

**OREGON HEALTH & SCIENCE UNIVERSITY**

**SCHOOL OF MEDICINE**

MEAL QUALITY AND TIMING OF NUTRIENT INTAKE AMONG ADOLESCENTS AND YOUNG  
ADULTS WITH TYPE 1 DIABETES: ASSOCIATIONS WITH GLYCEMIC CONTROL AND SLEEP  
DURATION.

By

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Thesis

Master of Science in Clinical Human Nutrition

September 9<sup>th</sup>, 2021

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# Table of Contents

<b>Use of Abbreviations</b> .....	<b>i</b>
<b>List of Tables</b> .....	<b>ii</b>
<b>List of Figures</b> .....	<b>iii</b>
<b>Acknowledgements</b> .....	<b>iv</b>
<b>Chapter 1: Specific Aims &amp; Hypotheses</b> .....	<b>1</b>
<b>Chapter 2: Background &amp; Review of Literature</b> .....	<b>3</b>
Pathophysiology and Incidence of T1DM .....	<b>3</b>
Assessment of Glycemic Control.....	<b>5</b>
Continuous Glucose Monitoring (CGMs) .....	<b>5</b>
Glycated Hemoglobin (HgA1c).....	<b>6</b>
Insulin Types .....	<b>7</b>
Insulin Delivery Methods .....	<b>8</b>
Insulin Sensitivity .....	<b>10</b>
Adolescent Meal Quality.....	<b>11</b>
Healthy Eating Index – 2015 (HEI-2015) .....	<b>13</b>
Adolescent Meal Frequency .....	<b>15</b>
Adolescent Behavioral Impacts.....	<b>15</b>
Sleep Patterns.....	<b>16</b>
Remote Food Photography Method (RFPM) .....	<b>18</b>
<b>Chapter 3: Materials &amp; Methods</b> .....	<b>20</b>
General Design.....	<b>20</b>
Continuous Glucose Monitoring (CGM).....	<b>20</b>
Remote Food Photography Method (RFPM) .....	<b>21</b>
Outcome Variables.....	<b>22</b>
Statistical Analysis.....	<b>22</b>
Dietary Intake Validations.....	<b>22</b>
Measure of Sleep .....	<b>23</b>
Descriptive Statistics .....	<b>24</b>

<b>Chapter 4: Results</b> .....	<b>25</b>
Subject Characteristics.....	<b>25</b>
HEI Score .....	<b>28</b>
HEI Component (13) Scores .....	<b>29</b>
Energy Distribution .....	<b>34</b>
Duration of Sleep .....	<b>39</b>
<b>Discussion</b> .....	<b>42</b>
<b>References</b> .....	<b>46</b>

## Use of Abbreviations

ADA	American Diabetes Association
AF	Activity Factor
CBG	Capillary Blood Glucose
CDC	Center for Disease Control
CGM	Continuous Glucose Monitoring
CI	Confidence Interval
CSII	Continuous Subcutaneous Insulin Infusion
DCCT	Diabetes Control and Complications Trial
DKA	Diabetic Ketoacidosis
HbA1C	Hemoglobin A1C
HEI	Healthy Eating Index
IBW	Ideal Body Weight
MDI	Multiple Daily Insulin Injections
MNT	Medical Nutrition Therapy
PPG	Postprandial Plasma Glucose
REE	Resting Energy Expenditure
RPFM	Remote Food Photography Method
SMBG	Self-Monitoring of Blood Glucose
T1DEXI	Type 1 Diabetes Exercise Initiative
T1DM	Type 1 Diabetes Mellitus
TEE	Total Energy Expenditure

## List of Tables

Table 1.1: Healthy Eating Index (HEI) Components and Scoring .....	<b>14</b>
Table 2.1: Hypotheses and Statistical Tests.....	<b>24</b>
Table 3.1: Subject Characteristics .....	<b>27</b>
Table 4.1: Subject Characteristics of Diabetes Markers. ....	<b>27</b>
Table 5.1: Total HEI Mixed-Effects Models.....	<b>33</b>
Table 6.1: Mixed-Effects Model of Calories (%) Consumed Past 5PM .....	<b>37</b>

## List of Figures

Figure 1.1: Flow chart of study design.....	26
Figure 2.1: Box Plot of an Average HEI Score (%) per subject .....	28
Figure 3.1: Mean Healthy Eating Index (HEI) component (13) scores.....	30
Figure 4.1: Scatterplot of All HEI Scores by Age .....	34
Figure 5.1: Box Plot of mean nutrient intake consumed past 5 PM.....	35
Figure 6.1: Scatterplot of calories (A) and fat (B) consumed past 5Pm by BMI .....	38
Figure 7.1: Box plot (A) and scatterplot (B) of duration of sleep per subject .....	39
Figure 8.1: Box plot (A) and scatterplot (B) of mean duration of sleep per subject .....	41

## Acknowledgements

Foremost, I'd like to express my sincere gratitude to my mentor Dr. Gillingham for her patience, guidance, and encouragement. Dr. Gillingham has been an outstanding role model and has played a key role in my aspiration to pursue a career in diabetes.

Thank you to my committee members, Dr. Clements, and Dr. Stadler, for guiding me along the way, challenging me, and providing me many opportunities to learn and grow. I'd also like to thank Ms. Carol DeFrancesco and Dr. Susana Patton for providing insight, expertise, and critical feedback throughout this entire journey.

My appreciation also extends to the Oregon Health & Science University library staff and biostatistics department. Thank you for providing me support as I navigated statistical analysis and coding, literature reviews, and reference sorting.

Finally, I would like to acknowledge with gratitude, the endless support and love of my family – my parents, Gregg and Melinda Whigham; and my brothers, Andrew and Benjamin Whigham. They all kept me going and grounded when I needed it the most.

My twin brother Benjamin, to whom my thesis is dedicate to, thank you for helping me find my passion in life. You continue to amaze me with your discipline, selflessness, and bravery in managing your Type 1 Diabetes. As I emerge into the nutrition profession, I am committed to helping individuals with Type 1 Diabetes, with you in mind.



## Chapter 1: Specific Aims & Hypotheses

Within the general population, diet quality among adolescents and young adults is suboptimal and eating patterns are often lower in nutrient quality and higher in saturated fat compared to older adults. Some studies report the diets of adolescents and young adults include a daily caloric intake high in ultra-processed foods, and low in nutrient-dense foods. Among adolescents and young adults with Type 1 Diabetes (T1DM) healthy eating patterns that consist of a variety of nutrient-dense foods and appropriate portion sizes are important components of optimal diabetes management. Psychosocial barriers to adhering to diabetes management are common among adolescents and young adults with T1DM. Typical adolescent eating patterns and behaviors may lead to chronic hyperglycemia and less optimal glycemic control, which ultimately results in elevated hemoglobin (HbA1c) values, increasing the risk for long-term complications associated with T1DM.

The timing of meals and the relative distribution of energy and nutrients throughout the day among adolescent and young adults with T1DM, compared to older adults with T1DM, has not been reported. Eating patterns common among adolescents include: skipping meals, particularly breakfast; irregular meals, with the majority of energy consumed during the evening hours; and frequent snacking, usually on energy-dense foods.<sup>1-3</sup> Consuming large amounts of energy later in the day can be problematic for adolescents and young adults with T1DM since insulin sensitivity declines over the course of the day resulting in lower sensitivity during the evening hours. These typical adolescent and young adult eating behaviors may impair overall glycemic control and

contribute to early development of life-threatening diabetes complications among adolescent and young adults with T1DM.

Sleep duration and sleep quality is also known to play a central role in desired food choices and energy distribution. Inadequate duration and quality of sleep affects the release of the energy sensing hormones ghrelin and leptin, by increasing levels of ghrelin and decreasing concentrations of leptin. As a result, individuals who consistently achieve poor sleep quality and quantity are known to seek high-calorie foods. Many adolescents in the United States do not achieve the recommended 8-10 hours of sleep per night, with this inadequate sleep duration getting progressively worse extending into adult years<sup>4</sup>. Poor sleep behavior may also impact the ability of adolescents and young adults with T1DM to adhere to adequate diabetes self-management practices<sup>5,6</sup>.

While all three lifestyle patterns, diet quality, energy distribution, and sleep behavior can influence diabetes management, limited research has evaluated how each individually and in combination affect glycemic control among adolescent and young adults with T1DM compared to older adults with T1DM. To address this gap, we propose to examine diet quality, meal timing specifically to energy distribution, and sleep behavior of adolescents and young adults with T1DM (n=15) compared to older adults with T1DM (n=33) who participated in the T1 DEXI pilot study.

Specific Aim 1: Compare meal quality as assessed by a mean Healthy Eating Index (HEI) score among adolescent/young adults and older adults.

Hypothesis: We hypothesize that the mean HEI score will be lower among adolescent/young adults compared to older adults.

Specific Aim 2: Compare mean percent of total energy consumed after 5 PM among adolescent/young adults compared to older adults.

Hypothesis 2a: We hypothesize that adolescent/young adults will consume a greater percent of their daily total energy after 5 PM compared to older adults.

Hypothesis 2b: We hypothesize that the mean percent of total energy from fat will be higher among adolescent/young adults than older adults.

Specific Aim 3: Compare mean sleep duration among adolescent/young adults to older adults.

Hypothesis: We hypothesize that mean sleep duration will be lower among adolescents/young adults than older adults.

Identifying differences in diet quality, meal timing with respect to energy distribution, and sleep behaviors between adolescent and young adults to older adults will contribute to improved medical nutrition therapy and lifestyle counseling strategies to reduce metabolic risk among individuals with T1DM.

