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Glycemic Control: Risk Factors, Quality of Life, Workforce Participation, and Mortality Among US Adults with Type 2 Diabetes

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GLYCEMIC CONTROL: RISK FACTORS, QUALITY OF LIFE, WORKFORCE

PARTICIPATION, AND MORTALITY AMONG US ADULTS WITH TYPE 2

DIABETES

A dissertation submitted in partial fulfillment of the

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in

PUBLIC HEALTH

by

Evelyn Patricia Davila

2010

To: Dean Fernando M. Treviño
       R.Stempel College of Public Health and Social Work

This dissertation, written by Evelyn Patricia Davila, and entitled Glycemic Control: Risk Factors, Quality of Life, Workforce Participation, and Mortality among US Adults with Type 2 Diabetes, having been approved in respect to style and intellectual content, is referred to you for judgment.

We have read this dissertation and recommend that it be approved.

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Mary Jo Trepka

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Date of Defense: March 11, 2010

The dissertation of Evelyn Patricia Davila is approved.

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R.Stempel College of Public Health and Social Work

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Interim Dean Kevin O'Shea
University Graduate School

Florida International University, 2010

DEDICATION

In loving memory of my mother Norma E. Davila (1955-1997)

ACKNOWLEDGMENTS

ABSTRACT OF THE DISSERTATION

GLYCEMIC CONTROL: RISK FACTORS, QUALITY OF LIFE, WORKFORCE

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Evelyn Patricia Davila

Florida International University, 2010

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Professor Theophile Niyonsenga, Major Professor

Despite research showing the benefits of glycemic control, it remains suboptimal

among adults with diabetes in the United States. Possible reasons include unaddressed

risk factors as well as lack of awareness of its immediate and long term consequences.

The objectives of this study were to, using cross-sectional data, 1) ascertain the

association between suboptimal (Hemoglobin A1c (HbA1c) $\geq$7%), borderline (HbA1c 7-

8.9%), and poor (HbA1c $\geq$9%) glycemic control and potentially new risk factors (e.g.

work characteristics), and 2) assess whether aspects of poor health and well-being such as

poor health related quality of life (HRQOL), unemployment, and missed-work are

associated with glycemic control; and 3) using prospective data, assess the relationship

between mortality risk and glycemic control in US adults with type 2 diabetes. Data from

the 1988-1994 and 1999-2004 National Health and Nutrition Examination Surveys were

used. HbA1c values were used to create dichotomous glycemic control indicators. Binary

logistic regression models were used to assess relationships between risk factors,

employment status and glycemic control. Multinomial logistic regression analyses were

conducted to assess relationships between glycemic control and HRQOL variables. Zero-inflated Poisson regression models were used to assess relationships between missed work days and glycemic control. Cox-proportional hazard models were used to assess effects of glycemic control on mortality risk. Using STATA software, analyses were weighted to account for complex survey design and non-response. Multivariable models adjusted for socio-demographics, body mass index, among other variables. Results revealed that being a farm worker and working over 40 hours/week were risk factors for suboptimal glycemic control. Having greater days of poor mental was associated with suboptimal, borderline, and poor glycemic control. Having greater days of inactivity was associated with poor glycemic control while having greater days of poor physical health was associated with borderline glycemic control. There were no statistically significant relationships between glycemic control, self-reported general health, employment, and missed work. Finally, having an HbA1c value less than 6.5% was protective against mortality. The findings suggest that work-related factors are important in a person's ability to reach optimal diabetes management levels. Poor glycemic control appears to have significant detrimental effects on HRQOL.

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LIST OF ACRONYMS

ACCORD   Action to Control Cardiovascular Risk in Diabetes

AACE   American Association of Clinical Endocrinologists

BMI   Body Mass Index

CDC   Centers for Disease Control and Prevention

CI   Confidence Interval

CV   Coefficient of Variation

CVD   Cardiovascular Disease

DCCT   Diabetes Control and Complications Trial

BRFSS   Behavior Risk Factor Surveillance System

HbA1c   Glycosylated Hemoglobin A1c

HR   Hazard Ratio

HRQOL   Health Related Quality of Life

HS   High School

ICD   International Classification of Diseases

QOL   Quality of Life

NCHS   National Center for Health Statistics

NH   Non-Hispanic

NHANES   National Health and Nutrition Examination Surveys

OR   Odds Ratio

PA   Physical Activity

PSU   Primary Sampling Units

SHS   Secondhand Smoke Exposure

US   United States

CHAPTER I.

INTRODUCTION

<u>Overview</u>

Diabetes mellitus is one of the most serious chronic diseases in the United States

(US) and in the world. In the US alone, diabetes affects an estimated 7.0% (20.8 million)

of the total population, and another 54 million are at risk.[1] The prevalence of diabetes in

the US is expected to rise in the future given the continued increase in the prevalence of

associated risk factors such as older age, obesity, and minority race and ethnicity (e.g.

