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Associations Between Low-Carbohydrate Diet Score and Prognostic Factors Among Adults With Diabetes Mellitus: An Analysis of the NHANES 2005-2016

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ASSOCIATIONS BETWEEN LOW-CARBOHYDRATE DIET SCORE AND
PROGNOSTIC FACTORS AMONG ADULTS WITH DIABETES MELLITUS:
AN ANALYSIS OF THE NHANES 2005-2016

by

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A thesis submitted in partial fulfillment of the requirement
for the Honors in the Major Program in Health Sciences
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ABSTRACT

Background: Type 2 diabetes mellitus is one of the leading chronic diseases affecting Americans. There is a lack of literature discussing the link between diet and prognosis of those already diagnosed with DM.

Objective: To provide insight into which diet is better for the outlook of diabetes mellitus by examining the associations between the low-carbohydrate diet (LCD) score and three diabetes-related health indicators: blood hemoglobin (HbA1c), triglycerides, and retinopathy.

Methods: A total of 3,313 U.S. adults with DM were selected from the National Health and Nutrition Examination Survey 2005-2016. Presence of retinopathy was ascertained through self-reporting. Dietary intake was measured with 24-hour dietary recalls, and LCD scores were calculated from the proportion of energy of three macronutrients. Scores ranged from 0-30, with a higher score indicating lower carbohydrate intake.

Results: There was no significant difference in HbA1c levels between the highest and the lowest quintile of LCD score (mean = 7.42% [95% CI: 7.23, 7.61] vs. 7.32% [95% CI: 7.13, 7.51]).

There was no significant association between blood triglyceride levels and LCD score, comparing quintile 1 to quintile 5 (mean= 168.64 mg/dl; 95% CI = [150.14, 187.14] vs. mean= 162.44 mg/dl; 95% CI = [143.76, 181.11]). In multivariable logistic regression analysis, the odds ratio of having retinopathy comparing the highest to the lowest quintile was 1.01 (95% CI: 0.59, 1.72).

Conclusion: Proportion of carbohydrate in diet was not associated with DM prognosis factors. Future studies should focus on carbohydrate quality as well as quantity.

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INTRODUCTION

Among numerous chronic diseases that trouble the American population, type 2 diabetes mellitus continues to be of concern. As of 2017, it has been estimated that 9.4% of the US population has diabetes and that 90-95% of all cases are type 2 diabetes (Centers for Disease Control and Prevention, 2017). Additionally, 33.9% of U.S. adults, age 18 years or older, have been classified as having prediabetes (Centers for Disease Control and Prevention, 2017). Insulin resistance is the primary cause of elevated blood sugars in both prediabetes and the resulting type 2 diabetes. As a result of the rising number of cases over the past few decades, many researchers have set out to examine what behaviors have been contributing to this epidemic.

The importance of a healthy diet in preventing diabetes is well-known to many. However, there is much controversy surrounding the main dietary contributors to the development of insulin resistance and consequently, type 2 diabetes. While popular belief holds that an excess of carbohydrates is to blame, there are still some opponents who believe that high consumption of fat is the culprit of this chronic disease (Marshall & Bessesen, 2002). Researchers and health professionals have emphasized that because high fat diets can contribute to weight gain and obesity, dietary fat plays a crucial role in the development of diabetes (Nettleton, Jebb, Riserus, Koletzko, & Fleming, 2014). Nonetheless, there are studies that emphasize quality of fat over quantity (Harding et al., 2004; Hu, van Dam, & Liu, 2001; Meyer, Kushi, Jacobs, & Folsom, 2001; Salmerón et al., 2001). In a cohort study of Japanese men and women, researchers found that women who consumed a diet with low-carbohydrate, high protein, and high fat had a decreased risk of type 2 diabetes, however, the association was not found in men (Nanri et al., 2015). However, another cohort study found that consuming a low-carbohydrate diet with high

animal protein and fat was positively associated with higher risk of diabetes in men (Lawrence de Koning et al., 2011). As shown, the research available on the association between various macronutrient intakes and type 2 diabetes varied and is mostly inconclusive. The literature available demonstrates the complexity of finding definitive associations between diet and diabetes.

A low-carbohydrate diet is among the many meal plans followed by those with diabetes as well as those attempting to lose weight. The American Diabetes Association (Nanri et al.) defines a low-carbohydrate diet as one in which “highly processed carbohydrate foods and grains are limited or avoided,” and the focus is shifted towards consumption of non-starchy vegetables and protein foods. The main reason why carbohydrates are the primary focus for diabetes is due to the relationship between the glycemic load, a measure of how much the carbohydrate content of our meals raise blood glucose, and the subsequent impact on insulin response (Linus Pauling Institute, 2003; Riccardi, Rivellese, & Giacco, 2008). Low-carbohydrate diets can be a popular choice for people with diabetes because of their inherent need to reduce spikes in insulin and blood sugar.

In 2006, Halton et al. developed a scale called the low-carbohydrate diet (LCD) score as a way to rank intake of carbohydrate in relation to the two other macronutrients, protein and fat (2006). After performing a study using data from the Nurses’ Health Study in 2008, it was found that having a diet high in LCD score, meaning low-carbohydrate, high protein and high fat, did not increase the risk of type 2 diabetes in women (Halton, Liu, Manson, & Hu, 2008). In fact, there was no association found between the LCD score and risk for diabetes. An association was only observed after creating a separate LCD score for carbohydrate with vegetable fat and

vegetable protein. After analyzing the data, researchers found that when comparing the 1st decile with the 10th decile for the LCD score, the multivariate relative risk (RR) for type 2 diabetes was 0.82 (95% CI: 0.71,0.94). They thus concluded that consumption of vegetable rather than animal sources of fat and protein may slightly reduce risk for type 2 diabetes. Other studies have attempted to find associations between the LCD score and diabetes, however only few have been successful (Namazi, Larijani, & Azadbakht, 2017).

The prognosis of individuals diagnosed with type 2 diabetes can be heavily dependent on what their diet consists of on a regular basis. Complications such as nerve damage, heart disease, and kidney disease can be caused by improper management of diabetes (Asif, 2014). While there are many studies examining the relationship between diet and risk of diabetes, there is a lack of literature regarding the prognosis of persons already diagnosed with diabetes with regard to diet changes. Doctors and dietitians may inform people with diabetes about many treatment options with regard to medications and lifestyle interventions to manage their symptoms and prevent complications, yet some individuals may want to know if there is a specific diet that is better for their prognosis after they are diagnosed.

BACKGROUND

Prevalence of Diabetes

According to the Centers for Disease Control and Prevention (CDC) 2017 report, about 30.3 million Americans have diabetes mellitus. Within this estimate, 30.2 million diabetes cases belong to adults aged 18 years and older. Using 2011-2014 National Health and Nutrition Examination Survey (NHANES) data, it was estimated that there are 7.2 million undiagnosed cases of diabetes among the U.S. adult population (Centers for Disease Control and Prevention, 2017).

Data from the 2013-2015 National Health Interview Survey (NHIS) also showed that the prevalence of diagnosed diabetes was highest in the American Indian/Alaska Native ethnic group for both males and females, 14.9% and 15.3% respectively. Other disparities in the prevalence of diabetes can be seen across geographic regions and socioeconomic status. According to 2017 Behavioral Risk Factor Surveillance System (BRFSS), the southeastern region of the United States contains the highest prevalence of diagnosed diabetes in the nation. States such as West Virginia, Mississippi, and Alabama, have diabetes rates of 15.2%, 14.2% and 14.1% respectively. Education level is an example of a socioeconomic factor that shows differences in diabetes prevalence. Data from 2013-2015 NHIS showed that prevalence of diagnosed diabetes was 12.6% in adults with less than high school education, in contrast to 9.5% of adults with high school education and 7.2% of adults with education above high school.