## **Chapter 2: Background & Review of Literature**

### **Pathophysiology and Incidence of T1DM**

Diabetes mellitus is a metabolic disease characterized by a chronic hyperglycemia. T1DM, a classification of diabetes, is an autoimmune illness caused by a

destruction of the insulin producing beta cells in the pancreas, often diagnosed in the pediatric population, and leading to insulin deficiency. Individuals with T1DM are dependent on insulin injections or an insulin pump to maintain near-normal blood glucose concentrations and metabolic homeostasis for the remainder of their lives. While insulin treatment prolongs life, individuals with T1DM are at risk for severe short- and long-term disease-related complications. Short term complications can be related to administrations of excessive insulin, hypoglycemia and hyperglycemic episodes, and diabetic ketoacidosis (DKA). Long term complications are related to microvascular insults that include retinopathy, nephropathy, neuropathy, and cardiovascular disease.

In the United States, nearly 1.6 million individuals are living with T1DM, including about 187,000 children and adolescents <sup>7-8</sup> A report published by the Centers for Disease Control and Prevention (CDC) in 2020 reported an unprecedented increase in the occurrence of T1DM diagnosis in the United States, with nearly a 30% increase in rate of new diagnosed cases since 2017<sup>9</sup>. Additional studies support the CDC's report suggesting an alarming increased incidence of T1DM in the United States<sup>10-12</sup>. However, the trend of increased T1DM incidence may in fact be due to an increase in new onset T1DM in adolescents and young adults. Historically, childhood T1DM incidence increased with age and reached a peak between 10 to 14 years of age<sup>12</sup>. The majority of epidemiological studies focus on the development of T1DM in early childhood defined as 0 – 14 years of age, with fewer studies reporting data on T1DM incidence among children over 14 years of age. Several studies conducted in the United Kingdom<sup>13</sup> and the United States<sup>14</sup> reported a significant increase in T1DM incidence in adolescents and

young adults between 15-34 years of age and 15-19 years of age, respectively<sup>12-14</sup>.

Studies that examined the impact of health behaviors among adolescents and young adults with T1DM compared to older adults with T1DM suggest that more research is needed to better tailor nutrition education and treatment to adolescents and young adults to achieve optimal glycemic control and reduce diabetes complications.

## **Assessment of Glycemic Control**

### **Continuous Glucose Monitoring (CGMs)**

While self-monitoring of blood glucose, (SMBG), concentrations provides a snapshot of glucose control and is considered important to diabetes management, it is limited by individual adherence to medical nutrition therapy recommendations and the number of capillary blood samples an individual is willing/able to obtain each day<sup>15</sup>. Alternatively, continuous glucose monitoring (CGM) measures glucose concentrations subcutaneously in interstitial fluid allowing the individual to receive more personalized data on glucose status as to avoid multiple capillary blood samples a day<sup>16</sup>. The CGM sensor is usually placed under the skin of an individual's stomach, arm, buttocks, or thigh and reports glucose concentration readings roughly every 5 minutes allowing for up to 288 individual glucose concentration readings per day, an impossible match for the SMBG technique<sup>16</sup>. The CGM sensor receives and stores glucose concentration data with the additional ability to show trends and patterns in glucose concentration readings. Furthermore, CGM sensors can be programmed to alert individuals to hyperglycemic ( $\geq 125$  mg/dL when fasting and  $\geq 200$  mg/dL 2 hours postprandial) or

hypoglycemia ( $\leq 70$  mg/dL) concentrations allowing the individual to make timely treatment adjustments.

More frequent glucose monitoring is associated with improved overall glycemic control among patients with T1DM. Some studies that compared the use of CGM and SMBG discovered that both methods decreased HbA1c values, suggesting improved glycemic control with either form of monitoring, but HbA1c values were lower among using the CGM method<sup>17,18</sup>. The authors concluded that for glycemic control, CGM is superior to SMBG. The T1DM Exchange Study supported these findings when concluding that CGM use is associated with significantly lower HbA1c values in some age-groups (children 8.3% vs. 8.6%,  $P < 0.001$  and adults 7.7% vs. 7.9%,  $P < 0.001$ ) especially when used more frequently<sup>19,20</sup>.

### **Glycated Hemoglobin (HgA1c)**

Glycated Hemoglobin is another biomarker available to assess the effectiveness of the management plan on glycemic control. HgA1c is an indicator of mean blood glucose concentrations, typically reflective of an average glycemia over several months as glucose molecules remain attached to the hemoglobin for the life of the red blood cells, which is typically 2 or 3 months. HgA1c plays a primary role in assessing the effectiveness of the management plan on glycemic control and predictive value for diabetes complications<sup>21</sup>. Improved (lower) HgA1c is associated with a reduced risk of the development of diabetes complications such as retinopathy and nephropathy, which was demonstrated in the 1993 Diabetes Control and Complications Trial (DCCT)<sup>6</sup>. The

DCCT was a prospective, randomized, controlled trial of intensive versus standard insulin management among patients with recent T1DM diagnosis. The study demonstrated that improved glycemic control with intensive insulin management was associated with decreases rates of retinopathy, nephropathy, as well as neuropathic complications. Additional findings in the DCCT trial showed adolescents had a 1% higher HbA1c compared to adults, despite similar therapeutic approaches, with higher doses of insulin<sup>6</sup>.

It should be noted that, the American Diabetes Association (ADA) HbA1c target as of 2018 of <7.5% was achieved by a smaller percentage of adolescents with T1DM (17%) than older adults with T1DM (37%)<sup>22</sup>. Clements et al. inspected the discrepancies between HbA1c values across the specific transition periods of pre-adolescence-to-adolescence and adolescent-to-young adults<sup>23</sup>. This study indicated that glycemic control among participants 8-18 years old worsened over time, through the age of 16 years old. HgA1c values observed in 18 years old begin to plateau into early adulthood. The study recognized the importance and need of focused diabetes management and education interventions to prevent deterioration in glucose control in pre-adolescence, adolescence, and early adulthood<sup>23</sup>.

### **Insulin Types**

Insulin is a potent anabolic hormone. Since the discovery of insulin in 1920's, it has been used as a source of treatment for diabetes. Exogenous insulin injections replace the normal pancreatic insulin release. Three primary characteristics of insulin

types are: onset of action, peak effect, and duration of action to meet specific needs of patients<sup>24</sup>. The different insulin formulations are described as rapid-acting insulin, regular or short-acting insulin, intermediate-acting insulin, and long-acting insulin<sup>25</sup>. Common intensive insulin regimens vary depending on preferred insulin delivery methods. Typically, individuals who are on continuous subcutaneous insulin infusion (CSII) use rapid-acting insulins or short-acting insulins since the pump delivers small amounts of insulin every few minutes. Individuals who use subcutaneous injections via an insulin pen will typically require a basal or background insulin dose of a long-acting insulin once or twice a day followed by a bolus dose of rapid-acting insulin or short-acting insulin before meals to cover the sugar and carbohydrate content in foods consumed as well as to correct high blood glucose concentrations.

### **Insulin Delivery Methods**

Adequate and correct technique in insulin delivery regimens, specific to and factoring in individual behavioral habits, is critical for optimal control of diabetes. Patients with T1DM require intensive insulin therapy, which can be administered using a range of insulin types and delivery methods. Delivery methods consist of subcutaneous injections via an insulin pen in multiple daily doses of insulin (MDI) or CSII via an insulin pump.

Insulin delivery methods vary among biological sex and between the age groups of children, adolescents, young adults, and older adults and are changing with the growing use of technology. In 2019, Louisa van den Boom et al. concluded in a



population of 96,547 patients with T1DM (median age of 17.9 years) that the percentage using insulin pump therapy increased from 1% in 1995 to 53% in 2017, with highest rates in the youngest patients (92% preschoolers, 74% in children, 56% in adolescents aged <15 years, 46% in adolescents ages > 15 years, 37% in adults)<sup>26</sup>. This increase in insulin pump use is largely associated with the rapid technological developments and demonstrated efficacy of insulin pumps, leading the children and adolescent population to be more likely to adopt these new technologies.

Variations between insulin delivery methods, with the highest use of insulin pump therapy in the youngest population, is an important factor to consider when examining meal timing, sleep behaviors, and diet quality of the adolescent and young adults' participants compared to older adults' participants.

The REPOSE (Relative Effectiveness of Pumps Over MDI and Structured Education) Trial by Heller et al. was a large randomized controlled trial of 267 individuals with T1DM that compared insulin pump therapy and insulin injection therapy on diabetes control over the course of 2 years.

This interventional clinical trial included testimonials from the participants using insulin pump therapy who expressed more flexibility, freedom in food choices, and dietary patterns<sup>27</sup>. Decreased diet restrictions were reported among participants using pump therapy. For instance, previous behavior of skipping meals or snacks because they did not want to have additional injections were eliminated along with reports of greater

confidence with dining out. The use of insulin pump therapy could contribute to an increase in energy consumption as it creates ease in last minute food intake decisions.

### **Insulin Sensitivity**

Insulin sensitivity refers to how insulin responsive tissues respond to a given insulin load. More specifically, insulin sensitive tissues such as skeletal muscle cells, adipose tissues, and the liver take up blood glucose in response to insulin, resulting in reduced blood glucose concentrations. Decreased insulin sensitivity or insulin resistance, occurs when higher insulin levels are needed to maintain euglycemia (70-180 mg/dL). An individual with T1DM can use the insulin sensitivity factor, which refers to the number of milligrams per deciliter (mg/dL) blood glucose concentrations fall when 1 unit of insulin is administered, to decide how much insulin is needed to keep their blood glucose concentrations within the target range. Established by the ADA, the blood glucose target range is between 70-130 mg/dL before a meal and no higher than 180 mg/dL up to 2 hours after a meal<sup>28</sup>. Insulin sensitivity can be highly individualized and change according to lifestyle factors, dietary factors, and time of day.

Insulin sensitivity has a diurnal pattern that varies during the day<sup>29</sup>. According to Poggiogalle et al. 2018, more than a dozen human studies have reported the existence of a diurnal rhythm in oral glucose tolerance, typically peaking in the morning, with impairments in glucose tolerance in the afternoon and evening hours<sup>30-36 37-46</sup>. Rhythms of peripheral insulin sensitivity appear to contribute to the diurnal variation in glycemic control. One study used a frequently-sampled intravenous glucose tolerance test in

normal-weight participants and found that insulin sensitivity was impaired by 34% in the evening relative to the morning<sup>47</sup>. Thus, glucose and or meal ingestion in the evening hours may result in a greater increase in plasma glucose concentration than in the morning hours due to diurnal changes in insulin sensitivity and glucose disposal.

