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## Longitudinal Association between Television Watching, Computer Use and Meal Frequency and Risk Markers in Diabetes among Youth with Diabetes

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LONGITUDINAL ASSOCIATION BETWEEN TELEVISION WATCHING, COMPUTER  
USE AND MEAL FREQUENCY AND RISK MARKERS IN DIABETES AMONG YOUTH  
WITH DIABETES

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## DEDICATION

This dissertation is lovingly dedicated to my mother, Beiling Chen. Her support, encouragement, and constant love have sustained me throughout my life.

This is also dedicated to my wife, Fei Xu, who have been very important in my life for her love and support.

I love you all.

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Again, I would like to declare my sincere gratitude for everyone.

## ABSTRACT

**BACKGROUND AND OBJECTIVES:** Television watching and computer use are considered to be the main sedentary behaviors in children and youth. However, their longitudinal impact on HbA1c and serum lipids among youth with type 1 diabetes (T1D) and type 2 diabetes (T2D) are under-studied. Sedentary behavior is normally assessed by questionnaire in large epidemiological studies, however, its measurement by questionnaire has not been evaluated among youth with diabetes. Also, no recent studies have evaluated the optimal meal frequency for glycemic control in youth with T1D and T2D; for this reason nutritional guidelines on meal frequency for youth with diabetes are vague. In this study we investigated the longitudinal relationship between television watching, computer use and meal frequency and HbA1c and serum lipids among youth with T1D and T2D; and evaluated the performance of questions to measure sedentary behavior in youth with diabetes.

**RESEARCH DESIGN AND METHODS:** This study included 1049 US youth ( $\geq 10$  years old at the initial visit) with T1D and T2D who participated in the SEARCH for Diabetes in Youth Study and provided baseline data from 2002 to 2005. These participants were followed-up prospectively at 1, 2 and 5 years after the initial visit. All participants included in these analyses had physician diagnosed diabetes, documented year of diagnosis, were less than 20 years old on December 31 of the year of diagnosis, and attended at least one follow-up visit. Data collection procedures were performed by

trained and certified staff following standardized protocols for both initial and follow-up visits,. Data collection approaches included questionnaires, physical examination and laboratory tests. Between July 2003 and March 2006, SEARCH cases aged  $\geq 10$  years who participated in the on-site SEARCH visit were invited to participate in the SEARCH-CC study in South Carolina and Colorado centers. All youth without diabetes were selected from health care provider offices in the same geographic areas as cases. Overall, 49% (n=220) of invited youth without diabetes participated in SEARCH CC study.

**RESULTS:** Increased television watching on weekdays and during the week over time was associated with larger increases in HbA1c among youth with T1D and T2D (p-value<0.05). Among youth with T1D, significant positive longitudinal associations were observed between television watching and TG (p-value<0.05) (week days and whole week), and LDL (p-value<0.05) (whole week). The overall correlations between hours of television watching from the YRBS and number of half hour television watching blocks from the 3DPAR were 0.30 (p<0.05) and 0.45 (p<0.05) among youth with T1D and T2D respectively, and 0.41 (p<0.05) among youth without diabetes. The correlations tended to be higher in females, older participants, normal weight T1D participants and overweight T2D participants. Similarly, African Americans and Hispanics with T2D tended to have higher Pearson correlations. The YRBS questions tended to overestimate (by 0.23, 0.54 and 0.40 for youth with T1D, T2D and without diabetes respectively) television watching compared with 3DPAR after adjusting for age, gender, and race. Among youth with T1D, HbA1c increase over time was higher for those who consumed 1-3 meals/day compared

with those who consumed 4-5 meals/day (reference group); changes in HbA1c for individuals who ate 6-10 meals/day were not different from the reference group after adjusting for potential confounders including BMI z-scores and total energy intake. This association was stronger among youth who were  $\geq 15$  years (p-value for interaction $<0.05$ ) and African Americans (p-value for interaction $<0.05$ ). Youth who consumed 6-10 meals/day consumed more calories on average than youth eating 4-5 meals/day. Meal frequency was not associated with changes in serum lipids among youth with T1D and T2D.

**CONCLUSIONS:** Youth with T2D who increased their television watching over time vs those that decreased it had larger increases in HbA1c over 5 years. Youth with T1D who increased their television watching over time had increases in LDL, TG and to a lesser extent HbA1c. Television watching measured by YRBS questions showed weak to moderate correlation with television watching measured by 3DPAR among youth with diabetes. The correlation was stronger among youth who were older, female, overweight, African American and Hispanic. Youth with T1D who ate 1-3 meals/day had higher HbA1c over 5 years compared with those who ate 4-5 meals/day, but not those who ate 6-10 meals/day. Frequent meals without increasing total energy intake may be beneficial for youth with T1D.



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# CHAPTER 1

## INTRODUCTION

### **1.1 Background**

Diabetes is a serious, costly, and potentially life-threatening disease. Diabetes is characterized by elevated blood glucose resulting from either insufficient insulin production or ineffective insulin action. Diabetes can cause both chronic and acute complications. Chronic complications of diabetes include cardiovascular disease, renal disease, nephropathy, and neuropathy, and can influence all segments of people with the disease.

There are mainly two types of diabetes which are type 1 diabetes (T1D) and type 2 diabetes (T2D). T1D is an autoimmune condition characterized by the progressive destruction of pancreatic beta cells leading to an absolute deficiency of insulin. T1D is possibly related to autoimmunity that is triggered by an interaction of genetic and environmental factors. T2D is usually a consequence of insulin resistance or impaired insulin action leading to hyperglycemia. In its early stages, T2D is characterized by increased insulin production to compensate for impaired insulin action. With the development of T2D, overproduction of insulin and chronic hyperglycemia impair beta cell function and reduce insulin production. T2D mainly occurs in persons genetically predisposed to the disease and is more likely to occur in the presence of other risk factors

such as obesity, insufficient physical activity, increased sedentary behavior, and poor diet.

The dramatic development of technology in the past few decades has resulted in changes in the environment, which have led to sedentary lifestyles. In this situation, youth spend more time on sedentary behavior that does not increase energy expenditure substantially<sup>1</sup>. One of the most common and important sedentary behaviors is television watching, which has been studied extensively in non-diabetic populations. Most youth in the United States are growing up in homes with television and spend more time on watching television than any other activity except sleep, and the time spent watching television may even exceed time spent in school<sup>2-5</sup>. Recent estimates indicate that children 2 to 18 years of age watch at least 2.5 hours of television each day and are exposed to about 6.5 hours of media per day from all sources<sup>6,7</sup>. This phenomenon is a major public health concern because watching television has an effect on obesity, metabolic and cardiovascular disease risk factors<sup>2,3,8-15</sup>. So, the American Academy of Pediatrics suggests that sedentary behavior, especially time watching television should be limited to less than 2 hours per day<sup>5</sup>.

Youth with T1D are particular at higher risk of developing cardiovascular disease than the general population<sup>16</sup>, and long-term glycemic control is a strong predictor for cardiovascular disease in T1D<sup>17-19</sup>. To our knowledge, there are few data specifically addressing the role of television watching and computer use in the adverse effect of T1D among youth. There is a potential inverse effect between physical activity and television

watching and computer use, which means, the more time youth spend on physical activity, the less time youth spend on television watching and computer use; the more time that is spent watching television and using the computer the less time is available for physical activity. Therefore, television watching and computer use are discouraged to improve physical activity. But the above association is still controversial; television watching and computer use may be independent of physical activity, which means, television watching and computer use and physical activity are not mutually exclusive. Each day, youth have the same opportunity to engage in many different activities that can be both physically active and sedentary. They can have different hours of television watching and computer use but still participate in one hour moderate-vigorous physical activity per day. So it is possible for a child to be both physically active and spend more hours watching television and using the computer. Furthermore, television watching is often accompanied with snacking and beverage intake which can increase intake of total energy. Moreover, youth are likely to be exposed to television advertising for unhealthy foods, which may trigger further unhealthy food consumption <sup>1,20-23</sup>.

Youth with T2D typically have been noted to be sedentary <sup>24</sup>. Based on data from NHANES III (1988-94), 26% of children watch 4 or more hours of television a day and 67% watch at least 2 hours a day <sup>25,26</sup>. Several studies have found a positive association between the amount of television watching and computer use and the prevalence of obesity <sup>13,26,27</sup>. Since obesity is an important risk factor of T2D diabetes in youth, hours of television watching and computer use may have influence on T2D in youth.



The Youth Risk Behavior Survey (YRBS) is an ongoing CDC surveillance program developed in 1989 to monitor health behaviors among US youth. The YRBS questions focus on the major risk behaviors and provide estimated prevalence of these risk behaviors among young people <sup>28</sup>. States and local districts use the YRBS data to assess and evaluate policies and programs to prevent health risk behaviors among youth <sup>29</sup>. Several studies have demonstrated the consistent reliability of the high school versions of the YRBS <sup>30-32</sup>.

The 3 Day Physical Activity Recall (3DPAR) is a self-reported measurement <sup>33</sup> that was designed to assess physical activity behavior of adolescents. The 3DPAR includes a list of 81 items related to physical activity and sedentary behavior for each of the previous 3 days. Each day is divided into 36 blocks of time (30 minutes per block) between 6:00 AM and midnight. Participants record their main activity (from the list of 81 items) and the intensity (light, moderate, hard and very hard) of that activity during each half hour block. The 3DPAR has been validated previously against an accelerometer ( $r=0.27-0.46$ ,  $p<0.05$ ) <sup>34,35</sup>.

Meal frequency has been recognized for over 20 years to be associated with metabolic changes in people with T2D <sup>36</sup>. The American Diabetes Association (ADA) guidelines on nutritional therapy in diabetes recognizes nutrition therapy as an essential component of diabetes treatment, and recommends individualized dietary counseling as part of the overall treatment plan <sup>37</sup>. Previous ADA statement of nutrition principles reported that increased meal frequency was related with lower mean glucose and insulin levels in T2D

<sup>38</sup>. While the most recent ADA guidelines on nutrition therapy do not specify the optimal meal frequency <sup>37</sup>. Jenkins et al <sup>36</sup> and Bertelsen et al <sup>39</sup> have compared the effects of 2 or 3 large meals/day with 6 to 13 small meals/day among adults with T2D in 2 days. Both studies showed that increased meal frequency could increase insulin sensitivity and lower blood glucose concentration over the day. Similar metabolic advantages, such as reduction in serum lipids and lipid concentration, have also been observed in healthy subjects <sup>40-42</sup>. However, a relatively longer (4 weeks) study conducted by Arnold et al <sup>43</sup> on the impact of meal frequency on metabolic effects among 13 adults with T2D did not confirm the potential benefits of increased meal frequency. Another randomized crossover study (24 weeks) conducted among adults with T2D reported eating two large meals a day could reduce body weight, hepatic fat content, fasting plasma glucose, C-peptide and glucagon, and increase oral glucose insulin sensitivity than six meals a day <sup>44</sup>.

There were several reasons to study television watching, computer use and meal frequency in youth with diabetes. 1) A sedentary lifestyle, particularly television watching and computer use, is common and is associated with numerous negative health behaviors and outcomes among children, including overweight <sup>12,45-47</sup>, irregular sleep <sup>48</sup>, insufficient consumption of fruits and vegetables <sup>49</sup>, and eating disorders <sup>50,51</sup>; 2) Meal frequency is particularly important for individuals with diabetes. For instance, although physical activity is recommended for youth with T1D, prolonged and moderate-vigorous physical activity can make it more difficult to monitor and regulate blood glucose levels before, during and after physical activity. Youth can experience unexpected hypoglycemia after physical activity as the body is replete with glycogen stores in the

liver<sup>52,53</sup>. So, in order to maintain blood glucose levels within the target range due to physical activity, extra monitoring of blood glucose concentration and a little snack are needed for every hour of physical activity to prevent hypoglycemia<sup>52,54</sup> which can increase number of consumed meals. Increased meal frequency can contribute to energy balance, such as increasing total energy intake that leads to over-weight and obesity which are risk factors of cardiovascular diseases. Currently, there are no clear guidelines for optimal meal frequency for youth with diabetes.

## **1.2 Aims and Research Questions**

Aim 1: Evaluate if change of hours of television watching and computer use are associated with change of HbA1c, LDL, HDL and TG in youth with T1D and T2D over time.

Research Question 1.1: Is the increase of hours of television watching and computer use associated with higher HbA1c longitudinally after adjusting for multiple covariates?

Research Question 1.2: Is the increase of hours of television watching and computer use associated with higher TG and LDL and lower HDL longitudinally after adjusting for multiple covariates?

Research Question 1.3: Is the association between the change hours of television watching and computer use and the change of HbA1c and serum lipids stronger among youth with T2D compared youth with T1D after adjusting for multiple covariates?

Aim 2: Evaluate the validity of self-reported television watching adapted from the YRBS compared with 3DPAR in SEARCH\_CC cases and controls?

Research Question 2.1: Are data collected on hours of television watching from the self-reported YRBS consistent with the 3DPAR in youth with and without diabetes?

Research Question 2.2: Do data collected on hours of television watching from the self-reported YRBS over or under estimate hours of television watching collected from the 3DPAR in youth with and without diabetes?

Aim 3: Evaluate if meal frequency is associated with HbA1c, LDL, HDL and TG in youth over time with T1D and T2D.

Research Question 3.1: What is the prevailing meal frequency pattern among youth with T1D and T2D?

Research Question 3.2: Is decreased meal frequency associated with higher HbA1c longitudinally after adjusting for multiple covariates among youth with T1D and T2D?

Research Question 3.3: Does the relationship between meal frequency and HbA1c, TG, LDL and HDL in research question 3.2 vary by diabetes type?

### **1.3 Significance**

Sedentary behavior, assessed as television watching and computer use, and meal frequency have potentially important effects on youth with diabetes but these relations are understudied in this population. In this dissertation I have studied the longitudinal relationship between television watching, computer use, and meal frequency on HbA1c and serum lipids (HDL, LDL and TG) in youth with diabetes using SEARCH for diabetes in youth data (Aim 1 and 3). The results characterized the relation between these potentially modifiable factors and markers of complications in children with diabetes. The information from these analyses will help clinicians providing care for children with diabetes to provide specific advice, and for researchers to conduct further studies. Ultimately this will improve the quality of life of youth with diabetes and reduce future complications.

Another aim of this dissertation related to the validation of self-reported hours of television watching among youth with diabetes. Television watching measured by questions adapted from the YRBS survey were compared an alternative method (3DPAR) which has been validated against an accelerometer. These results will help researchers to assess television watching in epidemiologic studies.

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## CHAPTER 2

### LITERATURE REVIEW

#### **2.1 Youth with Diabetes**

##### 2.1.1 Type 1 Diabetes in youth

##### 2.1.1.1 Definition, prevalence, incidence and trend

##### 2.1.1.1.1 Definition of T1D

T1D is an autoimmune condition characterized by the progressive destruction of pancreatic beta cells leading to an absolute deficiency of insulin.

##### 2.1.1.1.2 Prevalence of T1D

T1D prevalence of youth was estimated to be 1.48 per 1,000 in 2001 and 1.93 per 1,000 in 2009. Diabetes prevalence differed across major racial and ethnic groups, where white youth had the highest prevalence of T1D (2.55 per 1,000) and American Indian youth had the lowest prevalence of T1D (0.35 per 1,000) in 2009 <sup>1</sup>.

##### 2.1.1.1.3 Incidence of T1D

Based on 2002 and 2010 SEARCH for Diabetes in Youth (SEARCH) data, the incidence of youth T1D was 10.3 per 100,000 in 2002 and 17.0 per 100,000 in 2010 <sup>1</sup>. Among youth aged less than 10 years old, most diabetes cases are type 1 among all race/ethnic groups. In this age group, non-Hispanic Whites have the highest incidence of T1D.

Among older youth (ages 10-14 and 15-19 years), the highest incidence of T1D is still in

non-Hispanic White youth, followed by African American and Hispanic, and lowest among American Indian and Asian/Pacific Islanders <sup>1,2</sup>.

#### 2.1.1.1.4 Trend of T1D

The incidence of T1D is increasing in many countries of the world <sup>3-6</sup>. Most <sup>7-11</sup>, but not all <sup>2-4,12-20</sup> population-based registries showed an increasing incidence of T1D over time.

The average annual rates of T1D increased 2.8% globally based on data from the DIAMOND project which examined the trends in incidence of T1D from 1990 to 1999 in 114 populations from 57 countries among 84 million children less than 14 years of age <sup>5</sup>. In a similar analysis based on 20 population-based registries in 17 countries in Europe, the annual increase in T1D rate was 3.2% for the period from 1989 to 1998 <sup>21</sup> and 3.9% (95% CI, 3.6–4.2) from 1989 to 2003 <sup>22</sup>. The observed incidence rates confirmed, and in fact exceeded, the incidence predicted for 2010 by earlier projections <sup>4</sup>. In the European study <sup>22</sup>, estimates of the increased rates were highest in the youngest age group.

In the US, the SEARCH study estimated that the 2002–2005 incidence of T1D in non-Hispanic White youth less than 14 years old is 27.5 per 100,000 per year <sup>23</sup>, a rate that exceeded earlier estimates of T1D in the US <sup>4</sup>. By using data from the Colorado IDDM registry and the SEARCH-Colorado site, the incidence of T1D is shown to increase in youth less than 17 years of age over the past three decades <sup>12</sup>. During a 26-year period, the incidence of T1D increased by 2.3% per year and is much higher than predicted from earlier Colorado data <sup>4</sup>.

