International (Variety) and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQI-I (Variety) <18[1]					DQI-I (Variety) ≥18[1]					p-value[2]
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	
Weight for age z-score[3,4]	1.57	1.33	1.615	0.805	2.84	0.93	1.67	0.91	-0.48	2.67	0.28
Height for age z-score[3,4]	0.29	1.49	0.31	-0.32	1.03	0.42	0.91	0.37	-0.26	0.75	0.75
BMI for age z-score[3,4]	1.70	1.50	2.42	0.69	3.00	0.91	1.71	1.10	-0.35	2.70	0.20
Waist circumference (cm)[5]	83	16	85	74	95	78	21	65	63	90	0.40
Hip circumference (cm)[5]	100	15	95	87	114	94	17	91	83	107	0.37
Waist to hip[5]	0.84	0.12	0.85	0.75	0.94	0.82	0.09	0.81	0.74	0.88	0.54
Waist to height[5]	0.49	0.10	0.48	0.40	0.57	0.47	0.10	0.41	0.39	0.56	0.73
%Fat free mass[6]	73.6	15.8	77.5	57.6	87.1	78.8	12.0	80.6	68.4	89.5	0.62
Fat free mass (kg)[6]	52.3	16.7	48.9	42.9	67.2	48.8	14.2	47.7	39.1	61.9	0.57
%Body Fat[6]	26.3	15.8	22.5	12.9	42.4	21.2	12.0	19.4	10.5	31.6	0.62
Fat mass (kg)[6]	28.6	23.6	15.5	12.6	51.4	16.4	16.1	8.6	5.8	28.5	0.15

[1]DQI-I (Variety) is the sum score of the variety of food groups and within milk and meat products (Maximum score is 20).

[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 12 in children with DQI-I (Variety) <18 and n=19 in children with DQI-I (Variety) ≥18.
[5]N= 8-9 in children with DQI-I (Variety) <18 and n=17 in children with DQI-I (Variety) ≥18.
[6]N= 11 in children with DQI-I (Variety) <18 and n=15 in children with DQI-I (Variety) ≥18.
Abbreviations: BMI, Body Mass Index; DQI-I, Diet Quality Index- International; IQ, Interquartile range; SD, Standard Deviation.

Table J-25: The Interrelationship between Diet Quality Model within Healthy Eating Index-Canada (Adequacy and Moderation) and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQ Model within HEI-C <60[1]					DQ Model within HEI-C ≥60[1]					p-value[2]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Weight for age z-score[3,4]	1.85	1.46	2.46	1.42	2.87	0.47	1.36	0.18	-0.48	1.32	0.01
Height for age z-score[3,4]	0.34	1.24	0.39	0.08	0.87	0.40	1.07	0.16	-0.46	1.07	0.88
BMI for age z-score[3,4]	1.90	1.60	2.65	1.36	3.00	0.47	1.41	-0.17	-0.54	1.22	0.01
Waist circumference (cm)[5]	90	20	92	79	110	68	10	64	63	71	0.01
Hip circumference (cm)[5]	104	16	106	91	122	85	8	86	82	91	<0.01
Waist to hip[5]	0.85	0.10	0.86	0.80	0.91	0.79	0.01	0.76	0.71	0.85	0.10
Waist to height[5]	0.52	0.191	0.54	0.42	0.61	0.43	0.07	0.40	0.39	0.45	0.07
%Fat free mass[6]	70.5	13.8	68.4	57.6	84.2	82.7	10.8	83.4	77.5	89.8	0.04
Fat free mass (kg)[6]	60.6	13.1	61.9	49.1	71.3	40.0	8.6	41.1	36.1	47.7	<0.01
%Body Fat[6]	29.5	13.9	31.6	15.8	42.4	17.3	10.8	16.6	10.2	22.5	0.04

Fat mass (kg)[6]	34.3	21.1	30.7	15.5	51.5	8.8	6.8	7.21	4.0	8.7	<0.01

[1]DQ Model within HEI-C is the sum score of HEI-C (Adequacy), and HEI-C (Moderation) (Maximum score is 90).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group) (http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 16 in children with DQ Model within HEI-C <60 and n=15 in children with DQ Model within HEI-C ≥60.
[5]N= 14 in children with DQ Model within HEI-C <60 and n=11-12 in children with DQ Model within HEI-C ≥60.
[6]N= 13 in children with DQ Model within HEI-C <60 and n=13 in children with DQ Model within HEI-C ≥60.
Abbreviations: BMI, Body Mass Index; DQ, Diet Quality; HEI-C, Healthy Eating Index-Canada; IQ, Interquartile range; SD, Standard Deviation.

Table J-26: The Interrelationship between Diet Quality Model within Dietary Guideline Index for Children and Adolescents (Adequacy and Moderation) and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQ Model within DGI-CA <54[1]					DQ Model within DGI-CA ≥54[1]					p-value[2]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Weight for age z-score[3,4]	1.17	1.57	1.52	-0.45	2.68	1.19	1.59	1.23	-0.13	2.76	0.97
Height for age z-score[3,4]	0.29	1.29	0.38	-0.26	0.99	0.45	1.02	0.28	-0.24	0.89	0.71
BMI for age z-score[3,4]	1.18	1.76	1.54	-0.33	2.75	1.25	1.61	1.16	-0.31	2.89	0.91
Waist circumference (cm)[5]	83	19	83	64	96	76	19	66	63	87	0.27
Hip circumference (cm)[5]	100	17	98	88	109	91	15	86	83	98	0.18
Waist to hip[5]	0.83	0.09	0.81	0.78	0.90	0.83	0.11	0.81	0.73	0.92	0.97
Waist to height[5]	0.48	0.10	0.44	0.41	0.56	0.47	0.11	0.40	0.39	0.57	0.70
%Fat free mass[6]	76.6	14.4	82.9	67.1	87.1	76.6	13.6	77.5	68.4	83.7	0.80
Fat free mass (kg)[6]	52.2	14.1	49.1	42.9	62.6	48.4	16.4	47.7	37.0	49.4	0.54
%Body Fat[6]	23.4	14.4	17.1	12.9	32.9	23.4	13.6	22.5	16.3	31.6	0.80

Fat mass (kg)[6]	24.4	20.4	15.5	8.5	45.1	18.70	20.3	8.7	6.7	23.4	0.46

[1]DQ Model within DGI-CA is the sum score of DGI-CA (Adequacy), and DGI-CA (Moderation) (Maximum score is 80).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group) (http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 15 in children with DQ Model within DGI-CA <54 and n=16 in children with DQ Model within DGI-CA ≥54.
[5]N= 14 in children with DQ Model within DGI-CA <54 and n=11-12 in children with DQ Model within DGI-CA ≥54.
[6]N= 13 in children with DQ Model within DGI-CA <54 and n=13 in children with DQ Model within DGI-CA ≥54.
Abbreviations: BMI, Body Mass Index; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQ, Diet Quality; IQ, Interquartile range; SD, Standard Deviation.

Table J-27: The Interrelationship between Diet Quality Model within Diet Quality Index-International (Adequacy and Moderation) and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQ Model within DQI-I <45[1]					DQ Model within DQI-I ≥45[1]					p-value[2]
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	
Weight for age z-score[3,4]	1.85	1.46	2.46	1.42	2.87	0.47	1.36	0.18	-0.48	1.32	0.01
Height for age z-score[3,4]	0.34	1.24	0.39	0.08	0.87	0.40	1.07	0.16	-0.46	1.07	0.88
BMI for age z-score[3,4]	1.90	1.60	2.65	1.36	3.0	0.47	1.41	-0.17	-0.54	1.22	0.01
Waist circumference (cm)[5]	90	20	92	79	110	68	10	64	63	71	0.01
Hip circumference (cm)[5]	104	16	106	91	122	85	8	86	82	91	<0.01
Waist to hip[5]	0.85	0.10	0.86	0.80	0.91	0.79	0.10	0.60	0.71	0.85	0.10
Waist to height[5]	0.52	0.11	0.54	0.42	0.61	0.43	0.07	0.40	0.39	0.45	0.07
%Fat free mass[6]	70.5	13.9	68.4	57.6	84.2	82.7	10.8	83.4	77.5	89.8	0.04
Fat free mass (kg)[6]	60.6	13.1	61.9	49.1	71.3	40.0	8.6	41.1	36.1	47.7	<0.01
%Body Fat[6]	29.5	13.9	31.6	15.8	42.4	17.3	10.8	16.6	10.2	22.5	0.04

Fat mass (kg)[6]	34.3	21.1	30.7	15.5	51.5	8.8	6.8	7.21	4.0	8.7	<0.01

[1]DQ Model within DQI-I is the sum score of DQI-I (Adequacy), and DQI-I (Moderation) (Maximum score is 70).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group) (http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 16 in children with DQ Model within DQI-I <45 and n=15 in children with DQ Model within DQI-I ≥45.
[5]N= 14 in children with DQ Model within DQI-I <45 and n=11-12 in children with DQ Model within DQI-I ≥45.
[6]N= 13 in children with DQ Model within DQI-I <45 and n=13 in children with DQ Model within DQI-I ≥45.
Abbreviations: BMI, Body Mass Index; IQ, DQ, Diet Quality; DQI-I, Diet Quality Index-International; Interquartile range; SD, Standard Deviation.