Additionally, insulin sensitivity could be adversely affected by physiological changes during puberty in adolescents. A study, using a hyperinsulinemia clamp technique, concluded that there was a decrease in insulin sensitivity by 30% during mid-puberty when compared with prepubertal and adult subjects<sup>48</sup>. Puberty in individuals with T1DM may lead to decreased glycemic control because there is an increase in insulin resistance over the period of puberty, an increase in insulin needs as lean body mass increases during puberty, and behavioral changes and psychosocial issues occurring that contribute to less optimal glycemic control<sup>48</sup>.

### **Adolescent Meal Quality**

The Global Burden for Disease Study in 2013 concluded that obesity prevalence has increased among child and adolescent populations over the last three decades<sup>49</sup>. Positive associations between consumption of ultra-processed food and body fat during childhood and adolescence appear to be significant contributors<sup>50,51</sup>. Ultra-processed foods are generally manufactured from lower cost sources of energy, nutrients, and additives with ability for consumption anywhere and anytime. These foods are often higher in fat, saturated fat, and calories than less processed alternatives.

Adolescent and young adult individuals with T1DM may consume high fat and energy intakes. In 2011, Patton et al. and in 2006, Mayer et al. reviewed current dietary intake of youth with T1DM and concluded they consumed more fat and saturated fat than age-based recommendations and more than healthy controls<sup>52,53</sup>. In youth with T1DM, total percent of calories from fat ranged from 31-47%, which was higher than the Healthy People 2010 recommendations of <30%. Additionally, the youth's total percent of calories from saturated fat ranged from 11-15%, which was higher than the ADA recommendations of <7%<sup>52,53</sup>. Additional research compared dietary intakes of 108 adolescents with T1DM and grouped subjects based on glycemic control, hypoglycemia events and hospitalizations. Subjects with suboptimal glycemic control, increased hypoglycemic events and hospitalizations had total caloric intake as high as 3,000 to 4,000 kcal/day and calories from fat were as high as 50 to 70% of their diet<sup>54</sup>. Similar to the general population, consumption of high calorie and high fat diets are associated with poor health outcomes among adolescents with T1DM.

Not all research observed high calorie, high fat diets among adolescents and young adult individuals with T1DM. One study measured nutrient intake using a 24-hour diet recall of 61 adolescents with T1DM<sup>55</sup>. The subjects met the appropriate calories from fat guidelines averaging 30%, indicating no greater total fat intake in youth with T1DM. Likewise, Lodefalk and Aman 2006 reported that adolescents with T1DM had healthier food habits than healthy control subjects, potentially a result of nutritional education to the individuals<sup>56</sup>. Consequently, the percent of subjects using CSII versus MDI was 16% compared to 84% (n=160), supporting the premise that the use of insulin

pump therapy (CSII) could contribute to an increase in energy consumption potentially resulting in suboptimal glycemic control. The literature about nutrient intakes among adolescents with T1DM has been equivocal. Studies have compared nutrient intake of adolescents with T1DM to the general population or to current nutrition guidelines but not to adults with T1DM.

### **Healthy Eating Index – 2015 (HEI-2015)**

The HEI is a tool that is based on a scoring system (0 to 100) to measure individuals diet quality compared to the recommendations of the Dietary Guidelines for Americans. The Dietary Guidelines for Americans translate current nutrition science into recommendations for individuals to consume a nutrient dense healthful eating pattern associated with lower risk of chronic disease<sup>57</sup>. A perfect HEI score of 100 is reflective of food choices and eating patterns that align with the Dietary Guidelines for Americans, with a score of 81-100 being defined as ‘good’. The 13 components of the scoring standard in the HEI-2015 consist of intakes of total fruit, whole fruits, total vegetables, greens and beans, whole grains, dairy, total protein foods, seafood and plant proteins, fatty acids, refined grains, sodium, added sugars, and saturated fats<sup>57</sup>. This study will use HEI as a measure of overall diet quality in adolescent and young adults compared to adults with T1DM.

Adolescents and young adults with T1DM may consume a low-quality diet, with a lower HEI index score as a result of an overemphasis of carbohydrates to maintain euglycemia<sup>58</sup>. There has been a recent increase of individuals with T1DM who are

overweight and obese. One potential contributor could be excessive energy intake, particular excessive consumption of low nutrient dense, high calorie foods that lead to an overall low HEI score<sup>59</sup>. In a previous study, dietary intake in adolescents with T1DM fell well short of the US Dietary Guidelines, with the mean HEI-2005 score of  $53.4 \pm 11$ . (range = 26.4 to 81.2) falling at the low end of the “needs improvement” range, and <1% of the sample scoring in the “good” HEI-2005 range. Most notably, saturated fat intake exceeded guidelines, with intake nearly twice the recommended maximum and almost half of energy intake came from highly processed foods<sup>58</sup>. Poor dietary quality among adolescents is a common problem which may in turn lead to impaired glycemic control and comorbidities.

**Table 1. 1:** Healthy Eating Index (HEI) components and corresponding maximum score.

COMPONENT	MAXIMUM SCORE (%)
Total fruits	5
Whole fruits	5
Total Vegetables	5
Greens & beans	5
Whole grains	10
Dairy	10
Total protein foods	5
Seafood & plant protein	5
Fatty acids	10

Refined grains	10
Sodium	10
Added sugars	10
Saturated fats	10
<b>Total</b>	<b>100</b>

### **Adolescent Meal Frequency**

Meal frequency and meal timing is associated with adequate glycemic control among patients with T1DM. A meal pattern with smaller and more frequent meals has been associated with better glycemic control in individuals with T1DM, compared to irregular and infrequent meal consumption<sup>60</sup>. A study of 655 children and adolescents with T1DM observed that those who skipped meals were more likely to have suboptimal HbA1c concentrations. On the other hand, among the 687 participants in the intensive treatment arm of the DCCT trial, avoidance of extra snacks appeared beneficial to a lower HbA1c<sup>61</sup>. Optimal timing and frequency of meals to promote better glycemia continues to be debated in the literature. We will examine percentage of meals and snacks consumed in the late evening hours (after 5 PM) compared to early hours and number of meals and snacks between adolescent, young adults, and older adults with T1DM.

### **Adolescent Behavioral Impacts**

Postprandial blood glucose concentrations are significantly higher in the evening hours compared to the morning hours, making behavioral cycles of higher caloric intake in the evening hours among adolescents and young adults with T1DM more susceptible to impaired glycemic control. The “adolescent and young adult lifestyle” encourages teens to stay up later in the evening hours and socialize on cell phones and computers. Along with many psychosocial pressures adolescents experience, additional daily stress can contribute to reasons for staying up late which can lead to more opportunities for food intake.

Adolescence and young adulthood can be difficult phases in life to treat diabetes due to both physiological and psychosocial pressures<sup>62</sup>. During adolescents, young individuals with T1DM often seek independence and sometimes rebel against self-care behaviors. While adolescents with T1DM are at a greater risk for behavioral problems<sup>63</sup>, the psychosocial aspect of the disease is often missed with whole/most of the education given on the strict maintenance of blood glucose. Behavioral changes and psychosocial issues that can occur during adolescent and or adult years could contribute to suboptimal glycemic control<sup>64</sup>. This study will elevate the behavioral domain of sleep and examine the average sleep duration among adolescent and young adults with T1DM.

### **Sleep Patterns**

Preferred timing of sleep and duration vary largely between age groups with studies demonstrating adolescent individuals beginning their sleep on average later



than adults and compensating for accumulating sleep debts during the week with increased sleep on weekends<sup>65</sup>. Adolescence is a time of emerging independence and discovered social roles, all of which can affect sleep hygiene<sup>64,66</sup>. With rising concerns in the scientific literature, the adolescent's population might be especially vulnerable and prone to poor sleep habits. Sleep duration of adolescents has consistently decreased over several decades, with 71.5% of adolescent population in 1991 sleeping longer than 7 hours per night dropping to 63.0% of adolescent population in 2012 sleeping longer than 7 hours per night<sup>67</sup>.

Poor sleep habits may impact glycemic control among individuals with T1DM. Von Schnurbein et al. 2018 conducted a large (n=191) study among adolescents with T1DM that observed an association between lower sleep quality and increased HbA1c. For each 1-point increase in sleep quality, there was an associated 0.07% decrease in HbA1c (0.8 mmol/mol) <sup>68</sup>. A retrospective study conducted by Matejko, Kiec-Wilk et al. in 2015 examined whether short sleep duration is associated with glycemic control in continuous subcutaneous insulin infusion-treated T1DM individuals<sup>69</sup>. Shorter sleep duration was associated with worse glycemic control after adjustment for potential cofounders. Shorter sleep duration may contribute to the development of insulin resistance through the increased secretion of stress and appetite regulating hormones, such as ghrelin and leptin<sup>69</sup>. We propose comparing sleep duration among adolescent and young adults and older adult participants with T1DM to determine if younger age is in fact associated with decreased sleep quality.

## **Remote Food Photography Method (RFPM)**

Food habits and dietary intakes are traditionally measured by food frequency questionnaire, 24-hour diet recalls, or food records. Several validation studies of energy intake data has led to the widespread recognition that much of the dietary data on children and adolescents is prone to reporting error, mostly through biases and under-reporting<sup>70,71</sup>. Adolescents with higher body weight and adolescents with disordered eating tendencies are more likely to under-report food intake on dietary assessment tools. Studies that have analyzed the 24-hour diet recall method demonstrated misreporting of energy intake with a mean percentage of underreports that ranged from 21.5% - 67% and the percentage of under reporters in studies using estimated food records ranged from 11.9% to 44%<sup>72</sup>.