#### 2.1.1.2 Causes of T1D in youth

The exact cause of T1D is still unknown. What we know is that the immune system mistakenly destroys the insulin-producing (islet) cells in the pancreas in most people with T1D. Chronic inflammatory infiltrate has been observed to impact pancreatic islet.

Another possible reason would be that the pancreas loses cells producing insulin and the rest remaining  $\beta$ cells cannot regenerate enough these insulin-producing cells among patients with T1D. Also, genetics may play a role in this process, and exposure to certain viruses may trigger the disease.

#### 2.1.1.3 Clinical symptoms, treatment and management of T1D in youth

##### 2.1.1.3.1 Clinical symptoms

The signs and symptoms of T1D in children usually develop quickly, over a period of weeks, including increased thirst and frequent urination and weight loss. The condition may also present as diabetic ketoacidosis, the signs and symptoms of which include shallow rapid breathing, abdominal tenderness, and loss of consciousness <sup>24</sup>.

##### 2.1.1.3.2 Treatment and management

Treatment for T1D is a lifelong commitment of blood sugar monitoring, insulin administration, healthy eating and regular physical activity, even for children. As youth grows and changes so will his or her diabetes treatment plan. Over the years, youth may need different doses or types of insulin, new meal plans or other treatment changes <sup>24</sup>.

Blood sugar monitoring: The frequency of blood sugar monitoring varies depending upon the different types of insulin therapy used in youth, but it needs to be done at least three times a day to ensure the level of blood sugar is within target range <sup>24</sup>.

Continuous glucose monitoring (CGM): Continuous glucose monitoring is a way to monitor blood sugar levels, and may be most helpful for people who have developed hypoglycemia unawareness. Continuous glucose monitoring attaches to the body using a fine needle just under the skin that checks blood glucose level every few minutes. Since continuous glucose monitoring is not as accurate as standard blood sugar monitoring, so it's not considered as a replacement method for keeping track of blood sugar, but is used as an additional tool <sup>24</sup>.

Insulin and other medications: Individuals with T1D need lifelong insulin treatment. Because gastric enzymes interfere with insulin taken by mouth, taking oral insulin isn't an option for lowering blood sugar <sup>24</sup>. Basically, we have four available insulin types as follows: 1) Rapid-acting insulin, such as insulin lispro (Humalog) and insulin aspart (NovoLog), start working in five to fifteen minutes and peaks thirty to ninety minutes later; 2) Short-acting insulin, such as human insulin (Humulin R, Novolin R, others), starts working thirty to sixty minutes after injection and generally peaks in two to four hours; 3) Long-acting insulin, such as insulin glargine (Lantus) and insulin detemir (Levemir), has almost no peak and may provide coverage for as long as twenty to 26 hours; 4) Intermediate-acting insulin, such as NPH insulin (Humulin N, Novolin N), starts working one to three hours after it's taken and peaks in eight hours.

Healthy eating: The goal of healthy eating is to prevent youth from hypoglycemia and maintain blood glucose within an accepted range. Youth should adopt healthy eating habits to ensure adequate intake of essential vitamins and minerals by eating fruits, vegetables and whole grains which are high in nutrition and low in fat and calories <sup>25-28</sup>. All these recommendations are based on requirements for all healthy youth since there is no research which studies the nutrient requirements for youth with diabetes.

Physical activity: Youth with T1D are encouraged to engage in physical activity. Since physical activity can reduce blood sugar and continue affecting blood sugar for up to twelve hours. It is necessary to check the blood sugar before and after physical activity to prevent hypoglycemia. Also there may be a need to adjust food plans or insulin dose to compensate for the physical activity <sup>24</sup>.

#### 2.1.1.4 Complications of T1D in youth

Long-term complications of T1D develop gradually. Eventually, if blood sugar levels are not well controlled, diabetes complications may be disabling or even life threatening. Basically, T1D can have adverse effects on nearly every major organ in children's body, including heart disease, nerve damage, kidney damage, eye damage, foot damage, skin conditions, osteoporosis and brain problems <sup>24</sup>.

## 2.1.2 Type 2 Diabetes in youth

### 2.1.2.1 Definition, prevalence, incidence and trend

#### 2.1.2.1.1 Definition of T2D

T2D is usually a consequence of insulin resistance or impaired insulin action leading to hyperglycemia. In its early stages T2D is characterized by increased insulin production to compensate for impaired insulin action. With the development of T2D, overproduction of insulin and chronic hyperglycemia impair beta cell function and reduces insulin production.

#### 2.1.2.1.2 Prevalence of T2D

T2D prevalence of youth was estimated to be 0.34 per 1,000 in 2001 and 0.46 per 1, 1000 in 2009. Diabetes prevalence differed across major racial and ethnic groups, where American Indian youth had the highest prevalence of T1D (1.2 per 1,000) and white youth had the lowest prevalence of T1D (0.17 per 1,000) in 2009 <sup>1</sup>.

#### 2.1.2.1.3 Incidence of T2D

Based on 2002 and 2010 SEARCH data, the incidence of youth with T2D was 3.3 per 100,00 in 2002 and 5.2 per 100,000 in 2010. The incidence of T2D is the highest among Hispanics, followed by African Americans, Whites and American Indian, and is low among Asian Pacific islander<sup>1,2</sup>.

#### 2.1.2.1.4 Trend of T2D

An increasing proportion of youth with apparent T2D has been reported in the last decade<sup>1</sup>. One population-based study has reported a significant increased prevalence of diabetes among youth ages 10 to 19 from 1967 to 1996 derived from the Pima Indians. Another County-registry data also suggested that the incidence of pediatric diabetes is increasing. Outside North America, one study reported that the incidence of T2D among junior high school students increased from 3.2/100,000 per year between 1974-1981 to 13.9 between 1991-95 in Japan. Also, Libya, Bangladesh, Australia and Canada reported increasing incidence of T2D among youth in their population <sup>29</sup>. SEARCH data also indicated that the prevalence of T2D among children and youth increased from 2001 to 2009 in the United States <sup>1</sup>.

#### 2.1.2.2 Causes of T2D in youth

Overweight is the main risk factor for T2D in youth. In the United States, almost one fourth of children are considered to be overweight which doubles the chance of developing T2D. Besides overweight, the following factors may also contribute T2D <sup>30-33</sup>: family history, ethnicity, intrauterine exposure to maternal diabetes, low birth weight, pubertal augmentation of growth hormone/IGF secretory dynamics, sedentary lifestyle, and female gender.



### 2.1.2.3 Clinical symptoms, treatment and management of T2D in youth.

#### 2.1.2.3.1 Clinical presentation/symptoms

The symptoms of T2D in youth develop slowly. Initially, there may be no symptoms. Eventually, the following symptoms may occur: unexplained weight loss, increased hunger or thirst, dry mouth, frequent urination, fatigue, blurred vision, heavy breathing, slow healing of sores or cuts, itchy skin, numbness or tingling in the hands or feet.

#### 2.1.2.3.2 Treatment and management

**Metabolic control:** Diet and physical activity alone are effective for metabolic control in less than 10 percent of youths with T2D, and an oral medication or insulin is usually required to treat T2D. There may be a need for insulin treatment at later stages.

**Body weight management:** Since body weight has been shown to be associated with high-sweetened beverage intake <sup>24-27,34</sup>, television watching <sup>28,35</sup>, and physical activity <sup>28,35</sup>, so controlling for these risk factors would be beneficial for the body weight management leading to better control of blood sugar levels in diabetes.

#### 2.1.2.4 Complications of T2D in youth

T2D can have an influence on every major organ in youth, including the heart, blood vessels, nerves, eyes and kidneys. The long-term complications of T2D develop gradually. But eventually, T2D complications can be: heart disease, nerve damage (neuropathy), nonalcoholic fatty liver disease, kidney damage (nephropathy), eye damage, foot damage, skin conditions and brain problems.

## **2.2 HbA1c and serum lipids**

For years, HbA1c is widely used as the gold standard to assess glycemia and indicates the average blood glucose levels over a 2 to 3 month period <sup>25</sup>. HbA1c is recognized for several advantages in comparison to fasting plasma glucose level since its higher repeatability, low cost, free of fasting state and avoiding day to day variability <sup>25</sup>.

However, HbA1c can be influenced by genetic, hematologic, and illness-related factors <sup>25,36</sup>.

As a biomarker in the diagnosis and progression of diabetes in youth, HbA1c has been shown to be decreased by exercise and weight loss <sup>27</sup> and pharmacologic therapy <sup>28</sup> and increased in response to diets high in fats <sup>29</sup> in patients with diabetes.

Both serum lipids concentration and glycemic control can be considered as biomarkers for the quality of diabetes control and care. One study reported a positive correlation between glycemic control and serum lipids concentration in patients with T1D aged 13 to 40 years<sup>37</sup>, similar results have been reported in another study in patients with T2D <sup>38</sup>.

Also, results from SEARCH study have shown positive association between poor glycemic control and higher concentration of serum lipids in children and youth in all major ethnic/racial groups in the United States for both T1D and T2D <sup>39</sup>.

### **2.3 The relationship between television watching and computer use and HbA1c and serum lipids in youth with diabetes**

With the dramatic development of technology, changes in environment and society have created sedentary lifestyle in the past few decades. In this situation, youth spend more time engaged in sedentary behavior that does not increase energy expenditure substantially<sup>35</sup>. One of the most common and important sedentary behaviors is television watching, which has been studied extensively in non-diabetic populations. Most youth in the United States are growing up in homes with televisions and are spending more time on watching television than any other activity except sleep; the time spent watching television may even exceed time spent in school<sup>40-43</sup>. Recent estimates indicate that children 2 to 18 years of age watch at least 2.5 hours of television each day and are exposed to a total of 6.5 hours of media per day from all sources<sup>44</sup>. As a result, this phenomenon is a major public health concern because watching television has an effect on obesity, metabolic and cardiovascular disease risk factors<sup>40,41,45-52</sup>. The American Academy of Pediatrics suggests that sedentary behavior, especially time watching television should be limited to less than 2 hours per day<sup>43</sup>.

Studies examining the influence of television watching on childhood overweight proliferated since 1985 after Dietz and Gortmaker<sup>40</sup> found a positive association between television watching and obesity among children. Since then, four mechanisms have been proposed in attempt to explain this association as follows: (1) Television watching replaces time that would be used for physical activity; (2) Television watching increases between meal snacking causing greater total daily calorie intake; (3) Television content

plays a negative influence on children's food choices and attitudes towards health lifestyles through priming and/or cultivation <sup>53</sup> and (4) Television watching decreases one's metabolic rate (MET) <sup>50,54</sup>. However, the relative contribution of each of these mechanisms to obesity is unknown.

Youth with T1D are particular at higher risk of developing cardiovascular disease than the general population <sup>55</sup>, and long-term glycemic control is a strong predictor for cardiovascular disease in T1D <sup>56-58</sup>. To our knowledge, there are few data specifically addressing the role of television watching on health outcomes among youth with T1D. There is a potential inverse effect between physical activity and television watching, which means, the more time youth spend on physical activity and the less time youth spend on television watching; the more time television watching and the less time physical activity. Therefore, television watching is discouraged to improve physical activity. But the above association is still controversial, and television watching may have adverse effects on health independent of physical activity. Each day, youth have the same opportunity to engage in many different activities that can be both active and sedentary. They can have different hours of television watching but still participate in 1 hour moderate-vigorous physical activity per day. So it is possible for a child to be both physically active and more hours of television watching. Furthermore, television watching is often accompanied with snacking which can increase intake of total energy and refined, energy dense foods that are associated with over-weight and obesity. Moreover, youth are likely to be exposed to television advertising for unhealthy foods, which may trigger further unhealthy food consumption <sup>35,59-62</sup>.

Youth with T2D typically have been noted to be sedentary <sup>63</sup>. Based on data from NHANES III (1988-94), 26% of children watch 4 or more hours of television a day and 67% watch at least 2 hours a day <sup>64,65</sup>. Several studies have found a positive association between the amount of television watching and the prevalence of obesity <sup>50,65,66</sup>. Since obesity is an important risk factor of T2D diabetes in youth, hours of television watching may have influence on T2D in youth.

#### **2.4 The relationship between meal frequency and HbA1c and serum lipids in youth with diabetes**

Meal frequency has been recognized for over 20 years to be associated with metabolic changes in people with diabetes <sup>67</sup>. The American Diabetes Association (ADA) guidelines on nutritional therapy in diabetes recognize nutrition therapy as an essential component of diabetes treatment, and recommend individualized dietary counseling as part of the overall treatment plan <sup>68</sup>. Previous ADA statements of nutrition principles reported that increased meal frequency was related with lower mean glucose and insulin levels in T2D <sup>69</sup>; however, the most recent ADA guidelines on nutrition therapy do not specify the optimal meal frequency <sup>68</sup>. Considering the potential benefit of impaired glycemic control and cardiovascular risk profile with increased meal frequency while holding energy intake constant in people with diabetes, it is surprising that no long-term effects of meal frequency on lipid profiles has been reported. Jenkins et al <sup>67</sup> and Bertelsen et al <sup>70</sup> have compared the effects of 2 or 3 large meals/day with 6 to 13 small meals/day among adults with T2D in 2 days. Both studies showed that increased meal

frequency could increase insulin sensitivity and lower blood glucose concentration over the day. Similar metabolic advantages, such as reduction in serum lipids and lipid concentration, have also been observed in healthy subjects <sup>71-73</sup>. However, a relatively longer (4 weeks) study conducted by Arnold et al <sup>74</sup> on the impact of meal frequency on metabolic effects among 13 adults with T2D did not confirm the potential benefits of increased meal frequency. Another randomized crossover study (24 weeks) conducted among adults with T2D reported eating two large meals a day could reduce body weight, hepatic fat content, fasting plasma glucose, C-peptide and glucagon, and increase oral glucose insulin sensitivity than six meals a day <sup>75</sup>.

## **2.5 Validation of self-report television watching data and 3DPA data**

### **2.5.1. Measurement of self-reported television watching**

Since a sedentary lifestyle, particularly television watching, is associated with numerous negative health behaviors and outcomes among children, including overweight <sup>49,76-78</sup>, irregular sleep <sup>79</sup>, insufficient consumption of fruits and vegetables <sup>80</sup>, and disordered eating <sup>81,82</sup>, interest in the accurate assessment of sedentary time has increased <sup>83</sup>, however, validated methods to assess sedentary behavior (television watching) are limited <sup>84</sup>. Self-report questionnaires remain the most widely used method to evaluate behavior in adolescents <sup>85</sup>. In contrast to objective measurement like direct observation, self-report questionnaires provide a low cost and easy to use method for measuring sedentary behaviors (television watching). One of the limitations of self-reported behavioral questionnaires is response bias where respondents may intentionally provide incorrect answers due to pressure <sup>86-88</sup>. There is some evidence from studies of adults that

weight status may affect reporting of sedentary behaviors, with overweight adults underreporting minutes of sedentary activities compared to normal weight adults <sup>89</sup>. Another limitation is recall bias. Participants may not clearly remember their sedentary behavior in the past, especially for children and adolescent.

According to Bryant's <sup>90</sup> systematic review of measurement of television watching in children and adolescent, many television watching related questions were adapted from existing tools <sup>51,91-95</sup>. The most common used method was to differentiate weekdays from weekend days <sup>51,76,91-93,96-99</sup>, then average weekly hours of television watching was calculated by weighting the sum of the weekend and weekdays. Some other methods were performed by Janz and Mahoney <sup>95</sup>, who asked participants to recall the previous day and evening; and Shannon et al., <sup>97</sup> who supplied a 7-Day television watching recall with 30-min interval.

Although a self-reported questionnaire is the most common used method to assess television watching, but limited research has focused their validity and reliability, and it is still unclear whether a self-reported measure is superior to others. Schmitz et al. compared self-reported weekday television watching adapted from the YRBS with a 7-day television viewing log. This study was the first evaluation of reliability and validity of the YRBS television watching questions with middle school students and reported a moderate reliability ( $r = 0.68$ ) and fair validity ( $r = 0.46$ ) comparing with the 7-day television watching log, indicating that the YRBS questions are suitable to measure television watching in middle school students. This study also pointed out that the newly

developed YRBS questions for weekday and weekend day television watching and computer use also showed acceptable reliability and validity.

### 2.5.2. Measurement of 3-Day Physical Activity Recall

The 3-Day Physical Activity Recall (3DPAR) is a self-report instrument, based on the Previous Day Physical Activity Recall (PDPAR) <sup>100</sup>. The recall period was extended in the 3DPAR to provide more information about habitual patterns of activity than the original PDPAR <sup>101</sup>.