Table J-28: The interrelationship between Glycemic Index, Glycemic Load and Diet Quality Scores Anthropometric and Body Composition

Dependent variable[$]	Independent variables[*]	p-value of independent variables[#]	R^2	p-value of the model [#]
		Anthropometric		
BMI for age z-score	HEI-C GL HEI-C *GL	0.03 0.17 0.10	0.31	0.02
		Body composition		
Log % Fat free mass	HEI-C GL HEI-C *GL	0.04 0.02 0.57	0.40	0.01
Log % Fat free mass	DQI-I GL	0.03 0.01	0.35	<0.01
Log Fat mass	HEI-C GL HEI-C *GL	<0.01 0.06 0.09	0.61	<0.01
Log Fat mass	HEI-C GI	<0.01 0.09	0.53	<0.01

[$] Variables demonstrating skewed distributions were log transformed.
[*]All independent variables are category variables above and below the median: GI (≥ and <48), GL (≥ and <108) and HEI-C (≥ and <70) or above and below the cut-off of good vs poor diet quality DQI-I (≥ and <60).
[#]p-value<0.05 are considered statistically significant.
Abbreviations: BMI, body mass index; DQI-I, Diet Quality Index-International; GI, Glycemic Index; GL, Glycemic Load; HEI-C, Healthy Eating Index-Canada; NAFLD, Non-Alcoholic Fatty Liver Disease.

Table J-29: The Interrelationship between Glycemic Index and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	GI<48[1]					GI≥48[1]					p-value[2]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	26	15	19	15	32	57	57	27	14	93	0.30
AST (U/L)	25	6	26	19	32	38	22	32	20	49	0.16
γGT (U/L)	11	8	7	5	15	19	34	5	5	16	0.95
Glucose (mmol/L)	4.8	0.6	4.7	4.5	5.1	4.8	0.5	4.9	4.5	5.2	0.65
Insulin (mU/L)	14	13	11	5	15	21	17	18	9	24	0.14
HOMA-IR[3]	3.7	4.1	2.2	1.0	5.9	4.3	3.3	3.8	2.1	4.9	0.4
Triglyceride (mmol/L)	0.9	0.5	0.8	0.5	1.1	1.0	0.5	1.0	0.6	1.5	0.42
Total cholesterol (mmol/L)	3.5	1.0	3.6	3.2	3.9	4.1	0.7	4.2	3.6	4.5	0.02
HDL (mmol/L)	1.18	0.28	1.12	0.99	1.49	1.13	0.27	1.04	0.88	1.41	0.50
LDL (mmol/L)	2.4	1.1	2.3	1.6	2.5	2.5	0.6	2.5	2.0	2.7	0.11

[1]N= 14-15 in children with GI <48 and n=14-16 in children with GI ≥48.
[2]p-values <0.05 are considered statistically significant.
[3]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; GI, Glycemic Index; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-30: The Interrelationship between Glycemic Load and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	GL<108[1]					GL≥108[1]					p-value[2]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	35	36	28	13	45	48	52	19	16	75	0.59
AST (U/L)	29	17	26	19	32	34	18	29	22	37	0.13
γGT (U/L)	13	11	10	5	16	17	34	5	5	14	0.43
Glucose (mmol/L)	4.8	0.50	4.8	4.5	5.1	4.8	0.5	4.9	4.5	5.2	0.81
Insulin (mU/L)	18	17	14	7	25	15	14	10	5	19	0.32
HOMA-IR[3]	4.7	4.0	2.8	1.6	5.9	3.4	3.3	2.1	0.9	4.2	0.25
Triglyceride (mmol/L)	0.95	0.51	0.92	0.54	1.20	0.95	0.54	0.69	0.55	1.37	0.91
Total cholesterol (mmol/L)	3.7	1.0	3.7	3.2	4.2	4.0	0.8	3.9	3.5	4.4	0.32
HDL (mmol/L)	1.13	0.28	1.01	0.88	1.37	1.18	0.28	1.11	0.94	1.46	0.59
LDL (mmol/L)	2.5	1.0	2.3	2.0	2.6	2.4	0.7	2.4	1.8	2.7	0.95

[1]N= 13-15 in children with GL <108 and n=15-16 in children with GL ≥108.
[2]p-values <0.05 are considered statistically significant.
[3]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; GL, Glycemic Load; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-31: The Interrelationship between Healthy Eating Index-Canada and Liver Enzymes and Cardio-Metabolic in Children

with Non-Alcoholic Fatty Liver Disease and Lean Controls

	HEI-C <70[1]					HEI-C ≥70[1]					p-value[2]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	57	54	39	17	75	26	25	17	13	21	0.04
AST (U/L)	36	22	30	21	38	27	11	26	19	33	0.30
γGT (U/L)	16	11	15	5	21	15	35	5	5	5	<0.01
Glucose (mmol/L)	5.0	0.4	5.1	4.7	5.3	4.6	0.5	4.5	4.3	4.9	0.03
Insulin (mU/L)	24	18	18	12	42	11	9	9	5	10	0.01
HOMA-IR[3]	5.5	4.2	4.0	2.7	9.3	2.3	1.9	1.8	1.0	2.1	0.01
Triglyceride (mmol/L)	1.11	0.50	1.00	0.78	1.53	0.78	0.50	0.58	0.54	0.98	0.05
Total cholesterol (mmol/L)	4.0	0.9	3.9	3.3	4.4	3.6	0.9	3.7	3.5	4.2	0.64
HDL (mmol/L)	1.07	0.27	1.02	0.84	1.25	1.25	0.25	1.33	0.99	1.48	0.06
LDL (mmol/L)	2.6	1.1	2.5	1.7	3.0	2.23	0.5	2.3	1.9	2.6	0.65

[1]N= 13-15 in children with HEI-C <70 and n=15-16 in children with HEI-C ≥70.
[2]p-values <0.05 are considered statistically significant.
[3]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; HDL, High density lipoprotein; HEI-C, Healthy Eating Index-Canada; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-32: The Interrelationship between Dietary Guideline Index for Children and Adolescents and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DGI-CA <68[1]					DGI-CA ≥68[1]					p-value[2]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	47	42	25	17	75	37	48	17	13	45	0.24
AST (U/L)	34	18	32	21	38	29	17	25	19	32	0.19
γGT (U/L)	20	33	11	5	16	10	10	5	5	10	0.21
Glucose (mmol/L)	4.9	0.5	5.1	4.8	5.2	4.7	0.5	4.5	4.5	4.9	0.17
Insulin (mU/L)	18	17	13	7	21	17	14	10	7	25	0.81
HOMA-IR[3]	3.6	3.1	2.8	1.6	4.4	4.4	4.3	2.1	1.3	5.9	0.92
Triglyceride (mmol/L)	1.0	0.5	1.0	0.5	1.3	0.9	0.6	0.6	0.5	1.2	0.53
Total cholesterol (mmol/L)	4.0	0.8	4.1	3.5	4.5	3.6	1.0	3.6	3.2	4.0	0.15
HDL (mmol/L)	1.16	0.29	1.09	0.88	1.46	1.16	0.26	1.09	0.92	1.35	0.97
LDL (mmol/L)	2.4	0.7	2.5	1.9	2.6	2.5	1.0	2.3	1.8	2.8	0.50