Advanced technological abilities have led to the use of remote food photography as an alternative method to measure dietary intake, which allows researchers and clinicians to quickly and unobtrusively estimate food intake<sup>73</sup>. The addition of photography, while still experiencing limitations and imperfections, can improve the accuracy of dietary recalls<sup>74</sup>. This method consists of subjects capturing images of food selection and plate waste using a smartphone. These images are then wirelessly transmitted to a server for analysis by a trained professional. Subjects using the RFPM are counseled to label images of food items that are not easily recognizable with a brief description for the data analysis. There are many advantages to the innovative approach of RFPM as a form of food intake assessment, including reduced individual burden and the ability to quantify food intake at the group and individual level<sup>73</sup>.

An additional advantage of the RFPM is the ability to provide text reminders to subjects before meals to improve the capture of true dietary intake among users. Yet establishing the RFPM as a credible food intake assessment remains a challenge due to various external factors that could make it difficult to analyze the captured photos, one being the variations with human raters and analysts that sometimes determine quantity, macronutrient, and micronutrient content. Lassen et al. and a couple others demonstrated that registered dietitians significantly underreport (around 4.7%-13%) energy intake of subjects based on photographs of the subjects' meals compared to the actual weight of the meal<sup>75-77</sup>.

On the contrary, some studies have not found significant differences in estimated energy intake amid various diet recall methods. Delisle et al. found no statistical difference in the average estimated energy intake between the three methods: digital food photography analysis, 24-hour diet recall, and doubly labelled water<sup>78</sup>. Wang et al. found similar results to Delisle of no statistical differences in energy consumption when investigating differences in estimated median nutrient intake among the three methods: 1-day weighed food record, digital images, and 24-hour diet recall around twenty-eight college students majoring in food and nutrition<sup>79</sup>.

Regardless of questions as to whether the RFPM could potentially eliminate biases shown in self-reported dietary consumption, a common distinction seen among many studies is the subjects' preference of the RFPM for meal tracking due to the ease of documenting food intake and reduced burden<sup>80,81</sup>. The RFPM method, along with trained human raters that used a computer-assisted approach with nutrient references

in a nutrient database, was used for the T1 Diabetes Exercise Initiative Pilot Study (T1DExI).

## **Chapter 3: Materials & Methods**

### **General Design**

This proposed research was a secondary data analysis of data derived from the T1 Diabetes Exercise Initiative Pilot Study (T1DExI). Adolescents and adults with T1DM were enrolled in a 4-week study to evaluate the methods to collect and aggregate coordinated data around exercise events and to examine effects of various exercise modalities and nutrient intake on glycemic control. Major inclusion criteria included a diagnosis of T1DM for at least 2 years, age between 15 and 70 years, and the use of either multiple daily insulin injections or an insulin pump.

Study participants were trained to use a novel food and exercise tracking phone application, the T1-Dexi app, to record exercise events and to collect digital photographs of foods before and after meal consumption, on the day of and day after scheduled structured exercise during the 4-week protocol.

The methods for measuring food intake and glucose monitoring that were used for this proposed such analysis are described in further detail below.

### **Continuous Glucose Monitoring (CGM)**

Each subject used an existing Dexcom CGM device or was fitted with a subcutaneous continuous glucose monitor – Dexcom™ G4 or Dexcom™ G4 share

(Dexcom, Inc, San Diego, CA) which measured glucose concentrations every five minutes. CGM data was collected and aggregated to a central server.

A mean glucose concentration was then calculated for each subject per day. A “Time in Range” glucose concentration was calculated for each subject per day, expressed as a percentage, and defined as the percentage of measurements that were recorded with a blood glucose level within the target range of 70 to 180 mg/dl (euglycemic).

### **Remote Food Photography Method (RFPM)**

The RFPM was used to measure energy and nutrient intake. Participants were trained to use a novel food and exercise tracking phone app (T1-Dexi app) to record exercise events and to collect digital photographs of foods before and after meal consumption on the day of and day after scheduled structured exercise during the 4-week protocol. If a participant did not finish 100% of their meal, they were asked to take an after digital photograph to capture the food not consumed or “plate waste”. Participants were asked to capture images at an arm’s distance away from the plate and at a 45-degree angle, and with a reference card (which is like a driver’s license) for a fiducial marker. Participants were also asked to provide text details along with the digital photograph to provide a more detailed description. The photo, as well as the date, time, and location of the meal/snack from the smartphone assigned was uploaded and aggregated to a central server<sup>82</sup>.

After digital photographs were uploaded to the server, they were analyzed by a trained professional rater using a computer-assisted approach. The rater identified the foods in the images and linked them to a nutrient reference in the Food and Nutrient Database for Dietary Studies. The rater obtained a reference image from an archive of food images and then estimated the portion size of the participants foods by visually comparing the uploaded food image to the standard food image. This process relied on existing and validated visual comparison methodology to estimate food consumption and “plate waste”.

### **Outcome Variables**

The primary outcome variables that were assessed in this analysis were daily Healthy Eating Index score for all valid days of intake, percent of total energy intake from total fat and saturated fat, percent of total energy consumed between waking to 5 PM (early dietary intake) and percent of total energy consumed after 5 PM (late dietary intake), and sleep duration.

### **Statistical Analysis**

#### **Dietary Intake Validations**

Participants daily energy intake (kcal/d) for each day of RFPM capture were compared to estimated total energy expenditure (kcal/d) to confirm that the RFPM results capture most of the food consumed by participants.

Total energy expenditure (TEE) was calculated as resting energy expenditure (REE) using the Harris Benedict equation X 1.4 activity factor (AF). The T1DExI study

design included coordinated exercise events and various activity modalities for each participant, which was considered when deciding to use a 1.4 AF.

For participants that were classified as obese (class I, II, or III) the ideal body weight (IBW) was calculated and used in the Harris Benedict equation, to estimate REE and TEE. If in a 24-hour period, less than 70% of the calculated TEE is captured, those days were considered “underreported” and were excluded from our analysis. For all days with at least 70% TEE captured, an HEI score was calculated based on the USDA HEI scoring system. We estimated that each participant generated between 0-16 days of valid dietary intake information and HEI scores.

Each day of valid dietary intake were further analyzed to assess timing of meal consumption. Meals were time stamped in the T1-Dexi app and time of the meal photo was in the text notes. Meal timing was used to calculate as the percent of total energy consumed from waking to 5 PM (early dietary intake) and percent of total energy consumed after 5 PM (late dietary intake).

### **Measure of Sleep**

Sleep duration was calculated using the sleep start and end times recorded on the daily questionnaire in the T1-Dexi app. Sleep data was assessed for normality and all non-normal variables were transformed.

T tests were used to determine differences in means of primary outcome variables between the adolescent/young adults and older adults’ participants. Data was

analyzed using STATA (Version 16.1, College Station, Tx). Differences were considered significant when  $p < 0.05$ .

### Descriptive Statistics

Data was summarized by group (adolescent/young adults and older adults) and reported as mean  $\pm$  standard deviation and 95% confidence intervals. Subject characteristics were compared between adolescent/young adults and older adults. Study sample (n=38) characteristics included biological sex, pump use, race/ethnicity, BMI class, age, BMI ( $\text{kg}/\text{m}^2$ ), duration of T1DM, HbA1c (%), REE ( $\text{kcal}/\text{d}$ ), and TEE ( $\text{kcal}/\text{d}$ ).

**Table 2. 1:** Hypotheses and Statistical Tests.

HYPOTHESIS	STATISTICAL TEST
We hypothesize that the mean HEI scores will be lower among adolescent/young adults compared to older adults.	Continuous Mixed-Effects Model <ul style="list-style-type: none"> <li>- Dependent Variable: HEI Score</li> <li>- Predictors: Age, BMI, M/F (sex), Fat,</li> <li>- Random Variable: Persons</li> </ul>
2a. We hypothesize that adolescent/young adults will consume a greater percent of their daily total calories after 5 PM compared to older adults	Continuous Mixed-Effects Model <ul style="list-style-type: none"> <li>- Dependent Variable: Calories (%)</li> <li>- Fixed Variable: Age, BMI, M/F (sex)</li> </ul> Random Variable: Person



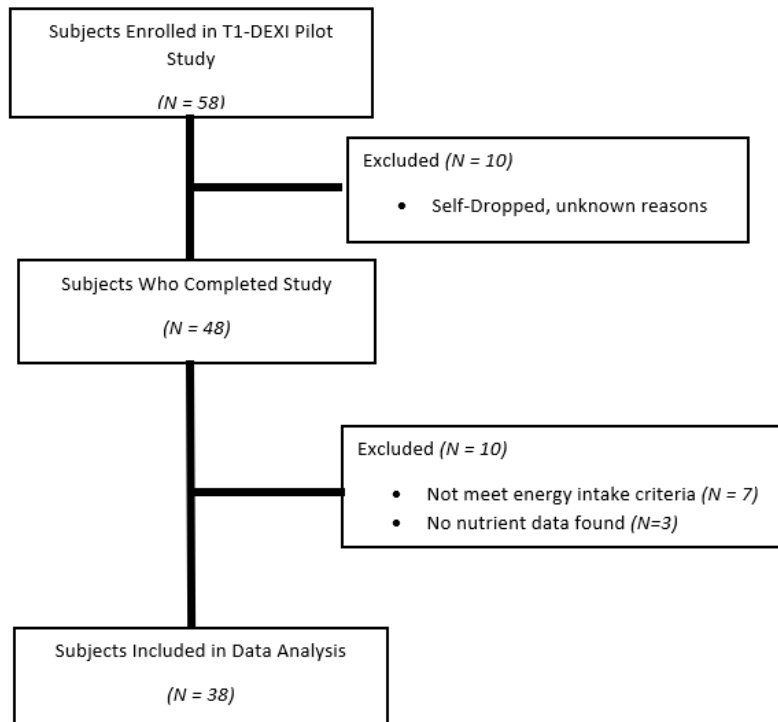
<p>2b. We hypothesize that the mean percent of total energy from fat will be higher among adolescents/young adults compared to older adults.</p>	<p>T test comparison of means</p>
<p>We hypothesize that the mean sleep duration will be lower among adolescents/young adults compared to older adults.</p>	<p>T test comparison of means</p>

## Chapter 4: Results

### **Subject Characteristics**

Initial subject characteristics were collected on 58 subjects. Throughout the 4-week duration of the study 10 of the subjects ‘dropped’ for reasons that were unreported, leaving a total of 48 subjects who ‘completed’ the study. An additional 7 subjects were excluded due to “underreporting”, as less than 70% of the calculated TEE was captured for all days of data. A total of 3 subjects were excluded because no nutrient data was recorded. The final study population was 38 (Figure 1.1).