Three validation studies <sup>101-103</sup> indicated moderate validity of 3DPAR. The first validation study compared the 3DPAR with a 7-day of accelerometer monitoring. They reported weak to moderate correlations for total ( $r = 0.46$ ;  $P < 0.001$ ), moderate-vigorous ( $r = 0.27$ ;  $P < 0.05$ ) and vigorous ( $r = 0.41$ ;  $P < 0.001$ ) physical activity respectively <sup>101</sup>. The other two validation studies indicated similar correlations when validated against accelerometer <sup>102</sup> and pedometer <sup>103</sup>. The validation against accelerometer found correlations of 0.28–0.31 ( $P < 0.01$ ) for moderate-vigorous physical activity and correlations of 0.16–0.19 ( $P > 0.05$ ) for vigorous physical activity. The validation against pedometer found correlation of 0.32 ( $P < 0.001$ ) for moderate-vigorous physical activity and correlation of 0.34 ( $P < 0.001$ ) for vigorous physical activity.



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## CHAPTER 3

### MANUSCRIPT 1

Longitudinal association between television watching and computer use and risk markers  
in diabetes in the SEARCH for Diabetes in Youth Study<sup>1</sup>

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## **Abstract**

**Background:** The study provides evidence of the longitudinal association between screen time with hemoglobin A1c and cardiovascular risk markers among youth with type 1 (T1D) and type 2 diabetes (T2D). **Objective:** To examine the longitudinal relationship of screen time with HbA1c and serum lipids among youth with diabetes. **Subjects:** Youth with T1D and T2D. **Methods:** We followed up 1049 youth ( $\geq 10$  yr. old) with recently diagnosed T1D and T2D participating in the SEARCH for Diabetes in Youth Study. **Results:** Increased television watching on weekdays and during the week over time was associated with larger increases in HbA1c among youth with T1D and T2D ( $p\text{-value} < 0.05$ ). Among youth with T1D, significant longitudinal associations were observed between television watching and TG ( $p\text{-value} < 0.05$ ) (week days and whole week), and LDL-c ( $p\text{-value} < 0.05$ ) (whole week). For example, for youth who watched 1 hour of television per weekday at the outset and 3 hours per weekday 5 years later, the longitudinal model predicted greater absolute increases in HbA1c (2.19% for T1D and 2.16% for T2D); whereas for youth who watched television 3 hours per weekday at the outset and 1 hour per weekday 5 years later, the model predicted lesser absolute increases in HbA1c (2.08% for T1D and 1.06% for T2D). **Conclusions:** Youth with T2D who increased their television watching over time vs those that decreased it had larger increases in HbA1c over 5 years. Youth with T1D who increased their television watching over time had increases in LDL-c, TG and to a lesser extent HbA1c.

**Key words:** Diabetes, youth, hemoglobin A1c, serum lipids, screen time.

## **Background**

Excessive time spent watching television, playing video games, and using computers is an emerging public health issue <sup>1</sup>. The American Academy of Pediatrics recommends that television watching among children should be limited to less than 2 hours per day <sup>2</sup>. This is based on cross-sectional and longitudinal studies conducted among children and adults without diabetes that link increased television watching to adverse health outcomes <sup>3-6</sup>.

US children spend more time watching television than any other activity besides sleep, and time spent watching television may even exceed time spent in school <sup>2, 7-9</sup>. Television watching is the most usual screen time which has been studied comprehensively in the non-diabetic population <sup>7, 9-14</sup>. Recent estimates indicate that children 2 to 18 years of age watch at least 2.5 hours of television, spend 1.5 hours playing video games and using computers each day, and are exposed to about 6.5 hours of media per day from all sources <sup>15-17</sup>.

Children with T1D or T2D are at increased risk of developing cardiovascular complications in later life <sup>18</sup>, and more television watching in children with T1D has been associated with poorer glycemic control and more adverse lipid profiles in cross-sectional studies <sup>19-21</sup>. However, to the best of our knowledge, the extent to which television watching and computer use influence the cardiovascular risk profile of youth with T1D and T2D has not been evaluated in longitudinal analyses. We therefore studied the longitudinal relationship between changes in television watching and computer use over time and changes in HbA1c and serum lipids over 5 years in youth with diabetes using the SEARCH for diabetes in youth data. These analyses will quantify the extent to which

television watching and computer use, potentially modifiable factors, impact the evolution of HbA1c and cardiovascular risk markers in youth with diabetes.

## **Research design and methods**

### **Study design and population**

The SEARCH study is an on-going multicenter, population-based, observational investigation of non-gestational diabetes among youth < 20 years old. The SEARCH study clinical centers that contributed data for this analysis are Ohio, Colorado, Washington, South Carolina, California and Hawaii. The SEARCH study has been previously described in detail <sup>22</sup>.

This analysis included 1049 multi-ethnic US youth ( $\geq 10$  years old at the initial visit) with T1D and T2D who participated in the SEARCH for Diabetes in Youth Study and provided baseline data from 2002 to 2005. These participants were followed-up prospectively at 1, 2 and 5 years after the initial visit (61% participants had 3 or more visits). All participants included in these analyses had physician diagnosed diabetes, documented year of diagnosis, were less than 20 years old on December 31 of the year of diagnosis, and attended at least one follow-up visit.

### **Data collection and measurement**

Before implementation of data collection, this study was reviewed and approved by each local institutional review board that had jurisdiction over the local study population. Also, written informed consent and child assent were obtained at the start of each study visit.

For both initial and follow-up visits, data collection procedures were performed by trained and certified staff following standardized protocols <sup>22</sup> . Data collection approaches included questionnaires, physical examination and laboratory tests.

#### Exposure:

Television watching and computer use questions were adapted from the Youth Risk Behavioral Survey (YRBS) questionnaires <sup>23</sup> and were asked at the initial visit and each follow-up visit. In this questionnaire, there were two items asking about television watching behavior. They were: “On each week day, about how much time do you usually spend watching television?” and “On each weekend day, about how much time do you usually spend watching television?” The two questions about computer use were: “On each week day, about how much time do you usually spend on the computer for fun, including playing video or computer games?” and “On each weekend day, about how much time do you usually spend on the computer for fun, including playing video or computer games?” The responses to these four questions were categorized as follows: “None”, “Less than 1 hour”, “1 hour”, “2 hours”, “3 hours”, “4 hours”, and “5 or more hours”. Weighted television watching and computer use per week were calculated as follows: weighted television watching per week=  $(5 \times \text{weekday television watching} / 7) + (2 \times \text{weekend television watching} / 7)$  and weighted computer use per week=  $(5 \times \text{weekday computer use} / 7) + (2 \times \text{weekend computer use} / 7)$ .

Outcomes from laboratory tests:

Blood samples were drawn at each visit under the condition of metabolic stability defined by 8 hours of fasting and no episode of diabetic ketoacidosis in the previous month.

Within 24 hours, these blood samples were shipped with dry ice to the central laboratory in Seattle, WA for the measurement of HbA1c, LDL-c, HDL and TG.

Other covariates:

Demographic information including gender, race/ethnicity, age, highest parental education, household income, type of insurance and family composition were obtained by an initial survey at baseline <sup>24</sup>.

Physical activity was assessed using a question adapted from the Youth Risk Behavioral Survey (YRBS) questionnaires <sup>23</sup> and was asked at the initial and each follow-up visit. Standardized physical examinations were conducted for all participants at each visit that included height, weight, waist circumference, and blood pressure.

Statistical methods

There were 1049 participants in this analysis with at least 2 visits; 61% had 3 or more visits. Demographic information is shown as means and standard deviation for continuous variables and frequencies and percents for categorical variables.

Television watching and computer use were evaluated separately for weekdays, weekends, and the whole week. One category increase in television watching and computer use corresponded to one hour increase in the longitudinal analyses.

Longitudinal mixed models were fit separately for individuals with T1D and T2D to characterize the relation between changes in television watching and computer use (initial and time-varying values) and time-varying HbA1c and serum lipids among youth with diabetes that were included as random effects. Multivariate mixed models tested the effects of television watching and computer use at the initial visit, and the time-varying effects of television watching and computer use measured at the 1 year, 2 year and or 5 year follow-up visits. In addition, an interaction term (initial television watching/ computer use\* time-varying television watching/ computer use) was added into the model to determine whether changes in HbA1c and serum lipids (HDL, LDL-c and log TG) over time varied with changes in television watching and computer use habits over time as a function of initial television watching and computer use. Duration of diabetes (number of months since diabetes diagnosis) was included in these models as an indicator of time for each participant. All models were expanded to include fixed/non-time varying effects, including gender, age at the initial visit, race/ethnicity, highest parental education, type of insurance and household income, and time-varying covariates including BMI- z score, waist circumference, physical activity and treatment for diabetes and dyslipidemia <sup>25, 26</sup>. To evaluate the role of dietary intake we further adjusted all models for usual intake of total calories measured at baseline. For all models, we further stratified by intensive use (insulin  $\geq 3$  times/day or insulin pump) and non-intensive

(insulin < 3 times/day) regimens for youth with T1D, and by insulin treatment and non-insulin treatment for youth with T2D.

Statistical analyses were conducted using SAS (version 9.1, 2003, SAS Institute Inc, Cary, NC). Mixed models were used to fit statistical models. We used  $p < 0.05$  as standard of significance.

## **Results**

### Characteristics of Study Population:

Participants with T1D consisted of 384 (46.8%) females and 437 (53.2%) males with a mean age of  $13.6 \pm 2.4$  years at the initial visit, and included 617 (75.1%) Non-Hispanic Whites, 81 (9.9%) African Americans, 90 (11.0%) Hispanics, and 33 (4.0%) individuals belonging to other race/ ethnic groups. Participants with T2D consisted of 139 (61.0%) females and 89 (39.0%) males with a mean age of  $15.1 \pm 2.5$  years at the initial visit, and included 49 (21.5%) Non-Hispanic Whites, 82 (36.0%) African Americans, 52 (22.8%) Hispanics, and 45 (19.7%) individuals belonging to other race/ ethnic groups (Table 1).

Youth with both T1D and T2D (2002-2005) tended to watch more television during weekends than weekdays (T1D: 29% vs. 15% watched more than 4 hours of television per day; T2D: 42% vs. 30% watched more than 4 hours of television per day). Computer use during weekends and weekdays was low among youth with T1D and T2D during the study period (Figures 1 and 2).

### Longitudinal Mixed Models:

Increased television watching on weekdays, and during the entire week (weighted whole week as described in methods), was positively associated with changes in HbA1c among youth with T1D and T2D after adjusting for age at the initial visit, gender, race, physical activity, computer use on weekdays, parental education, household income, insurance type, BMI z-score, family composition, and treatment for diabetes and dyslipidemia. Similar significant longitudinal associations were observed between weekday television watching and changes in log TG levels, weighted whole week television watching and changes in LDL-c levels among youth with T1D, and weekend television watching and changes in HbA1c levels among youth with T2D (p-values for interaction between the initial and time-varying visits  $<0.01$ ) (Tables 2 and 3). The relationship between television watching and HbA1c was similar among youth with T1D when stratifying by intensive versus non-intensive treatment, and among youth with T2D stratified by insulin versus no insulin treatment. We did not find significant associations between changes in television watching and changes in HDL-c among youth with T1D or T2D, or log TG and LDL-c among youth with T2D. Computer use was not associated with any of the outcomes in this analysis. Further adjustment for total usual caloric intake did not materially alter the results.

### Predicted Models

The data presented in Table 4 are statistically significant results from multivariable mixed models described in Tables 2 and 3. Table 4 illustrates the predicted time varying changes at selected time points in HbA1c among youth with T1D and T2D, LDL-c and



TG among youth with T1D from the initial visit (n=1049) to 5 years (n=575) of follow-up. Predicted mean values of outcomes were estimated for 1 hour/day and 3 hours/day of television watching at the initial and 5 year follow-up visits respectively.

HbA1c increased on average from the initial visit to the 5 year follow-up visit among youth with both T1D and T2D (Table 4). However, the magnitude of HbA1c increase was smaller in those who decreased television watching over time and larger in those who increased it. For example, the HbA1c value for youth who watched television on weekdays for 3 hours/d at the initial visit and 1 hour/d at the 5 year follow-up visit rose less than for those who watched television on weekdays for 1 hour/d at the initial visit and 3 hour/d the 5 years follow-up visit were (T1D: 2.08% vs. 2.19%; T2D: 1.06% vs. 2.16%) (Table 4).

LDL-c and TG levels also increased on average from the initial visit to the 5 year follow-up visit among youth with T1D (Table 4). LDL-c and TG increased less in who decreased television watching over time and more in those who increased it. For example, LDL-c and TG increased less among youth who watched television for 3 hours/d at the initial visit and 1 hour/d at the 5 year follow-up visit and more among those who watched television for 1 hour/d at the initial visit and 3 hour/d the 5 years follow-up visit (LDL-c-weighted whole week television watching: 6.27 mg/dl vs. 9.32 mg/dl; TG-weekdays television watching: 8.43 mg/dl vs. 13.47 mg/dl) (Table 4).

## Discussion

In this study HbA1c, LDL-c and TG levels increased over time in all youth with T1D and T2D. However, the magnitude of increase was significantly greater among those who watched more television and increased their television watching behavior over time, compared to those who watched less TV, after adjusting for several important confounders. Computer use was not associated with HbA1c and serum lipids in this analysis.

Our results are consistent with previous cross-sectional studies evaluating the relationship between television watching and HbA1c in youth with T1D<sup>19-21</sup>. Margeirsdottir et al.<sup>19</sup> reported in a cross-sectional study in Norway that among 538 children and adolescents with T1D aged approximately 13 years on average, HbA1c was 9.4% for those who watched television for  $\geq 4$  hours/d versus 8.2% for those who watched television for  $< 1$  hour/d. Michaliszyn and Faulkner reported that US youth with T1D aged 14.5 years on average<sup>21</sup> spent about 10 hours per day in sedentary activities and more sedentary time was correlated with increased total cholesterol, LDL-c and TG ( $p < 0.05$ ). In another study among 2093 youth with T1D with mean age of 14.5 years from 19 countries, Aman et al.<sup>20</sup> indicated that HbA1c was not correlated with total hours of television watching in a week ( $r = 0.04$ ,  $P > 0.1$ ). However, these were descriptive cross-sectional studies and were unable to demonstrate the long-term impact of television watching on glycemic control and cardiovascular markers among youth with T1D.

The influence of sedentary behavior on health is a public health concern <sup>27</sup>. Youth on average watch at least 2.5 hours of television, 1.5 hours of video games playing and computer use each day and are exposed to about 6.5 hours of media per day from all sources<sup>15-17</sup>. Research studies commonly use screen-based media use, including television watching, video game playing, and computer use, to measure the sedentary behavior, although we know these behaviors are not completely representative.

Several mechanisms might explain the positive longitudinal association between television watching and changes in HbA1c, LDL-c and TG. First, television watching may replace time that would be used for physical activity that can improve insulin sensitivity <sup>2</sup> and increase energy expenditure leading to lower HbA1c and improved lipid profile. However, some other studies report poor correlation between television watching and physical activity <sup>12,14,28</sup>. Second, television watching is associated with snacking and sweetened beverage consumption causing increased total calorie intake <sup>29-31</sup>. Television contents, including advertisements for fast food and sweetened beverages, can negatively influence youth's food choices causing unhealthy dietary behavior<sup>32-36</sup>. Third, a recent study evaluating 2003/2004 and 2005/2006 NHANES data found a positive association between time spent in sedentary behavior and insulin resistance among youth with diabetes<sup>37,38</sup>. In addition, television watching is a lower energy expenditure behavior compared with other sedentary activities like writing and driving <sup>12</sup>. Thus, it has been hypothesized that increased television watching may lead to less physical activity, reduced energy expenditure, increased food and energy intake, and increased insulin resistance. However, in our study, adjustment for physical activity and total calories did

not attenuate the associations in this study, possibly due to measurement error in assessing these variables.

A minimum of 2 hours per week of physical activity on average can significantly increase HDL-c levels among individuals without diabetes <sup>39</sup>. However, change in sedentary time measured by accelerometer was not associated with HDL-c in a longitudinal analysis of adults with T2D <sup>37</sup>, similar to what we observed. The reasons for this are not clear. Moreover, in our analyses, sedentary time was measured using a questionnaire which would lead to attenuation of any associations due to measurement error. There were no reports, to the best of our knowledge, of a longitudinal relationship between sedentary behavior and T1D.

This study had several potential limitations. First, the exposure variable, television watching, was assessed through self-report questionnaire. However, because participants did not know their HbA1c or serum lipid values when television watching was assessed, it is unlikely that the outcome contributed to error related to assessment of television watching. Therefore, measurement error associated with assessment of television watching in this study would bias the result towards the null. Second, the estimated changes in HbA1c (particularly for T1D), LDL-c and TG over time attributed to television watching were small. Television watching was collected in 7 categories to make it easier for respondents to estimate, but this strategy resulted in the television watching categories to be more homogeneous. Moreover, more than half the youth watched 2 or more hours of television on weekdays and more than two thirds did so on

weekends. The lower estimated changes in HbA1c , LDL-c and TG attributed to change in television watching in our study may be due to the smaller contrast between the comparison groups (1 and 3 hours of television watching) resulting from the homogeneous estimates of television watching categories and the large proportion of individuals watching more television. However, the results were statistically significant and therefore provide evidence supporting the hypothesis that reducing television watching favorably impacts changes in metabolic markers over several years in youth with T1D and T2D. The magnitude of change in HbA1c was small for T1D, but relatively stronger for lipids in youth with T1D vs those with T2D and for HbA1c in youth with T2D vs those with T1D. Moreover, as small reductions in HbA1c contribute to large declines in diabetes related complications<sup>40</sup>, including the recommendation to reduce television watching on top of other advice on self-care may provide additive benefits to youth with diabetes. Our data suggest that most youth with diabetes do not make large changes in their television watching practices. In our study, only approximately 10% of the youth who completed the 5-year follow-up visit reported reducing their televisions watching practices by 2 hours. Third, baseline data were collected between 2002 and 2005 and then followed up for 5 years when television watching was the main contributor to screen time and sedentary behavior<sup>2, 7-9</sup>. Even though computer time was not related to the outcomes in our analyses, time spent using smart phones, tablets and other such devices may increasingly contribute to sedentary behavior today, data not captured herein. Another limitation was the potential for residual confounding because of the observational study design. However, we adjusted for many potential confounders including age, gender, race, physical activity, computer use on

weekdays parental education, household income, insurance type, BMI z-score, family composition, and treatment for diabetes, and dyslipidemia. The associations reported in this paper were independent of these potential confounders.