[1]N= 15-16 in children with DGI-CA <68 and n=14-15 in children with DGI-CA ≥68.
[2]p-values <0.05 are considered statistically significant.
[3]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST; Aspartate aminotransferase, DGI-CA, Dietary Guideline Index for Children and Adolescents; γ-GT, γ-glutamyltransferase; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-33: The Interrelationship between Diet Quality Index-International and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQI-I <60[1]	DQI-I ≥60[1]	p-value[2]

	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	53	45	45	13	92	36	45	18	15	32	0.42
AST (U/L)	34	20	30	19	38	31	16	26	20	33	0.82
γGT (U/L)	15	11	11	5	16	16	31	5	5	12	0.16
Glucose (mmol/L)	5.0	0.5	5.1	4.7	5.3	4.7	0.5	4.7	4.5	5.1	0.13
Insulin (mU/L)	26	18	19	13	47	12	11	10	5	13	0.02
HOMA-IR[3]	5.4	3.8	4.2	2.7	8.8	3.2	3.5	2.1	1.0	4.9	0.06
Triglyceride (mmol/L)	1.0	0.5	1.0	0.6	1.4	0.9	0.5	0.7	0.5	1.2	0.39
Total cholesterol (mmol/L)	4.0	0.9	4.0	3.3	4.5	3.7	0.9	3.6	3.4	4.3	0.56
HDL (mmol/L)	1.03	0.25	0.88	0.83	1.16	1.23	0.26	1.31	1.00	1.47	0.05
LDL (mmol/L)	2.5	0.7	2.5	2.0	2.6	2.4	0.9	2.3	1.8	2.7	0.44

[1]N= 10-11 in children with DQI-I <60 and n=18-20 in children with DQI-I ≥60.

[2]p-values <0.05 are considered statistically significant.

[3]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].

Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; DQI-I, Diet Quality Index-International; γ-GT, γ-glutamyltransferase; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-34: The Interrelationship between Healthy Eating Index-Canada (Adequacy) and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	HEI-C (Adequacy) <34[1,2]					HEI-C (Adequacy) ≥34[1,2]					p-value[3]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	

ALT (U/L)	58	55	33	17	92	26	25	17	13	21	0.02
AST (U/L)	38	22	32	25	38	27	11	25	19	33	0.10
γGT (U/L)	16	11	14	5	21	15	34	5	5	8	0.01
Glucose (mmol/L)	5.1	0.4	5.1	4.7	5.4	4.6	0.4	4.5	4.4	4.9	<0.01
Insulin (mU/L)	24	18	18	12	42	11	8	9	5	10	0.01
HOMA-IR[4]	5.1	3.8	3.8	2.7	8.8	2.9	3.3	2.0	2.0	4.4	0.03
Triglyceride (mmol/L)	1.1	0.6	1.0	0.8	1.6	0.8	0.4	0.6	0.5	1.0	0.06
Total cholesterol (mmol/L)	3.7	1.2	3.7	3.1	4.2	3.9	0.5	3.7	3.5	4.3	0.36
HDL (mmol/L)	1.05	0.24	1.01	0.85	1.16	1.26	0.27	1.34	0.98	1.49	0.04
LDL (mmol/L)	2.4	0.8	2.5	1.7	2.8	2.5	0.9	2.4	2.0	2.6	0.95

[1]HEI-C (Adequacy) is the sum score of fruit and vegetables, grains, milk and alternatives and meat and alternatives (Maximum score is 50).
[2]N= 13-15 in children with HEI-C (Adequacy) <34 and n=15-16 in children with HEI-C (Adequacy) ≥34.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; HEI-C, Healthy Eating Index-Canada; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-35: The Interrelationship between Dietary Guideline Index for Children and Adolescents (Adequacy) and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DGI-CA (Adequacy) <26[1,2]					**DGI-CA (Adequacy) ≥26[1,2]**					**p-value[3]**
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	

ALT (U/L)	62	55	39	28	92	25	24	16	13	19	<0.01
AST (U/L)	40	22	34	27	44	26	10	24	19	27	0.01
γGT (U/L)	16	12	12	5	21	15	32	5	5	10	0.03
Glucose (mmol/L)	5.2	0.3	5.1	5.0	5.4	4.5	0.4	4.5	4.3	4.8	<0.01
Insulin (mU/L)	25	18	19	12	42	11	8	9	5	15	0.01
HOMA-IR[4]	5.3	3.8	4.0	2.7	8.8	2.9	3.3	2.0	1.0	3.6	0.02
Triglyceride (mmol/L)	1.2	0.6	1.0	0.8	1.6	0.8	0.4	0.6	0.5	1.0	0.04
Total cholesterol (mmol/L)	3.8	1.2	3.7	3.1	4.2	3.9	0.5	3.7	3.5	4.3	0.55
HDL (mmol/L)	1.03	0.22	1.00	0.85	1.12	1.26	0.27	1.33	1.01	1.48	0.02
LDL (mmol/L)	2.5	0.8	2.5	1.8	2.8	2.4	0.9	2.3	2.1	2.6	0.77

[1]DGI-CA (Adequacy) is the sum score of fruit and vegetables, grains, milk and alternatives and meat and alternatives (Maximum score is 40).
[2]N= 13-15 in children with DGI-CA (Adequacy) <26 and n=15-17 in children with DGI-CA (Adequacy) ≥26.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DGI-CA, Dietary Guideline Index for Children and Adolescents; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-36: The Interrelationship between Diet Quality Index-International (Adequacy) and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQI-I Adequacy <26[1,2]					DQI-I Adequacy ≥26[1,2]					p-value[3]
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	
ALT (U/L)	58	57	33	17	92	28	25	17	14	21	0.07
AST (U/L)	38	23	30	21	44	28	10	26	20	33	0.31

γGT (U/L)	16	12	12	5	21	15	32	5	5	10	0.03
Glucose (mmol/L)	5.1	0.4	5.1	4.9	5.4	4.6	0.4	4.5	4.5	4.8	<0.01
Insulin (mU/L)	24	18	17	12	42	11	8	9	5	19	0.01
HOMA-IR[4]	5.2	3.8	3.6	2.7	8.8	2.9	3.3	2.0	1.0	4.1	0.03
Triglyceride (mmol/L)	1.1	0.6	1.0	0.8	1.4	0.8	0.4	0.6	0.5	1.0	0.15
Total cholesterol (mmol/L)	3.7	1.2	3.6	3.1	4.2	3.9	0.5	3.8	3.6	4.3	0.25
HDL (mmol/L)	1.05	0.20	1.02	0.88	1.16	1.25	0.30	1.33	0.95	1.49	0.06
LDL (mmol/L)	2.4	0.8	2.3	1.7	2.8	2.5	0.9	2.4	2.1	2.6	0.83

[1]DQI-I (Adequacy) is the sum score of fruit and vegetables, grains, fibre, protein, iron, calcium, vitamin C (Maximum score is 40).
[2]N= 12-14 in children with DQI-I (Adequacy) <26 and n=15-17 in children with DQI-I (Adequacy) ≥26.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DQI-I, Diet Quality Index-International; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-37: The Interrelationship between Healthy Eating Index-Canada (Moderation) and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	HEI-C (Moderation) <30[1,2]					HEI-C (Moderation) ≥30[1,2]					p-value[3]
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	
ALT (U/L)	49	42	33	16	57	36	47	17	14	32	0.21
AST (U/L)	35	18	33	21	38	30	17	26	20	32	0.26
γGT (U/L)	12	10	11	5	16	17	32	5	5	12	0.40
Glucose (mmol/L)	4.9	0.4	4.9	4.7	5.1	4.8	0.6	4.8	4.5	5.2	0.59

Insulin (mU/L)	21	17	17	11	21	15.	14	10	5	24	0.22
HOMA-IR[4]	4.8	4.0	3.8	2.2	4.9	3.4	3.3	2.1	1.0	4.9	0.20
Triglyceride (mmol/L)	1.0	0.5	1.0	0.5	1.4	0.9	0.5	0.7	0.6	1.1	0.45
Total cholesterol (mmol/L)	4.2	0.9	4.2	3.7	4.7	3.5	0.8	3.6	3.2	3.9	0.03
HDL (mmol/L)	1.12	0.31	1.06	0.85	1.37	1.18	0.25	1.105	0.99	1.45	0.38
LDL (mmol/L)	2.9	1.1	2.6	2.1	3.4	2.1	0.5	2.3	1.8	2.5	0.03