**Figure 1.1:** Flow chart of study design.



There were 10 subjects in the adolescent/young adult group and 28 in the older adult group (Table 3.1). The groups were similar in distribution of males and females, pump use and BMI categories. All were white, non-hispanic. Adolescent/young adults had T1DM for a shorter period of time, had higher energy expenditure and HBGA1C. Glycemic control during the study enrollment period is provided in Table 4.1.

**Table 3. 1:** Subject characteristics

	Adolescent/Young Adult (n=10, 26.31%)	Older Adult (n=28, 73.68%)
Variable	Obs. (%)	Obs. (%)
<b>Biological Sex</b>	10	28
Female	3 (30.00%)	10 (35.71%)
Male	7 (80.00%)	18 (64.29%)
<b>Pump Use</b>	10	28
Yes	8 (80.00%)	23 (82.14%)
No	2 (20.00%)	5 (17.86%)
<b>Race</b>	10	28
White	10 (100%)	28 (100%)
<b>Ethnicity</b>	10	28
Hispanic or Latino	0 (0%)	0 (0%)
<b>BMI Class</b>	10	28
Under Wt.	0 (0%)	0 (0%)
Normal Wt.	2 (20.00%)	12 (42.86%)
Over Wt.	7 (70.00%)	12 (42.86%)
Obese I	1 (10.00%)	2 (7.14%)
Obese II	0 (0%)	1 (3.57%)
	Mean ± Std. Dev, Min/Max	Mean ± Std. Dev, Min/Max
<b>Age (year)</b>	21.3 ± 2.86, 15/25	41.03 ± 13.27, 26/68
<b>BMI (kg/m<sup>2</sup>)</b>	26.94 ± 2.65, 22.49/31.60	26.46 ± 3.78, 20.74/39.86
<b>T1DM Duration (year)</b>	11.4 ± 4.19, 5/17	22.21 ± 13.61, 3/57
<b>HbA1c (%)</b>	9.33 ± 2.56, 6/13.4	7.08 ± 0.90, 5.8/9.3
<b>TEE (kcal/d)</b>	3598 ± 2127, 2099/8293	2335 ± 401, 1735/3335
<b>REE (kcal/d)</b>	1766 ± 160, 1499/1967	1668 ± 287, 1239/2382
<b># of Valid Days</b>	6.7 ± 4.21, 1/15	7.46 ± 5.25, 1/16

*Table 3.1 A comparison of characteristics between Adolescent/young adults subjects and Older adult subjects with T1DM enrolled in the T1Dexi Pilot study. Results are means ± standard deviation of the mean (SD). Range of values expressed as the low – high observations.*

**Table 4. 1:** Subject characteristics of diabetes markers.

	Adolescent/Young Adult (52 observations)	Older Adult (173 observations)
Variable	Mean ± Std. Dev, Min/Max	Mean ± Std. Dev, Min/Max
<b>Time In Range (%)</b>	47.92 ± 25.7 0/93.68	63.85 ± 20.03 17.7/100
<b>Mean Glucose (mg/dL)</b>	179 ± 63.95 98.4/307.3	145 ± 37.91 86.45/264.8
	Adolescent/Young Adult (50 observations)	Older Adult (165 observations)
<b>Insulin per Kg</b>	.588 ± .27 .081/1.11	.430 ± .137 0/.81

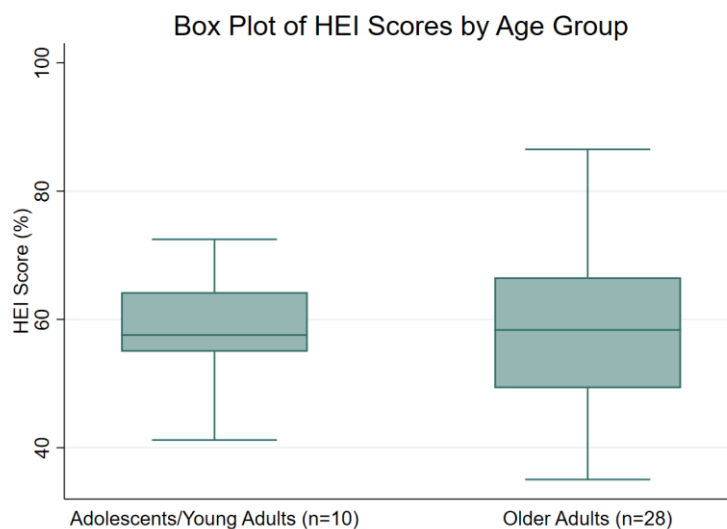
*Table 4.1 A comparison of diabetes/glucose marker characteristics between adolescents/young adults subjects and older adult subjects within T1DM enrolled in the T1Dexi Pilot study. Results are means ± standard deviation of the mean (SD). Range of values expressed as the low – high observations.*

## HEI Score

A daily HEI score, expressed as a 1 to 100, along with the 13 component sub scores were calculated for all valid (at least 70% or more captured TEE) recorded days of food intake per subject. Some subjects had 1 valid HEI score while others had upwards of 16 valid HEI scores. On average adolescents/young adults had 6.7 ( $\pm$  4.21) valid days of nutrient intake and older adults had 7.46 ( $\pm$  5.25) valid days of nutrient intake. Subjects were categorized in age groups for the mean analysis, adolescents/young adults were 25 years or younger, older adults were 26 years or older.

The adolescents/young adults average HEI score was 58.92 ( $\pm$  8.8, 41.2/72.48) and the older adults average HEI score was 57.55 ( $\pm$  11.26, 35.04/86.52), with both groups showing a diet that “needs improvement”. No statistical differences between the mean age group HEI scores were observed (p value = 0.73). Notably, the older adults had a higher variation of HEI scores, as seen in the box plot below.

**Figure 2. 1:** A Box Plot of a mean HEI Score (%) per subject (n=38) sorted by age group.

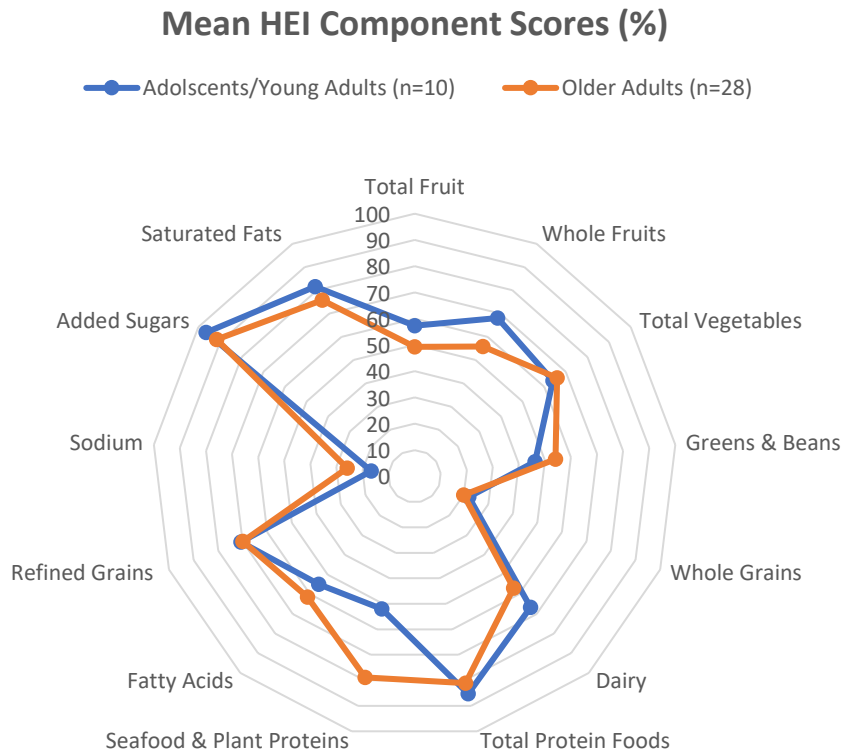


*Figure 2. 1 The Adolescents/young adults recorded a mean HEI score of 58.92 while the older adults recorded a mean HEI score of 57.55, according to the HEI-2015. HEI scores >80 indicate a “good” diet, scores ranging from 51 to 80 reflect a diet that “needs improvement”, and HEI scores <51 imply a “poor” diet.*

### **HEI Component (13) Scores**

We further explored the relationship between HEI scores and age groups by individually looking at the 13 component scores of the HEI. A mean sub score was calculated per subject for each of the 13 components scores and then one mean score was calculated per adolescent/young adult and older adult. Results are demonstrated in a radar graph (Figure 3). Though the average HEI scores among the two groups showed no statistical differences, there are some variations within the 13 components among the age groups.

**Figure 3. 1:** Mean Healthy Eating Index (HEI) component (13) scores.



*Figure 3. 1 The outer edge of the circle represents 100% of the maximum score for that component, while the center of the circle represents a score of 0% for that component. Ideally you would want a full circle. Average total scores per component are displayed as adolescent/young adults and older adults respectively. Total fruit 57.29% and 49.31%. Whole fruits 68.03% and 55.85%. Total vegetables 63.99% and 65.93%. Green & Beans 46.21% and 54.03%. Whole grains 22.08% and 19.99%. Dairy 66.63% and 56.80%. Total protein foods 85.31% and 81.12%. Seafood and plant proteins 52.05% and 78.91%. Fatty acids 54.96% and 61.42%. Refined grains 70.68% and 69.91%. Sodium 16.60% and 25.91%. Added sugars 96.42% and 91.60%. Saturated fat 81.56% and 75.75%.*

There are two groupings within the HEI components categories: adequacy components and moderation components. Adequacy components represent the foods groups that are encouraged, for these components higher scores reflect high intakes, because higher intakes are desirable. Total fruit, whole fruit, total vegetables, greens &

beans, total protein foods, and seafood & plant proteins are the adequacy components within the HEI scoring subsystem. Moderation components represent food groups for which there are recommended limits to consumption, for these components higher scores reflect lower intakes because lower intakes are desirable. Refined grains, sodium, saturated fats, and added sugars are the moderation components within the HEI scoring subsystem.