Definition and Diagnosis of Type 2 Diabetes Mellitus

Type 2 diabetes mellitus is categorized as a metabolic disease that stems from the inability of bodily cells to properly manage insulin levels (Institute for Quality and Efficiency in

Health Care, 2008). In a healthy individual, the pancreas contains beta cells that store and release the hormone insulin in response to increases in blood glucose levels, which occurs after consumption of food. Upon insulin secretion into the blood, blood glucose levels are lowered to maintain homeostasis (National Institute of Diabetes and Digestive and Kidney Diseases, 2018). However, when this system is altered due to lifestyle and genetic factors, insulin resistance occurs. Insulin resistance implies that when insulin attempts to bind to cell receptors for the cell to uptake glucose, the signaling pathway is no longer effective (Kharroubi & Darwish, 2015). As a consequence, glucose remains in the bloodstream and leads to chronic hyperglycemia and, thus, type 2 diabetes. In some cases, the pancreas may not produce sufficient amounts of insulin, which can also contribute to the expression of the disease (National Institute of Diabetes and Digestive and Kidney Diseases, 2018). The diagnostic criteria for type 2 diabetes is typically based on one of four laboratory measures: hemoglobin A1c (HbA1c), fasting plasma glucose (FPG), oral glucose tolerance test (OGTT), or random blood glucose test (RPG) (American Diabetes Association, 2015a). The criteria utilized for diagnosis of diabetes as well as pre-diabetes from the American Diabetes Association are summarized in Appendix: Table 1.

Clinical and Nutritional Guidelines for Persons Diagnosed with Diabetes

Upon diagnosis of type 2 diabetes, patients are instructed by their clinicians to follow guidelines for pharmaceutical intervention using drugs designed to lower blood sugar, such as metformin, as well as lifestyle changes to improve nutrition and physical well-being (Inzucchi et al., 2012). While the general recommendations are given for those with diabetes, clinicians sometimes provide individuals with pre-diabetes status with a treatment plan to prevent or delay a transition to diabetes (American Diabetes Association, 2015b; Mainous, Tanner, Scuderi,

Porter, & Carek, 2016). Lifestyle modifications in terms of diet and nutrition are personalized for each particular case, however, adherence to guidelines for certain food groups are emphasized.

According to the American Diabetes Association (Nanri et al.), there is insufficient evidence to recommend an ideal percentage of carbohydrates, fat, or protein for people with diabetes (Evert et al., 2013). Instead they suggest that the source of each macronutrient food should be beneficial to overall health. In other words, individuals should choose higher quality foods that are nutrient dense. Nonetheless, monitoring carbohydrate intake for every meal is imperative for preventing complications for diabetes, as spikes in blood glucose should be avoided (American Diabetes Association, 2018). Carbohydrate sources such as fruits, vegetables, and whole grains should be chosen over foods with a lot of added sugars like sugar-sweetened beverages (Evert et al., 2013). Protein sources are recommended to be rich in biological value and made with essential amino acids. Both animal and plant sources of protein are acceptable including foods such as poultry, fish, eggs and soy (Gray, 2015). Dietary fat intake should be rich in mono- and polyunsaturated fats and limited in saturated and trans-fat (Gray, 2015).

Low Carbohydrate Diets and the LCD Score

Many researchers have studied the efficacy of different diets that are meant to vary the macronutrient composition in the management of diabetes. Low carbohydrate diets are frequently used as a method to restrict excess consumption of carbohydrates and increase diet quality, therefore improving glycemic control (Spritzler, 2012). However, this does not come without possible complications. The most current United States Department of Agriculture (U.S. Department of Health and Human Services and USDA) dietary guidelines recommends that 45

to 65 percent of total calories should come from carbohydrates, based on a standard 2,000 calorie diet. Lowering the intake of carbohydrates inevitably increases consumption of fat and protein which can in turn cause concerns for renal function, heart health and other systemic effects (Spritzler, 2012).

In spite of the risks that improper management of a low carbohydrate diet can cause, potential benefits have been illustrated by some studies. For instance, a meta-analysis of cohort studies on macronutrient intake and development of type 2 diabetes found that high total carbohydrate may be associated with increased risk for type 2 diabetes while high consumption of vegetable fat significantly lowered risk of type 2 diabetes (Alhazmi, Stojanovski, McEvoy, & Garg, 2012) . Salmeron et al. reported that risk of diabetes was increased by 58% by replacing 5% of energy from polyunsaturated fat with an equivalent amount of energy from carbohydrates (Salmerón et al., 2001). This indicated that replacing carbohydrates with healthier fats may decrease chances for development of diabetes. A cohort study by Gower et al. found that participants who consumed a lower-carbohydrate diet compared to a low-fat diet lost more total fat mass, had 11% less intra-abdominal fat, and had better improvement of glucose metabolism among those were at-high risk for type 2 diabetes (Gower & Goss, 2015).

Halton et al. created the LCD score which was in turn used by other researchers as a scale for measuring adherence to a particular intake of the three macronutrients: carbohydrate, protein, and fat (Halton et al., 2006). The three categories were broken into deciles to form a score ranging from 0 to 30. A score of 0 would represent highest intake of carbohydrate with lowest intake of fat and protein, while a score of 30 represents lowest intake of carbohydrate and highest intake of fat and protein. The score is meant to represent an individual's adherence to a low-

carbohydrate diet, thus a higher score indicates that the participant followed the diet more closely and consumed least amount of carbohydrates. A meta-analysis of four cohort studies that examined the association between the highest versus lowest LCD score and risk for diabetes only found a slight association (overall RR=1.17; 95% CI: 0.90,1.51), which warrants further investigations to clarify the effect of the LCD score (Namazi et al., 2017).

Diabetes-Related Conditions and Prognostic Factors

When improperly controlled, type 2 diabetes is known for causing microvascular as well as macrovascular complications due to its severe damage to blood vessels. Common microvascular complications include retinopathy, nephropathy, and neuropathy, which cause stress to the eyes, renal system, and peripheral nerves, respectively (Fowler, 2008). It is even possible for retinopathy to start developing as early as seven years before type 2 diabetes is clinically diagnosed (Fong, Aiello, Ferris, & Klein, 2004). According to the National Kidney Foundation, diabetic nephropathy is the leading cause of kidney failure in the U.S. (National Kidney Foundation, 2017). Diabetic neuropathy is commonly associated with the tingling and burning sensation that people with diabetes tend to feel, especially in their feet. Neuropathy increases the risk for foot ulcers and infections which can eventually require amputations (Boulton et al., 2005).

The most common macrovascular complication is the development of atherosclerosis which manifests as narrowing of arterial walls and plaque formation (Fowler, 2008). Oxidation of LDL cholesterol particles combined with injury and inflammation of the endothelial lining of arteries eventually leads to high risk for occlusion and cardiovascular disease, the number one cause of mortality in people with diabetes (Fowler, 2008). High plasma triglyceride levels are

also an important indicator of possible macrovascular complications due to their frequent associations with cardiovascular disease and other comorbidities (Yuan, Al-Shali, & Hegele, 2007). Hypertension is also frequently occurring, with a prevalence of 50% to 80% in patients with type 2 diabetes (Landsberg & Molitch, 2004).