[1]HEI-C (Moderation) is the sum score of fat, saturated fat, cholesterol, and *other foods* groups (Maximum score is 40).
[2] N= 11-13 in children with HEI-C (Moderation) <30 and n=17-18 in children with HEI-C (Moderation) ≥30.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; HDL, High density lipoprotein; HEI-C, Healthy Eating Index-Canada; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-38: The Interrelationship between Ditary Guideline Index for Childern and Adolescents (Moderation) and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DGI-CA (Moderation) <28[1,2]					**DGI-CA (Moderation) ≥28[1,2]**					**p-value[3]**
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	
ALT (U/L)	41	32	28	16	57	42	55	18	14	39	0.35
AST (U/L)	31	12	29	20	35	32	22	26	19	33	0.57
γGT (U/L)	19	34	11	5	16	12	12	5	5	10	0.20
Glucose (mmol/L)	4.8	0.5	4.9	4.5	5.3	4.8	0.5	4.8	4.5	5.1	0.75
Insulin (mU/L)	20.2	17.0	15.1	11.8	20.6	15	14	10	6	23	0.26
HOMA-IR[4]	4.7	3.9	3.4	2.7	4.9	3.4	3.4	2.0	1.1	5.4	0.21

Triglyceride (mmol/L)	1.1	0.5	1.0	0.8	1.5	0.8	0.5	0.6	0.5	1.0	0.09
Total cholesterol (mmol/L)	4.1	0.8	4.1	3.7	4.6	3.6	0.9	3.6	3.3	3.9	0.048
HDL (mmol/L)	1.10	0.29	1.01	0.85	1.44	1.21	0.25	1.31	1.00	1.41	0.24
LDL (mmol/L)	2.7	1.0	2.5	2.1	3.0	2.2	0.6	2.2	1.8	2.5	0.11

[1]DGI-CA (Moderation) is the sum score of *other foods* groups, beverage and food choice (saturated fatty) (Maximum score is 40).
[2]N= 12-15 in children with DGI-CA (Moderation) <28 and n=15-16 in children with DGI-CA (Moderation) ≥28.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DGI-CA, Dietary Guideline Index for Children and Adolesacents; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation .

Table J-39: The Interrelationship between Diet Quality Index-International (Moderation) and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQI-I (Moderation) <21[1,2]					DQI-I (Moderation) ≥21[1,2]					p-value[3]
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	
ALT (U/L)	35	28	21	13	52	48	56	20	16	52	0.68
AST (U/L)	28	10	26	19	34	35	22	27	21	34	0.55
γGT (U/L)	9	5	5	5	15	21	34	7	5	26	0.47
Glucose (mmol/L)	4.7	0.5	4.7	4.5	4.9	4.9	0.6	5.1	4.5	5.3	0.19
Insulin (mU/L)	19	17	14	9	21	16	14	10	5	24	0.60
HOMA-IR[4]	4.3	4.0	2.8	2.0	4.9	3.7	3.5	2.1	1.0	5.9	0.66
Triglyceride (mmol/L)	1.0	0.5	1.0	0.5	1.4	0.9	0.5	0.7	0.5	1.0	0.48
Total cholesterol (mmol/L)	4.2	0.9	4.1	3.7	4.7	3.5	0.8	3.5	3.2	4.0	0.01
HDL (mmol/L)	1.15	0.31	1.09	0.85	1.45	1.16	0.25	1.07	0.97	1.36	0.77

LDL (mmol/L)	2.8	1.0	2.5	2.1	3.4	2.1	0.5	2.2	1.7	2.5	0.04

[1]DQI-I (Moderation) is the sum score of fat, saturated fat, cholesterol, sodium and *other foods* groups (Maximum score is 30).
[2]N= 13-15 in children with DQI-I (Moderation) <21 and n=15-16 in children with DQI-I (Moderation) ≥21.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DQI-I, Diet Quality Index-International; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-40: The Interrelationship between Dietary Guideline Index for Children and Adolescents (Foods) and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DGI-CA (Foods) <5.2[1,2]					DGI-CA (Foods) ≥5.2[1,2]					p-value[3]
	Mean	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	
ALT (U/L)	50	61	17	15	45	30	24	20	14	32	0.75
AST (U/L)	34	24	26	19	36	28	9	26	21	33	0.79
γGT (U/L)	14	13	5	5	16	9	5	5	5	10	0.42
Glucose (mmol/L)	4.9	0.6	5.1	4.7	5.2	4.7	0.5	4.7	4.5	5.0	0.33
Insulin (mU/L)	23	20	15	7	42	12	8	10	7	18	0.36
HOMA-IR[4]	4.8	4.3	2.9	1.3	8.8	2.6	1.7	2.1	1.6	3.8	0.33
Triglyceride (mmol/L)	0.9	0.4	1.0	0.6	1.1	0.9	0.6	0.6	0.5	1.2	0.48
Total cholesterol (mmol/L)	3.7	0.5	3.6	3.3	4.0	3.9	1.2	3.9	3.5	4.4	0.31
HDL (mmol/L)	1.20	0.30	1.16	0.88	1.48	1.20	0.24	1.21	1.01	1.37	0.94
LDL (mmol/L)	2.1	0.5	2.0	1.8	2.5	2.59	0.73	2.53	2.33	2.78	0.05

[1]DGI-CA (Foods) is the sum score of whole grains and low fat milk (Maximum score is 10).

[2]N= 12-13 in children with DGI-CA (Foods) <5.2 and n=13-14 in children with DGI-CA (Foods) ≥5.2.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DGI-CA, Dietary Guideline Index for Children and Adolescents; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-41: The Interrelationship between Dietary Guideline Index for Children and Adolescents (Grains) and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DGI-CA (Grains) <6[1,2]					DGI-CA (Grains) ≥6[1,2]					p-value[3]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	57	57	33	14	93	25	16	17	15	31	0.25
AST (U/L)	37	23	33	20	49	26	5	26	21	27	0.28
γGT (U/L)	20	34	10	5	15	10	8	5	5	16	0.35
Glucose (mmol/L)	5.0	0.4	5.1	4.7	5.3	4.6	0.5	4.7	4.3	4.9	0.03
Insulin (mU/L)	22	17	19	10	25	13	12	9	5	15	0.09
HOMA-IR[4]	5.3	4.0	4.4	2.1	8.8	2.8	3.0	2.0	1.0	2.8	0.04
Triglyceride (mmol/L)	1.1	0.6	1.0	0.6	1.6	0.8	0.4	0.6	0.5	1.0	0.13
Total cholesterol (mmol/L)	3.7	1.1	3.6	3.3	4.3	4.0	0.7	3.9	3.5	4.4	0.45
HDL (mmol/L)	1.1	0.3	1.0	0.9	1.3	1.23	0.27	1.33	1.01	1.48	0.15
LDL (mmol/L)	2.5	1.0	2.2	1.8	2.7	2.38	0.61	2.36	2.07	2.60	0.86

[1]DGI-CA (Grains) is the sum score of the total grains and whole grains (Maximum score is 10).
[2]N= 14-16 in children with DGI-CA (Grains) <6 and n=14-15 in children with DGI-CA (Grains) ≥6.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DGI-CA, Dietary Guideline Index for Children

and Adolescents; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-42: The Interrelationship between Dietary Guideline Index for Children and Adolescents (Milk) and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DGI-CA (Milk) <7[1,2]					DGI-CA (Milk) ≥7[1,2]					p-value[3]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	53	53	33	17	57	28	28	17	13	21	0.05
AST (U/L)	37	22	32	25	34	26	9	23	19	34	0.23
γGT (U/L)	22	33	11	5	24	7	5	5	5	5	0.01
Glucose (mmol/L)	4.8	0.5	4.7	4.5	5.2	4.8	0.5	4.9	4.5	5.1	0.92
Insulin (mU/L)	23	16	21	12	30	11	12	9	5	12	0.01
HOMA-IR[4]	5.3	3.9	4.6	2.4	7.3	2.5	2.8	1.8	1.1	2.8	0.01
Triglyceride (mmol/L)	1.2	0.5	1.0	0.9	1.5	0.7	0.4	0.6	0.5	0.8	0.01
Total cholesterol (mmol/L)	3.8	1.0	3.8	3.3	4.3	3.9	0.8	3.7	3.5	4.2	1.00
HDL (mmol/L)	1.08	0.28	0.99	0.88	1.33	1.25	0.25	1.32	1.06	1.45	0.08
LDL (mmol/L)	2.5	0.9	2.45	2.0	2.6	2.3	0.8	2.4	1.9	2.6	0.49