This study had several strengths. The sample for this analysis was drawn from the SEARCH for Diabetes in Youth study population, which is the largest prospective investigation among youth with T1D and T2D, and includes all major US ethnic groups. The longitudinal study design, including 5 years of follow-up, and the ability to adjust for many important potential confounders were also important strengths of this study. Also, we can evaluate the comprehensive longitudinal effect of television watching and computer use on HbA1c and serum lipids since we had the chance to measure television watching and computer use on both weekdays and weekends.

In conclusion, HbA1c, LDL-c and TG increased in all youth with T1D and T2D over 5 years. Youth with T2D who increased their television watching time had larger increases in HbA1c over 5 years. Youth with T1D who increased their television watching time had larger increases in LDL-c, TG and to a lesser extent HbA1c. Television watching may contribute to poor glycemic control and dyslipidemia in youth with diabetes and can be a potentially modifiable behavior to improve health outcomes in youth with diabetes.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention and the National Institute of Diabetes and Digestive and Kidney Diseases.



Table 3.1. Demographic and clinical characteristics of participants at the initial visit: SEARCH for Diabetes in Youth, 2002-2005

		T1D (n=821)	T2D (n=228)
Demographics			
Gender: n (%)	Female	384 (46.8)	139 (61.0)
	Male	437 (53.2)	89 (39.0)
Race: n (%)	Non-Hispanic White	617 (75.1)	49 (21.5)
	African American	81 (9.9)	82 (36.0)
	Hispanic	90 (11.0)	52 (22.8)
	Others <sup>a</sup>	33 (4.0)	45 (19.7)
Age: mean± SD		13.6±2.4	15.1±2.5
Parental highest education: n (%)	Bachelor degree or more	383 (46.9)	36 (16.0)
	Some college with associate degree	279 (34.2)	80 (35.4)
	High school	122 (14.9)	76 (33.6)
	Less than high school	33 (4.0)	34 (15.0)
Annual household income: n (%)	<\$25,000	106 (13.0)	95 (41.6)
	\$25,000-49,000	160 (19.6)	58 (25.4)
	\$50,000-74,000	172 (21.1)	25 (11.0)
	≥75,000	327 (40.0)	20 (8.8)
	DK/Ref	51 (6.3)	30 (13.2)
Insurance: n (%)	Medicaid/Medicare	128 (15.7)	90 (39.7)
	Private	660 (81.1)	119 (52.4)
	Other	9 (1.1)	10 (4.4)
	None	17 (2.1)	8 (3.5)
Television watching, computer use and physical activity			
Physical activity (days/week)		2.9±2.3	2.9±2.4
Weekday television watching: hours		2.0±1.3	2.6±1.5
Weekend television watching: hours		2.6±1.5	3.0±1.7
Weighted television watching: hours		2.2±1.3	2.7±1.4
Weekday computer use: hours		1.3±1.1	1.2±1.3
Weekend computer use: hours		1.5±1.4	1.3±1.5
Weighted computer use: hours		1.3±1.1	1.2±1.3
Clinical characteristics			
HbA1c: n (%)	<8%	505 (63.5)	171 (77.7)
	8-9.5%	208 (26.1)	22 (10.0)
	≥9.5%	83 (10.4)	27 (12.3)
BMI z-score: mean ± SD		0.6±0.9	2.1±0.6
Caloric intake (cal): mean ±SD		1869.8±842.1	1761.5±850.5

Diabetes treatment: n (%)	Insulin pump	71 (8.7)	0 (0.0)
	Insulin 3+ times per day	428 (52.4)	25 (11.0)
	Insulin <3 times per day	305 (37.3)	50 (22.0)
	No treatment or Oral meds only	13 (1.6)	152 (67.0)
HDL: n (%)	Normal HDL (> 40 mg/dl)	648 (78.9)	100 (43.9)
	Low HDL ( $\leq$ 40 mg/dl)	173 (21.1)	128 (56.1)
LDL: n (%)	Normal LDL (<100 mg/dl)	546 (66.5)	125 (54.8)
	High LDL ( $\geq$ 100 mg/dl)	275 (33.5)	103 (45.2)
TG: n (%)	Normal TG (< 110 mg/dl)	735 (89.5)	123 (53.9)
	High TG ( $\geq$ 110 mg/dl)	86 (10.5)	105 (46.1)

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a: Other races: Asian Indian, American Indian or Alaska Native, Native Hawaiian, and Asian etc.

Table 3.2. Adjusted<sup>c</sup> longitudinal associations<sup>b</sup> of changes in means of HbA1c and serum lipids among youth with T1D: SEARCH for Diabetes in Youth

		HbA1c (%)	HDL (mg/dl)	LDL (mg/dl)	Log TG <sup>d</sup> (mg/dl)
Weekday television watching	Diabetes duration ( $\beta_1$ )	0.034 <sup>a</sup>	0.13 <sup>a</sup>	0.11 <sup>a</sup>	0.003 <sup>a</sup>
	Baseline ( $\beta_2$ )	0.20 <sup>a</sup>	0.11	1.73	0.023
	Time-varying ( $\beta_3$ )	0.15 <sup>a</sup>	-0.36	1.31	0.046 <sup>a</sup>
	Baseline*time-varying ( $\beta_4$ )	-0.06 <sup>a</sup>	0.05	-0.49	-0.013 <sup>a</sup>
Weekend television watching	Diabetes duration ( $\beta_1$ )	0.034 <sup>a</sup>	0.13 <sup>a</sup>	0.11 <sup>a</sup>	0.003 <sup>a</sup>
	Baseline ( $\beta_2$ )	0.12	-0.11	1.01	-0.013
	Time-varying ( $\beta_3$ )	0.02	-0.16	1.18	-0.0071
	Baseline*time-varying ( $\beta_4$ )	-0.03	0.1	-0.33	0.001
Weighted television watching per week	Diabetes duration ( $\beta_1$ )	0.034 <sup>a</sup>	0.13 <sup>a</sup>	0.11 <sup>a</sup>	0.003 <sup>a</sup>
	Baseline ( $\beta_2$ )	0.23 <sup>a</sup>	0.13	2.21 <sup>a</sup>	0.014
	Time-varying ( $\beta_3$ )	0.16 <sup>a</sup>	-0.17	2.09 <sup>a</sup>	0.040 <sup>a</sup>
	Baseline*time-varying ( $\beta_4$ )	-0.07 <sup>a</sup>	0.03	-0.66 <sup>a</sup>	-0.01
Weekday computer use	Diabetes duration ( $\beta_1$ )	0.035 <sup>a</sup>	0.13 <sup>a</sup>	0.12 <sup>a</sup>	0.003 <sup>a</sup>
	Baseline ( $\beta_2$ )	0.11	-0.01	1.09	0.017
	Time-varying ( $\beta_3$ )	0.13	-0.5	0.09	0.022
	Baseline*time-varying ( $\beta_4$ )	-0.03	0.13	-0.31	-0.008
Weekend computer use	Diabetes duration ( $\beta_1$ )	0.035 <sup>a</sup>	0.13 <sup>a</sup>	0.12 <sup>a</sup>	0.003 <sup>a</sup>
	Baseline ( $\beta_2$ )	0.04	0.07	0.97	0.0011
	Time-varying ( $\beta_3$ )	-0.02	-0.46	-0.46	0.0012

	Baseline*time-varying ( $\beta_4$ )	0.01	0.08	-0.16	-0.0044
	Diabetes duration ( $\beta_1$ )	0.035 <sup>a</sup>	0.13 <sup>a</sup>	0.12 <sup>a</sup>	0.003 <sup>a</sup>
Weighted	Baseline ( $\beta_2$ )	0.07	-0.04	1.5	0.011
computer use per week	Time-varying ( $\beta_3$ )	0.05	-0.42	-0.24	0.016
	Baseline*time-varying ( $\beta_4$ )	-0.01	0.11	-0.29	-0.005

a:  $p < 0.05$ ; b: Outcome =  $\beta_0 + \beta_1(\text{duration}) + \beta_2(\text{initial exposure}) + \beta_3(\text{time-varying exposure}) + \beta_4(\text{initial exposure} \times \text{time-varying exposure}) + \beta_5(\text{other covariates}) + \varepsilon$ ; c: Adjusted variables: Age at the initial visit, gender, race, parental education, household income, family composition, insurance type, physical activity, and treatment for diabetes and dyslipidemia; d: Coefficients are unchanged since log-transformation means that unit conversion is captured in the intercept term.

Table 3.3. Adjusted<sup>c</sup> longitudinal associations<sup>b</sup> of changes in means of HbA1c and serum lipids among youth with T2D: SEARCH for Diabetes in Youth

		HbA1C (%)	HDL (mg/dl)	LDL (mg/dl)	Log TG <sup>d</sup> (mg/dl)
Weekday television watching	Diabetes duration ( $\beta_1$ )	0.019 <sup>a</sup>	0.078 <sup>a</sup>	0.056	-0.001
	Baseline ( $\beta_2$ )	0.43 <sup>a</sup>	-0.43	0.99	0.075 <sup>a</sup>
	Time-varying ( $\beta_3$ )	0.53 <sup>a</sup>	-1.01	2.35	0.064 <sup>a</sup>
	Baseline*time-varying ( $\beta_4$ )	-0.13 <sup>a</sup>	0.29	-0.18	-0.016
Weekend television watching	Diabetes duration ( $\beta_1$ )	0.021 <sup>a</sup>	0.066 <sup>a</sup>	0.038	-0.001
	Baseline ( $\beta_2$ )	0.44 <sup>a</sup>	-0.01	0.09	0.056
	Time-varying ( $\beta_3$ )	0.38 <sup>a</sup>	-0.19	2.91	0.015
	Baseline*time-varying ( $\beta_4$ )	-0.11 <sup>a</sup>	-0.01	-0.43	-0.005
Weighted television watching per week	Diabetes duration ( $\beta_1$ )	0.019 <sup>a</sup>	0.074 <sup>a</sup>	0.065	-0.001
	Baseline ( $\beta_2$ )	0.52 <sup>a</sup>	-0.32	-0.42	0.078 <sup>a</sup>
	Time-varying ( $\beta_3$ )	0.62 <sup>a</sup>	-1.38	1.37	0.046
	Baseline*time-varying ( $\beta_4$ )	-0.15 <sup>a</sup>	0.3	0.18	-0.013
Weekday computer use	Diabetes duration ( $\beta_1$ )	0.025 <sup>a</sup>	0.067 <sup>a</sup>	0.038	-0.001
	Baseline ( $\beta_2$ )	0.45	0.73	2.88	0.033
	Time-varying ( $\beta_3$ )	0.08	-0.13	0.87	0.045
	Baseline*time-varying ( $\beta_4$ )	-0.08	-0.07	-0.4	-0.022
Weekend computer use	Diabetes duration ( $\beta_1$ )	0.027 <sup>a</sup>	0.064 <sup>a</sup>	0.042	-0.0003
	Baseline ( $\beta_2$ )	0.17	0.17	1.49	0.008

Weighted computer use per week	Time-varying ( $\beta_3$ )	0.01	0.14	1.07	-0.005
	Baseline*time-varying ( $\beta_4$ )	0.02	0.01	-0.08	0.0003
	Diabetes duration ( $\beta_1$ )	0.026 <sup>a</sup>	0.065 <sup>a</sup>	0.037	-0.001
	Baseline ( $\beta_2$ )	0.4	0.13	2.24	0.052
	Time-varying ( $\beta_3$ )	0.03	0.03	0.96	0.031
	Baseline*time-varying ( $\beta_4$ )	-0.04	0.01	-0.16	-0.019

a:  $p < 0.05$ ; b: Outcome =  $\beta_0 + \beta_1(\text{duration}) + \beta_2(\text{initial exposure}) + \beta_3(\text{time-varying exposure}) + \beta_4(\text{initial exposure} \times \text{time-varying exposure}) + \beta_5(\text{other covariates}) + \epsilon$ ; c: Adjusted variables: Age at the initial visit, gender, race, parental education, household income, family composition, insurance type, physical activity, and treatment for diabetes and dyslipidemia; d: Coefficients are unchanged since log-transformation means that unit conversion is captured in the intercept term..

Table 3.4. Estimated<sup>a,b</sup> HbA1c , LDL and TG resulting from change in television watching and computer use after a 5 year interval: SEARCH for Diabetes in Youth,2002-2005

			1 hour to 3 hours	3 hours to 1 hour
T1D	Weekday television watching	HbA1c (%) -Initial visit	8.23	8.45
		HbA1c (%) -5 year follow-up visit	10.42	10.53
		Change	2.19	2.08
		TG (mg/dl) -Initial visit	53.30	55.33
		TG (mg/dl) -5 year follow-up visit	66.77	63.76
		Change	13.47	8.43
	Weighted television watching per week	HbA1c (%) -Initial visit	8.15	8.41
		HbA1c (%) -5 year follow-up visit	10.35	10.5
		Change	2.20	2.09
		LDL (mg/dl) -Initial visit	89.54	92.84
		LDL (mg/dl) -5 year follow-up visit	98.86	99.11
		Change	9.32	6.27
T2D	Weekday television watching	HbA1c (%) -Initial visit	7.55	8.45
		HbA1c (%) -5 year follow-up visit	9.71	9.51
		Change	2.16	1.06
	Weekend television watching	HbA1c (%) -Initial visit	7.57	8.33
		HbA1c (%) -5 year follow-up visit	9.38	9.5
		Change	1.81	1.17
	Weighted television watching per week	HbA1c (%) -Initial visit	7.25	8.36
		HbA1c (%) -5 year follow-up visit	9.55	9.36
		Change	2.30	1.00

a: Estimates were generated from the followed mixed model: Outcome =  $\beta_0 + \beta_1(\text{duration}) + \beta_2(\text{initial exposure}) + \beta_3(\text{time-varying exposure}) + \beta_4(\text{initial exposure} \times \text{time-varying exposure}) + \beta_5(\text{other covariates}) + \varepsilon$ ; b: Reference of adjusted covariates in mixed models: age at initial visit=10 years old, gender=male, race=Non-Hispanic White, physical activity=0 day, higher parental education=less than high school, income= less than \$25k per year, insurance=none, family composition= both parents, BMI z-score=0, diabetes treatment=insulin pump, and lipids treatment=none; c: only presented significant results from mixed models in table 3.2 and table 3.3.