Blacks and Hispanics).[2] Projections have indicated that the prevalence of diabetes will

increase to 366 million worldwide by the year 2030,[3] with 39 million in the US by the

year 2050.[4] In the US, the death rate for diabetes increased by 45% from 1970 to 2002,[5]

and in 2006, diabetes was the sixth leading cause of death in the US.[6] In addition to the

high risk of mortality associated with diabetes, diabetes is also associated with great

morbidity and disability. For example, among adults over 20 years of age, diabetes is the

leading cause of blindness, leg amputations, and kidney disease.[1, 7] Consequently, both

indirect (e.g. due to disability, unemployment, premature death) and direct (e.g. medical

costs including hospitalizations and treatment) costs associated with diabetes are high,

with the total costs estimated at about $174 billion, of which $116 billion are medical.[7] In

fact, the medical expenditures among those individuals with diabetes are estimated to be

more than twice of those without.[7] Therefore, the public health and economic burden

associated with diabetes is large and is likely to increase.

Diabetes is generally diagnosed using a fasting plasma glucose test with a glucose

result of 126 mg/dl after an eight-hour fast or by a two hour oral glucose tolerance test

with a glucose result of 200 mg/dl or more.[8] Diabetes is primarily categorized as type 1 or type 2. Type 1 diabetes is the least common, accounting for less than 10% of all cases; it is caused by almost complete lack of insulin secretion, usually due to the autoimmune destruction of pancreatic beta cells.[9] Type 2 diabetes is much more common accounting for 90-95% of cases. Type 2 diabetes is characterized by impaired insulin secretion that could arise due to insulin resistance and it is highly associated with obesity.[9] Although diabetes can be diagnosed at any age, individuals diagnosed at an older age are usually diagnosed with type 2 diabetes. Regardless of the classification of diabetes, the outcome is the same, namely high levels of blood glucose or hyperglycemia due to a combination of an increase in insulin resistance, a decrease in beta cell function, and a decrease in insulin secretion by the pancreas.[1]

People can live with diabetes without major complications as long as it is well controlled and managed. The aim of diabetes management is to adequately maintain normal blood glucose levels (i.e. 70-130 mg/dl) in order to prevent microvascular (e.g., retinopathy, neuropathy, nephropathy) and macrovascular (e.g., peripheral vascular or cardiovascular disease [CVD]) complications.[10] A key element in diabetes management is glycemic control, which may be indicated by a person's HbA1c. The hemoglobin A1C test measures the percent of glucose in the bloodstream attached to hemoglobin molecules in the previous two to three months, which is the lifespan of red blood cells. Thus, the more excess glucose in the bloodstream, the higher the percentage of hemoglobin molecules attached, the higher the HbA1c level. This test has been considered the gold standard for assessing glycemic control in diabetes care for the last 25 years.[10, 11] Although there are other methods of assessing glycemic control, the HbA1c

test has been shown to be better than serum fructosamine tests because the latter only measures glycemic control in the last 2 weeks.[12] Although continuous (daily) blood glucose monitoring would provide the most accurate evaluation of a person's average blood glucose levels, the HbA1c test is more practical, less costly, and more convenient than continuous blood glucose monitoring.

Several guidelines for glycemic control currently exist. The American Diabetes Association (ADA) treatment goals for glycemic control recommend HbA1c values of < 7.0%.[9] The International Diabetes Federation and the American Association of Clinical Endocrinologists (AACE) recommend an HbA1c value of <6.5 %.[13] However, an HbA1c value of <7.0% is not always realistic for individuals who are older and with several co-existing conditions and/or those facing terminal illness.[14] Thus, two commonly used thresholds for glycemic control are a HbA1c value of ≥ 7%, which is generally considered suboptimal glycemic control, and a HbA1c value of ≥ 9%, which is an indicator of poor glycemic control and more often used as a target value for patients in worse health (e.g., greater comorbidity and/or terminally ill).[15-18]

Research has shown clear evidence of the benefits of good glycemic control in terms of diabetes-related complications. For example, it has been noted that a 1% decrease in the HbA1c value can lead to a 10% reduction in risk of coronary artery disease.[19, 20] Moreover, good glycemic control has been associated with fewer diabetic complications and better metabolic control.[11] Studies have also shown that macrovascular and microvascular complications are related to poor glycemic control. For example, poor glycemic control has been associated with severe periodontitis,[21] incidence of proteinuria and symptoms consistent with diabetic neuropathy,[22] and elevated C-

reactive protein, a marker of systemic inflammation and risk factor for cardiovascular disease.[23]

Given the medical benefits of good glycemic control, strong efforts by public health advocates and the medical community have been made to improve glycemic control among adults with diabetes. For example, national diabetes programs, targeted at the general public, such as the National Diabetes Education Program have launched campaigns like the "Control the ABC's" campaign, which stresses the importance of the HbA1c test, in addition to frequent blood pressure and cholesterol check-ups.[24] The Diabetes Quality Improvement Project is another diabetes program that has been developed in order to improve diabetes management.[25] This program's mission is to develop a set of standardized performance and outcome measures in order to make equal comparisons of diabetes management health care plans across the US.[25]