The blood glycosylated hemoglobin, HbA1c, test is an important indicator not only for diagnosis of diabetes but also for evaluating prognosis of patients. HbA1c can measure the average plasma glucose concentration from the previous two to three months (Sherwani, Khan, Ekhzaimy, Masood, & Sakharkar, 2016). Elevated HbA1c levels can be a risk factor for diabetes-related complications such as those previously mentioned. For example, HbA1c levels showed a positive correlation with total cholesterol ($r= 0.127$, $p < 0.001$), low-density lipoprotein cholesterol (LDL, $r= 0.142$, $p = 0.001$), and triglycerides ($r= 0.153$, $p < 0.001$) in patients with diabetes (Khan, Sobki, & Khan, 2007).

Managing diet with special attention to macronutrient intake is imperative for preventing or slowing the progression of diabetes comorbidities. There is a need for more large-scale randomized controlled trials (RCT) to investigate the effect of different dietary approaches on diabetes management (Ley, Hamdy, Mohan, & Hu, 2014). Garg et al. found in a study of non-insulin-dependent patients with type 2 diabetes that high-carbohydrate diets led to exacerbation of diabetes-related conditions such as elevated very low-density lipoprotein (VLDL) cholesterol levels, and hyperinsulinemia (Garg et al., 1994). A meta-analysis of high-monounsaturated-fatty acid (MUFA) versus high-carbohydrate diets also found that a high-carbohydrate diet worsened diabetes conditions, and emphasized the role of healthy fats, like MUFAs in diet therapy for diabetes (Garg, 1998).

RESEARCH PURPOSE AND IMPORTANCE

The need to determine a direct correlation between macronutrient composition and diabetes is imperative for the depleting health of millions of Americans. Although many dietary guidelines are available to the public, it has been stated that only about half of U.S. adults receive proper nutrition education for their diabetic condition and less than half see a registered dietitian, leaving the remainder of people with diabetes with a lot of unawareness about how to maintain a healthy diet (Evert et al., 2013). Knowing which particular macronutrient intakes are more associated with worsening diabetes conditions will be very helpful in educating patients who are concerned about their health. This investigation will contribute to literature regarding the relationship between diet and diabetes prognosis.

Objective

The purpose of this study is to assess the dietary behavior of American adults with diabetes mellitus and examine the relationship between the LCD score and three diabetes-related health indicators: HbA1c, blood triglyceride levels, and retinopathy.

Hypotheses

H1: Participants with a higher LCD score, indicating lower carbohydrate intake, will have lower HbA1c levels than participants with lower LCD scores.

H2: Participants with a higher LCD score will have a lower prevalence of retinopathy than participants with lower LCD scores.

H3: Participants with a higher LCD score will have lower blood triglyceride levels than participants with lower LCD scores.

METHODS

Study Design and Population

For this investigation, a representative sample of adults from the NHANES will be used. The NHANES is a cross-sectional survey done by the CDC on a yearly basis to collect data about diet, medical conditions, lifestyle and health indicators. The NHANES started in the 1960s and became a continuous program in 1999 (CDC, 2017). A national sample of about 5,000 individuals is examined every year, consisting of all ages and races/ethnicities. For dietary interviews and medical examinations, participants see a physician. Interviews are also conducted in the participant's home by medical/health professionals using computer systems. Information is de-identified and made available publicly for research purposes by the National Center for Health Statistics (NCHS), which is a part of the CDC. All participants signed an informed consent form to be a part of the NHANES. The current study has been reviewed and approved by the Institutional Review Board of University of Central Florida (IRB # SBE-18-14542).

The population for this present study includes both adult participants, minimum age 20 years with reliable dietary records in NHANES from 2005 to 2016. From this eligible sample, female participants who were either pregnant or lactating were excluded.

Ascertainment of Diabetes

Presence of diabetes mellitus was determined by both questionnaire responses and HbA1c lab values. Diabetes diagnosis was designated by a response of "YES" to the question, "Have you ever been told by a doctor or health professional that you have diabetes?" and an HbA1c \geq 6.4%.

Dietary Intake

Macronutrients and micronutrient intakes of participants were examined using the NHANES dietary data, which contains the results of 24-hour dietary recalls. NHANES food intake data was also linked to USDA Food Patterns Equivalent Database (FPED) to obtain participant's intakes for each MyPyramid food group.

From daily macronutrient intakes and total calorie intakes, LCD scores were calculated by grouping the proportion of daily calories/energy from each macronutrient into deciles. Each point for carbohydrate, total protein, and total fat intake (0 to 10 for each macronutrient) was then added together to form the LCD score, ranging from 0 to 30. LCD scores were further categorized into quintiles, with the first quintile representing the lowest LCD scores and the fifth quintile representing the highest LCD scores.

Prognostic Factors

The health status of participants was examined using three prognostic indicators: HbA1c, blood triglyceride levels, and presence of retinopathy.

Table A. NHANES variable information for prognostic indicators

Variable	NHANES Variable Name	Note
HbA1c	LBXGH	N/a
Triglyceride	LBXTR	N/a
Retinopathy	DIQ080	“Has a doctor ever told you that diabetes has affected your eyes or that you had retinopathy?”

Demographic Information

The following demographic characteristics about participants were included in the study:

Table B. NHANES demographic variable information

Variable	NHANES Variable Name	Note
Age	RIDAGEYR	Age at screening
Gender	RIAGENDR	N/a
Race/Ethnicity	RIDETH1	N/a
BMI	BMXBMI	Calculated with measured height and weight (kg/m ²)
Smoking status	SMQ040	“Do you now smoke cigarettes?” * * Answer should be: “Every day” or “Some days” to be classified as a “current smoker”
Alcohol intake	ALQ120Q	“How often did you drink alcohol over the past 12 months?” or “In the past 12 months, how often did you drink any type of alcoholic beverage”
Physical activity	PAQ_ ¹	New variables created from physical activity questionnaire ¹
Family history of type 2 diabetes	DIQ175A	“Why do you think you are at risk for diabetes or prediabetes?”
Education level	DMDEDUC2	“What is the highest grade or level of school you have completed or the highest degree you have received?”
Marital Status	DMDMARTL	N/a
Income (Annual family & PIR)	INDFMINC (2005-2006) INDFMIN2 (After 2006) INDFMPIR (Family income to poverty ratio)	N/a
High Cholesterol	LBXTC or BPQ100D	Total cholesterol \geq 240 mg/dl or if answered “Yes” to the question “Are you now taking prescribed medicine for high cholesterol?”
Hypertension	SBP140/DBP90 BPQ050A	Diagnosed if SBP \geq 140 or DBP \geq 90 or if answered “Yes” to the question “Are you now taking prescribed medicine for HBP?”

¹ Physical activity defined as either: 1= below criteria of 150 min/week, 2= met criteria, 3= exceeded criteria

Statistical Analysis

The NHANES data was exported and analyzed using Statistical Analysis System software (version 9.4, SAS Institute Inc, Cary, NC). Because multiple years of continuous NHANES data were combined, an appropriate weight variable was created following the Analytic and Reporting Guidelines which is available from the CDC website. All analyses were weighted using the NHANES examination sample weights and adjusted for the complex sample design of NHANES using the SAS Survey Analysis Procedures. Statistical significance was set at $p < 0.05$.