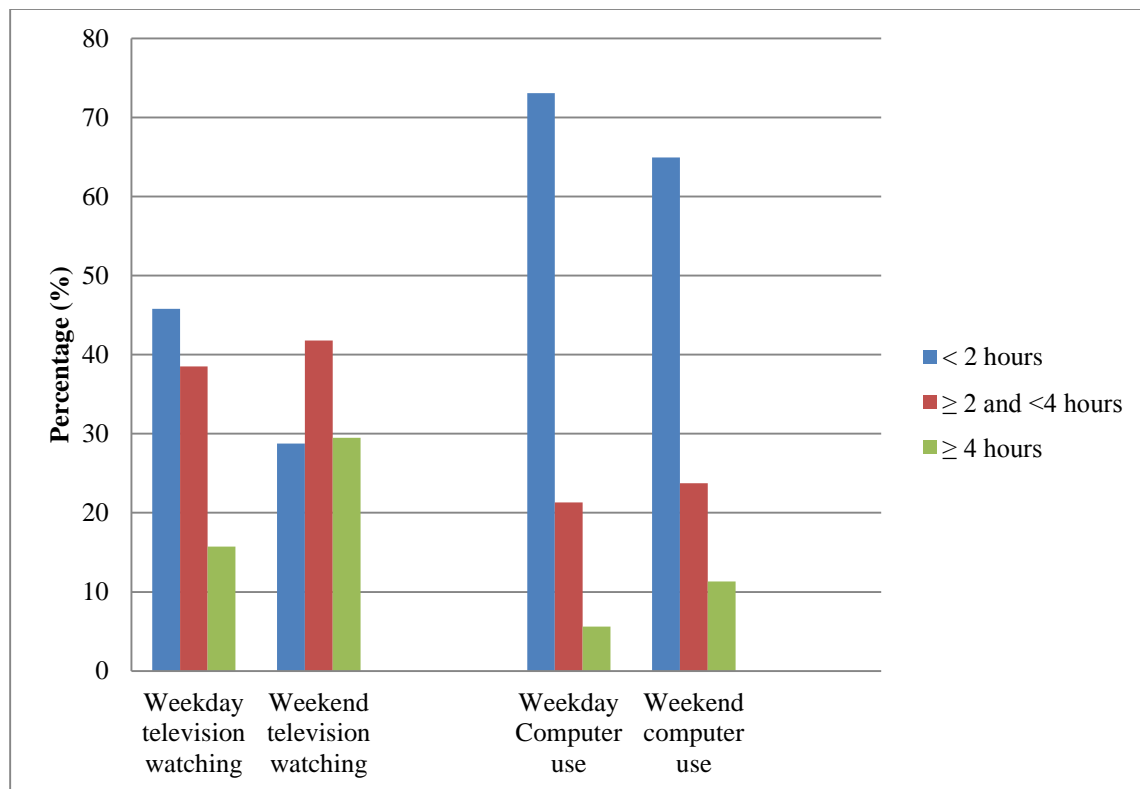


Figure 3. 1 Frequency of television watching and computer use among youth with T1D at the initial visit: SEARCH for Diabetes in Youth, 2002-2005



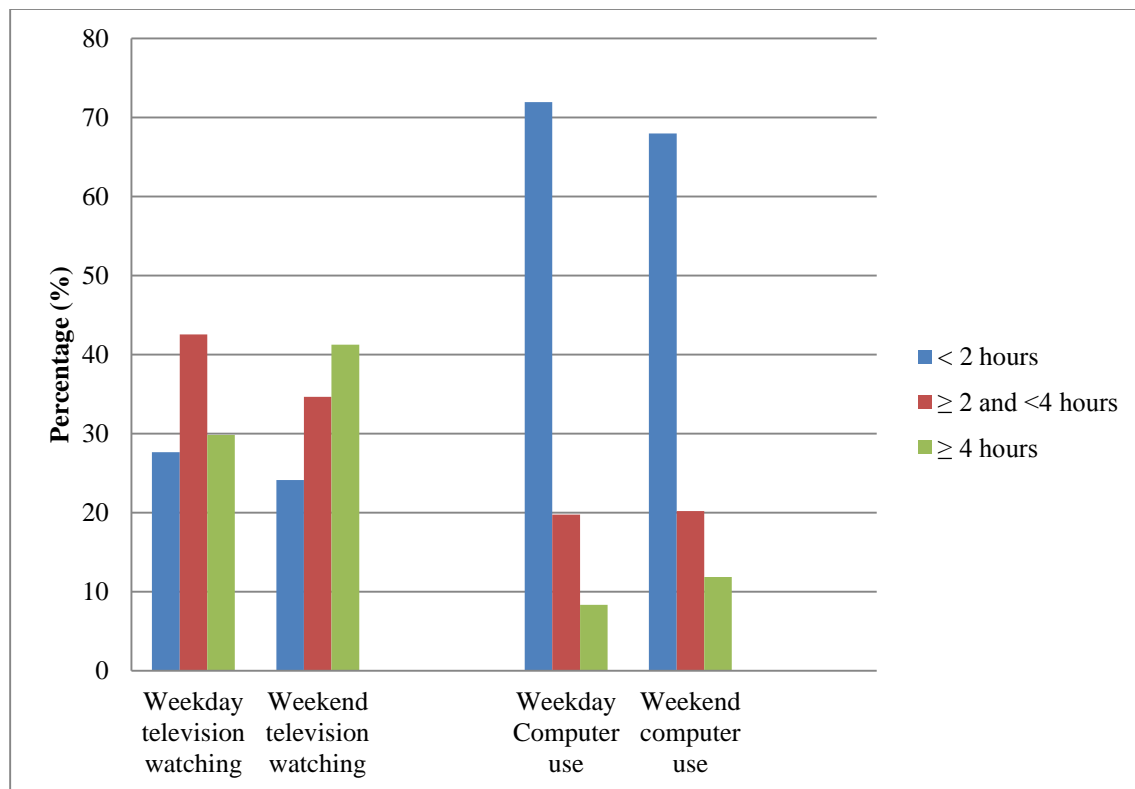


Figure 3. 2 Frequency of television watching and computer use among youth with T2D at the initial visit: SEARCH for Diabetes in Youth, 2002-2005

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## CHAPTER 4

### MANUSCRIPT 2

Validity of a questionnaire to assess television watching in youth with and without  
diabetes: The SEARCH Case-Control Study<sup>1</sup>

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<sup>1</sup> Chao Li, Elizabeth J. Mayer-Davis, Ralph B. D'Agostino Jr., Dana Dabelea, Angela D. Liese, Russell Pate, Ronny A. Bell, and Anwar T. Merchant. To be submitted to Journal of Physical Activity & Health.

## **Abstract**

**Background:** Sedentary behavior is an important contributor to future complications among youth with diabetes. However, there are few validated methods to assess sedentary behavior among youth with diabetes. This study evaluated the validity of television watching assessed by Youth Risk Behavior Survey questions (YRBS) against a 3 Day Physical Activity Recall (3DPAR) among youth with and without diabetes.

**Methods:** A sample of 578 youth with type 1 diabetes (T1D), 119 youth with type 2 diabetes (T2D) and 220 youth without diabetes participated in the SEARCH for Diabetes in Youth-Case Control study. Weekday and weekend television watching were assessed by the YRBS questions and three days of self-reported number of half-hour time blocks designated of television derived from the 3DPAR. Television watching was compared between the two instruments.

**Results:** The overall correlations between hours of television watching from the YRBS and number of half hour television watching blocks from the 3DPAR were 0.30 ( $p<0.05$ ) and 0.45 ( $p<0.05$ ) among youth with T1D and T2D respectively, and 0.41 ( $p<0.05$ ) among youth without diabetes. The correlations tended to be higher in females (T1D:  $r=0.31$ ; T2D:  $r=0.51$ ; Control:  $r=0.54$ ) than in males (T1D:  $r=0.30$ ; T2D:  $r=0.37$ ; Control:  $r=0.25$ ). Also, the correlations were higher in older participants (T1D:  $r=0.43$ ; T2D:  $r=0.52$ ; Control:  $r=0.50$ ) than in younger participants (T1D:  $r=0.19$ ; T2D:  $r=0.32$ ; Control:  $r=0.31$ ). Also, the correlations were higher in normal weight T1D participants ( $r=0.35$ ) and overweight T2D participants ( $r=0.46$ ) compared to over-weight T1D

participants ( $r=0.18$ ) and normal weight T2D participants ( $r=0.22$ ). When stratified by race/ethnicity, African Americans and Hispanics with T2D tended to have higher Pearson correlations (African Americans:  $r=0.50$ ; Hispanics:  $r=0.55$ ) than non-Hispanic Whites ( $r=0.31$ ). The YRBS questions tended to overestimate (by 0.23, 0.54 and 0.40 for youth with T1D, T2D and without diabetes respectively) television watching compared with 3DPAR after adjusting for age, gender, and race/ethnicity.

**Conclusions:** Television watching measured by YRBS questions showed weak to moderate correlation with television watching measured by 3DPAR among youth with diabetes. The correlation was stronger among youth who were older, female, overweight, African American and Hispanic. Using YRBS questions may be a viable option to measure television watching in youth with diabetes, particularly in large epidemiologic studies when alternative assessment methods are either too costly or complex making them not feasible.

## Background

Television watching is a sedentary behavior that is associated with adolescent obesity <sup>1</sup> and higher levels of diabetes risk factors in overweight youth <sup>2,3</sup> based on few cross-sectional and longitudinal studies conducted among children and adults without diabetes <sup>4-7</sup>. However, the influence of television watching on youth with diabetes remains understudied. Only few cross-sectional studies reported associations between more television watching and poorer glycemic control and more adverse lipid profiles among youth with type 1 diabetes (T1D) <sup>8-10</sup>. A possible reason for this situation could be the lack of a reliable method to measure television watching. Self-reported questionnaires have been widely developed to measure behaviors in youth <sup>11</sup> because questionnaires are inexpensive, easy to administer, and feasible for large studies. However, responses from self-reported questionnaires are prone to bias and measurement error <sup>12,13</sup>.

The Youth Risk Behavior Survey (YRBS) is an ongoing CDC surveillance program developed in 1989 to monitor health behaviors among US youth. In this survey, television watching is determined by the following question: “On an average school day, how many hours do you watch television?” This YRBS question has been validated by Schmitz et al. <sup>14</sup> among middle school students and the results indicated that it had adequate reliability and validity. However, its validity has not been assessed among youth with diabetes.

The purpose of this study was to evaluate the validity of television watching assessed by the YRBS questions against a 3 Day Physical Activity Recall (3DPAR). The 3DPAR is a



self-reported instrument that assesses the frequency and intensity of physical activity and sedentary behaviors during the previous 3 sequential days and has been validated in female youth <sup>15</sup>. To our knowledge, this is the first study to evaluate television watching assessed by the YRBS questions against a validated survey among youth with type 1 (T1D) and type 2 diabetes (T2D).

### **Research design and methods**

All data for this study were derived from the SEARCH Case-Control (SEARCH-CC) study. The SEARCH-CC is an ancillary study to the SEARCH for Diabetes in Youth (SEARCH) study, which is an ongoing multicenter cohort study that conducts population based ascertainment of youth aged <20 years diagnosed with diabetes. A detailed description of SEARCH study methods has been published previously <sup>16</sup>. The SEARCH-CC study was designed to study and evaluate selected risk factors for childhood diabetes, and conducted at two the SEARCH clinical sites, South Carolina and Colorado <sup>17,18</sup>.

#### **SEARCH-CC case and control inclusion**

Diabetes cases were identified through a variety of methods and the diagnosis and type of diabetes was confirmed by a health care provider. Between July 2003 and March 2006, SEARCH cases aged  $\geq 10$  years who participated in the SEARCH study baseline visit were invited to participate in the SEARCH-CC study in the South Carolina and Colorado centers. Detailed information about sampling and recruitment for SEARCH-CC has been published <sup>19,20</sup>.

Youth without diabetes were selected from health care provider offices in the same geographic areas as cases. We over-sampled youth without diabetes based upon the distribution of age, gender and race/ethnicity characteristics of cases. Overall, 49% (n=220) of invited youth without diabetes participated in SEARCH-CC. Control youth with fasting glucose values indicative of diabetes at the time of the SEARCH-CC visit were excluded from the analysis.

Before implementation of data collection, the study protocol was reviewed and approved by each local institutional review board that had jurisdiction over the local study population. Written informed consent and child assent were obtained at the start of the study visits.

The analyses in this report included all SEARCH-CC cases and controls, who responded to several questions on physical activity and sedentary behaviors based on the YRBS questionnaire as part of the standardized SEARCH study protocol and completed the 3DPAR as part of the SEARCH-CC protocol. Both the YRBS questionnaire and 3DPAR measured physical activity and sedentary behavior in the same week.

#### Data collection and measurements

##### 3-Day Physical Activity Recall data

The 3DPAR is a self-report measurement that was designed to assess physical activity behavior of adolescents <sup>21</sup>. The 3DPAR includes a list of 81 items related to physical activity and sedentary behavior for each of the previous 3 days. Each day is divided into

36 blocks of time (30 minutes per block) between 6:00 AM and midnight. Participants record their main activity (from the list of 81 items) and the intensity (light, moderate, hard and very hard) of that activity during each half hour block. The 3DPAR has been validated previously<sup>22,23</sup>. From the 3DPAR data, we calculated the number of half hour blocks designated as television watching. This information from the 3DPAR was used as the standard against which to validate television watching reported as on the YRBS.

#### Youth Risk Behavior Survey data

Two questions regarding television watching were adapted from the YRBS questions<sup>24</sup>. They were: “On each week day, about how much time do you usually spend watching television?” and “On each weekend day, about how much time do you usually spend watching television?” The responses to these two questions were categorized as follows: “None”, “Less than 1 hour”, “1 hour”, “2 hours”, “3 hours”, “4 hours”, and “5 or more hours”. Weighted hours of television watching per week were calculated as follows:  
$$\text{weighted television watching per week} = (5 * \text{weekday television watching} / 7) + (2 * \text{weekend television watching} / 7).$$

Demographic information (age, gender, and race/ethnicity) were collected from self-reported questionnaires administrated by trained and certified study staff at the SEARCH-CC visit.

## Statistical Analysis

Statistical analyses were performed by using SAS (version 9.1, 2003, SAS Institute Inc, Cary, NC). Significant level was set at  $p < 0.05$ . Pearson correlation was used to measure the relationship between data from the YRBS questions and the 3DPAR. We used Dancey and Reidy's categorization<sup>25</sup> to define strength of Pearson correlations ( $r=0$ : zero;  $r=0.10-0.39$ : weak;  $r=0.40-0.69$ : moderate;  $r=0.70-0.99$ : strong;  $r=1$ : perfect). Kappa statistics and percent of agreement were calculated to evaluate the agreement of dichotomized television watching determined by median from both the YRBS and 3DPAR. In order to evaluate the extent to which the YRBS questionnaire over or under estimated television watching measured by 3DPAR, linear regression was performed with 3DPAR television watching as the outcome and YRBS television watching as the independent variable adjusted for age, gender and race/ethnicity. The coefficient for television watching measured by YRBS would be zero if there was no over or under estimation, positive if there was overestimation, and negative if there was underestimation. Television watching measured by both YRBS and 3DPAR were codes as half hour of television watching.

## Results

The study sample was composed of 578 youth with T1D, 119 with T2D, and 220 without diabetes, with mean ages (SD) of youth by diabetes type were 14.6 (SD=3.4), 15.9 (SD=2.8) and 14.5 (SD=2.9) respectively (Table 4.1). There were 286 (49.5%) females and 292 (50.5%) males who had T1D, 83 (69.8%) females and 36 (30.2%) males who

had T2D, 133 (60.5%) females and 87 (39.5%) males who were free of diabetes. Youth with T1D were more likely to have normal weight (68.4%) and youth with T2D tended to be overweight (89.1%). Most participants with T1D (79.4%) and without diabetes (53.9%) were non-Hispanic White, and participants with T2D were primarily African American (56.3%).

All correlations, percent agreement and Kappa between the YRBS questions and 3DPAR are presented in Table 4.2. The overall correlations between hours of television watching from the YRBS and number of half hour television watching blocks from the 3DPAR were 0.30 ( $p<0.05$ ) and 0.45 ( $p<0.05$ ) among youth with T1D and T2D respectively, and 0.41 ( $p<0.05$ ) among youth without diabetes. The correlations tended to be higher in females (T1D:  $r=0.31$ ; T2D:  $r=0.51$ ; youth without diabetes:  $r=0.54$ ) than in males (T1D:  $r=0.30$ ; T2D:  $r=0.37$ ; youth without diabetes:  $r=0.25$ ). Also, the correlations were higher in older participants (T1D:  $r=0.43$ ; T2D:  $r=0.52$ ; youth without diabetes:  $r=0.50$ ) than in younger participants (T1D:  $r=0.19$ ; T2D:  $r=0.32$ ; youth without diabetes:  $r=0.31$ ). Moreover, the correlations were higher in normal weight T1D participants ( $r=0.35$ ) and overweight T2D participants ( $r=0.46$ ) compared to over-weight T1D participants ( $r=0.18$ ) and normal weight T2D participants ( $r=0.22$ ). When stratified by race/ethnicity, African Americans and Hispanics with T2D tended to have higher Pearson correlations (African Americans:  $r=0.50$ ; Hispanics:  $r=0.55$ ) than non-Hispanic Whites ( $r=0.31$ ).

The results of the regression models are presented in Table 4.3. The YRBS questions tended to overestimate (by 0.23, 0.54 and 0.40 for youth with T1D, T2D and without

diabetes respectively) television watching compared with 3DPAR after adjusting for age, gender, and race/ethnicity. For example, for a normal weight non-Hispanic White male participant aged 15 years old, the half hour of television watching collected from the YRBS were 2.0 (T1D), 1.5 (T2D) and 1.3 (without diabetes) respectively times higher than half hour television watching blocks collected from the 3DPAR.

## **Discussion**

In this validation study conducted among youth with and without diabetes, self-reported hours of television watching evaluated by the YRBS questions were weakly to moderately correlated with responses obtained from the 3DPAR. The correlations were higher (i.e. in the moderate range) for youth with T2D, and who were also females,  $\geq 15$  years of age, and African Americans and Hispanics. The YRBS questions tended to overestimate television watching among youth with and without diabetes compared with 3DPAR after adjusting for age, gender, and race/ethnicity.

The YRBS questions focus on the major risk behaviors and provide estimated prevalence of these risk behaviors among young people <sup>26</sup>. States and local districts health departments use the YRBS data to assess and evaluate policies and programs to prevent health risk behaviors among youth <sup>27</sup>, so several studies have demonstrated the consistent reliability of the high school versions of the YRBS <sup>28-30</sup>. However, to our knowledge, this study is the first attempt to validate report of television watching from the YRBS questions among youth with T1D and T2D against a previously validated survey instrument. According to Bryant's <sup>17</sup> systematic review of measurement of television

watching in children and adolescent, many television watching related questions were adapted from existing tools<sup>17,18,31,32</sup>. The most commonly used method was to differentiate weekdays from weekend days<sup>18,31-36</sup>, then average weekly television watching was calculated by weighting the sum of the weekdays and weekend. Schmitz et al.<sup>14</sup> compared self-reported weekly television watching adapted from the YRBS questions with 7-day television watching log among middle school students and found out a moderate reliability ( $r=0.68$ ) and validity ( $r_{\text{weekday television watching}} = 0.46$ ,  $r_{\text{weekend television watching}} = 0.37$ ,  $r_{\text{average television viewing over the week}} = 0.47$ ) comparing with the 7-day television watching log. Their findings suggest that the YRBS questions were suitable to measure television watching in middle school students.