Despite research showing the importance of lower HbA1c levels for preventing diabetic complications and despite public health efforts towards diabetes management, glycemic control remains a serious public health problem in the US. For example, in the 1980s and 1990s, only about 37% of US adults diagnosed with diabetes had HbA1c levels < 7% (i.e. optimal glycemic control).[25] Others have noted that 18% of the US population with diabetes in the 1980s and 1990s had HbA1c values of >9.5%.[26] More recent data have shown slight improvements, yet still about 44% of the population with diabetes has an HbA1c value of suboptimal glycemic control.[27]

There are several possible reasons why adults with diabetes are not reaching optimal (i.e. HbA1c of <7%) or good (HbA1c of < 9%) glycemic control. One of the reasons could be the presence of unknown risk factors for suboptimal or poor glycemic

control that may be acting as barriers to proper diabetes management. Another reason could be the fact that information about the known morbidity outcomes does not promote a sense of urgency to the individuals with diabetes that would otherwise motivate them to adhere to their diabetes treatment regimen. Thus, it is important to assess potentially new risk factors for suboptimal, borderline, and poor glycemic control, as well as to learn about the consequences of suboptimal, borderline, and poor glycemic control other than those that are traditionally studied and reported (e.g., macrovascular and microvascuar complications).

The objectives of this study were to: 1) ascertain whether suboptimal, borderline, or poor glycemic control are associated with factors such as numbers of hours worked, type of occupation, secondhand smoke (SHS) exposure, and desire to lose weight in US adults with type 2 diabetes; 2) assess whether aspects of poor health and well-being such as poor quality of life, unemployment and missed work days are associated with suboptimal, borderline, and poor glycemic control in US adults with type 2 diabetes; and 3) assess the relationship between the risk of mortality and suboptimal, borderline, and poor glycemic control in US adults with type 2 diabetes.

Research questions and hypotheses

This research used secondary, cross-sectional data from a nationally representative sample survey (1999-2004 NHANES) and a prospective study design (1988-1994 NHANES and its linked mortality file) to assess the relationship between suboptimal, borderline, and poor glycemic control and potentially four new risk factors i) number of hours worked per week, (ii) type of occupation, (iii) SHS exposure, and (iv)

desire to lose weight. In addition, this study assessed the relationship between suboptimal, borderline, and poor glycemic control and employment status, absenteeism and mortality. NHANES is a series of population based surveys conducted by the Centers for Disease Control and Prevention (CDC) and designed to monitor several aspects of health, thereby providing a nationally representative picture of the health and nutritional status of the US population.[28] A summary of the research questions and hypotheses for this study is shown in figure 1.

Figure 1. A diagrammatic view of study hypotheses

Research Question 1:   Research Questions 2 and 3:

| Employed in service or blue-collar industry |

| Greater hours worked |

| Secondhand smoke exposure |

| Desire to lose weight |

| Suboptimal/ borderline/poor glycemic control |

| Greater days of inactivity, poor mental, and physical health |

| Greater missed work days |

| Unemployment |

| All-cause and CVD mortality |
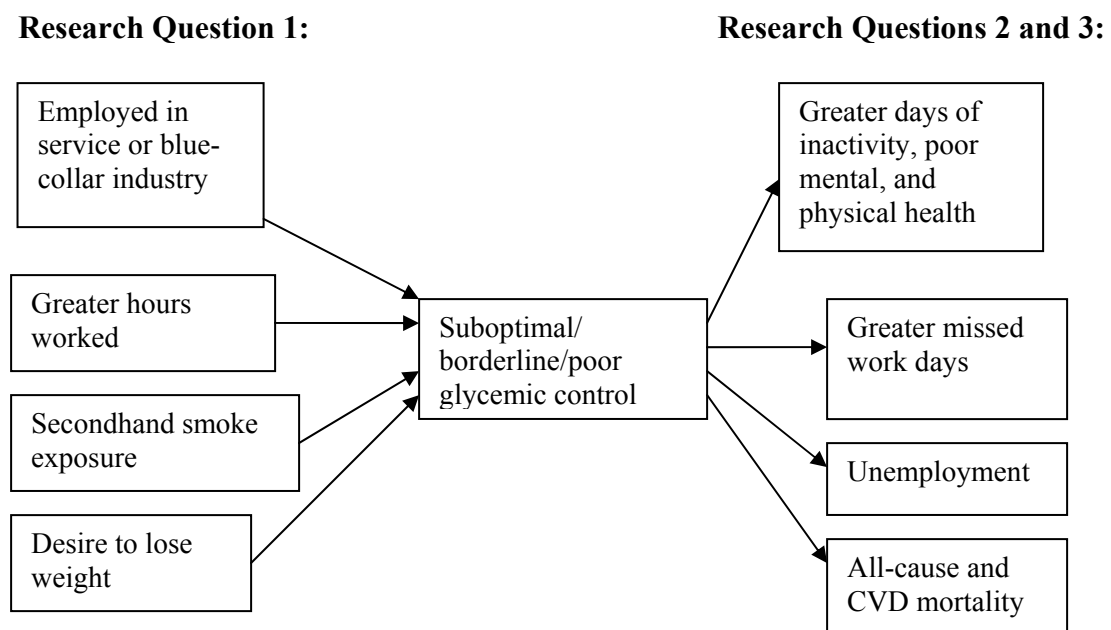
Research Question 1: Are suboptimal (HbA1c $\geq$ 7%), borderline (HbA1c 7-8.9%), and poor (HbA1c $\geq$ 9%) glycemic control associated with potentially new risk factors such as i) number of hours worked per week, (ii) type of occupation, (iii) SHS

exposure, and (iv) desire to lose weight among US adults with type 2 diabetes? This question leads to the following hypotheses.