[1]DGI-CA (Milk) is the sum score of milk and alternatives and low fat milk (Maximum score is 10).
[2]N= 15-17 in children with DGI-CA (Milk) <7 and n=14 in children with DGI-CA (Milk) ≥7.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DGI-CA, Dietary Guideline Index for Children and Adolescents; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-43: The Interrelationship between Diet Quality Index-International (Variety) and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQI-I (Variety) <18[1,2]					DQI-I (Variety) ≥18[1,2]					p-value[3]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	51	45	37	16	77	36	45	17	14	33	0.34
AST (U/L)	35	19	30	22	42	29	16	26	20	33	0.61
γGT (U/L)	26	38	13	8	26	8	7	5	5	9	0.01
Glucose (mmol/L)	4.9	0.5	5.0	4.6	5.2	4.7	0.5	4.7	4.5	5.1	0.29
Insulin (mU/L)	17	13	15	5	22	18	17	10	7	24	0.69
HOMA-IR[4]	3.8	3.3	2.8	1.0	4.9	4.1	3.9	2.1	1.6	5.9	0.81
Triglyceride (mmol/L)	0.9	0.5	0.9	0.5	1.0	1.0	0.6	0.9	0.6	1.4	0.56
Total cholesterol (mmol/L)	3.8	0.9	3.6	3.2	4.0	3.9	0.9	4.0	3.5	4.4	0.27
HDL (mmol/L)	1.15	0.28	1.04	0.91	1.42	1.16	0.27	1.12	0.91	1.44	0.92
LDL (mmol/L)	2.2	0.7	2.1	1.7	2.5	2.6	0.9	2.5	2.1	2.8	0.17

[1]DQI-I (Variety) is the sum score of the variety of food groups and within milk and meat products (Maximum score is 20).
[2]N= 11-12 in children with DQI-I (Variety) <18 and n=17-19 in children with DQI-I (Variety) ≥18.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DQI-I, Diet Quality Index- International; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-44: The Interrelationship between Diet Quality Model within Healthy Eating Index-Canada (Adequacy and Moderation) and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQ Model within HEI-C <60[1,2]					DQ Model within HEI-C ≥60[1,2]					p-value[3]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	57	54	39	17	75	26	25	17	13	21	0.04
AST (U/L)	36	22	30	21	38	27	11	26	19	33	0.30
γGT (U/L)	16	11	15	5	21	15	35	5	5	5	<0.01
Glucose (mmol/L)	5.0	0.4	5.1	4.7	5.3	4.6	0.5	4.5	4.3	4.9	0.03
Insulin (mU/L)	24	18	18	12	42	11	9	9	5	10	0.01
HOMA-IR[4]	5.5	4.2	4.0	2.7	9.3	2.3	1.9	1.8	1.0	2.1	0.01
Triglyceride (mmol/L)	1.1	0.5	1.0	0.8	1.5	0.8	0.5	0.6	0.5	1.0	0.05
Total cholesterol (mmol/L)	4.0	0.9	3.9	3.3	4.4	3.6	0.9	3.7	3.5	4.22	0.64
HDL (mmol/L)	1.07	0.27	1.02	0.84	1.25	1.25	0.25	1.33	0.99	1.48	0.06
LDL (mmol/L)	2.63	1.1	2.5	1.7	3.0	2.3	0.5	2.3	1.9	2.6	0.65

[1]DQ Model within HEI-C tool is the sum score of HEI-C (Adequacy) and HEI-C (Moderation) (Maximum score is 90).
[2]N= 14-16 in children with DQ Model within HEI-C <60 and n=14-15 in children with DQ Model within HEI-C ≥60.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DQ, Diet Quality; HEI-C, Healthy Eating Index-Canada; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-45: The Interrelationship between Diet Quality Model within Dietary Guideline Index for Children and Adolescents (Adequacy and Moderation) and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQ Model within DGI-CA <54 (n=14-15)[1,2]					DQ Model within DGI-CA ≥54[1,2]					p-value[3]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	43	41	21	16	57	41	49	18	14	49	0.50
AST (U/L)	33	17	29	21	35	31	19	26	19	33	0.43
γGT (U/L)	12	9	11	5	16	19	35	5	5	15	0.54
Glucose (mmol/L)	4.9	0.5	5	4.7	5.1	4.7	0.5	4.6	4.5	5.1	0.31
Insulin (mU/L)	18	117	13	7	21	17	14	10	7	25	0.81
HOMA-IR[4]	3.6	3.1	2.8	1.6	4.4	4.4	4.3	2.1	1.3	5.9	0.92
Triglyceride (mmol/L)	1.0	0.5	0.9	0.5	1.3	0.9	0.6	0.7	0.6	1.3	0.81
Total cholesterol (mmol/L)	4.0	0.8	4.0	3.3	4.6	3.6	0.9	3.6	3.3	4.1	0.25
HDL (mmol/L)	1.17	0.30	1.12	0.88	1.48	1.15	0.26	1.06	0.94	1.34	0.78
LDL (mmol/L)	2.4	0.7	2.5	1.9	2.6	2.5	1.0	2.3	1.9	2.7	0.68

[1]DQ Model within DGI-CA tool is the sum score of DGI-CA (Adequacy) and DGI-CA (Moderation) (Maximum score is 80).
[2]N= 14-15 in children with DQ Model within DGI-CA <54 and n=14-16 in children with DQ Model within DGI-CA ≥54.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQ, Diet Quality; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-46: The Interrelationship between Diet Quality Model within Diet Quality Index-International (Adequacy and Moderation)and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQ Model within DQI-I <45[1,2]					DQ Model within DQI-I ≥45[1,2]					p-value[3]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	57	54	39	17	75	26	25	17	13	21	0.04
AST (U/L)	36	22	29.5	21	38	27	11	26	19	33	0.30
γGT (U/L)	16	11	15	5	21	14.6	35	5	5	5	<0.01
Glucose (mmol/L)	5.0	0.4	5.1	4.7	5.3	4.6	0.5	4.5	4.3	4.9	0.03
Insulin (mU/L)	24	18	18	12	42	11	9	9	5	10	0.01
HOMA-IR[4]	5.5	4.2	4.0	2.7	9.3	2.3	1.9	1.8	1.0	2.1	0.01
Triglyceride (mmol/L)	1.1	0.5	1.0	0.8	1.5	0.8	0.5	0.6	0.5	1.0	0.05
Total cholesterol (mmol/L)	4.0	0.9	3.9	3.3	4.4	3.6	0.9	3.7	3.5	4.2	0.64
HDL (mmol/L)	1.07	0.27	1.02	0.84	1.25	1.25	0.24	1.33	0.99	1.48	0.06
LDL (mmol/L)	2.6	1.1	2.5	1.7	3.0	2.3	0.5	2.3	1.9	2.6	0.65

[1]DQ Model within DQI-I tool is the sum score of DQI-I (Adequacy) and DQI-I (Moderation) (Maximum score is 70).
[2]N= 14-15 in children with DQ Model within DQI-I <45 and n=14-16 in children with DQ Model within DQI-I ≥45.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DQ, Diet Quality; DQI-I, Diet Quality Index-International; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-47: The Post Hoc Power analysis of Glycemic Index, Glycemic Load and Diet Quality Tools in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	Power (%)
Glycemic Index	18
Glycemic Load	33
Total Diet Quality Score	
Healthy Eating Index-Canada	86
Dietary Guideline Index for Children and Adolescents	65
Diet Quality Index-International	69
Antioxidants[1]	
Vitamin A	44
Vitamin C	82
Vitamin E	8
The Components of Diet Quality: Adequacy	
HEI-C[2]	85
DGI-CA[3]	71
DQI-I[4]	90
The Components of Diet Quality: Moderation	
HEI-C[5]	62
DGI-CA[6]	28
DQI-I[7]	23
The Components of Diet Quality: Variety	
HEI-C (Variety)[8]	41
DGI-CA Food[9]	46
DGI-CA Grains[10]	29
DGI-CA Milk[11]	90
DQI-I[12]	8
The Components of Diet Quality: **Overall Balance (DQI-I)[13]**	17
DQ Model Within Diet Quality Tool[14]	
HEI-C[13]	92
DGI-CA[14]	48
DQI-I[15]	91