The present study has several limitations: 1) unlike physical activity, it is very hard to measure television watching and there is no gold standard. In this study, we used the self-reported YRBS questions as an alternative way to measure television watching comparing with the 3DPAR which is also a self-reported measurement, although the 3DPAR has been validated by accelerometer<sup>15</sup>; 2) in this study, 54.6% of participants were less than 14 years old (middle school students) while the original target population of YRBS were high school students; 3) the assessment of time spent in front of the television may be inaccurate as the YRBS questions measure television watching with error. However, it may still be possible to rank individuals by less or more television watching using this instrument.

This study also has several strengths. All data were from the population based SEARCH-CC study with a large sample size and diverse racial/ethnic mix of participants. Second, the YRBS questions were brief, which increases their potential for use in a variety of settings. Third, regression models allow us to estimate the relationship between the YRBS data and the 3DPAR data adjusting for multiple covariates.

In conclusion, among youth with diabetes, television watching measured by the YRBS questions showed weak to moderate correlation with television watching measured by the 3DPAR. The correlation was stronger among youth who were older, female, overweight, African American and Hispanic. Using YRBS questions may be a viable option to measure television watching in youth with diabetes, particularly in large epidemiologic studies when alternative assessment methods are either too costly or complex.

### **Acknowledgment**

The SEARCH for Diabetes in Youth Study and SEARCH Case-Control study are indebted to the many youth and their families, and their health care providers, whose participation made this study possible.

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Table 4.1. Demographic information between youth with and without diabetes: The SEARCH Case Control Study

		T1D	T2D	Without Diabetes
3-Day Physical Activity Recall (3DPAR): n (%)	≤2h television watching	442 (76.5%)	81 (68.1%)	150 (68.2%)
	>2h television watching	136 (23.5%)	38 (31.9%)	70 (31.8%)
Number of blocks per day of 3DPAR: (n± STD)		3.5±3.3	4.9±4.1	4.1±3.6
Youth Risk Behavior Survey (YRBS): n (%)	≤2h television watching	208 (36.0%)	25 (21.0%)	66 (30.0%)
	>2h television watching	370 (64.0%)	94 (79.0%)	154 (70.0%)
Gender: n (%)	Female	286 (49.5%)	83 (69.8%)	133 (60.5%)
	Male	292 (50.5%)	36 (30.2%)	87 (39.5%)
Race <sup>▲</sup> : n (%)	Non-Hispanic White	455 (79.4%)	33 (27.7%)	117 (53.9%)
	African American	49 (8.5%)	67 (56.3%)	60 (27.7%)
	Hispanic	56 (9.8%)	18 (15.1%)	35 (16.1%)
	Others	13 (2.3%)	1 (0.9%)	5 (2.3%)
BMI_z20: n (%)	≤1	401 (69.4%)	13 (10.9%)	131 (59.6%)
	>1	177 (30.6%)	106 (89.1%)	89 (40.4%)
Age(years): (mean ± STD)		14.6±3.4	15.9±2.8	14.5±2.9

▲: Other races: Asian and multiple races

Table 4.2. Validation of television watching measured by the YRBS and 3DPAR: The SEARCH Case Control Study

		T1D	T2D	Without Diabetes
Overall	Pearson correlation	0.30*	0.45*	0.41*
	Kappa (95 C.I.) <sup>♦</sup>	0.18 (0.091, 0.25)	0.42 (0.26, 0.58)	0.25 (0.13, 0.38)
	Percent of agreement (%) <sup>♦</sup>	61.77	71.43	62.72
Gender				
Female	Pearson correlation	0.31*	0.51*	0.54*
	Kappa (95 C.I.) <sup>♦</sup>	0.24 (0.12, 0.35)	0.43 (0.24, 0.62)	0.35 (0.19, 0.51)
	Percent of agreement (%) <sup>♦</sup>	65.38	72.29	67.67
Male	Pearson correlation	0.30*	0.37*	0.25*
	Kappa (95 C.I.) <sup>♦</sup>	0.11 (-0.0027, 0.23)	0.39 (0.083, 0.69)	0.11 (-0.095, 0.31)
	Percent of agreement (%) <sup>♦</sup>	58.22	69.45	55.17
Age				
<15 years	Pearson correlation	0.19*	0.32*	0.31*
	Kappa (95 C.I.) <sup>♦</sup>	0.12 (0.011, 0.23)	0.39 (0.12, 0.66)	0.29 (0.12, 0.45)
	Percent of agreement (%) <sup>♦</sup>	58.93	69.77	64.23
≥15 years	Pearson correlation	0.43*	0.52*	0.50*
	Kappa (95 C.I.) <sup>♦</sup>	0.25 (0.13, 0.38)	0.43 (0.23, 0.64)	0.21 (0.016, 0.40)
	Percent of agreement (%) <sup>♦</sup>	65.70	72.37	60.82
Race				
Non-Hispanic White	Pearson correlation	0.28*	0.31	0.34*
	Kappa (95 C.I.) <sup>♦</sup>	0.18 (0.087, 0.27)	0.18 (-0.14, 0.51)	0.21 (0.039, 0.39)

	Percent of agreement (%) ♦	62.85	60.60	62.40
African American	Pearson correlation	0.18	0.50*	0.33*
	Kappa (95 C.I.) ♦	-0.07 (-0.34, 0.19)	0.49 (0.29, 0.70)	0.16 (-0.092, 0.41)
	Percent of agreement (%) ♦	44.90	74.63	58.33
Hispanic	Pearson correlation	0.38*	0.55*	0.67*
	Kappa (95 C.I.) ♦	0.24 (-0.020, 0.50)	0.51 (0.010, 0.91)	0.37 (0.062, 0.68)
	Percent of agreement (%) ♦	66.07	77.78	68.57
Others	Pearson correlation	0.79*	N/A★	N/A★
	Kappa (95 C.I.) ♦	0.35 (-0.17, 0.87)	N/A★	N/A★
	Percent of agreement (%) ♦	69.23	N/A★	N/A★
BMI_Z20				
>1	Pearson correlation	0.18*	0.46*	0.41*
	Kappa (95 C.I.) ♦	0.10 (-0.047, 0.25)	0.41 (0.24, 0.58)	0.32 (0.13, 0.52)
	Percent of agreement (%) ♦	56.5	70.76	66.29
≤1	Pearson correlation	0.35*	0.22*	0.40*
	Kappa (95 C.I.) ♦	0.20 (0.10, 0.30)	0.42 (-0.12, 0.96)	0.18 (0.0089, 0.34)
	Percent of agreement (%) ♦	64.09	76.92	60.03

\*: p<0.05; ♦: categorized into two groups by median ; ★: not applicable due to small sample size

Table 4.3. Associations of television watching measured by the YRBS and 3DPAR: The SEARCH Case Control Study

		T1D			T2D			Without Diabetes		
		Estimate	F	P	Estimate	F	P	Estimate	F	P
Intercept		4.05			0.65			-1.32		
YRBS		0.23	18.25	<.01	0.54	17.62	<.01	0.40	24.83	<.01
Age		-0.15	9.56	<.01	0.02	0.01	0.91	0.15	3.01	0.08
Gender (ref: Male)		-0.11	0.13	0.72	-0.46	0.27	0.60	-0.26	0.25	0.62
Race (ref=White)	African American	1.12			-0.38			0.51		
	Hispanic	0.26	1.5	0.21	-0.61	0.25	0.86	2.98	5.66	<.01
	Others	0.17			-3.09			-1.27		

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CHAPTER 5

MANUSCRIPT 3

Longitudinal association between meal frequency and risk markers in diabetes in the  
SEARCH for Diabetes in Youth Study<sup>1</sup>

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<sup>1</sup> Chao Li, Elizabeth J. Mayer-Davis, Ralph B. D'Agostino Jr., Dana Dabelea, Larry Dolan, Angela D. Liese, Russell Pate, and Anwar T. Merchant. To be submitted to American Journal of Nutrition.



## **Abstract**

**Background:** Few studies have evaluated the long-term association between meal frequency and risk markers in diabetes among youth with diabetes. **Objective:** The objective was to examine the longitudinal association over 5 years between meal frequency and HbA1c and serum lipids among youth with type 1 diabetes (T1D) and type 2 diabetes (T2D). **Design:** 1049 youth ( $\geq 10$  yr. old) with recently diagnosed T1D and T2D participated in the SEARCH for Diabetes in Youth Study from 2002-2005. Meal frequency (1 to 3, 4 to 5 and 6 to 10 meals/day) measured at the initial visit was related to HbA1c and serum lipids repeatedly measured over 5 years. **Results:** Meal frequency was associated with changes in HbA1c among youth with T1D ( $n=821$ ), but not T2D ( $n=228$ ), after multivariable adjustment. HbA1c increased constantly by 0.43% ( $p<0.05$ ) among youth with T1D who ate 1-3 meals/day than those ate 4-5 meals/day; and there was no difference in change of HbA1c comparing individuals eating 4-5 meals/day and 6-10 meals/day. This association was stronger among youth who were  $\geq 15$  years ( $p$ -value for interaction $<0.05$ ) and African American ( $p$ -value for interaction $<0.05$ ). Meal frequency was not associated with changes in serum lipids among youth with T1D and T2D.

**Conclusions:** Youth with T1D who ate 1-3 meals/day had higher HbA1c over 5 years compared with those who ate 4-5 meals/day, but not with those who ate 6-10 meals/day. Frequent meals without increasing total energy intake may be beneficial for youth with T1D.

## Background

Increased meal frequency has been associated with multiple metabolic benefits in adults with diabetes <sup>1</sup>. Consuming 6 to 13 small meals/day over 2 days had beneficial effects on insulin sensitivity and blood glucose compared with those consuming 2 or 3 large meals/day among adults with type 2 diabetes (T2D) <sup>1,2</sup>. But this benefit was not confirmed in a relatively longer-term (4 weeks) study <sup>3</sup> conducted among 13 adults with T2D. More recent studies <sup>4,5</sup> reported similar metabolic benefits, including more favorable glucose response, increased insulin sensitivity and improved lipids profiles, were associated with increased meal frequency in healthy people.

Reduced meal frequency has been linked to reduced postprandial energy expenditure which may lead to increased weight <sup>5</sup>. Meanwhile, increased meal frequency could reduce insulin secretion and increase fractional clearance of insulin <sup>2,6</sup>. Also, increased meal frequency could prolong absorption of carbohydrate, fiber and enzyme inhibitor that can be linked to reduce mean insulin levels postprandial <sup>1,6,7</sup>, lower postprandial glucose profile <sup>1,6,7</sup>, decrease 24-h urinary C-peptide output <sup>1,8</sup>, flatter gastric inhibitory polypeptide response <sup>1,2,6</sup>, decrease unitary catecholamine output <sup>6</sup>, reduce fasting and postprandial serum total and LDL cholesterol levels <sup>8-10</sup>, prolong suppression of plasma free fatty acids <sup>6</sup>, enhance urinary uric acid excretion <sup>10</sup>, reduce serum apolipoprotein B levels <sup>11</sup> and serum uric acid levels <sup>10</sup>, and lower hepatic cholesterol synthesis <sup>7</sup>.

To our knowledge, no published studies have evaluated the long-term effect of meal frequency on glycemic and metabolic control among youth with type 1 diabetes (T1D)

and T2D, even though diabetes is a growing public health concern in youth <sup>12</sup>. Therefore, in this study, we assessed the longitudinal relation over 5 years between meal frequency and HbA1c and serum lipids among youth with both T1D and T2D using data from the SEARCH for Diabetes in Youth Study.

## **Research design and methods**

### **Study design and population**

The SEARCH for Diabetes in Youth study is an on-going population-based, observational study of non-gestational diabetes among youth < 20 years old. The multiple clinical centers of SEARCH study that contributed data for this analysis are Ohio, Colorado, Washington, South Carolina, California and Hawaii. The SEARCH study has been previously described in detail <sup>13</sup>.

There were 1049 T1D and T2D youth ( $\geq 10$  years old at the initial visit) who joined the SEARCH study and provided baseline data from 2002 to 2005. Participants were re-examined one and five years after the initial visit. All participants in this study had documented physician-diagnosed diabetes and information on year of diagnosis. Also, they were less than 20 years old on December 31 of the year of diagnosis, and participated in at least one follow-up visit.

## Data collection and measurement

Local institutional review boards that had jurisdiction over the local study population reviewed and approved this study before implementation of data collection. Also, we obtained written informed consent and child assent at the beginning of each study visit.

Trained and certified staff collected data by following standardized protocols for initial and follow-up visits<sup>13</sup>. Data were collected by questionnaires, physical examination and laboratory tests.

## Exposure:

In our food frequency questionnaire (FFQ), there was one question asking about meal frequency behavior. It was: “Last week, about how many times each day did you eat (including meals & snacks)?” The responses to this question were categorized as follows: “0”, “1”, “2”, “3”, “4-5”, “6-7”, and “8-10” meals/day. Meal frequency was further categorized as follows: “0-3”, “4-5” and “6-10” meals/day adapted from previous similar studies<sup>14,15</sup>.

## Outcomes from laboratory tests:

SEARCH staff drew blood samples under the condition of metabolic stability (8 hours of fasting and no episode of diabetic ketoacidosis in the previous month) at each visit. The blood samples were shipped with dry ice to the central laboratory in Seattle, WA within 24 hours to measure HbA1c, LDL cholesterol, HDL cholesterol and triglyceride (TG). An ion exchange high-performance liquid chromatography instrument (TOSOH,

Bioscience, Inc., Dan Francisco, CA) was used to measure HbA1c. LDL, HDL and TG were analyzed enzymatically on a Hitachi 917 auto analyzer (Boehringer Mannheim Diagnostics, Indianapolis, Ind). Friedewald equation <sup>16</sup> and lipid research clinics beta quantification <sup>17</sup> were used to calculate LDL for individuals with TG concentrations less and more than 400 mg/dl (4.52 mmol/L) respectively.

Other covariates:

Demographic information including gender, age, race/ethnicity, type of insurance, household income, and highest parental education were obtained from an initial survey at baseline <sup>18</sup>.

Physical activity was evaluated by a question adapted from the Youth Risk Behavioral Survey questionnaires <sup>19</sup> and asked at each study visit. The physical activity question was: “On how many of the past 7 days did you exercise or participate in a physical activity for at least 20 minutes that made you sweat and breathe hard, such as basketball, soccer, running, swimming laps, fast bicycling, fast dancing, or similar aerobic activities?” The responses to this question were: “None”, “1 day”, “2 days”, “3 days”, “4 days”, “5 days”, “6 days”, and “7 days”.

All youth participated in standardized physical examinations. Height and weight were measured by a stadiometer and electronic scale, respectively, at each visit. Dividing weight (kg) by squared height (m) was used to calculate body mass index ([BMI] kg/m<sup>2</sup>),

and age and gender specific BMI z-scores were obtained by using the Centers for Disease Control and Prevention growth curves <sup>20</sup>.

### Statistical methods

Demographic information is shown as means and standard deviation for continuous variables and frequencies and percents for categorical variables.

Longitudinal mixed models were fit separately for individuals with T1D and T2D to characterize the relation between fixed meal frequency (meal frequency at each visit was carried over as initial value) and time-varying HbA1c and serum lipids among youth with diabetes that were included as random effects. Multivariate mixed models tested the effects of meal frequency on HbA1c and serum lipids measured at the initial, 1 year and or 5 year follow-up visits. In addition, an interaction term (duration of diabetes\*initial meal frequency) was added into the model to determine whether changes in HbA1c and serum lipids (HDL, LDL and TG) over time varied by the initial meal frequency.

Duration of diabetes (number of months since diabetes diagnosis) was included in these mixed models as an indicator of time for each participant. All models were expanded to include fixed/non-time varying covariates, including gender, age at the initial visit, race/ethnicity, highest parental education, type of insurance and household income, and time-varying covariates including BMI- z score, total intake of calorie, physical activity and treatment for diabetes and dyslipidemia <sup>21,22</sup>.

All statistical analyses were performed in SAS (version 9.1, 2003, SAS Institute Inc, Cary, NC). Mixed models were used to fit longitudinal statistical models.  $P < 0.05$  was used as standard of significance.

## **Results**

There were 821 youth with T1D and 228 youth with T2D in this study (Table 5.1).

Frequency of meal consumption was different in youth with

T1D and T2D. Among youth with T1D, 184 (22.4%) had 1-3 meals/day, 246 (30.0%) had 4-5 meals/day and 391 (47.6%) had 6-10 meals/day. In comparison, of youth with T2D, 94 (41.2%) had 1-3 meals/day, 32 (14.0%) had 4-5 meals/day, and 102 (44.8%) had 6-10 meals/day. The participants were similar with respect to age, gender, race, socioeconomic, and insurance status across categories of meal consumption among those with T1D and T2D. Youth with T1D who ate 4-5 meals/day were leaner (mean BMI z-score 0.4) than those eating 1-3 and 6-10 meals/day (mean BMI z-scores 0.6). No such difference was seen in youth with T2D (Table 5.1).