Components with the highest scores for the adolescent/young adult subjects were added sugars, whole fruits, dairy, and total protein foods, whereas components with the lowest scores were sodium, whole grains, greens & beans, and seafood & plant proteins. Components with the highest scores for the older adult subjects were added sugars, total protein foods, seafood & plant protein, and total vegetables, whereas components with the lowest scores were whole grains, sodium, greens & beans, and whole fruits.

The most noticeable mean difference is the older adult population scored significantly higher in the Seafood & Plant Protein component compared to the adolescent/young adult group (78.9% vs. 52.05%, respectively).

Both groups are doing “good” in the added sugar components (94.6% and 91.6%, labeled adolescent/young adult and older adult respectively) with a higher score reflecting a lower intake as lower intakes are desirable for the moderation components. This indicates that the current education recommendations to limit foods and beverages that are high in added sugar is being understood within the T1DM population.

Contrastingly, both groups are doing “poor” in the sodium component (16.6% and 25.8%, labeled adolescent/young adult and older adult respectively) with a higher score being desirable for this component. Furthermore, both groups demonstrated that the whole grains component was significantly lower than any other adequacy component with 22.0% of desired intake being achieved by adolescent/young adults and 19.9% of desired intake being achieved by older adults.

Diving deeper, we ran a mixed-effects model using all the HEI scores, with an effective sample size of 268, compared to a mean HEI score per subject by age group, to increase the statistical power. The fixed effects were as followed: Age, BMI, and biological sex. The random effect was the subject (Table 4 model 1). A reduced model that removed BMI and biological sex, non-significant factors, was run (model 2). The BMI and biological sex of the subject did not have a significant effect on HEI score in the mixed effect model. However, age of the subject did have a significant effect on HEI score in the mixed model indicating an increase in diet quality with age. The relationship between age and HEI score is graphed in Figure 4.1

The variability within subjects across the different days of HEI score was greater than the variability between subjects (Table 4 model 2). Both parameters, within subject and between subject, variability had a strong impact on the model but the effects of the within subject variability (coefficient 135.8157) was greater than between subjects (coefficient 54.84011).



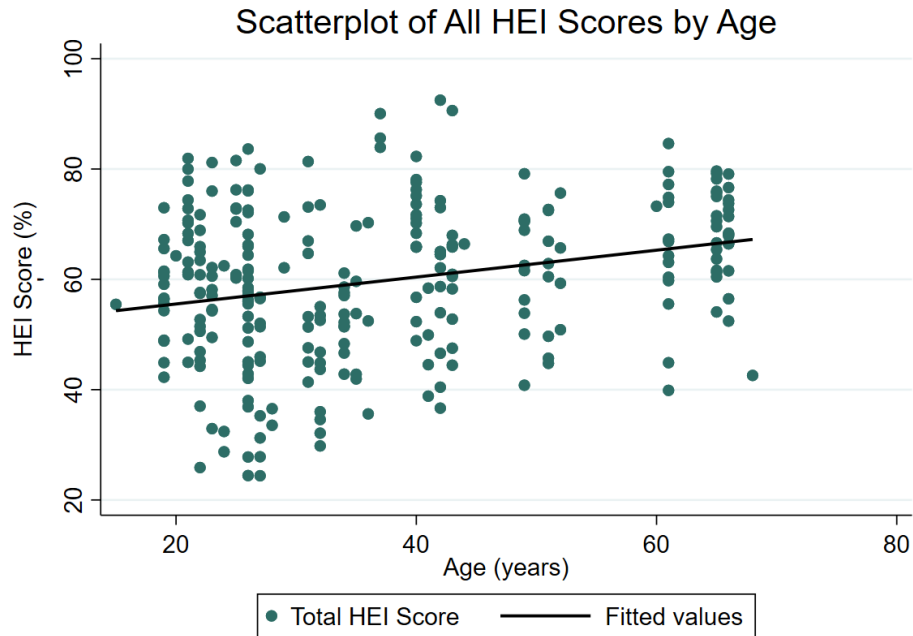
Many factors contribute to overall glycemic control among subjects with Type 1 diabetes. We next examined if diet quality, as measured by HEI score, was a predictor of glycemia measured by either time in range (70-180 mg/dl) or mean glucose. We conducted similar mixed effects models with glycemic control (time in range or mean glucose) as the dependent variable and HEI score, age, BMI and biological sex as the fixed effects. Subject was the random effect. HEI was not a significant predictor of glycemic control in our models (results not shown). It is possible we did not observe a significant relationship due to a small population (n) size and insufficient power to observe the relationship. It is also possible overall diet quality is not a significant predictive factor for glycemic control.

**Table 5. 1:** Total HEI mixed-effects models among 268 observations within 38 subjects.

Mixed Effects Model								
	Model 1				Model 2			
	Coef.	Std. Err.	P >  z	95% CI	Coef.	Std. Err.	P >  z	95% CI
<b>Fixed Effects</b>								
Age	.1736192	.1110082	0.118	-0.439529 .3911914	.2201953	.1062789	0.038	.0118926 .4284981
BMI	.0465987	.5149119	0.928	-.9626101 1.055808				
Biological Sex	-5.360511	3.487855	0.124	-12.19658 1.475559				
<b>Random Effects Parameter</b>								
	Estimate	Std. Err.	95% CI		Estimate	Std. Err.	95% CI	
<b>Between subject variability</b>	56.08547	21.847	26.13855 120.3426		54.84011	21.49167	25.43988 118.2174	
<b>Within subject variability</b>	135.2255	12.64153	112.586 162.4176		135.8157	12.75406	112.9838 163.2615	

*Table 5. 1 Model 1 used a mixed model effects model. Model 2 used a mixed model effects model. Fixed effects with p>0.05 were considered insignificant and excluded.*

**Figure 4. 1:** Scatterplot of all HEI Scores (n=268) among the 38 subjects by Age.



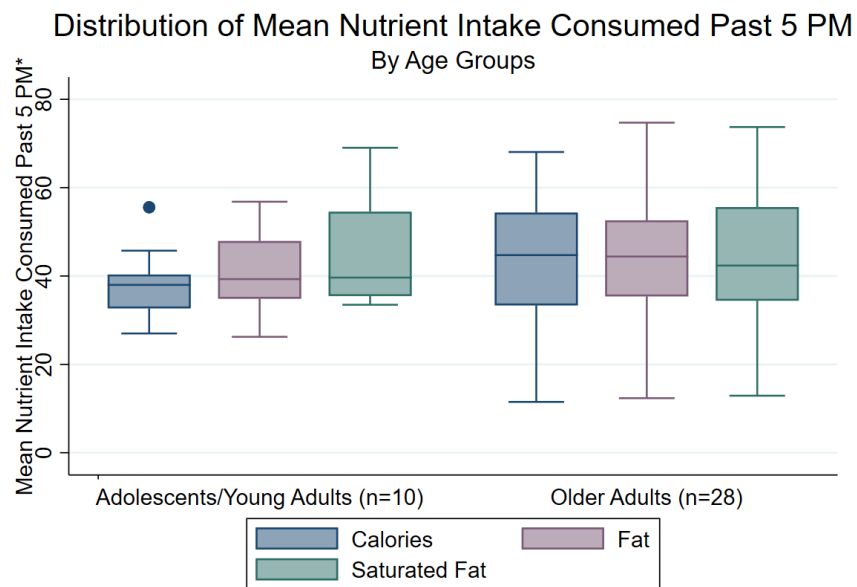
*Figure 4.1 The HEI score is expressed as a percentage. There is a moderate linear trend between HEI score and age (Pearson  $r = 0.2688$ )*

### **Energy Distribution**

Daily totals of calories, fat, and saturated fat intakes were calculated for all valid (at least 70% or more captured TEE) recorded days of food intake per subject. Of those daily totals of calories, fat, and saturated fat intake the percentage of calories, fat, and saturated fat intake consumed past 5 PM was then calculated per subject and expressed as a mean percentage. Subjects were categorized in age groups for the mean analysis: adolescents/young adults were 25 years or younger and older adults were 26 years or older.

Adolescent/young adults consumed a mean of 38.45 ( $\pm$  8.05, 27/55.56) % of total calories past 5 PM and the older adults consumed a mean of 43.91 ( $\pm$  15.11, 11.5/68) % of total calorie intake past 5 PM; there was no difference between groups (p value of 0.2863). Similarly, adolescents/young adults consumed a mean of 41.56 ( $\pm$  10.4, 26.24/56.81) % of total fat past 5 PM and older adults consumed a mean of 44.27 ( $\pm$  14.67, 12.35/74.71) % of total fat past 5 PM. Again, there was no difference between groups (p value = 0.5942). Lastly, adolescents/young adults consumed a mean of 45.27 ( $\pm$  12.2, 33.49/69.03)% of total saturated fat intake past 5 PM and older adults consumed a mean of 44.71 ( $\pm$  15.62, 12.9/73.71)% of total saturated fat past 5 PM with no difference between means (p value =0.9194).