Hypothesis 1a: Suboptimal, borderline, and poor glycemic control are associated with greater number of hours worked per week after controlling for potential confounders such as (i) duration of diagnosis, (ii) body mass index (BMI), (iii) alcohol use, (iv) greater number of non-CVD chronic conditions, (v) family history of diabetes, (vi) insurance status, (vii) sex, (viii) physical activity, (ix) diabetes treatment, and (x) race/ethnicity.

Hypothesis 1b: Suboptimal, borderline, and poor glycemic control are associated with occupational groups with greater time constraints or demands such as blue collar and service workers versus white collar workers after controlling for potential confounders such as (i) duration of diagnosis, (ii) BMI, (iii) alcohol use, (iv) greater number of non-CVD chronic conditions, (v) family history of diabetes, (vi) insurance status, (vii) sex, (viii) physical activity, (ix) diabetes treatment, and (x) race/ethnicity.

Hypothesis 1c: Among self-reported non-smokers, suboptimal, borderline, and poor glycemic control are associated with being exposed to secondhand smoke after controlling for potential confounders such as (i) duration of diagnosis, (ii) BMI, (iii) alcohol use, (iv) greater number of non-CVD chronic conditions, (v) family history of diabetes, (vi) insurance status, (vii) sex, (viii) physical activity, (ix) diabetes treatment, and (x) race/ethnicity.

Hypothesis 1d: Suboptimal, borderline, and poor glycemic control are associated with desire to lose weight after controlling for potential confounders such as (i) duration of diagnosis, (ii) BMI, (iii) alcohol use, (iv) greater number of non-CVD chronic

conditions, (v) family history of diabetes, (vi) insurance status, (vii) sex, (viii) physical activity, (ix) diabetes treatment, and (x) race/ethnicity.

Research Question 2: Are a) health-related quality of life (HRQOL) measures indicative of poor health [i.e. (i) poor self-reported general health and greater number of days (ii) poor physical health, (iii) poor mental health and (iv) limited activity in the past 30 days]; b) greater days of missed work in the past 12 months (i.e. absenteeism), and c) unemployment, associated with suboptimal (HbA1c $\geq$ 7%), borderline (HbA1c 7-8.9%), and poor (HbA1c $\geq$ 9%) glycemic control among US adults with type 2 diabetes, after controlling for potential confounders (mentioned in hypothesis 1)? This research question leads to the following hypotheses:

Hypothesis 2a: All four HRQOL measures are associated with suboptimal, borderline, and poor glycemic control, after controlling for potential confounders.

Hypothesis 2b: Greater number of missed work days in the past 12 months is associated with suboptimal, borderline, and poor glycemic control, after controlling for potential confounders.

Hypothesis 2c: Unemployment is associated with suboptimal, borderline, and poor glycemic controls, after controlling for potential confounders.

Research Question 3: Greater mortality risk among are associated with suboptimal (HbA1c $\geq$ 7%), borderline (HbA1c 7-8.9%), and poor (HbA1c $\geq$ 9%) glycemic control among US adults with type 2 diabetes after controlling for potential confounders as noted in hypothesis 1? Two hypotheses are derived from this research question.

Hypothesis 3a: All-cause mortality risk is associated with suboptimal, borderline, and poor glycemic control, after controlling for potential confounders.

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Hypothesis 3b: CVD mortality risk is associated with suboptimal, borderline, and poor glycemic control, after controlling for potential confounders.

Significance of the present study

Results from this study will provide information of public health significance for several reasons. First, by using a nationally representative sample of adults, this proposed study will allow generalization of the findings related to glycemic control among US adults with a self-reported diagnosis of diabetes. Second, by using a large nationally representative database, a comprehensive and thorough statistical assessment of the relationship between potentially new risk factors (e. g. type of occupation, hours worked, secondhand smoke exposure, and desire to lose weight) with suboptimal, borderline, and poor glycemic control, while adjusting for potential confounders, will be possible. Third, by studying the relationship between glycemic control and HRQOL, as well as employment and absenteeism, a better understanding of the overall well-being and the disability/dysfunction associated with poorly managed diabetes will be gained; thus, providing an estimate of the impact of disease that is not obtained in traditional morbidity and mortality outcome measures.[29] Fourth, by studying the association between glycemic control and mortality risk using prospective data, the long-term benefits due to good diabetes management will be elucidated.

CHAPTER II.

LITERATURE REVIEW

Overview

The literature search for this study included a comprehensive review of scientific articles

in English available in databases such as MEDLINE using MeSH and keywords such as

glycemic control, A1C, diabetes management, diabetes control, hemoglobin, diabetes

treatment, among others from all years, as early as from 1950. In addition, articles that

were found to be relevant from these searchers were used to capture additional articles by

examining their reference lists as well as by looking at others who cited them. The

literature review is presented separately for each research question and hypothesis.