[1]Vitamin A, vitamin E and vitamin C are treated as categorical variable (**J-1**). Scores of 5, 2.5, or 0 were signed for meeting 100% of the RDA, 50 to <100% of RDA, or <50% of the RDA, respectively (similar to the DQI-I approach) (16).
[2]HEI-C (Adequacy): sum score of fruit and vegetables, grain products, milk and alternatives, and meat and alternatives.
[3]DGI-CA (Adequacy): sum score of fruit and vegetables, grain products, milk and alternatives, and meat and alternatives.
[4]DQI-I (Adequacy): sum score of fruit and vegetables, grain products, fibre, protein, iron, calcium, and vitamin C.
[5]HEI-C (Moderation): sum score of fat, saturated fat, cholesterol, and *other foods* group.
[6]DGI-CA (Moderation): sum score of *other foods* group and food choice (saturated fat).
[7]DQI-I (Moderation): sum score of fat, saturated fat, cholesterol, sodium, and *other foods* group.
[8] HEI-C (Variety): the score of Variety.
[9]DGI-CA (Foods): sum score of whole grains, land ow fat milk.
[10]DGI-CA (Grains): sum score of the total grains and whole grains.
[11]DGI-CA (Milk): sum score of milk and alternatives and low fat milk.
[12]DQI-I (Variety): sum score of the variety of food groups and within milk and meat products.
[13]DQI-I (Overall balance): sum score of macronutrient ratios as %Kcal and fatty acid ratios (saturated fat: monounsaturated fatty acid: polyunsaturated fatty acid).
[14]DQ Model is the sum score Adequacy and Moderation within DQ tool (HEI-C, DGI-CA and DQI-I).
Abbreviations: DGI-CA; Dietary Guideline Index for Children and Adolescents; DQ, Diet Quality; DQI-I, Diet Quality Index-International; HEI-C, Healthy Eating Index-Canada.

Table J-48: The 95% Confidence Interval and Coefficient of Variation in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	NAFLD (n=15)				Lean Control (n=16)			
	CI	Mean+CI (>95% CI)	Mean-CI (<95% CI)	CV	CI	Mean+CI (>95% CI)	Mean-CI (<95% CI)	CV
Energy (kcal)	216.17	1776.38	1344.05	0.27	169.27	1860.03	1521.49	0.20
Protein (g)	10.51	88.17	67.16	0.27	9.50	80.63	61.64	0.27
% Protein	3.26	24.15	17.63	0.31	2.28	19.43	14.87	0.27
Carbohydrate (g)	32.95	227.20	161.31	0.34	29.35	278.69	219.99	0.24
% Carbohydrate	4.16	53.51	45.19	0.17	3.65	62.72	55.41	0.13
Total Sugar (g)	16.37	87.06	54.31	0.46	23.00	133.37	87.37	0.43
Fibre (g)	2.02	17.39	13.36	0.26	3.19	21.97	15.59	0.35
Fat (g)	10.17	64.75	44.41	0.37	8.64	58.39	41.10	0.35
% Fat	2.69	33.67	28.29	0.17	3.45	29.56	22.66	0.27
SFA (g)	3.68	22.16	14.79	0.39	3.31	21.23	14.61	0.38
% SFA	1.12	11.55	9.32	0.21	1.45	10.87	7.97	0.31
Trans Fat (g)	0.16	0.57	0.24	0.76	0.09	0.30	0.11	0.92
Cholesterol (mg)	36.32	239.99	167.34	0.35	26.30	192.48	139.88	0.32
PUFA (g)	2.64	13.48	8.20	0.48	2.08	10.32	6.16	0.52
% PUFA	1.33	7.62	4.95	0.42	0.81	5.06	3.44	0.39
MUFA (g)	4.93	24.67	14.81	0.49	3.97	20.12	12.17	0.50
% MUFA	1.52	12.52	9.48	0.27	1.61	9.96	6.73	0.39
Vitamin A (RAE)	134.19	584.49	316.10	0.59	150.67	758.84	457.51	0.51
Vitamin B1 (mg)	0.26	1.79	1.27	0.33	0.25	1.93	1.43	0.31
Vitamin B2 (mg)	0.25	1.80	1.30	0.32	0.31	2.19	1.57	0.34
Vit B3-NE (mg)	5.10	38.74	28.54	0.30	4.81	35.38	25.77	0.32
Vitamin B6 (mg)	0.17	1.58	1.25	0.23	0.26	1.81	1.29	0.34
Vitamin B12 (mg)	1.32	5.39	2.75	0.64	1.25	5.40	2.90	0.62
Vitamin C (mg)	40.12	120.86	40.62	0.98	47.04	187.49	93.41	0.68
Vitamin D (IU)	35.10	160.49	90.30	0.55	87.65	350.92	175.62	0.68
Folate-DFE (mg)	59.63	326.25	206.99	0.44	33.13	300.22	233.97	0.25
Calcium (mg)	134.17	849.72	581.39	0.37	159.45	1081.17	762.27	0.35
Copper (mg)	0.18	1.16	0.81	0.36	0.18	1.48	1.11	0.29
Iron (mg)	2.43	15.00	10.14	0.38	1.68	15.21	11.86	0.25

Magnesium (mg)	33.14	263.33	197.05	0.28	41.55	321.61	238.52	0.30
Potassium (mg)	298.68	2443.83	1846.46	0.28	379.19	3077.86	2319.48	0.29
Selenium (mg)	10.51	94.59	73.57	0.25	14.41	94.59	65.78	0.37
Sodium (mg)	314.21	2409.14	1780.72	0.30	282.39	2599.20	2034.42	0.25
Zinc (mg)	2.53	12.58	7.53	0.50	0.93	9.93	8.06	0.21
EI/BMR	0.17	1.27	0.93	0.31	0.14	1.32	1.05	0.24
Grains	0.80	5.66	4.07	0.32	0.65	6.45	5.14	0.23
F/V	1.12	4.97	2.73	0.57	1.41	7.21	4.39	0.50
Milk	0.54	2.25	1.18	0.62	0.53	2.89	1.83	0.46
Meat	0.64	3.07	1.80	0.52	0.33	2.10	1.43	0.39
GI	4.07	55.23	47.10	0.16	1.86	50.44	46.73	0.08
GL	22.71	123.97	78.54	0.44	16.89	140.07	106.29	0.28
HEI-C	4.80	71.20	61.60	0.14	5.34	82.21	71.54	0.14
DGI-CA	6.58	68.19	55.02	0.21	6.02	78.13	66.09	0.17
DQI-I	4.13	64.32	56.07	0.14	3.95	71.55	63.65	0.12

Abbreviations: BMR, Basal Metabolic Rate; CI, Confidence interval; CV, Coefficient of variation; DFE, Dietary Folate Equivalent; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-I, Diet Quality Index-International; EI, Energy Intake; F/V, Fruits and Vegetables; GI, Glycemic index; GL, Glycemic load; HEI-C, Healthy Eating Index-Canada; MUFA, Monounsaturated Fatty Acid; NAFLD, Non-Alcoholic Fatty Liver Disease; PUFA, Polyunsaturated Fatty Acid; RAE, Retinol Activity Equivalent; SFA, Saturated Fat.

Table J-49: The Interrelationship between Diet Quality Model Score between Diet Quality Tools [Diet Quality Index-International (Adequacy) and Healthy Eating Index-Canada (Moderation)] and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQ Model <53[1]					DQ Mode ≥53[1]					
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	p-value[2]
Weight for age z-score[3,4]	1.94	1.47	2.65	1.63	2.92	0.36	1.21	0.18	-0.48	1.32	<0.01
Height for age z-score[3,4]	0.35	1.26	0.39	0.08	0.87	0.39	1.05	0.16	-0.46	1.07	0.92
BMI for age z-score[3,4]	2.06	1.56	2.73	1.94	3	0.31	1.24	-0.17	-0.54	1.1	<0.01
Waist circumference (cm)[5]	90	19	93	79	110	67	8	64	63	71	0.01
Hip circumference (cm)[5]	104	17	106	91	122	85	8	86	82	91	<0.01
Waist to hip[5]	0.86	0.10	0.89	0.780	0.92	0.78	0.09	0.76	0.71	0.81	0.03
Waist to height[5]	0.53	0.11	0.55	0.42	0.61	0.42	0.05	0.40	0.39	0.42	0.02
%Fat free mass[6]	69.4	13.25	68.4	57.6	74.5	83.84	10.09	83.7	80.6	89.8	0.01
Fat free mass (kg)[6]	59.1	13.41	57.55	47.69	71.3	41.54	11.31	41.12	36.12	48.0	<0.01
% Body Fat[6]	30.6	13.25	31.6	25.5	42.4	16.16	10.09	16.3	10.2	19.4	0.01
Fat mass (kg)[6]	34.9	20.6	30.7	16.8	51.45	8.19	5.92	7.21	4.03	8.67	<0.01

[1]DQ Model is the sum score of Diet Quality Index-International (Adequacy) and Healthy Eating Index-Canada (Moderation) (Maximum score is 80).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group, http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 16 in children with DQ Model <53 and n=15 in children with DQ Model ≥53.
[5]N= 14 in children with DQ Model <53 and n=11-12 in children with DQ Model ≥53.
[6]N= 13 in children with DQ Model <53 and n=13 in children with DQ Model ≥53.
Abbreviations: BMI, Body Mass Index; DQ, Diet Quality; IQ, Interquartile range; SD, Standard Deviation.