The differences in 1-day dietary nutrient intakes, MyPyramid food group equivalents, and LCD scores were compared using analysis of variance (ANOVA, proc surveymeans procedure). The group with highest quintile of LCD score was compared to the group with lowest quintile of LCD score with respect to their diabetes-related health indicators (i.e., HbA1c, triglycerides, and retinopathy) using t-tests or chi-squared tests as appropriate: for continuous variables, t-tests will be used and for categorical variables, chi-squared tests was used. Additionally, a multivariable regression analysis using SAS PROC SURVEYREG/SURVEYLOGISTIC procedure was used to evaluate the estimates of the effects of LCD score on diabetes-related health conditions, after adjustment of potential confounding variables such as total energy intake, age, gender, race/ethnicity, and physical activity.

RESULTS

Participants

After excluding participants with missing data and those who were ineligible, we obtained a final sample of 3,313 adults with diabetes mellitus from the NHANES, years 2005-2016. Among the selected participants, 90.3% of adults were age 45 years and above (Table 1). Approximately 50.4% of adults with diabetes were male and 49.6% were female. Female participants were more likely to have a low LCD score compared to males (LCD Quintile 1-59.5% female: vs 40.5% male). The majority of participants were either non-Hispanic white (36.6%) or non-Hispanic black (28.6%). Among participants whose BMI was reported, 58.3% had a BMI classified as obese.

Shared characteristics for participants with retinopathy, high triglycerides, and high HbA1c levels included: being of the non-Hispanic white race, married; having an education restricted to 12th grade or below and an annual family income below \$75,000; being obese, hypertensive, and having high cholesterol; and to be below the recommended physical activity level (Tables 2-1 through 2-3). Participants with retinopathy and high HbA1c levels were more likely to be male, while those with high triglycerides were more likely to be female. Participants with retinopathy were mostly 65 years of age and above, while participants with high triglycerides and high HbA1c levels were mostly middle aged (45-64 years of age) (Tables 2-1 through 2-3).

Table 1. Demographic characteristics of adult study participants by low-carbohydrate diet (LCD) score from NHANES 2005-2016

Variable	Low-Carbohydrate Diet (LCD)Score					Total
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	
No. of participants	617	655	728	594	719	3,313
Age: mean (SD)						
20-29	10 (1.6)	6 (0.9)	13 (1.8)	5 (0.8)	10 (1.4)	44 (1.3)
30-44	55 (8.9)	40 (6.1)	57 (7.8)	54 (9.1)	72 (10.0)	278 (8.4)
45-64	260 (42.1)	273 (41.7)	328 (45.1)	268 (45.1)	346 (48.1)	1,475(44.5)
65+	292 (47.3)	336 (51.3)	330 (45.3)	267 (44.9)	291 (40.5)	1,516 (45.8)
	Mean (95% Confidence Interval)					
Age at screening	60.04 (58.76, 61.32)	62.71 (61.58, 63.85)	60.45 (59.15, 61.75)	61.16 (59.97, 62.35)	57.92 (56.66, 59.18)	60.33 (50.72, 60.94)
Age when first told you had diabetes	49.98 (48.66, 51.29)	51.93 (50.70, 53.17)	50.01 (48.37, 51.65)	49.52 (48.25, 50.78)	48.07 (46.64, 49.50)	49.80 (49.14, 50.45)
Time since diagnosis	9.94 (9.19, 10.69)	10.71 (9.90, 11.53)	10.43 (9.32, 11.53)	11.57 (10.59, 12.56)	9.80 (8.87, 10.73)	10.48 (10.11, 10.84)
Family poverty-Income ratio	2.48 (2.287, 2.68)	2.42 (2.24, 2.60)	2.70 (2.53, 2.87)	2.84 (2.66, 3.03)	2.99 (2.82, 3.16)	2.71 (2.62, 2.80)
	N (%)					
Gender						
Male	250 (40.5)	283 (43.2)	367 (50.4)	340 (57.2)	429 (59.7)	1,669 (50.4)
Female	367 (59.5)	372 (56.8)	361 (49.6)	254 (42.8)	290 (40.3)	1,644 (49.6)
BMI (kg/m²)						
Normal	85 (13.8)	93 (14.2)	94 (12.9)	68 (11.4)	82 (11.4)	422 (12.7)
Overweight	152 (24.6)	170 (26.0)	209 (28.7)	161 (27.1)	191 (21.6)	883 (26.7)
Obese	360 (58.3)	373 (56.9)	407 (55.9)	356 (59.9)	434 (60.4)	1,930 (58.3)
Race/Ethnicity						
Non-Hispanic White	171 (27.7)	226 (34.5)	277 (38.0)	270 (45.5)	269 (37.4)	1,213 (36.6)
Non-Hispanic Black	197 (31.9)	176 (26.9)	205 (28.2)	132 (22.2)	237 (33.0)	947 (28.6)
Mexican American	121 (19.6)	128 (19.5)	123 (16.9)	106 (17.8)	117 (16.3)	595 (18.0)
Other	128 (20.7)	125 (19.1)	123 (16.9)	86 (14.5)	96 (13.4)	558 (16.8)
Education						
< 12th grade	241 (39.1)	245 (37.4)	224 (30.8)	201 (33.8)	232 (32.3)	1,143 (34.5)
HS Graduate	130 (21.1)	170 (26.0)	192 (26.4)	143 (24.1)	159 (22.1)	947 (28.6)
AA or some college	145 (23.5)	165 (25.2)	208 (28.6)	145 (24.4)	205 (28.5)	595 (18.0)
College graduate +	99 (16.0)	74 (11.3)	102 (14.0)	105 (17.7)	123 (17.1)	558 (16.8)
Marital status						
Married/Partner	332 (53.8)	369 (56.3)	419 (57.6)	367 (61.8)	458 (63.7)	1,945 (58.7)
Widowed	104 (16.9)	129 (19.7)	110 (15.1)	86 (14.5)	71 (9.9)	500 (15.1)
Divorced/Separated	121 (19.6)	108 (16.5)	135 (18.5)	86 (14.5)	127 (17.7)	577 (17.4)
Single	58 (9.4)	49 (7.5)	63 (8.7)	55 (9.3)	62 (8.6)	287 (8.7)
Smoking status						
Never	339 (54.9)	340 (51.9)	364 (50.0)	258 (43.4)	332 (46.2)	1,633 (49.3)
Former	173 (28.0)	231 (35.3)	257 (35.3)	242 (40.7)	267 (37.1)	1,170 (35.3)
Current	105 (17.0)	84 (12.8)	107 (14.7)	94 (15.8)	120 (16.7)	510 (15.4)
Income						
< 20,000	199 (32.3)	222 (33.9)	215 (29.5)	152 (25.6)	166 (23.1)	954 (28.8)
20,000-75,000	318 (51.5)	317 (48.4)	364 (50.0)	317 (53.4)	394 (54.8)	1,710 (51.6)
≥ 75,000	74 (12.0)	84 (12.8)	117 (16.1)	106 (17.8)	133 (18.5)	514 (15.5)

Table 2-1. Demographic and clinical characteristics of adult study participants with diabetes by retinopathy status from NHANES 2005-2016