Risk factors of suboptimal and poor glycemic control

There have been several national and international studies assessing factors

associated with poor glycemic control such as (i) minority race-ethnicity (e.g. Blacks and

Hispanics), (ii) older age, (iii) male sex, (iv) drinking alcohol, (v) longer duration of

diabetes, (vi) diabetes treatment (e.g., insulin or oral antidiabetic drugs), (vii) lack of

insurance, (viii) having a CVD-related comorbidity (e.g. hypercholesterolemia,

hypertension, microalbuminuria, kidney disease), (ix) positive family history of diabetes,

BMI, smoking, (x) greater physical activity, (xi) lack of adherence to diabetes

management, and (xii) certain non-CVD chronic conditions (such as depression).[30-39]

Though these traditionally studied factors are important in glycemic control, research has

suggested that other factors such as work characteristics (e.g. an individual's occupation[40]

and the number of hours worked per week),[41, 42] secondhand smoke exposure,[43] and the

desire to lose weight may also influence glycemic control; yet the nature of the relationship between these factors and glycemic control has not been well studied.

Potentially new risk factors for suboptimal and poor glycemic control

Work constitutes an important part of most adult lives, and under several conditions can be the cause of the ill health. Thus, it is possible that glycemic control is also affected by work factors. However, few studies exist relating work characteristics with glycemic control among adults with diabetes.

The number of hours a person works is one factor that may be associated with poor glycemic control. Indeed, it is plausible that individuals working long hours are less likely to be able to properly manage their diabetes due to the lack of time to check their blood glucose levels, inject insulin, take oral agents when necessary, or eat well-balanced meals at regular time intervals, all factors that may affect glucose levels. Furthermore, research has shown that individuals with diabetes do consider their disease as an issue of concern affecting the type of jobs they seek, as well as the breaks and the work schedule they need.[44, 45] Although work-hours alone have not been linked to glycemic control, a related variable, job stress, has been associated with greater HbA1c levels even among employed individuals without diabetes in non-US studies.[42, 46, 47] Job stress, a term used to describe the psychological and physiological effects resulting from being employed in a high pressure and pace job coupled with lack of workplace decision or control, has even been associated with other cardiovascular risk factors.[48-51]

Work characteristics including the length of and control over work schedules may also affect glycemic control. In fact, commercial truck drivers reported problems

regulating their glucose levels and have blamed their unhealthy dietary patterns due to being on the road.[52] In relation to diabetes, certain occupations that are characterized as having high work demands (e.g. long work hours with limited breaks) have been shown to have a higher prevalence of diabetes.[53] For example, in a study of industrial factory workers in Japan, Japanese transport workers (e.g. those picking up and delivering factory materials) were shown to have greater risk of developing type 2 diabetes, compared to Japanese managers, clerical workers, and technical workers, even after adjusting for obesity and other potential confounders.[54] Industrial male workers and female nurses have also been shown to have greater risk of type 2 diabetes.[41, 55] Nonetheless, office workers have also been shown to be at lower risk for incidence of diabetes.[56] In the only known study relating occupation to glycemic control, which was based on data of adults with diabetes in New Zealand, the authors showed that glycemic control, as measured by fructosamine levels, did not vary by type of occupation (i.e. no difference found among administrative, clerical/sales/service, skilled trades, and unskilled manual workers).[57] Given the few studies relating occupation to glycemic control diabetes,[41, 54-57] more research is needed to determine the association between glycemic control and occupational factors.

Another factor that has not been fully investigated but is gaining recognition as a major determinant of several chronic conditions is passive smoking, also known as SHS exposure or environmental tobacco smoke. Aside from its effects on lung and respiratory functions, SHS exposure has been associated with greater acute coronary syndromes and an increase in inflammatory markers.[58] Research has shown that there is an association between diabetes and smoking.[59] Specifically, studies have shown that smoking

contributes to worse metabolic control among individuals with diabetes,[60] greater

likelihood of both microvascular[61] and macrovascular complications,[62] and worse

glycemic control.[63, 64] There have been fewer studies on the relationship between SHS

and diabetes.[43, 65] Nevertheless, these studies have shown a relationship between SHS and

glucose intolerance among young adults[43] as well as incidence of diabetes.[65] To date,

there are very few if any studies, to the author's knowledge based on a robust MEDLINE

search of published articles since 1950, investigating the effects of SHS and glycemic

control.

Another potential risk factor for suboptimal and poor glycemic control is an

individual's desire to lose weight or control their weight. For example, it is possible that

some adults with diabetes who want to lose or control their weight avoid taking insulin as

recommended by their physician knowing that weight gain is one of the potential side

effects of insulin use.[66-69] Thus, not taking insulin when needed may result in poor

glycemic control, particularly if the individual has other unhealthy dietary and eating

behaviors. In fact, poor glycemic control has been found among adolescents and young

adult females with eating disorders[70-72] and among adolescents that perceived themselves

as being overweight.[73] Furthermore, not taking insulin in order to avoid weight gain is

actually considered one of the DSM-IV diagnostic criteria for bulimia.[72] However, there

are very few if any studies specifically assessing the relationship between the desire to

lose weight and glycemic control among US adults with diabetes.