Youth who eating 6-10 meals/day consumed more energy than those eating 4-5 meals/day (mean 1965.8 versus 1774.2 calories/day for T1D and mean 2184.7 versus 1703.9 calories/day for T2D) (Table 5.1). Mean caloric intakes for those eating 1-3 meals/day and 4-5 meals/day were similar in youth with T1D and T2D (Table 5.1). Youth with T2D who consumed 1-3 meals/day had diets with a higher glucose and fructose composition compared with those eating 4-5 meals/day (mean glucose 15.9 versus 12.8 g/1000 calories, and mean fructose 15.8 versus 12.1 g/1000 calories) (Table 5.1). The

distribution of other nutrients was similar across categories of meal frequency in youth with T1D and T2D (Table 5.1).

#### Longitudinal Mixed Models:

HbA1c significantly increased over time among youth with T1D and T2D. LDL and TG only significantly increased over time among youth with T1D. Meal frequency at baseline was associated with changes in HbA1c among youth with T1D after adjusting for age at the initial visit, gender, race, physical activity, parental education, household income, insurance type, BMI z-score, treatment for diabetes and dyslipidemia and total calorie intake. HbA1c increased constantly by 0.43% ( $p < 0.05$ ) among youth with T1D who ate 1-3 meals/day than those ate 4-5 meals/day (Table 5.2); and there was no difference in change of HbA1c comparing individuals eating 4-5 meals/day and 6-10 meals/day. The relation between meal frequency and HbA1c did not depend on the initial meal frequency measured at baseline ( $p$ -value for interaction between duration of diabetes and meal frequency  $> 0.05$ ). The number of meals eaten per day was not associated with changes in HDL, LDL and TG among youth with T1D and T2D, or HbA1c among youth with T2D.

We further examined the relation between meal frequency and HbA1c among youth with T1D stratified by gender, age ( $< 15$  years old and  $\geq 15$  years old), and race (Non-Hispanic white, African American, Hispanic, others) in Figure 5.1-5.3 and Table 5.3. For youth with T1D, the effect estimates of having 4-5 meals per day vs. 1-3 meals per day



on HbA1c were similar in males and females, but was stronger for older participants ( $\geq 15$  years), and African Americans comparing with Non-Hispanic Whites.

## **Discussion**

In the present study youth with T1D who consumed 1-3 meals/day had a greater increase in mean HbA1c over 5 years compared with those consumed 4-5 meals/day, after accounting for energy intake and other factors. This longitudinal association was stronger among older and African American youth with T1D. There was no difference between eating 4-5 meals/day and 6-10 meals/day in changes of HbA1c, even though individuals who ate more frequent meals consumed more calories. Meal frequency was not associated with HbA1c among youth with T2D, and serum lipids among youth with both T1D and T2D. To our knowledge, this is the first study to prospectively evaluate potential long-term metabolic effects of meal frequency in youth with diabetes.

Meal frequency has been recognized for over 20 years to be associated with metabolic changes in people with diabetes <sup>1</sup>. The American Diabetes Association (ADA) guidelines on nutritional therapy in diabetes recognizes nutrition therapy as an essential component of diabetes treatment, and recommends individualized dietary counseling as part of the overall treatment plan <sup>23</sup>. Previous ADA statement of nutrition principles reported that increased meal frequency was related with lower mean blood glucose and insulin levels in T2D <sup>24</sup>. While the most recent ADA guidelines on nutrition therapy do not specify the optimal meal frequency <sup>23</sup>. Jenkins et al <sup>1</sup> and Bertelsen et al <sup>2</sup> have compared the effects

of 2 or 3 large meals/day with 6 to 13 small meals/day among adults with T2D in 2 days. Both studies showed that increased meal frequency could increase insulin sensitivity and lower blood glucose concentration over the day. Similar metabolic advantages, such as reduction in serum lipids and lipid concentration, have also been observed in healthy subjects <sup>4,5,8</sup>. However, a relatively longer (4 weeks) study conducted by Arnold et al <sup>25</sup> on the impact of meal frequency on metabolic effects among 13 adults with T2D did not confirm the potential benefits of increased meal frequency. Another randomized crossover study (24 weeks) conducted among adults with T2D reported eating two large meals a day could reduce body weight, hepatic fat content, fasting plasma glucose, C-peptide and glucagon, and increase oral glucose insulin sensitivity than six meals a day <sup>26</sup>.

It is biologically plausible that spreading the nutrient and energy load by increased meal frequency may be beneficial for youth with diabetes. First, reduced meal frequency has been linked to reduced postprandial energy expenditure which may lead to increased weight <sup>5</sup>. One study showed increased thermogenic response with reduced meal frequency in humans <sup>27</sup>. Second, increased meal frequency could prolong absorption of carbohydrate, fiber and enzyme inhibitor that can be linked to reduce mean insulin levels postprandial <sup>1,6,7</sup>, lower postprandial glucose profile <sup>1,6,7</sup>, decrease 24-h urinary C-peptide output <sup>1,8</sup>, flatter gastric inhibitory polypeptide response <sup>1,2,6</sup>, decrease unitary catecholamine output <sup>6</sup>, reduce fasting and postprandial serum total and LDL cholesterol levels <sup>8-10</sup>, prolong suppression of plasma free fatty acids <sup>6</sup>, enhance urinary uric acid excretion <sup>10</sup>, reduce serum apolipoprotein B levels <sup>11</sup> and serum uric acid levels <sup>10</sup>, and

lower hepatic cholesterol synthesis <sup>7</sup>. Third, increased meal frequency could reduce insulin secretion and increase fractional clearance of insulin <sup>2,6</sup>.

The main purpose of increasing meal frequency is to spread nutrient load and avoid hyperglycemia and hypoglycemia while holding constant total intake of calories.

However, we found that youth with both T1D and T2D eating 6-10 meals/day also consumed more total calories. Similar findings were also reported by studies conducted among adults free of diabetes <sup>28</sup> and those with T2D <sup>29</sup>. We adjusted for total energy intake, BMI, and physical activity in our analyses to account for these differences. Nevertheless, these findings are important because even small amounts of excess energy intake can lead to weight gain over time. Individuals making dietary recommendations to children with diabetes need to consider this.

There is no ideal percentage of calories from carbohydrate, fat and protein for all people with diabetes based on the most recent standards of medical care in diabetes from the American Diabetes Association <sup>30</sup>. Several studies reported that, on average, total intake of calories were about 45% from carbohydrate, 36-40% from fat and 16-18% from protein in people with diabetes <sup>31-33</sup>. In our study, we found similar macronutrient distribution among youth with T1D and T2D. Also, youth with T1D who ate 6-10 meals/day tends to have a lower percentages of calories from carbohydrate and more from fat than who ate 4-5 meals/day.

This study had several potential limitations. First, the exposure variable, meal frequency, was assessed through self-report questionnaire. However, because participants did not know their HbA1c or serum lipid values when meal frequency was assessed, it is unlikely that the outcome contributed to error related to assessment of meal frequency. Therefore, measurement error associated with assessment of meal frequency in this study would bias the result towards the null. Second, meal frequency was treated as fixed in this analysis, although eating habits may slightly change over time. Third, residual confounding was possible because of the observational study design. However, in the analyses we adjusted for many potential confounders including age, gender, race, total caloric intake, physical activity, parental education, household income, insurance type, BMI z-score, and treatment for diabetes and dyslipidemia. The associations reported in this paper were independent of these potential confounders. Fourth, our analysis was not able to separate breakfast from the total number of meals consumed of a day, since several previous study have shown breakfast was positively associated with T2D risk in adults <sup>14,15</sup>. Fifth, we have not found any association between meal frequency and HbA1c and serum lipids in T2D. This is probably due to the small sample size of youth with T2D. Finally, total caloric intake is usually underreported by the FFQ, so that, our adjustment for calculated total caloric intake seemed to be incomplete.

Despite these limitations, this study also had several strengths. First, the large sample for this analysis was drawn from the SEARCH for Diabetes in Youth Study population, which is the largest prospective investigation among youth with T1D and T2D, and includes all major US ethnic groups. Second, to our knowledge, this was the first

longitudinal study design, including 5 years of follow-up, to evaluate the relationship between meal frequency and HbA1c and serum lipids. Third, meal frequency was able to be analyzed independently with other dietary variables, and ability to adjust for many important potential confounders was also an important strengths of this study.

In conclusion, the HbA1c increase was smaller among youth with T1D consuming 4-5 meals/day than those consuming 1-3 meals/day over 5 years. This relation was stronger among African Americans and those  $\geq 15$  years. There was no difference in HbA1c levels among youth with T1D consuming 4-5 and 6-10 meals/day. However the latter group consumed more calories. Eating more frequent meals in a day without increasing total energy intake may be beneficial for youth with T1D.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention and the National Institute of Diabetes and Digestive and Kidney Diseases.

Table 5.1: Demographic, clinical and nutrient characteristics of participants at the initial visit: SEARCH for Diabetes in Youth, 2002-2005.

		T1D (n=821)			T2D (n=228)		
		1-3 meals/day	4-5 meals/day	6-10 meals/day	1-3 meals/day	4-5 meals/day	6-10 meals/day
Demographics							
Gender: n (%)	Female	85 (46.2)	115 (46.8)	184 (47.1)	58 (61.7)	20 (62.5)	61 (59.8)
	Male	99 (53.8)	131 (53.2)	207 (52.9)	36 (38.3)	12 (37.5)	41 (40.2)
Race: n (%)	Non-Hispanic White	123 (66.9)	187 (76.0)	307 (78.5)	21 (22.3)	3 (9.4)	25 (24.5)
	African American	25 (13.6)	21 (8.5)	35 (9.0)	33 (35.1)	16 (50.0)	33 (32.4)
	Hispanic	26 (14.1)	29 (11.8)	35 (9.0)	23 (24.5)	5 (15.6)	24 (23.5)
	Others <sup>1</sup>	10 (5.4)	9 (3.7)	14 (3.5)	17 (18.1)	8 (25.0)	20 (19.6)
Age: mean± SD		14±2.6	13.3±2.4	13.7±2.3	15.4±2.3	14.9±2.6	14.9±2.6
Parental highest education: n (%)	Bachelor degree or more	79 (43.2)	118 (48.0)	186 (48.0)	13 (14.0)	10 (31.3)	13 (12.9)
	Some college with associate degree	64 (35.0)	76 (30.9)	139 (35.8)	30 (32.3)	8 (25.0)	42 (41.5)
	High school	28 (15.3)	45 (18.3)	49 (12.6)	31 (33.3)	12 (37.5)	33 (32.7)
	Less than high school	12 (6.5)	7 (2.8)	14 (3.6)	19 (20.4)	2 (6.2)	13 (12.9)
Annual household income: n (%)	<\$25,000	42 (23.1)	39 (15.9)	79 (20.4)	27 (28.7)	9 (28.1)	22 (21.5)
	\$25,000-49,000	30 (16.5)	56 (22.8)	86 (22.2)	10 (10.7)	4 (12.5)	11 (10.8)
	\$50,000-74,000	67 (36.8)	100 (40.6)	160 (41.2)	6(6.4)	3 (9.4)	11 (10.8)
	≥75,000	29 (15.9)	37 (15.0)	40 (10.3)	38 (40.4)	10 (31.3)	47 (46.1)
	DK/Ref	14 (7.7)	14 (5.7)	23 (5.9)	13 (13.8)	6 (18.7)	11 (10.8)
Insurance: n (%)	Medicaid/Medicare	35 (19.1)	37 (15.2)	56 (14.5)	35 (37.6)	14 (43.8)	41 ((40.3)
	Private	143 (78.1)	198 (81.1)	319 (82.4)	49 (52.7)	15 (46.9)	55 (53.9)
	Other	1 (0.6)	6 (2.5)	2 (0.5)	5 (5.4)	1 (3.1)	4 (3.9)
	None	4 (2.2)	3 (1.2)	10 (2.6)	4 (4.3)	2 (6.2)	2 (1.9)
Clinical characteristics							
HbA1c: mean ± SD		8.0 <sup>2</sup> ±2.0	7.5±1.5	7.8±1.7	7.0±1.8	7.3±2.3	7.2±2.3

BMI z-score: mean $\pm$ SD		0.6 $\pm$ 0.9	0.4 $\pm$ 0.9	0.6 $\pm$ 1.0	2.2 $\pm$ 0.5	2.2 $\pm$ 0.7	2.1 $\pm$ 0.7
Diabetes treatment: n (%)	Insulin pump	9 (4.9)	16 (6.5)	46 (11.9)	0 (0.0)	0 (0.0)	0 (0.0)
	Insulin 3+ times/day	113 (61.4)	95 (38.6)	220 (56.9)	10 (10.6)	1 (3.1)	14 (13.9)
	Insulin <3 times/day	58 (31.5)	133 (54.1)	114 (29.4)	26 (27.7)	10 (31.3)	14 (13.9)
	No treatment	4 (2.2)	2 (0.8)	7 (1.8)	58 (61.7)	21 (65.6)	73 (72.2)
HDL: mean $\pm$ SD		52.3 $\pm$ 13.3	51.2 $\pm$ 11.9	52.4 $\pm$ 11.7	40.0 $\pm$ 9.1	41.7 $\pm$ 9.6	41.7 $\pm$ 9.5
LDL: mean $\pm$ SD		93.7 $\pm$ 25.6	91.4 $\pm$ 24.2	95.1 $\pm$ 29.8	101.2 $\pm$ 29.0	103.1 $\pm$ 27.9	93.8 $\pm$ 28.4
TG: mean $\pm$ SD		83.8 $\pm$ 99.3	68.1 $\pm$ 38.3	71.6 $\pm$ 47.4	141.1 $\pm$ 91.1	138.4 $\pm$ 95.2	125.0 $\pm$ 97.8
Nutrient characteristics							
Total calorie intake(cal):mean $\pm$ SD		1762 $\pm$ 803	1774 $\pm$ 683	1965 $\pm$ 788	1634 $\pm$ 704	1703 $\pm$ 707	2184 $\pm$ 858
Total carbohydrate (g/1000cal):mean $\pm$ SD		116 $\pm$ 18	113 $\pm$ 18	118 $\pm$ 19	120 $\pm$ 24	114 $\pm$ 20	114 $\pm$ 21
Percent of calories from carbohydrate (%)		46.5	47.1	45.2 <sup>2</sup>	47.9	45.6	45.8
Fructose(g/1000cal):mean $\pm$ SD		10.5 $\pm$ 5.7	9.8 $\pm$ 6.3	10.8 $\pm$ 6.9	15.8 $\pm$ 9.7	12.1 $\pm$ 9.5	13.6 $\pm$ 10.1
Glucose (g/1000cal): mean $\pm$ SD		11.4 $\pm$ 4.7	10.9 $\pm$ 5.5	12.0 $\pm$ 5.8	15.9 $\pm$ 8.4	12.8 $\pm$ 8.6	13.8 $\pm$ 8.9
Total fat (g/1000cal):		43.3 $\pm$ 6.7	44.1 $\pm$ 6.6	42.4 $\pm$ 6.7	42.0 $\pm$ 7.6	43.7 $\pm$ 7.5	43.8 $\pm$ 7.4
Percent of calories from fat (%)		39	38.2	39.7 <sup>2</sup>	38	39.4	39.4
Total protein (g/1000cal):mean $\pm$ SD		39.9 $\pm$ 5.2	40.5 $\pm$ 5.6	39.8 $\pm$ 5.9	37.4 $\pm$ 7.8	39.5 $\pm$ 6.0	40.0 $\pm$ 6.6
Percent of calories from protein (%)		15.9	16	16.2	15.1	16	15.8
Total sugar (g/1000cal):mean $\pm$ SD		54.2 $\pm$ 17.3	51.8 $\pm$ 18.1	55.72 $\pm$ 18.0	61.3 $\pm$ 24.4	53.8 $\pm$ 23.0	54.7 $\pm$ 26.0

1:Other races: Asian Indian, American Indian or Alaska Native, Native Hawaiian, Asian etc.; 2: p<0.05 from ANOVA test



Table 5.2. Adjusted<sup>3</sup> longitudinal associations of changes in HbA1c and serum lipids among youth with diabetes: SEARCH for Diabetes in Youth, 2002-2005

Mixed models (ref=4-5 meals/day) <sup>2</sup>			T1D				T2D			
			HbA1c	HDL	LDL	TG	HbA1c	HDL	LDL	TG
			(%)	(mg/dl)	(mg/dl)	(mg/dl)	(%)	(mg/dl)	(mg/dl)	(mg/dl)
model 1	DM Duration		0.032 <sup>1</sup>	0.14 <sup>1</sup>	0.10 <sup>1</sup>	0.46 <sup>1</sup>	0.022 <sup>1</sup>	0.080 <sup>1</sup>	-0.011	0.044
	DM Duration		0.033 <sup>1</sup>	0.14 <sup>1</sup>	0.10 <sup>1</sup>	0.37 <sup>1</sup>	0.023 <sup>1</sup>	0.06 <sup>1</sup>	0.02	0.15
model 2	MF	<=3meals	0.43 <sup>1</sup>	1.90	1.67	7.52	-0.16	-2.71	-2.58	14.49
		6-10meals	0.16	0.54	1.78	0.97	-0.11	-0.75	-8.43	0.64
	DM Duration		0.035 <sup>1</sup>	0.15 <sup>1</sup>	0.12 <sup>1</sup>	0.49 <sup>1</sup>	0.025 <sup>1</sup>	0.033 <sup>1</sup>	-0.070	0.026
	MF	<=3meals	0.35 <sup>1</sup>	1.80	1.60	7.59	0.10	-2.43	-0.60	29.05
model 3		6-10meals	0.12	0.77	1.73	2.82	-0.012	-1.58	-11.59	-3.65
	DM	<=3meals	-0.001	-0.003	-0.032	-0.352	-0.004	0.046	0.133	0.116
	Duration*MF	6-10meals	-0.004	-0.024	-0.017	-0.13	-0.002	0.058	0.18	0.30

1:  $p < 0.05$ ; 2: Model 1: Outcome =  $\beta_0 + \beta_1(\text{duration of diabetes}) + \epsilon$ ; Model 2: Outcome =  $\beta_0 + \beta_1(\text{duration of diabetes}) + \beta_2(\text{fixed meal frequency at baseline}) + \epsilon$ ; Model 3: Outcome =  $\beta_0 + \beta_1(\text{duration of diabetes}) + \beta_2(\text{fixed meal frequency at baseline}) + \beta_3(\text{duration of diabetes} * \text{fixed meal frequency at baseline}) + \epsilon$ ; 3: Adjusted variables: Gender, age at the initial visit, race/ethnicity, highest parental education, type of insurance, household income, BMI- z score, total intake of calorie, physical activity and treatment for diabetes and dyslipidemia.