Variable	Retinopathy N (%)	No Retinopathy N (%)
Gender		
Male	367 (53.8)	1,292 (49.6)
Female	315 (46.2)	1,314 (50.4)
Age		
20-29	9 (1.3)	35 (1.3)
30-44	48 (7.0)	230 (8.8)
45-64	302 (44.3)	1,163 (44.6)
65 and above	323 (47.4)	1,178 (45.2)
Race/Ethnicity		
Non-Hispanic White	226 (33.1)	978 (37.5)
Non-Hispanic Black	207 (30.4)	735 (28.2)
Mexican American	118 (17.3)	468 (18.0)
Other	131 (19.2)	425 (16.3)
Education		
12th grade and below	258 (37.8)	871 (33.4)
High School Graduate	169 (24.8)	619 (23.8)
Some college or AA degree	175 (25.7)	689 (26.4)
College graduate or above	79 (11.6)	423 (16.2)
Marital status		
Married/Partner	384 (56.3)	1,545 (59.3)
Widowed	107 (15.7)	389 (14.9)
Divorced/Separated	136 (19.9)	436 (16.7)
Single	55 (8.1)	232 (8.9)
Income		
< 20,000	230 (33.7)	715 (27.4)
20,000-75,000	320 (46.9)	1,377 (52.8)
≥ 75,000	93 (13.6)	420 (16.1)
BMI (kg/m²)		
Normal	85 (12.5)	335 (12.9)
Overweight	182 (26.7)	694 (26.6)
Obese	388 (56.9)	1,527 (58.6)
Smoking status		
Never	332 (48.7)	1,288 (49.4)
Former	256 (37.5)	908 (34.8)
Current	94 (13.8)	410 (15.7)
High Cholesterol		
Yes	417 (61.1)	1,496 (57.4)
No	244 (35.8)	1,042 (40.0)
Hypertension		
Yes	500 (73.3)	1,815 (69.6)
No	152 (22.3)	732 (28.1)
Physical Activity Adherence¹		
Below	439 (64.4)	1,480 (56.8)
Meet	66 (9.7)	253 (9.7)
Exceed	177 (26.0)	873 (33.5)

¹ Physical activity guidelines were established by the Department of Health and Human Services (Department of Health & Human Services, 2018)

Table 2-2. Demographic and clinical characteristics of adult study participants with diabetes by HbA1c level from NHANES 2005-2016

Variable	Blood Hemoglobin (HbA1c) Level	
	Normal (< 6.5 %) N (%)	High (≥ 6.5 %) N (%)
Gender		
Male	516 (47.3)	1,093 (52.4)
Female	575 (52.7)	994 (47.6)
Age		
20-29	17 (1.6)	27 (1.3)
30-44	95 (8.7)	174 (8.3)
45-64	454 (41.6)	969 (46.4)
65 and above	525 (48.1)	917 (43.9)
Race/Ethnicity		
Non-Hispanic White	444 (40.7)	738 (35.4)
Non-Hispanic Black	297 (27.2)	573 (27.5)
Mexican American	172 (15.8)	409 (19.6)
Other	178 (16.3)	367 (17.6)
Education		
12th grade and below	350 (32.1)	745 (35.7)
High School Graduate	270 (24.7)	485 (23.2)
Some college or AA degree	284 (26.0)	552 (26.4)
College graduate or above	186 (17.0)	301 (14.4)
Marital status		
Married/Partner	639 (58.6)	1,245 (59.7)
Widowed	178 (16.3)	292 (14.0)
Divorced/Separated	184 (16.9)	366 (17.5)
Single	90 (8.2)	181 (8.7)
Income		
< 20,000	324 (29.7)	592 (28.4)
20,000-75,000	574 (52.6)	1,067 (51.1)
≥ 75,000	169 (15.5)	330 (15.8)
BMI (kg/m²)		
Normal	142 (13.0)	253 (12.1)
Overweight	337 (30.9)	518 (24.8)
Obese	592 (54.3)	1,267 (60.7)
Smoking status		
Never	523 (47.9)	1,048 (50.2)
Former	407 (37.3)	716 (34.3)
Current	161 (14.8)	323 (15.5)
High Cholesterol		
Yes	576 (52.8)	1,282 (61.4)
No	501 (45.9)	790 (37.9)
Hypertension		
Yes	765 (70.1)	1,467 (70.3)
No	306 (28.0)	559 (26.8)
Physical Activity Adherence¹		
Below	653 (59.9)	1,190 (57.0)
Meet	113 (10.4)	197 (9.4)
Exceed	325 (29.8)	700 (33.5)

¹ Physical activity guidelines were established by the Department of Health and Human Services (Department of Health & Human Services, 2018)

Table 2-3. Demographic and clinical characteristics of adult study participants with diabetes by triglyceride level from NHANES 2005-2016

Variable	Blood Fasting Triglycerides Level	
	Normal (≤ 200 mg/dL) N (%)	High (> 200 mg/dL) N (%)
Gender		
Male	611 (50.6)	155 (47.5)
Female	596 (49.4)	171 (52.5)
Age		
20-29	12 (1.0)	5 (1.5)
30-44	80 (6.6)	36 (11.0)
45-64	529 (43.8)	171 (52.5)
65 and above	586 (48.6)	114 (35.0)
Race/Ethnicity		
Non-Hispanic White	434 (36.0)	158 (48.5)
Non-Hispanic Black	368 (30.5)	38 (11.7)
Mexican American	204 (16.9)	69 (21.2)
Other	201 (16.7)	61 (18.7)
Education		
12th grade and below	414 (34.3)	128 (39.3)
High School Graduate	280 (23.2)	79 (24.2)
Some college or AA degree	307 (25.4)	88 (27.0)
College graduate or above	202 (16.7)	31 (9.5)
Marital status		
Married/Partner	726 (60.1)	195 (59.8)
Widowed	173 (14.3)	40 (12.3)
Divorced/Separated	200 (16.6)	65 (19.9)
Single	107 (8.9)	25 (7.7)
Income		
< 20,000	309 (25.6)	110 (33.7)
20,000-75,000	665 (55.1)	167 (51.2)
$\geq 75,000$	184 (15.2)	34 (10.4)
BMI (kg/m²)		
Normal	165 (13.7)	26 (8.0)
Overweight	327 (27.1)	93 (28.5)
Obese	690 (57.2)	198 (60.7)
Smoking status		
Never	644 (53.4)	133 (40.8)
Former	405 (33.6)	121 (37.1)
Current	158 (13.1)	72 (22.1)
High Cholesterol		
Yes	677 (56.1)	213 (65.3)
No	530 (43.9)	113 (34.7)
Hypertension		
Yes	848 (70.3)	234 (71.8)
No	331 (27.4)	87 (26.7)
Physical Activity Adherence¹		
Below	673 (55.8)	194 (59.5)
Meet	131 (10.9)	31 (9.5)
Exceed	403 (33.4)	101 (31.0)

¹Physical activity guidelines were established by the Department of Health and Human Services (Department of Health & Human Services, 2018)

Prognostic Factors and Clinical Characteristics

The average HbA1c% of the lowest quintile for LCD score, in comparison to the highest quintile, was lower by 0.10% (mean= 7.32% [95% CI: 7.13, 7.51] vs. mean= 7.42% [95% CI: 7.23,7.61]). The association, however, was not significant as displayed by the confidence intervals (Table 3). A second variable for HbA1c was created to categorize participants into 2 groups: normal versus high HbA1c range. Surprisingly, 32.9% of participants scored within the normal level, less than 6.4%. Yet, across the different quintiles the ratio of normal to high HbA1c remained quite similar, around 1:2.