Table J-50: The Interrelationship between Diet Quality Model Score between Diet Quality Tools [Diet Quality Index-International (Adequacy) and Healthy Eating Index-Canada (Moderation)] and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQ Model <53[1,2]					DQ Model ≥53[1,2]					p-value[3]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	57	54	39	17	75	25	25	17	13	21	0.04
AST (U/L)	37	22	33	21	38	27	11	26	19	32	0.19
γGT (U/L)	15	11	12	5	16	15.4	35	5	5	5	0.01
Glucose (mmol/L)	5.0	0.5	5.1	4.7	5.4	4.6	0.5	4.5	4.3	4.9	0.01
Insulin (mU/L)	24	17	19	12	42	10	8	9	5	10	0.01
HOMA-IR[4]	5.7	4.1	4.3	2.7	9.3	2.1	1.6	1.8	1.0	2.1	<0.01
Triglyceride (mmol/L)	1.2	0.6	1.0	0.8	1.7	0.7	0.33	0.6	0.5	0.9	0.01
Total cholesterol (mmol/L)	3.8	1.2	3.8	3.2	4.4	3.8	0.5	3.7	3.5	4.2	0.84
HDL (mmol/L)	1.07	0.27	1.01	0.84	1.25	1.25	0.24	1.33	1.01	1.48	0.06
LDL (mmol/L)	2.6	1.1	2.5	1.7	3.1	2.3	0.5	2.3	1.9	2.5	0.46

[1]DQ Model is the sum score of Diet Quality Index-International (Adequacy) and Healthy Eating Index-Canada (Moderation) (Maximum score is 80).
[2]N= 14-16 in children with DQ Model <53 and n=14-15 in children with DQ Model ≥53.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DQ, Diet Quality; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-51: The Interrelationship between Diet Quality Model between Diet Quality Tools [Diet Quality Index-International (Adeqauecy), Healthy Eating Index-Canada (Moderation), Dietary Guideline Index for Children and Adolescents (Meat), and Dietary Guideline Index for Children and Adolescents (Milk)] and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQ Model <62[1]					DQ Model ≥62[1]					p-value[2]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Weight for age z-score[3,4]	1.79	1.49	2.28	1.32	3.00	0.60	1.42	0.36	-0.46	1.515	0.03
Height for age z-score[3,4]	0.32	1.28	0.38	-0.06	0.99	0.42	1.04	0.24	-0.36	0.89	0.81
BMI for age z-score[3,4]	1.84	1.63	2.6	1.17	3	0.62	1.49	-0.05	-0.45	1.87	0.04
Waist circumference (cm)[5]	88	19	89	79	98	71	16	64	63	74	0.05
Hip circumference (cm)[5]	104	17	106	91	122	87	10	86	82.5	91.5	0.01
Waist to hip[5]	0.84	0.09	0.84	0.78	0.90	0.81	0.11	0.78	0.72	0.88	0.41
Waist to height[5]	0.51	0.10	0.54	0.42	0.58	0.45	0.10	0.41	0.39	0.51	0.25
%Fat free mass[6]	70.6	14.5	70.5	56.5	84.3	81.7	11.1	83.2	77.0	89.8	0.07
Fat free mass (kg)[6]	60.5	13.7	60.1	47.1	73.8	41.6	10.1	42.1	36.1	48.0	<0.01
%Body Fat[6]	29.4	14.5	29.5	15.7	43.5	18.3	11.1	16.9	10.2	23	0.07
Fat mass (kg)[6]	34.8	22.0	35.1	14.8	52.2	10.2	8.4	7.8	4.0	14.2	<0.01

[1]DQ Model between DQ tools is the sum score of DQI-I (Adequacy), HEI-C (Moderation), DGI-CA (Milk), and DGI-CA (Meat) (Maximum score is 90).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group) (http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 15 in children with DQ Model between DQ tools <62 and n=16 in children with DQ Model between DQ tools ≥62.
[5]N= 13 in children with DQ Model between DQ tools <62 and n=12-13 in children with DQ Model between DQ tools ≥62.
[6]N= 12 in children with DQ Model between DQ tools <62 and n=14 in children with DQ Model between DQ tools ≥62.
Abbreviations: BMI, Body Mass Index; DQ, Diet Quality; IQ, Interquartile range; SD, Standard Deviation.

Table J-52: The Interrelationship between Diet Quality Model between Diet Quality Tools [Diet Quality Index-International (Adeqauecy), Healthy Eating Index-Canada (Moderation), Dietary Guideline Index for Children and Adolescents (Meat), and Dietary Guideline Index for Children and Adolescents (Milk)] and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQ Model <62[1,2]					DQ Model ≥62[1,2]					p-value[3]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	47	39	33	16	57	37	50	17	13.5	27	0.15
AST (U/L)	32	17	27	21	34	31	18	26	19.5	34	0.68
γGT (U/L)	15	10	14	5	16	16	34	5	5	7	0.02
Glucose (mmol/L)	5.0	0.5	5.0	4.7	5.3	4.6	0.5	4.6	4.4	5.0	0.06
Insulin (mU/L)	22	18	17	12	22	13	12	9	5	24	0.05
HOMA-IR[4]	5.2	4.2	3.8	2.7	8.8	2.8	2.6	2.0	1.0	4.9	0.03
Triglyceride (mmol/L)	1.1	0.5	1.0	0.8	1.4	0.9	0.6	0.6	0.5	1.1	0.15
Total cholesterol (mmol/L)	4.0	0.9	4.0	3.3	4.5	3.6	0.8	3.6	3.4	4.1	0.50
HDL (mmol/L)	1.07	0.28	1.01	0.83	1.33	1.24	0.24	1.31	1.00	1.47	0.08
LDL (mmol/L)	2.7	1.1	2.5	1.8	3.4	2.2	0.5	2.3	1.9	2.6	0.37

[1]DQ Model between DQ tools is the sum score of DQI-I (Adequacy), HEI-C (Moderation), DGI-CA (Milk), and DGI-CA (Meat) (Maximum score is 90).
[2]N= 13-15 in children with DQ Model <61 and n=15-16 in children with DQ Model ≥62.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DQ, Diet Quality; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Table J-53: The Interrelationship between Diet Quality Model between Diet Quality Tools [Diet Quality Index-International (Adeqauecy), Healthy Eating Index-Canada (Moderation), and Dietary Guideline Index for Children and Adolescents (Meat)] and Anthropometrics and Body Composition in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQ Model <61[1]					DQ Model ≥61[1]					p-value[2]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Weight for age z-score[3,4]	1.85	1.46	2.46	1.42	2.87	0.47	1.36	0.18	-0.48	1.32	0.01
Height for age z-score[3,4]	0.34	1.24	0.39	0.08	0.87	0.40	1.07	0.16	-0.46	1.07	0.88
BMI for age z-score[3,4]	1.90	1.60	2.65	1.36	3	0.47	1.41	-0.17	-0.54	1.22	0.01
Waist circumference (cm)[5]	90	20	92	79	110	68	10	64	63	71	0.01
Hip circumference (cm)[5]	104	16	106	91	122	85	8	86	82	91	<0.01
Waist to hip[5]	0.85	0.10	0.86	0.80	0.91	0.79	0.10	0.76	0.71	0.85	0.10
Waist to height[5]	0.52	0.11	0.54	0.42	0.61	0.43	0.07	0.40	0.39	0.45	0.07
%Fat free mass[6]	70.5	13.9	68.4	57.6	84.2	82.7	10.8	83.4	77.5	89.8	0.04
Fat free mass (kg)[6]	60.6	13.1	61.9	49.1	71.3	40.0	8.6	41.1	36.1	47.7	<0.01
%Body Fat[6]	29.5	13.9	31.6	15.8	42.4	17.3	10.8	16.6	10.2	22.5	0.04
Fat mass (kg)[6]	34.3	21.1	30.7	15.5	51.5	8.8	6.8	7.2	4.0	8.7	<0.01