**Figure 5. 1: Box Plot of the distribution of mean nutrient intake consumed past 5 PM by age groups.**



*Figure 5. 1 Box Plot of meal nutrient distribution (calories, fat, and saturated fat) consumed past 5 PM among adolescents/young adults and older adults' subjects.*

*\*Means of the meal nutrient intakes consumed past 5 PM are expressed as a percentage of the total nutrient intake of that day, per subject.*

Similar to the pattern with HEI score, the older adult subjects had a high variation within calories, fat, and saturated fat intake consumption past 5 PM. This was contrary to our initial hypothesis, so we further explored the relationship between energy distribution among age groups. We ran a mixed-effects model using all valid days with total calories (%) consumed past 5PM, for greater statistical power. The sample size was 259. The fixed effects were as followed: Age, BMI, Biological Sex, Fat, and Saturated Fat. The random effect was the subject. (Table 4, model 1). Both Fat and Saturated Fat were expressed as percentages consumed past 5PM. A reduced model that removed Age, Biological Sex, and Saturated Fat, non-significant factors, was run (model 2). The age, biological sex, and saturated fat consumption did not have a significant relationship with total calories (%) consumed past 5PM. However, higher BMI and higher fat consumption were significantly associated with increased calories (%) consumed past 5 PM. The relationships between BMI and fat consumption past 5 PM and total calories consumed past 5 PM are illustrated in Figure 6.1

**Table 6. 1:** Mixed-effects model of calories (%) consumed past 5PM among 268 observations within 38 subjects.

Mixed Effects Model								
	Model 1				Model 2			
	Coef.	Std. Err.	P >  z	95% CI	Coef.	Std. Err.	P >  z	95% CI
<b>Fixed Effects</b>								
Age	.0050860	.0618257	0.411	-.0703158 .1720364				
BMI	.7833796	.2964288	0.008	.2023898 1.364369	.7556908	.2773622	0.006	.2120708 1.299311
Biological Sex	-.4527664	1.948748	0.816	-4.272241 3.366712				
Fat*	.6591728	.0559848	0.000	.5494446 .7689011	.7152509	.0246128	0.000	.6670107 .7634911
Saturated Fat*	.0603817	.054373	0.267	-.0461875 .1669509				
<b>Random Effects Parameter</b>								
	<b>Estimate</b>	<b>Std. Err.</b>	<b>95% CI</b>		<b>Estimate</b>	<b>Std. Err.</b>	<b>95% CI</b>	
<b>between subject variability</b>	13.63434	6.030269	5.730075 32.44204		13.5272	5.6859	5.935015 30.83147	
<b>within subject variability</b>	67.10542	6.187297	56.01116 80.39714		66.91881	6.144242	55.8977 80.1129	

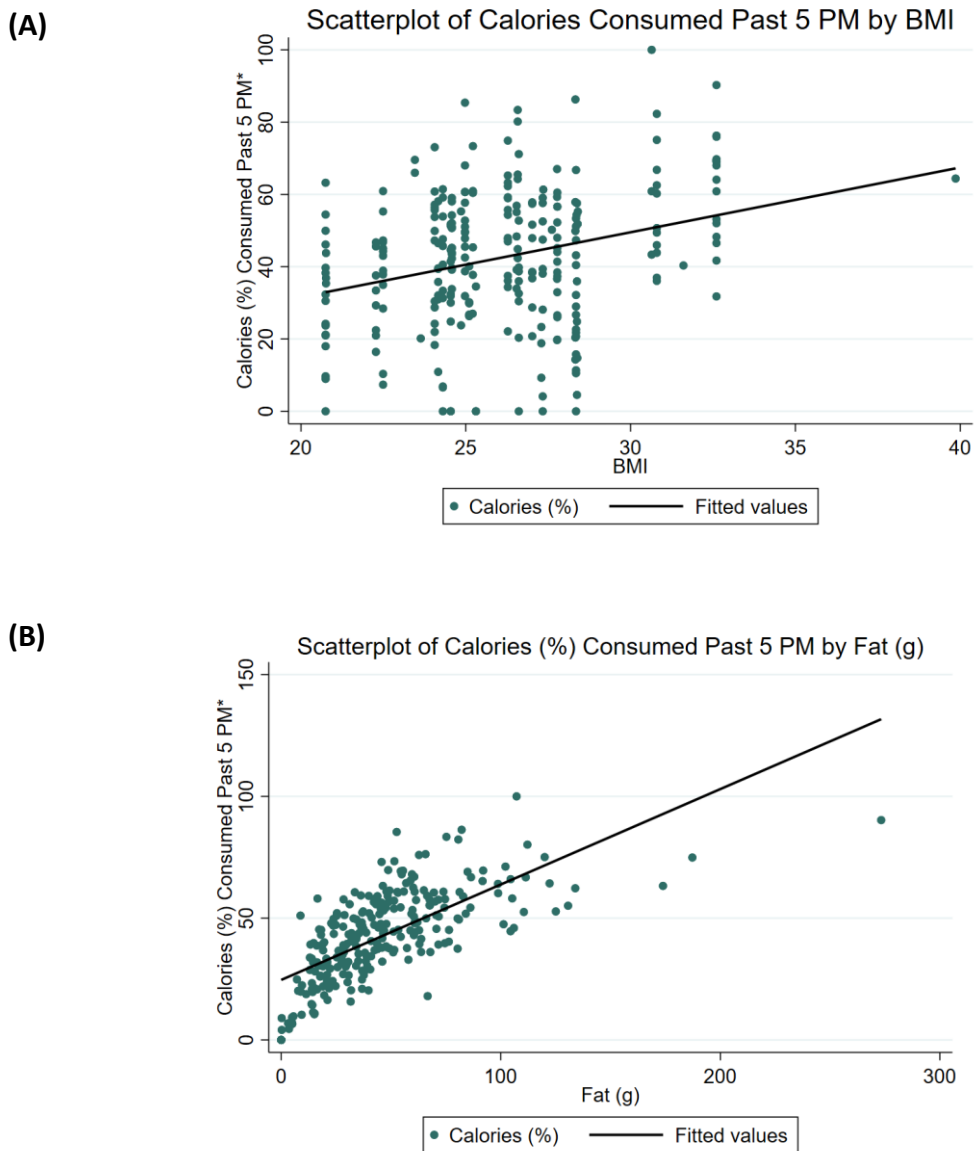
Table 6. 1 Model 1 used a mixed model effects model. Model 2 used a mixed model effects model. Fixed effects with  $p > 0.05$  were considered insignificant and excluded.

\*= The total percentage of calories consumed past 5 PM from fat and saturated fat.

Insulin sensitivity can be lower later in the day and we further examined if % of total energy consumed past 5 PM was a significant predictor of glycemic control. We ran a mixed effects model with either time in range or mean glucose as the dependent variable. Age, biological sex, BMI and % of energy consumed past 5 PM were the fixed effects; subject was the random effect. Similar to the results with the HEI score, % of energy, fat, or saturated fat consumed past 5 PM was not a predictor of time in range or mean glucose in this population (data not shown). This could be due to a small population (n) size with insufficient power to detect a relationship. There was not a lot

of variation across subjects in the % of total energy, fat and saturated fat consume past 5 PM in this population that may have masked any association if one exists, or it is possible that no relationship exists.

**Figure 6. 1:** Scatterplot of calories by BMI **(A)** and calories by fat **(B)**.



*Figure 6. 1* Calories and fat are expressed as a percentage. Sample size for both **(A)** and **(B)**  $n=268$ . **(A)** Pearson  $r = .2910$  and **(B)** Pearson  $r = .6890$

*\*Means of the meal energy intakes consumed past 5 PM are expressed as a percentage of the total energy intake of that day, per subject.*

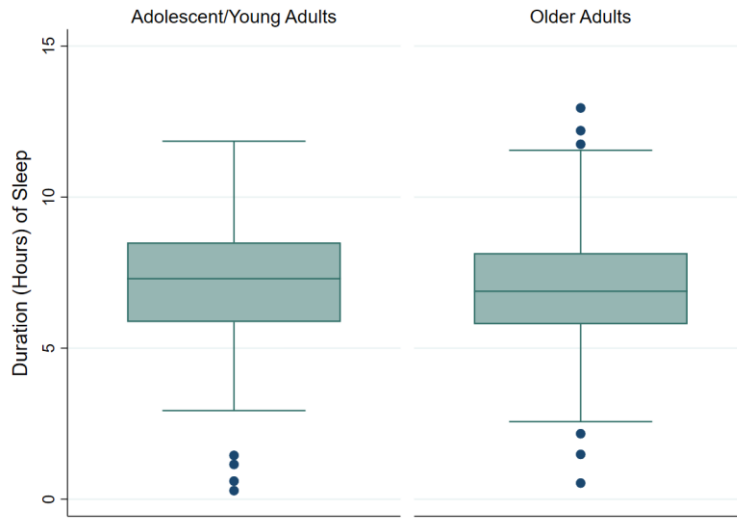
### **Duration of Sleep**

A total of 26 subjects were included in the duration of sleep analysis. Subjects (6) enrolled in the remote pilot arm of the study did not have recorded sleep data and an additional 6 subjects had missing sleep data. Within the adolescent/young adults' population there were 9 subjects, and within the older adult population there were 17 subjects. The duration, expressed in hours, of sleep was calculated for each day by taking the difference between the "Start Sleep Time" and the "Start Wake Time".

The adolescent/young adults (observation of n=193) averaged  $7.03 \pm 2.01$  hours of sleep a night while the older adults (observations of n=443) averaged  $6.80 \pm 1.98$  hours of sleep a night. A box plot of this distribution is displayed in Figure 6a below, and a scatterplot showing the relationship of total sleep hours by age in Figure 6b. In addition to a shorter duration of sleep, there is also a higher variability in duration of sleep among the older adults' subjects compared to the adolescent/young adult subjects. It is important to note the number of observations between the adolescent/young adult subjects and the older adult subjects is almost 2-fold different.

**Figure 7. 1:** Box plot of all sleep data days per adolescent/young adult subjects and older adult subjects **(A)** and a scatterplot of all sleep data days per adolescent/young adults subjects and older adult subjects by age **(B)**.