<u>Consequences of suboptimal and poor glycemic control</u>

Increasing the years of healthy life and improving the quality of life (QOL) are some of the overarching goals of Healthy People 2010.[74] Although the term QOL is mostly used by the social sciences, in public health and the medical professions, the focus has been placed on the concept of Health Related Quality of life (HRQOL). The CDC defines HRQOL as an individual's "perceived physical and mental health over time", a measure which provides a better insight into how an illness or condition can affect everyday life.[75] In general, HRQOL indicators can be thought of as a way to assess overall disability and poor function resulting from a disease or condition, aspects that may not be determined when looking at traditional measures of morbidity and mortality.[76] In addition, HRQOL measures can be especially useful when assessing the long term consequences of chronic conditions since poor disease management can take years to develop as a clinical or medical outcome,[77] impairing a person's overall health status and well-being, particularly one's mental health.

Since the 1990s, there has been growing interest in HRQOL, partly due to the growth of the US aging and chronically-ill population.[76] Consequently, the CDC developed four "core" HRQOL questions, also referred to as "Core Healthy Day" measures, which were first included in the Behavioral Risk Factor Surveillance System (BRFSS) in 1993, and were then included in the National Health and Nutrition Examination Surveys (NHANES) beginning with the 2001-2002 cycle. These four questions measure: 1) overall self-rated general health [fair/poor versus excellent/very good/good]; 2) physical health based on the number of days with poor physical health in the past 30 days; 3) mental health based on the number of days with poor mental and

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emotional health in the past 30 days; and 4) disability and loss in productivity based on the number of days with activity limitation in the past 30 days. These core HRQOL questions have been found to have an acceptable validity and reliability when compared to the Medical Outcomes Short-Form 36 (SF-36).[78] The SF-36 is a validated instrument with 36 questions about perceived health status and number of disability days, and is considered the gold standard for evaluating overall health including physical and mental health.[78]

Diabetes, glycemic control and health related quality of life

Individuals with diabetes have been shown to have poor quality of life.[79] One of the reasons for such poor quality of life could be the increased number of daily medical (or health) responsibilities adults diagnosed with diabetes have. The constant reminder of the importance and necessity of responsibilities and activities such as taking insulin or oral diabetic medication at regular time intervals (e.g. after consuming certain meals or performing various physical activities) can take its toll in a person's life.[79] In fact, because of the potential effects on HRQOL, it is believed that some physicians delay the initiation of insulin treatment, although a study showed that initiation of insulin treatment does not necessarily alter quality of life in a negative way.[80] Nevertheless, it is possible that adults with diabetes have poor quality of life because of the health complications related to poorly managed diabetes, such as retinopathy, neuropathy, and cardiovascular conditions.[77, 81, 82] Furthermore, given that fewer diabetic complications are found among those with better glycemic control, HRQOL is likely to be associated with glycemic control. However, the effect of glycemic control on HRQOL among diabetics is not clear.

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Indeed, while some studies have found poor glycemic control to be associated with poor quality of life,[83-85] other studies have not found any association.[86-89] For example, functional disability, which is a component of HRQOL, has shown an inconsistent relationship with glycemic control among adults with diabetes.[90, 91]

None of the studies relating QOL and glycemic control were based on a nationally representative data of adults with diabetes. In addition, the discrepancies in the results of these studies could be a function of the different QOL measurement instruments employed. For example, while some studies have used what are known as "generic" QOL measures such as those developed and used by the CDC, others have used more "illness oriented" measures that are developed specifically for health conditions such as diabetes and include the Diabetes Qualify of Life Measure, the Diabetes Treatment Satisfaction Questionnaire, and the Problem Areas in Diabetes.[77, 79] Thus, there is a need of nationally representative studies aimed at understanding the association between poor glycemic control and HRQOL among US adults with diabetes using validated measures.

Workforce participation: unemployment and absenteeism

As the US population continues to change, so does the US workforce. Specifically, the workforce is expected to become increasingly diverse with growing number of elderly and minority workers. In fact, Hispanics are projected to represent 17% of the workforce by 2020, an increase of 11% from the1980s.[40] Moreover, by the year 2012, there will be over 40 million American workers aged 65 and older.[92] Since the elderly, racial and ethnic subgroups such as Hispanics and Blacks are known to have a higher prevalence of many chronic health conditions such as diabetes,[93] the number of

workers with these chronic conditions is expected to steadily increase. The consequences

of these increases are likely to adversely impact workplace productivity, resulting in

economic losses not only to the individual or the employer, but also to the nation as a

whole.[94] Furthermore, a person's employment status, and consequently economic status,

may directly influence their access to health care and their ability to pay for medications

or treatment requirements, which in turn affect proper management of the disease, and

therefore may worsen patient prognosis. In addition to employment status, the number of

missed work days is another individual-level measure for monitoring the impact of

chronic disease on worker productivity. Missed work or "absenteeism" may provide a

reflection of the disability that is experienced by diabetics with poor health and well-

being that may perhaps not be obtainable by employment statistics.[95, 96] The disability

and consequently diminished productivity at work may be of particular concern for

employers given the financial implications such as decreased productivity.