At first glance, there is a difference in triglyceride levels between the lowest and highest quintile for LCD score (mean= 168.64 [95% CI: 150.14,187.14] vs. mean= 162.44 [95% CI: 143.76, 181.11]) (Table 3). Yet, after considering the confidence intervals, there was no significant difference between blood triglyceride levels and LCD score. Similarly, a second variable for triglycerides was utilized to classify participants by high levels (>200 mg/dl) and low levels (<200 mg/dl). Comparing quintile 1 to quintile 5, the percentage of participants with high triglycerides was relatively the same (9.4% vs. 9.8%).

About 21% of participants reported that they had retinopathy. Among participants with retinopathy, 23.8% ranked within the 2nd quintile for LCD score, indicating a relatively high consumption of carbohydrates. Additional clinical characteristics that may have an association with the primary prognostic factors were included in the analysis. Hypertension and high blood cholesterol were both in high prevalence among all 5 quintiles of LCD score. On average, between 69.4%-73.1% of participants were classified as having hypertension, and 54.7%-61.1% of participants were classified as having high blood cholesterol (Table 3).

Table 3. Clinical characteristics of adult study participants by LCD score from 2005-2016

Variable	Low-Carbohydrate Diet Score					Total
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	
No. of participants	617	655	728	594	719	3,313
Triglycerides (mg/dl)						
Mean	168.64	196.15	179.02	179.22	162.44	168.89
(95% CI)	(150.14, 187.14)	(147.31, 244.99)	(150.89, 207.16)	(138.34, 220.10)	(143.76,181.1)	(155.31, 182.47)
Normal (range <200 mg/dl) ¹	207 (17.1)	234 (19.4)	263 (21.8)	209 (17.3)	294 (24.4)	1,207 (78.7)
High (range ≥ 200 mg/dl) ¹	58 (17.8)	69 (21.2)	73 (22.4)	64 (19.6)	62 (19.0)	326 (21.3)
HbA1c (%)						
Mean	7.32	7.19	7.24	7.23	7.42	7.28
(95% CI)	(7.13,7.51)	(7.05, 7.32)	(7.07, 7.42)	(7.07, 7.38)	(7.23,7.61)	(7.20, 7.37)
Normal (range <6.5%)	216 (35.0)	215 (32.8)	240 (33.0)	185 (31.1)	235 (32.7)	1091 (32.9)
High (range ≥ 6.5%)	380 (61.6)	406 (62.0)	462 (63.5)	374 (63.0)	465 (64.7)	2087 (63.0)
Retinopathy						
Yes	122 (19.8)	156 (23.8)	141 (19.4)	134 (22.6)	129 (17.9)	682 (20.6)
No	493 (79.9)	497 (75.9)	579 (79.5)	454 (76.4)	583 (81.1)	2606 (78.7)
High Cholesterol						
Yes	377 (61.1)	392 (59.8)	407 (55.9)	358 (60.3)	393 (54.7)	1927 (58.2)
No	225 (36.5)	241 (36.8)	301 (41.3)	217 (36.5)	311 (43.3)	1295 (39.1)
Hypertension						
Yes	434 (70.3)	459 (70.1)	505 (69.4)	434 (73.1)	500 (69.5)	2332 (70.4)
No	163 (26.4)	176 (26.9)	203 (27.9)	140 (23.6)	208 (28.9)	890 (26.9)

¹ Mean (95% CI) calculated using the total participants that were eligible for inclusion based off their fasting blood triglyceride levels (N=1,533)

Dietary Information

The average carbohydrate consumption among participants in quintile 1 for LCD score was 63.56% (95% CI: 62.58, 64.44) of total calories and 34.1% (95% CI: 33.55, 34.64) of total calories for participants in quintile 5 (Table 4). Fat consumption averaged at 24.24% (95% CI: 23.38, 26.09) for quintile 1 and 45.08 (95% CI: 44.34, 45.83) for quintile 5. Protein consumption averaged at 12.20% (95% CI: 11.90, 12.50) for quintile 1 and 20.82% for quintile 5 (95% CI: 20.22, 21.41). The average saturated fat percentage and fatty acid ratios were both higher in quintile 5 for LCD score consistent with the higher intake of fat in participants consuming a low-carbohydrate diet. Average consumption of seafood and plant protein, cholesterol, sodium and alcohol was much higher for quintile 4, in comparison to quintile 1. Alcohol consumption, in particular, was on average ten times higher in quintile 4 (mean=10.43, 95% CI: 6.96, 13.90) compared to quintile 1 (mean=1.18, 95% CI: 0.61, 1.74). Total fruit consumption was on average about 2.37 times higher in quintile 1 compared to quintile 5 (mean=0.83, 95% CI: 0.73, 0.92 vs. mean= 0.35, 95% CI: 0.31, 0.39).

Table 4. Dietary intake of adult study participants by LCD Score from 2005-2016

Variable	Low-Carbohydrate Diet Score				
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
No. of Participants	617	655	728	594	719
	Mean (95% Confidence Interval)				
Energy (kcal)	1713.82 (1624.51, 1803.12)	1797.83 (1708.90, 1886.76)	1918.04 (1825.69, 2010.40)	2005.64 (1892.55, 2118.73)	2053.82 (1961.04, 2146.59)
Carbohydrate (% energy)	63.56 (62.68, 64.44)	54.53 (54.17, 54.89)	48.20 (47.99, 48.41)	41.73 (41.35, 42.10)	34.1 (33.55, 34.64)
Fat (% energy)	24.24 (23.38, 25.09)	30.01 (29.36, 30.66)	35.32 (34.80, 35.84)	41.25 (40.51, 41.99)	45.08 (44.34, 45.83)
Saturated Fat (% energy)	9.60 (9.27, 9.92)	10.30 (10.05, 10.55)	12.40 (12.07, 12.74)	12.40 (12.07, 12.74)	13.12 (12.81, 13.42)
Fatty Acid Ratio	1.91 (1.84, 1.98)	1.97 (1.92, 2.02)	1.90 (1.82, 1.98)	1.90 (1.84, 1.95)	1.94 (1.88, 2.00)
Protein (% energy)	12.20 (11.90, 12.50)	15.47 (15.12, 15.81)	16.48 (16.09, 16.88)	17.02 (16.54, 17.50)	20.82 (20.22, 21.41)
Seafood and Plant Protein (oz/ 1000 kcal)	0.77 (0.67, 0.87)	0.91 (0.81, 1.00)	0.99 (0.88, 1.10)	0.96 (0.83, 1.08)	1.10 (0.97, 1.23)
Cholesterol (mg)	151.07 (133.78, 168.36)	209.87 (192.18, 227.56)	268.35 (249.84, 286.86)	319.53 (296.14, 342.92)	466.36 (438.85, 493.87)
Sodium (g/ 1000 kcal)	1.63 (1.58, 1.67)	1.77 (1.74, 1.81)	1.80 (1.76, 1.84)	1.84 (1.80, 1.88)	1.99 (1.94, 2.04)
Added sugars (% energy)	15.50 (14.40, 16.60)	10.97 (10.22, 11.72)	10.00 (9.46, 10.55)	7.85 (7.38, 8.32)	6.62 (6.18, 7.07)
Total sugars (gm)	136.55 (124.70, 148.41)	105.16 (97.32, 112.99)	89.65 (85.40, 93.91)	72.95 (67.82, 78.08)	58.50 (54.56, 62.44)
Refined grains (oz/ 1000 kcal)	2.79 (2.66, 2.92)	2.89 (2.76, 3.00)	2.85 (2.75, 2.95)	2.79 (2.68, 2.89)	2.49 (2.39, 2.59)
Total Vegetables (c/ per 1000 kcal)	0.95 (0.88, 1.03)	1.03 (0.95, 1.11)	0.91 (0.85, 0.96)	0.90 (0.84, 0.97)	0.92 (0.86, 0.98)
Dark green vegetables & beans (c/1000 kcal)	0.14 (0.11, 0.17)	0.17 (0.13, 0.22)	0.14 (0.11, 0.17)	0.12 (0.10, 0.14)	0.14 (0.11, 0.16)
Total fruit (c/ 1000 kcal)	0.83 (0.73, 0.92)	0.67 (0.61, 0.73)	0.54 (0.49, 0.60)	0.45 (0.40, 0.50)	0.35 (0.31, 0.39)
Dairy (c/ 1000 kcal)	0.71 (0.65, 0.77)	0.80 (0.74, 0.85)	0.80 (0.73, 0.87)	0.78 (0.72, 0.84)	0.70 (0.65, 0.76)
Alcohol (gm)	1.18 (0.61, 1.74)	1.89 (1.03, 2.75)	4.65 (3.14, 6.16)	10.43 (6.96, 13.90)	7.44 (5.22, 9.66)