(A)



(B)

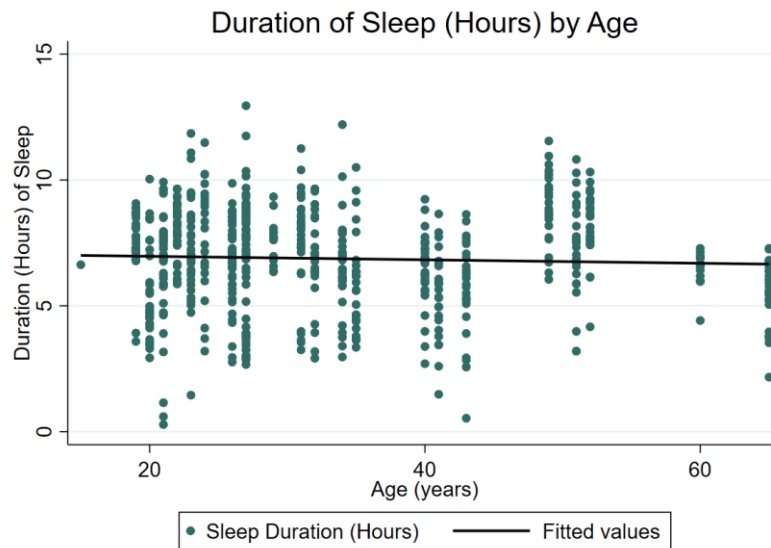


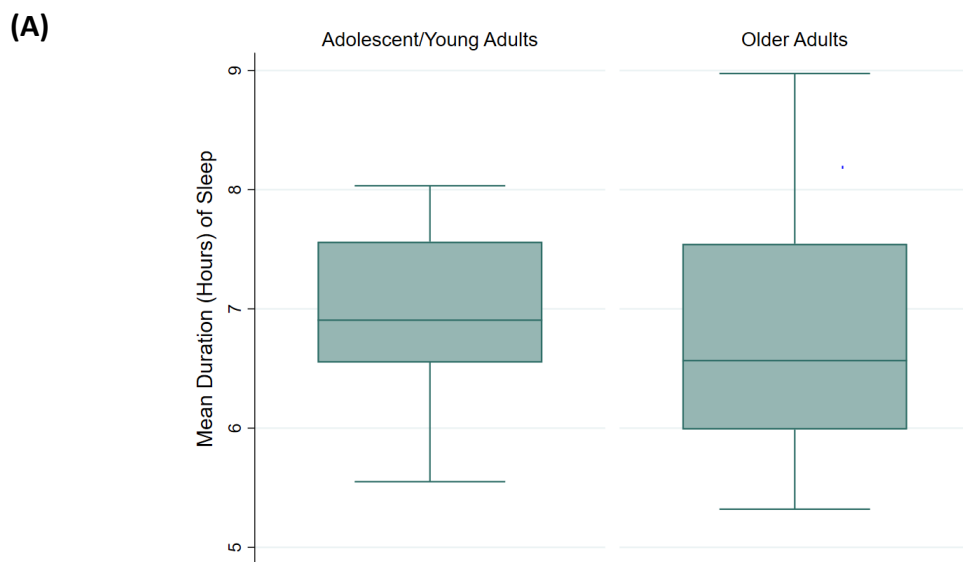
Figure 7. 1 Adolescent/young adults subjects (n=193) and older adult subjects (n=448). There appears to be no significant difference between sleep duration (hours) among adolescents/young adults and older adults. Pearson  $r = -0.0435$ .

A mean of sleep hours was then calculated per subject to correct for some potential outliers shown in Figure 6. When calculating a mean average sleep hours per subject the adolescent/young adults averaged 6.94 (observations of n=9) hours of sleep



a night while the older adults averaged 6.80 (observations of n=17) hours of sleep a night. This distribution is shown in a Figure 7a below, and a scatterplot showing the relationship of average sleep hours by age in Figure 7b. In this small cohort of patients with type 1 diabetes, there was no significant difference in the duration of sleep between adolescent/young adults and older adults.

**Figure 8. 1:** Box plot of calculated mean sleep data per adolescent/young adults subjects and older adult subjects **(A)** and a scatterplot of calculated mean sleep data per adolescent/young adults subjects and older adult subjects **(B)**.



(B)

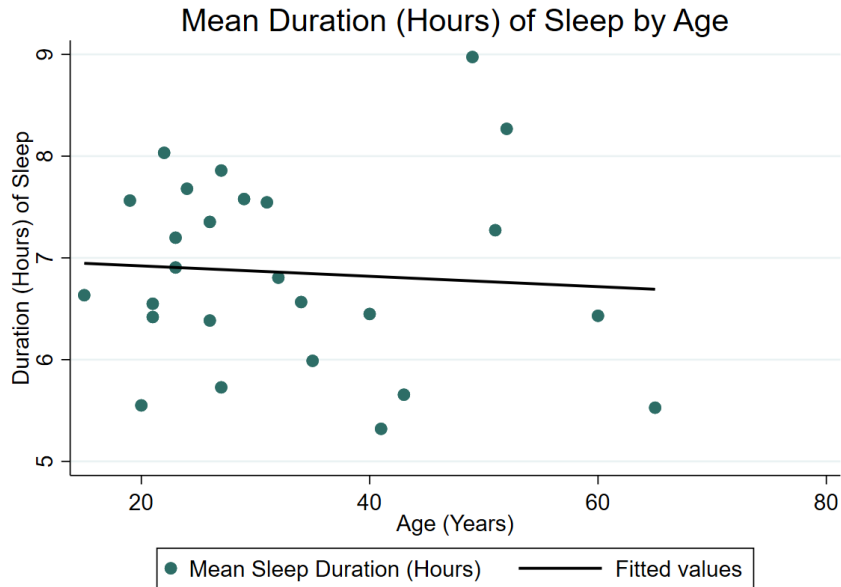


Figure 8. 1 Sleep data for adolescent/young adults subjects ( $n=9$ ) and sleep data for older adult subjects ( $n=17$ ). There is a weak linear negative trend in (B). Pearson  $r = -0.0730$  for mean duration (hours) of sleep by age.

## Discussion

In this cohort of individuals living with type 1 diabetes, the overall diet quality among adolescents/young adults and older adults was very similar as illustrated by similar means and standard deviations within the overall HEI index between age groups (Figure 2. 1). We initially hypothesized that the mean HEI score will be lower among adolescents/young adults compared to the older adults. However, when we looked at age as a continuous variable rather than by two age groupings, we did see some association with HEI and age (years). The association was moderate as shown with a Pearson correlation coefficient of 0.2688 (Figure 4. 1).

Further research with a larger sample size is needed to further interrogate this relationship, if any, between overall diet quality measured by HEI and age (years). When assessed to see if diet quality was associated with measures of glycemic control, either time in range or mean glucose during the day, we concluded that overall diet quality was not a substantial predictive factor for glycemic control. This may be related to a lack of statistical power to detect this association.

We initially hypothesized that adolescent/young adults will consume a greater percent of their daily total energy after 5 PM compared to older adults and that the mean percent of total energy from fat will be higher among adolescent/young adults than older adults. We did not observe any significant differences between the two age groups. When looking at the subjects outside the age groups, there was a moderate relationship between calories (%) consumed past 5 PM and BMI shown with a Pearson correlation coefficient of 0.2910 and we did see a strong relationship between calories (%) consumed past 5 PM and fat (g) as shown with a Pearson correlation coefficient of 0.6890. The data suggests that calories consumed after 5 PM are most likely high fat and high calorie foods. Additionally, we initially hypothesized that the mean sleep duration would be lower among adolescents/young adults than the older adults. We also did not observe a significant difference between the mean sleep duration among the two groups.

Previous literature have suggested differences between the psychosocial behaviors in the general adolescent/young adult populations. In most of the studies, the

general adolescent/young adult population reports skipping meals, consuming large amounts of energy later in the day, and achieving undesirable sleep duration of less than 7 hours of sleep per night. Our results were not consistent with the previous literature. We did see some subjects consume large amounts of energy later in the day in both young and older adults and this was tightly associated with increased fat intake. Interestingly, there was high variability across different days in both diet quality and timing of nutrient intake consumed by a particular participant. The variability across different days for a given subject was greater than the variability between different subjects. This high day to day variability was unexpected and most likely impacted our ability to detect differences in outcomes by age group.

Notable, the overall population of the study in general did not consume particularly healthy diets as the mean HEI scores among both age groups were categorized in the “needs improvement” category. There are many areas where a Registered Dietitian can focus on increasing overall diet quality among all aged individuals with type 1 diabetes: increasing whole grains consumption, reducing sodium intake, and encouraging more greens & beans. Even if overall diet quality is not related to overall glycemic control, it is still an important factor for overall health and reducing potential for the development of comorbidities such as cardiovascular disease.

There were some strengths within our study. The diets of the participants were captured using the remote food photography method (RFPM). The RFPM improves dietary reporting and estimation of meal nutrient composition when compared to the

traditional dietary assessment tools like the 24-hour recall and diet food frequency questionnaires.

Limitations of this study include the following: a non-diverse/inclusive population being assessed, missing CGM and insulin data, a small sample size, and missing sleep data. The population being assessed all identified as white individuals, which does not accurately represent all individuals or all individuals with T1DM. Missing CGM and insulin data values impacted the power of our analysis and ability to observe a relationship between adolescent/young adult psychosocial behaviors relative to a marker of glycemic control. We were also not able to control for insulin dose in our models. Similarly, due to a small population size (n) of individuals enrolled who met our inclusion criteria, our statistical tests were considered underpowered. The sleep data could have exhibited self-reporting bias as data collection consisted of a pre-programmed question prompt asking the subject to record “Sleep Start Time” and “Sleep Awake Time”. Limitations could be present on how accurately subjects reported these data points.

In conclusion, there is a weak association between diet quality, measured by HEI, and age within the T1-DEXI pilot study. However, there is no association between HEI and glycemic control which may be due to a lack of statistical power. Alternatively, diet quantity, exercise, insulin sensitivity, insulin dosed and previous glycemic control may all play a larger role in overall glycemic control and diet quality, as measured by HEI may not be a major factor. We have previously published that exercise improves time in range the day after formal exercise (Riddell et al). Further research needs to be done to

determine the relationship between diet quality and timing of nutrient intake among adolescents/young adults with type 1 diabetes and impacts, if any, on glycemic control.

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