Workforce participation and glycemic control

        There are various studies assessing the relationship between diabetes status and

workforce participation. For example, studies have shown that diabetics are both less

likely to be represented in the workforce and more likely to miss work,[57, 97-99] particularly

among those individuals with more severe diabetic complications.[94, 100, 101]

What makes some adults with diabetes more likely to miss work or be unemployed

versus other adults with diabetes is not entirely clear. However, one of the reasons could

be a person's level of glycemic control.

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There are few studies assessing the relationship between glycemic control and workforce participation. In a double-blind randomized controlled trial of adults with type 2 diabetes, the treatment group with more strict diabetes treatment regimens (e.g. lower HbA1c target) had a more favorable outcome in terms of retained employment and less absenteeism.[102] In a cross-sectional study of diabetic patients from Michigan, having more hours of missed work in the past month was associated with poor glycemic control.[103] However, in a study of adults with diabetes referred to a multi-center diabetes program in the US, there appeared to be no significant relationship between glycemic control and the risk of days lost from school or work even after controlling for confounders.[104] Thus, the association between glycemic control and missed work days requires further study.

Glycemic control and mortality risk

Along with improved quality of life and reduction in health disparity, increased life expectancy is a major goal of Healthy People 2010. Most studies that have assessed the relationship between glycemic control and mortality have been based on international studies, adults without diabetes, and/or chronically-ill populations. These studies have found that greater mortality risk is associated with poor glycemic control. For example, greater mortality risk among advanced chronic kidney disease and dialysis patients with poor glycemic control has been observed.[105-107] In a prospective study of individuals in the United Kingdom to assess the relationship between HbA1c levels and all-cause and CVD mortality (after a 6 year follow-up), it was shown that the all-cause and CVD mortality risk increased with greater HbA1c levels.[108]

Furthermore, most of the studies investigating the relationship between diabetes management measures (e.g., fasting blood glucose, HbA1c) and CVD events, including mortality risk, have been primarily of men.[108] The few studies that do exist among women have suggested differences in risk for CVD events and/or mortality, with most of them noting a lower mortality risk among women.[108-110] Some studies have even found a counterintuitive relationship between HbA1c and mortality, suggesting that strict diabetic treatment regimes may eventually be more harmful than beneficial in certain populations such as those with greater comorbidity.[111, 112] Thus, more research is needed to determine the association between glycemic control and mortality risk among US adults with diabetes.

CHAPTER III.

METHODOLOGY

Overview

This study used cross-sectional secondary data from a nationally representative survey sample (1988-1994 NHANES [also known as NHANES III] and 1999-2004 NHANES) to assess the relationship between four potentially new risk factors (type of occupation, number of hours worked per week, SHS exposure, and desire to lose weight) and suboptimal, borderline, and poor glycemic control. In addition, this study estimated the association between suboptimal, borderline, and poor glycemic control and employment status, missed work, and mortality.

Sample and description of data sets

The National Health and Nutrition Examination Survey (NHANES) is a health survey developed by the National Center for Health Statistics (NCHS) to gather information about the health status of the US population. NHANES uses a stratified, multi-stage complex probability design that allows for a nationally representative estimation of the non-institutionalized US population.[28]

Briefly, the sampling scheme in NHANES consists of four stages. The first stage involves selecting primary sampling units (PSU) from the entire nation. These are approximately the size of a large county or several small ones. The second stage involves the PSU units being divided in to small sections, usually about the size of city blocks. The third stage consists of selecting households at random within each of the sectors. Finally, stage four is where individuals are chosen from selected households, and

selection is based on age-sex-race screening strata. Weights are based on the probability of a person being selected at each of these stages. Sampling weights are created to provide unbiased national estimates, and are adjusted for non-response and then post-stratified to match with the US population census counts of subpopulations.[28]

NHANES data are collected by a trained team of professionals through a series of in-person interviews and medical examinations conducted at mobile examination clinics or at home. All NHANES data are de-identified, with only sequential numbers identifying each participant in order to protect participant confidentiality. Most NHANES data files are public-use files and the NHANES files used in this study were all public-use files that were downloaded from the NCHS website. The NHANES III linked Mortality File used in this study was the public-use file that contains data of the major causes of death (i.e. not specific cause of death) from the National Death Index, with follow-up through December 31, 2000.[113] Depending on the hypotheses being tested in this study, different NHANES survey years were used. The reason for this is because not all variables were available in all survey years. In addition, depending on the sampling methodology, NCHS does not recommend merging of the older NHANES (i.e. 1988-1994) with the more recent NHANES survey years. NHANES 1999-2004 was used for hypotheses 1, 2b, and 2c for utilized. NHANES 2001-2004 was used for hypothesis 2a, while NHANES 1988-1994 and its Mortality file for hypothesis 3a and 3b was used.