[1]DQ Model between DQ tools is the sum score of DQI-I (Adequacy), HEI-C (Moderation), and DGI-CA (Meat) (Maximum score is 85).
[2]p-values <0.05 are considered statistically significant.
[3]Weight-for-age z-score, Height-for-age z-score and body mass index for-age z score were calculated using World Health Organization Growth Charts for Canada (the Canadian Pediatric Endocrine Group) (http://cpeg-gcep.net/sites/default/files/plotter/index.html) (30).
[4]N= 16 in children with DQ Model <61 and n=15 in children with DQ Model ≥61.
[5]N= 14 in children with DQ Model <61 and n=11-12 in children with DQ Model ≥61.
[6]N= 13 in children with DQ Model <61 and n=13 in children with DQ Model ≥61.
Abbreviations: BMI, Body Mass Index;; DQ, Diet Quality; IQ, Interquartile range; SD, Standard Deviation.

Table J-54: The Interrelationship between Diet Quality Model between Diet Quality Tools [Diet Quality Index-International (Adeqauecy), Healthy Eating Index-Canada (Moderation), and Dietary Guideline Index for Children and Adolescents (Meat)] and Liver Enzymes and Cardio-Metabolic Parameters in Children with Non-Alcoholic Fatty Liver Disease and Lean Controls

	DQ Model <61[1,2]					DQ Model ≥61[1,2]					p-value[3]
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
ALT (U/L)	57	54	39	17	75	26	25	17	13	21	0.04
AST (U/L)	36	22	30	21	38	28	11	26	19	33	0.30
γGT (U/L)	16	11	15	5	21	15	35	5	5	5	<0.01
Glucose (mmol/L)	5.0	0.4	5.1	4.7	5.3	4.6	0.5	4.5	4.3	4.9	0.03
Insulin (mU/L)	24	18	18	12	42	11	9	9	5	10	0.01
HOMA-IR[4]	5.5	4.2	4.0	2.7	9.3	2.3	1.9	1.8	1.0	2.1	0.01
Triglyceride (mmol/L)	1.1	0.5	1.0	0.8	1.5	0.8	0.5	0.6	0.5	1.0	0.05
Total cholesterol (mmol/L)	4.0	1.0	3.9	3.3	4.4	3.6	0.9	3.7	3.5	4.2	0.64
HDL (mmol/L)	1.07	0.27	1.02	0.84	1.25	1.25	0.25	1.33	0.99	1.48	0.06
LDL (mmol/L)	2.6	1.1	2.5	1.7	3.0	2.3	0.5	2.3	1.9	2.6	0.65

[1]DQ Model between DQ tools is the sum score of DQI-I (Adequacy), HEI-C (Moderation), and DGI-CA (Meat) (Maximum score is 85).
[2]N= 13-15 in children with DQ Model <61 and n=15-16 in children with DQ Model ≥61.
[3]p-values <0.05 are considered statistically significant.
[4]HOMA-IR = fasting insulin (μU/mL)/22.5 x [glucose (mmol/L)].
Abbreviations: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; γ-GT, γ-glutamyltransferase; DQ, Diet Quality; HDL, High density lipoprotein; HOMA-IR, Homeostasis model of assessment of insulin resistance; IQ, Interquartile range; LDL, Low density lipoprotein; SD, Standard Deviation.

Appendix K : The Components of Diet Quality Tools and Recommended Foods and Nutrients Should Be Assessed Using a Diet Quality Tool

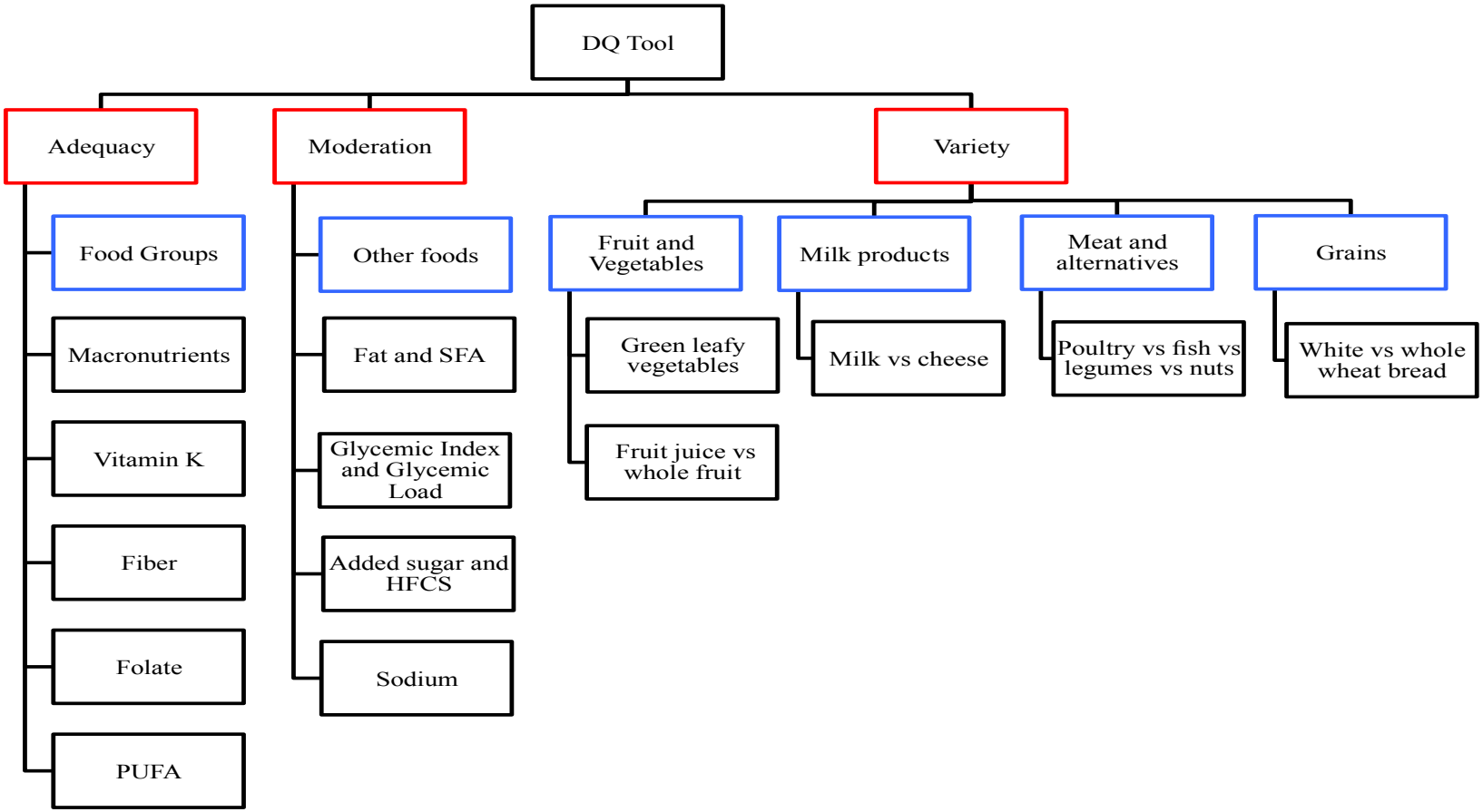


Figure K–1: The Components of Diet Quality Tools and Recommended Foods and Nutrients Should Be Assessed Using a Diet Quality Tool. Red boxes represent the components of diet quality tools; Blue boxes represents *food groups* that should be evaluated in each component; Black boxes represents *foods and nutrients* that should be evaluated in each component.
Abbreviations: DQ, Diet Quality; HFCS, High Fructose Corn Syrup; PUFA, Polyunsaturated Fatty Acid; SFA, Saturated Fatty Acid.