Table 5.3. Stratified analysis for the significant longitudinal relation between meal frequency and HbA1c among youth with T1D

		Estimate	95% confidence interval		P for interaction <sup>1</sup>
			Lower limit	Upper limit	
Overall		0.430	0.163	0.719	
Gender	Female	0.437	0.017	0.858	0.470
	Male	0.414	0.028	0.800	
Age	<15 yrs	0.368	0.075	0.662	0.031
	≥15 yrs	0.485	0.134	0.836	
Race	Non-Hispanic White (ref)	0.310	0.051	0.569	.
	African American	1.552	0.471	2.633	<0.0001
	Hispanic	0.365	-0.531	1.260	0.075
	Others 2	1.210	-0.757	3.177	0.064

1: interaction between stratified variables and meal frequency: Outcome =  $\beta_0 + \beta_1(\text{duration of diabetes}) + \beta_2(\text{fixed meal frequency at baseline}) +$

$\beta_3(\text{fixed meal frequency at baseline} \times \text{stratified variable}) + \epsilon$ ; 2: Other races: Asian Indian, American Indian or Alaska Native, Native Hawaiian, Asian

etc.

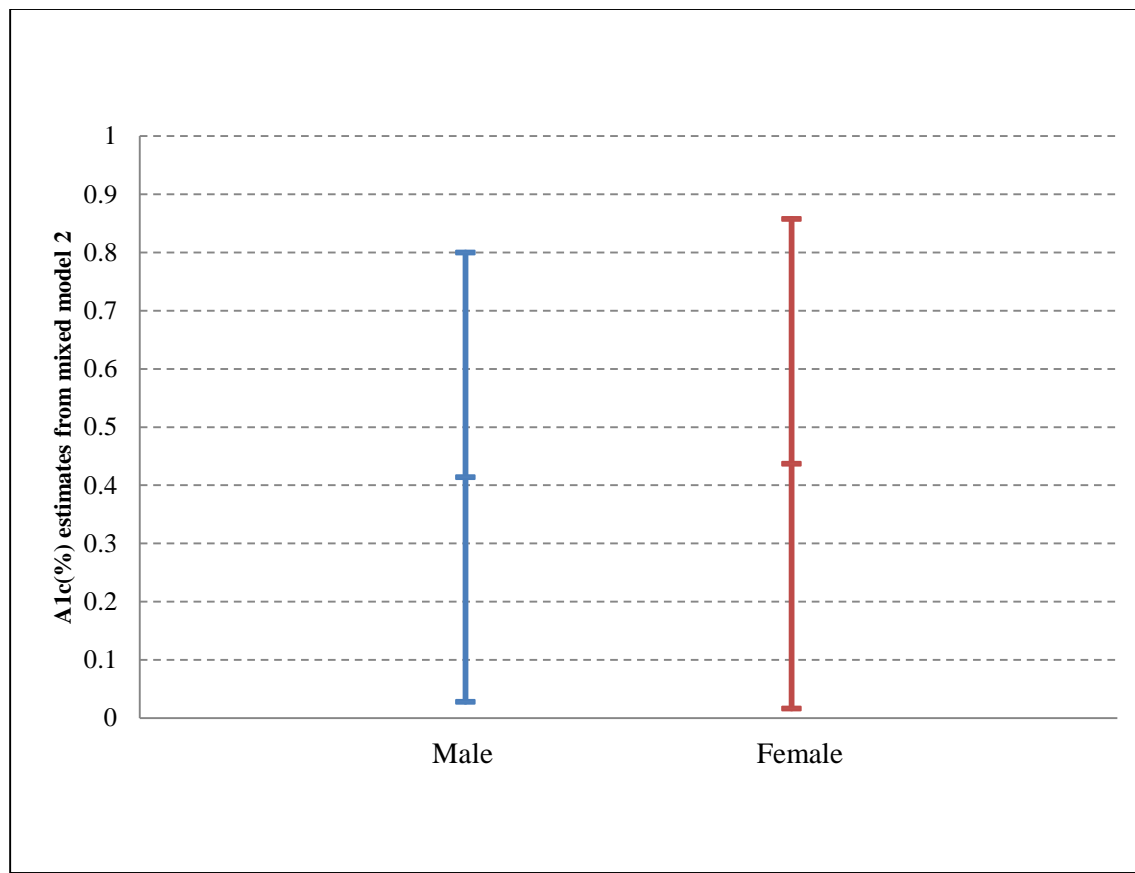


Figure 5. 1 Estimates and 95% confidence interval of HbA1c in males and females with T1D: SEARCH for Diabetes in Youth, 2002-2005

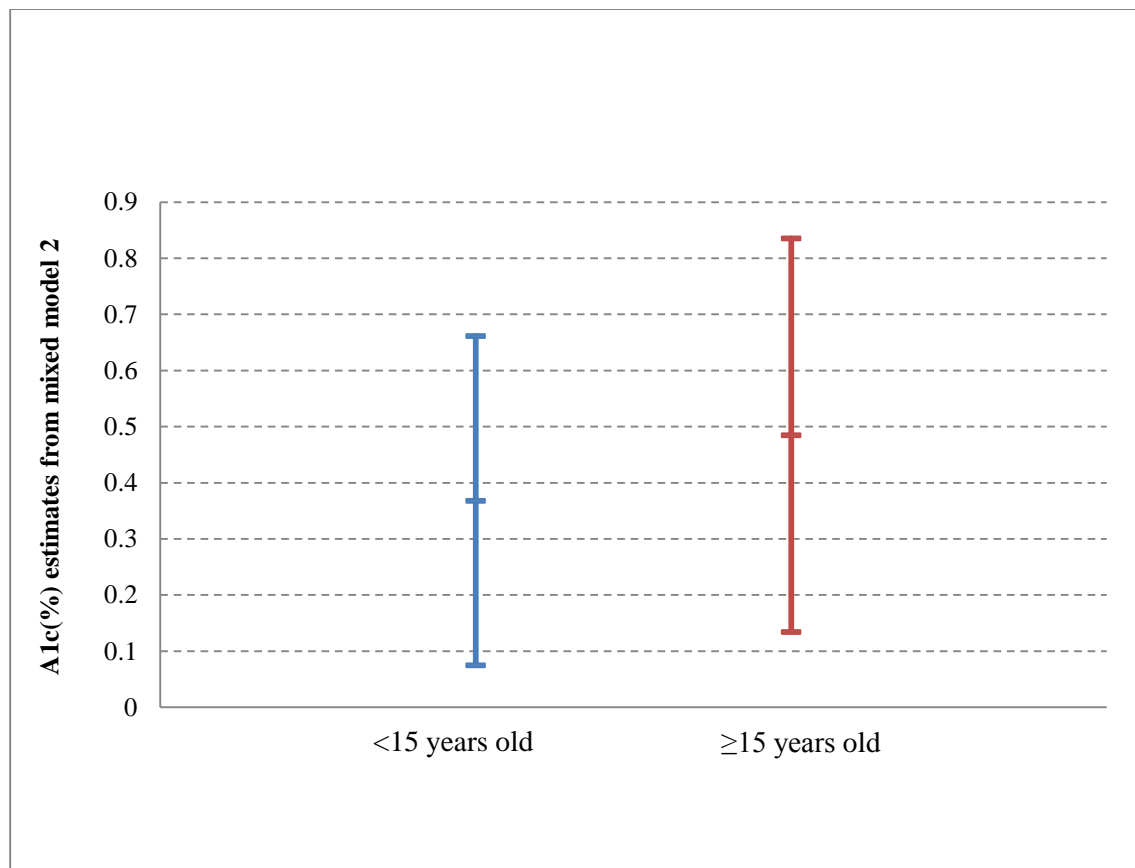


Figure 5. 2 Estimates and 95% confidence interval of HbA1c in younger and older youth with T1D: SEARCH for Diabetes in Youth, 2002-2005

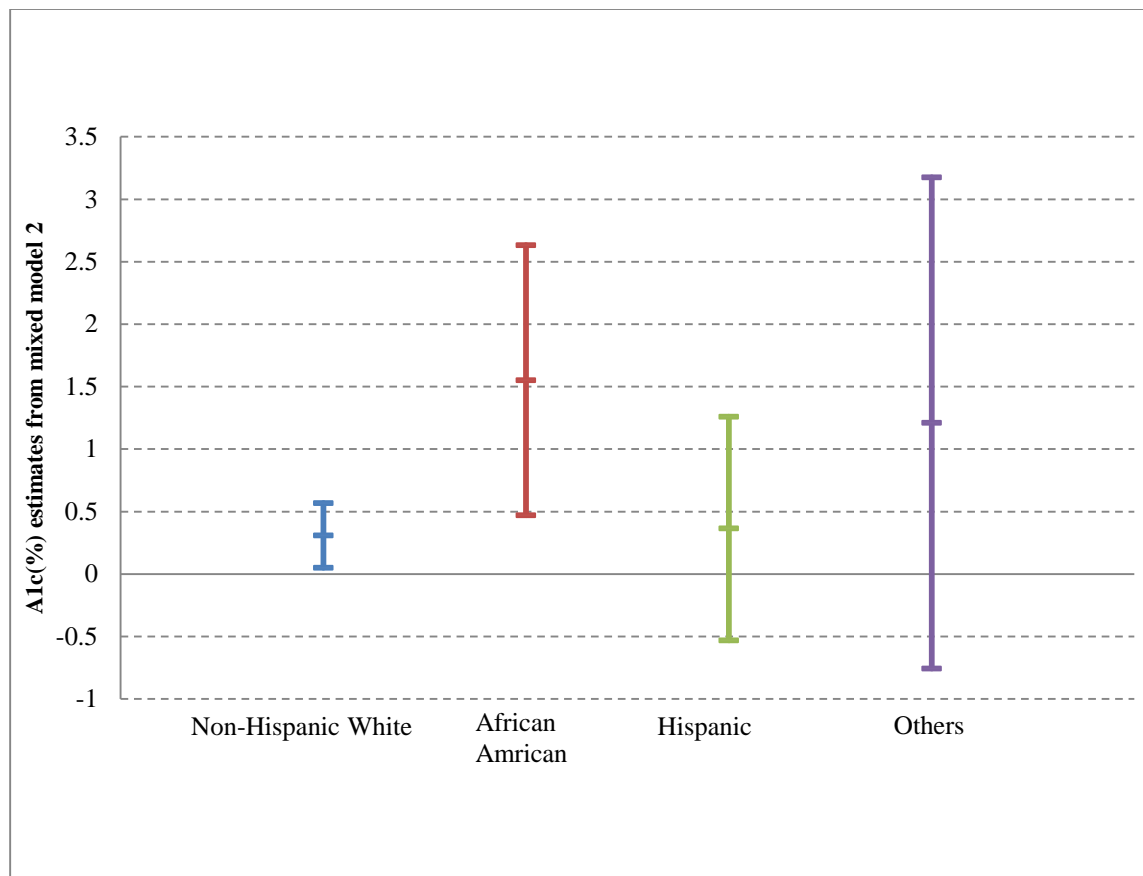


Figure 5. 3 Estimates and 95% confidence interval of HbA1c in Non-Hispanic White, African American, Hispanic and others races with T1D: SEARCH for Diabetes in Youth, 2002-2005

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## CHAPTER 6

### SUMMARY

The aims of this dissertation were developed to add new knowledge in the area of youth diabetes, sedentary behavior, meal frequency, validity of self-reported sedentary behavior questions and HbA1c and cardiovascular risk markers.

To fulfill these aims we studied the largest and representative sample of youth with T1D and T2D from the SEARCH and SEARCH-CC study in which we evaluated: 1. The longitudinal association between television watching and computer use and HbA1c and serum lipids among youth with diabetes; 2. The validity of self-reported television watching questions adapted from the YRBS against the 3DPAR among youth with and without diabetes; 3. The longitudinal association between meal frequency and HbA1c and serum lipids among youth with diabetes;

The main findings were that HbA1c, LDL-c and TG levels increased over time in all youth with T1D and T2D. However, the magnitude of increase was significantly greater among those who watched more television and increased their television watching behavior over time, compared to those who watched less TV, after adjusting for several important confounders. Computer use was not associated with HbA1c and serum lipids in this analysis.

Self-reported hours of television watching evaluated by the YRBS questions were weakly to moderately correlated with responses obtained from the 3DPAR. The correlations were higher (i.e. in the moderate range) for youth with T2D, and who were also females,  $\geq 15$  years of age, and African Americans and Hispanics. The YRBS questions tended to overestimate television watching among youth with and without diabetes compared with 3DPAR after adjusting for age, gender, and race.

Youth with T1D who consumed 1-3 meals/day had a greater increase in mean HbA1c over 5 years compared with those consumed 4-5 meals/day or more, after accounting for energy intake and other factors. This longitudinal association was stronger among older and African American youth with T1D. There was no difference between eating 4-5 meals/day and 6-10 meals/day in changes of HbA1c, even though individuals who ate more frequent meals consumed more calories. Meal frequency was not associated with HbA1c among youth with T2D. Meal frequency was not associated with longitudinal changes in serum lipids either among youth with T1D or T2D.

Sedentary behavior, including television watching and computer use, is an increasing public health concern, because the duration of sedentary behavior is increasing<sup>1-4 5,6</sup> and sedentary behavior has been reported to be associated with multiple adverse health outcome in the population of non-diabetic youth<sup>1,2,7-14</sup>. The first aim of this dissertation added knowledge and evidence that increased sedentary behavior was associated with poorer glycemic control in youth with diabetes over time. As mentioned in the background section, several cross-sectional studies have reported that sedentary behavior,

mainly including television watching and computer use, was associated with unhealthy dietary behaviors in children and youth <sup>15,16 17-19</sup>. For example, children may be placed in front of a television with a snack or a meal when their parents need to do some other household work. Some children and youth consumed a large proportion of energy when they watched television <sup>20</sup>. This kind of behavior can result in an increased number of meals consumed in a day among children and youth. Especially for youth with diabetes, the number of meals consumed a day can also be increased by consuming snacks before and after physical activity in order to prevent hypoglycemia<sup>21,22</sup>. Although this dissertation did not evaluate the above two possible associations between television watching and meal frequency, we found that increased meal frequency was associated with lower HbA1c among youth with T1D over time under the condition of consistent energy intake.

This dissertation had several potential limitations. First, the exposure variable, television watching, computer use and meal frequency, were assessed through self-report questionnaire. However, because participants did not know their HbA1c or serum lipid values when television watching, computer use and meal frequency were assessed, it is unlikely that the outcome contributed to error related to assessment of these exposures. Therefore, measurement error associated with assessment of television watching, computer use and meal frequency in this study would bias the result towards the null. Another limitation was the potential for residual confounding because of the observational study design. However, we adjusted for many potential confounders including age, gender, race, physical activity, computer use on weekdays parental

education, household income, insurance type, BMI z-score, family composition, and treatment for diabetes, and dyslipidemia. The associations reported in this dissertation were independent of these potential confounders.

Despite these limitations, this dissertation also had several strengths. The sample for this analysis was drawn from the SEARCH for Diabetes in Youth study population, which is the largest prospective investigation among youth with T1D and T2D, and includes all major US ethnic groups. The longitudinal study design, including 5 years of follow-up, and the ability to adjust for many important potential confounders were also important strengths of this study.

To sum up, first, television watching may contribute to poor glycemic control and dyslipidemia in youth with diabetes and can be a potentially modifiable behavior to improve health outcomes in youth with diabetes. Second, using YRBS questions may be a viable option to measure television watching in youth with diabetes, particularly in large epidemiologic studies when alternative assessment methods are either too costly or complex making them not feasible. Third, eating more frequent meals in a day without increasing total energy intake may be beneficial for youth with T1D.

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