Multivariate Analysis

The odds ratio of having retinopathy comparing the lowest and highest quintile of LCD score was 1.01 (95% CI: 0.72,1.42). Adjustment for age, gender, and race/ethnicity showed a slight increase in the odds ratio (OR=1.04, 95% CI: 0.74,1.46) but it was not statistically significant (Table 5). After multivariable adjustment, the odds ratio still showed no significant difference (OR=1.03, 95% CI: 0.71, 1.50). There was no significant association between having a high HbA1c level and LCD score, (OR= 1.17, 95% CI: 0.82, 1.67). After adjustment for age, gender, and race/ethnicity, the odds ratio slightly decreased (OR=1.15, 95% CI: 0.81, 1.63). The multivariate analysis of the relationship between HbA1c and high versus low LCD score showed another decreased in the odds ratio, but it remained insignificant (OR=1.10, 95% CI: 0.77, 1.56). There was no difference in presence of high triglycerides between quintile 1 and quintile 5 for LCD score (OR= 0.69, 95% CI: 0.43, 1.13). After multivariable adjustment, the odds ratio of having high triglycerides comparing the lowest and highest LCD quintiles was 0.67 (95% CI: 0.39, 1.13).

Table 5. Associations of LCD score with prognostic factors for diabetes mellitus

Outcomes	Low- Carbohydrate Diet Score				
	Quintile 1*	Quintile 2	Quintile 3	Quintile 4	Quintile 5
Retinopathy					
Unadjusted	1.0	1.45 (1.01, 2.06)	1.01 (0.73,1.40)	1.32 (0.94, 1.84)	1.01 (0.72,1.42)
Age- gender- and race/ethnicity- adjusted	1.0	1.45 (1.01, 2.10)	1.05 (0.75,1.45)	1.39 (1.00,1.93)	1.04 (0.74,1.46)
Multivariate ⁺	1.0	1.50 (1.00, 2.26)	1.02 (0.72, 1.46)	1.21 (0.84, 1.74)	1.03 (0.71, 1.50)
High HbA1c					
Unadjusted	1.0	1.01 (0.71, 1.44)	1.05 (0.74, 1.50)	1.21 (0.87, 1.69)	1.17 (0.82, 1.67)
Age- gender- and race/ethnicity- adjusted	1.0	1.02 (0.71, 1.46)	1.06 (0.74,1.51)	1.22 (0.81,1.53)	1.15 (0.81, 1.63)
Multivariate ⁺⁺	1.0	1.03 (0.72, 1.47)	1.07 (0.73, 1.56)	1.12 (0.80, 1.58)	1.10 (0.77, 1.56)
High Triglycerides					
Unadjusted	1.0	0.96 (0.60, 1.52)	0.91 (0.53, 1.57)	0.89 (0.52, 1.53)	0.69 (0.43, 1.13)
Age, gender, and race/ethnicity- adjusted	1.0	0.94 (0.59, 1.49)	0.88 (0.51, 1.53)	0.87 (0.49, 1.54)	0.65 (0.39, 1.10)
Multivariate ⁺	1.0	0.91 (0.56, 1.49)	0.99 (0.54, 1.82)	0.90 (0.49, 1.65)	0.67 (0.39, 1.13)

*Quintile 1 is the reference group; each odds ratio (OR) is in relation to quintile 1.

⁺ Multivariate model included age (continuous), gender (male vs. female), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Mexican American, Other (including multiracial), body-mass index (normal: <25, overweight: 25-30, obese: ≥ 30), high-blood pressure (dichotomous: yes or no) , HbA1c (continuous), high cholesterol (dichotomous: yes or no), daily energy intake (continuous), time since diagnosis (1 year increments; continuous)

⁺⁺ Multivariate model included for age (continuous), gender (male vs. female), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Mexican American, Other (including multiracial), body-mass index (normal: <25, overweight: 25-30, obese: ≥ 30), daily energy intake (continuous), time since diagnosis (1 year increments; continuous), physical activity adherence (below 150 min/day, met 150 min/day, exceed 150 min/day)

DISCUSSION

Hemoglobin-A1c

An examination of HbA1c levels as a continuous variable among different LCD scores displayed that there were no significant associations. Between the highest (quintile 1) and lowest (quintile 5) consumption of carbohydrates HbA1c levels remained similar, contrary to our hypothesis. The odds of having a higher HbA1c level from decreasing LCD score, thus increasing carbohydrate consumption, was no different from the odds of increasing an LCD score. Participants in both low and high LCD score quintiles had a similar outcome in terms of the proportion of normal to high HbA1c levels.

Although we could not find past research studies in which the association between LCD score and clinical factors of type 2 diabetes was examined, there are many studies that investigate the risk of type 2 diabetes based on this LCD score. One original LCD score study found no association between the score and the risk for type 2 diabetes, after stratifying the data by other factors such as physical activity and family history of diabetes (Halton et al., 2008). Only after creating a separate LCD score for proportion of energy from carbohydrates with vegetable fats and vegetable proteins did the researchers find an association. Comparing the highest to lowest LCD score deciles, the relative risk of type 2 diabetes was 0.82 (95% CI: 0.71, 0.94). This indicated that higher LCD scores were associated with a reduced risk for type 2 diabetes. Further separation of the score from its effect on risk showed even stronger associations. Carbohydrate consumption was positively associated with type 2 diabetes when

comparing the 1st to 10th decile of LCD score (multivariate RR: 1.26; 95% CI: 1.07, 1.49) (Halton et al., 2008) .

Sainsbury et al. conducted a systematic review and meta-analysis of the effect of carbohydrate restriction on glycemic control for adults with diabetes and found that restriction is beneficial in reducing HbA1c levels only when it is done for a short period of time (3-6 months). In fact, they found that after 12 months, the effectiveness of a carbohydrate-restricted diet on HbA1c levels was no longer present (Sainsbury et al., 2018).

Results from a randomized controlled trial in China, showed a stronger positive association with a decreased HbA1c for patients who consumed a low-carbohydrate diet rather than a low-fat diet (Wang et al., 2018).

Presence of Retinopathy

According to the analysis, only 20.6% of participants were diagnosed with retinopathy. However, both the unadjusted and adjusted odds ratio of having retinopathy, comparing the lowest and highest LCD scores showed no difference.

A recent systematic review investigated the relationship between dietary intake and diabetic retinopathy through 31 published studies (Wong et al., 2018). It reported a protective effect of dietary fiber, fruits and vegetables, oily fish, and a Mediterranean diet on risk of diabetic retinopathy. The results also emphasized that a general reduction in caloric intake had some effect on lowering the risk for diabetic retinopathy. The review notes that focusing on the consumption of quality, low-glycemic index carbohydrates, may be more beneficial as it pertains to prevention of the disease and its progression (Wong et al., 2018).

Other studies have described the positive relationship between low-glycemic index diet and blood glucose control in diabetes (Chiu & Taylor, 2011; Thomas & Elliott, 2009)

While it is intuitive that carbohydrate load would have an effect on glycemic control in diabetes, there has not yet been a study with strong evidence for an association between carbohydrate intake and retinopathy. More research is necessary to determine which dietary factors have the most influence on diabetic retinopathy, as the LCD score was not associated with this condition.

Blood Triglyceride Levels

Data showed no difference between blood triglyceride levels by LCD score. The odds ratio of having high triglycerides comparing the lowest to the highest LCD score was insignificant both before and after adjustment for possible covariates.

While previous studies have shown a clear relationship between higher consumption of carbohydrates and elevated triglyceride levels (Min, Kang, Sung, & Kim, 2016) (Bazzano et al., 2014) (Maki et al., 2017) (Sainsbury et al., 2018), the association can be easily influenced by other factors such as BMI, hormone replacement therapy, and insulin sensitivity (Parks, 2001). Vitale et al. did a study on adults, aged 50-75, with type 2 diabetes and found that increasing carbohydrate intake actually lowered triglyceride levels. However, they specified that “slowly absorbable carbohydrates” were the primary source of carbohydrate for participants in the study (Vitale et al., 2016). Another study found that increased carbohydrate intake subsequently increased triglyceride levels in individuals who previously gained weight or had undiagnosed diabetes prior to the study (Mayer-Davis, Levin, & Marshall, 1999). A randomized clinical trial

reported a strong effect of low carbohydrate and low-glycemic index diet on lowering triglycerides and postprandial glucose in individuals with type 2 diabetes (Wolever et al., 2013)

Despite the many findings of previous research, there are many issues with comparing results across the board because there is no standard definition for a low-carbohydrate diet and the quality of carbohydrates is not always accounted for (Vitale et al., 2016).

Dietary Intake

While the macronutrient proportions found for each quintile of LCD score seemed to be reasonable for each category, the stark differences in micronutrients and some food groups was surprising. Total fruit intake was more than two times higher in quintile 1, while alcohol intake was more than 10 times greater in quintile 4. These factors bring about many questions regarding what is considered to be a balanced diet by each participant, and whether or not particular guidelines are being followed.

Few studies focus on food quality and it may be possible that many participants do not have a strong understanding of what a balanced diet would entail for their particular health condition. Type 2 diabetes would call for a decrease in the consumption of carbohydrates but not an elimination of important foods such as fruits and vegetables and other nutrient dense foods.

A study found that just a 1-standard deviation increase in diet quality scores was associated with a 9-13% reduced risk of type 2 diabetes in men (L. de Koning et al., 2011). Among the diet scores included, most of scores that were associated with lower risk for type 2 diabetes followed dietary patterns with low intake of refined sugar, meats, sodium, and trans fat, high intake of plant-based foods and grains, and moderate alcohol consumption (L. de Koning et

al., 2011). Hu et al. reported that poor diet was associated with a significantly higher risk of diabetes, even with adjustment for BMI (Hu, Manson, et al., 2001)

While our study could not find associations between diet and diabetes, countless research supports the notion that healthy eating patterns help to prevent the symptoms of this chronic disease.

Limitations and Strengths

There are both limitations and strengths of this study. One major limitation of this study is missing data for certain participants and variables. Due to the nature of NHANES data, which is collected and assessed annually, information may not be available immediately for use in research. This played a significant role in our selection of prognostic factors for the study. Additionally, questionnaires were primarily used to determine dietary intakes, demographic factors, and certain clinical characteristics. Participants may not provide an answer to a question for many reasons including misunderstanding, non-compliance, protection of privacy, or lack of information. In terms of the prognostic factors, data for triglyceride counts could not be reported for 1,525 of the participants because data could only be included from the blood test if participants had fasted prior. Another limitation is that this study uses cross-sectional data, therefore it cannot determine a cause and effect relationship unlike studies performed over long periods of time. Also, diets were self-reported by participants which may introduce the possibility of recall bias.

Lastly, the NHANES does not use separate terminology for type 1 and type 2 diabetes mellitus. While we tried to limit study participants to just adults with type 2 diabetes mellitus, there is the possibility that some participants may have had type 1 diabetes.

Despite these limitations, there are still several strengths of this study. One of the major strengths of this study is that it is the first to examine the associations of the low-carbohydrate diet score with various prognostic factors in adults with type 2 diabetes. Other studies have focused on the relationship between the LCD score and the risk for disease outcome. This study also used cross-sectional data from the United States so it is more representative of the population. Additionally, data was obtained from 6 cycles of the NHANES, years 2005-2016. This may also give a more representative view of both the diets and characteristics of adults throughout the U.S. Another strength of this study is the magnitude of information included in the analysis. In addition to the primary prognostic factors being assessed by LCD score, dietary intake ranging from micronutrients to food groups, as well as demographic factors for each LCD quintile, can be seen and analyzed.

CONCLUSIONS

The results of this study showed that the low-carbohydrate diet score was not associated with the odds of having retinopathy, abnormal triglycerides, or high HbA1c levels. These outcomes suggest that the quantity of macronutrients in one's diet may not have a direct correlation with diabetes-related conditions. The implication of this study is that it may be more beneficial for future research studies to assess diet quality in patients with type 2 diabetes. Having a clear understanding of the dietary patterns that contribute to better outcomes for individuals with diabetes helps millions of Americans and provides health professionals with better tools to educate the community.

APPENDIX: TABLES

Appendix Table 1: Criteria for the diagnosis of diabetes and prediabetes

	Diabetes ¹	Prediabetes ²
Glycated hemoglobin (HbA1c) ^a	≥ 6.5%	5.7-6.4%
Fasting Plasma glucose (FPG) ^b	≥ 126 mg/dL	100-125 mg/dL
2-hour Postprandial glucose (PG) ^c	≥ 200 mg/dL	140- 199 mg/dL
Random plasma glucose (RPG) ^d	≥ 200 mg/dL	N/A

¹ In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing

² For all three tests, risk is continuous extending below the lower limit of the range and becoming disproportionately greater at higher ends of the range

^aThe test should be performed in a laboratory using a method that is National Glycohemoglobin Standardization Program (NGSP) certified and standardized to the Diabetes Control and Complications Trial (DCCT) assay

^b Fasting is defined as no caloric intake for at least 8 h

^c During an oral glucose tolerance test of 75g anhydrous glucose dissolved in water

^d For a patient with classic symptoms of hyperglycemia or hyperglycemic crisis

Data source: American Diabetes Association. (2015). Classification and Diagnosis of Diabetes. *Diabetes Care*, 38 (Supplement 1), S8-S16. doi:10.2337/dc15-S005

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