<u>Inclusion and exclusion criteria</u>

Individuals with a self-report of diabetes, aged 20 years or older, and not pregnant were included in the study. Individuals defined as having type 1 diabetes were excluded; the remaining sample was considered to have type 2 diabetes, as defined in previous studies.[31, 36, 40]

<u>Variables used for inclusion/exclusion criteria:</u>

<u>Self-report of diabetes</u>: This was a categorical variable defined as: 1) yes and 2) no, based to the question "Other than during pregnancy, have you been ever been told by a physician that you have diabetes or sugar diabetes?" Participants who were diagnosed with diabetes before the age of 30 (see variable question below), and were treated with insulin only were further classified as having type 1 diabetes. This definition is consistent with that used in previous studies utilizing NHANES data and is due to the agreement within clinicians that an individual diagnosed with diabetes before the age of 30 is more likely to have type 1 diabetes, but since type 2 diabetes is becoming more prevalent among youth, taking insulin only is likely a result of having type 1 diabetes.[31, 36, 40] Those individuals considered not to have type 1 diabetes, were classified as having type 2 diabetes, a definition consistent with previous NHANES analyses.[31, 36, 40]

<u>Age at diabetes diagnosis:</u> This was a continuous variable expressed in years based on the question "How old were you when a doctor or health care professional told you that you had diabetes or sugar diabetes?" and asked among all individuals that self-reported being diagnosed with diabetes.

Outcome and predictor variables:

     Glycemic control: the HbA1c value was a continuous variable expressed as a percentage of glucose in the bloodstream that is attached to hemoglobin molecules.

     Suboptimal and poor glycemic control: An individual with a HbA1c value equal to or greater than 7% was said to have suboptimal glycemic control. On the other hand, an individual with a HbA1c value equal to or greater than 9% was said to have poor glycemic control. To be consistent with many of the studies using glycemic control variables, suboptimal glycemic control was defined as: 1) yes, if HbA1c $\geq$ 7%, and 2) no, if HbA1c < 7% (reference group); while poor glycemic control was defined as: 1) yes, if HbA1c $\geq$ 9%, and 2) no, if HbA1c < 9% (reference group).

     Since a response of "yes" to the suboptimal glycemic control variable actually includes individuals with poor glycemic control and there are clinical differences or manifestations between suboptimal and poor glycemic control, a third glycemic control variable was also created, labeled "borderline" glycemic control, for the purposes of this study. This variable was defined as: 1) yes if HbA1c $\geq$7% but HbA1c <9%, and 2) no, if HbA1c < 7% (reference group); thus, for this variable all individuals with HbA1c $\geq$9% were excluded from the analyses. All analyses were repeated for this new glycemic control variable.

     In the 1999-2004 NHANES, glycosylated hemoglobin in whole blood was measured by the Diabetes Diagnostic Laboratory at the University of Missouri-Columbia using Primus CLC330 and Primus CLC 385 (Primus Corporation, Kansas City, MO) with a high performance liquid chromatography system among all participants age 12 years of age or older.[114] Several quality control procedures were taken to ensure accuracy

of measures. These measures included verifying and repeating plasma (or blood) specimens of HbA1c that were above 14% or below 4% (the accepted range for HbA1c measures were from 2% to 20%).[114] From the measurements that were repeated, a few were selected at random and the coefficient of variation (CV) calculated. The CV provides an estimate of the amount of dispersion in the measure, in other words, how much one measure differs from the second measure taken, with a lower CV indicating lower dispersion and less measurement error. The CV for these specimens ranged from 1.53 to 1.29, which indicates adequate similarity in the specimens when repeated.[114]

Health related quality of life: HRQOL was based on four different variables: self-rated general health, number of days of poor mental health, days of poor physical health, and days of activity limitation. Each HRQOL measure, except for the general health variable, was categorized into three levels in order to be consistent with previous studies while the general health variable was dichotomized.[115, 116]

General health: General health was a categorical variable based on the question "Would you say your health in general is fair, poor, good, very good, and excellent?" It was recoded to include only two categories: 1) fair/poor and 2) good/very good/excellent (reference group).

Days with poor mental health: This was a discrete variable expressed in days and based on the question "Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?." This variable was recoded into a categorical variable as follows: 1) ≥ 14 days, 2) 1-13 days, and 3) none (reference group).

Days with poor physical health: This was a discrete variable expressed as days,

and based on the question "Now thinking about your physical health, which includes physical illness and injury, for how many days during the past 30 days was your physical health not good?." For purpose of the analyses, this variable was redefined into a categorical variable as follows: 1) ≥ 14 days, 2) 1-13 days, 3) none (reference group).

Days with limited activity: This was a discrete variable expressed as days, and based on the question "During the past 30 days, for about how many days did poor physical or mental health keep you from doing your usual activities, such as self-care, work, school or recreation?." For the analyses, this variable was redefined into a categorical variable as follows: 1) ≥14 days, 2) 1-13 days, and 3) none (reference group).

All-causes and CVD mortality: The all-cause mortality variable was defined consistent with NCHS standards. Among participants in the NHANES III file, those that were found in the NHANES III Linked Mortality public-use file were considered dead, but if the person was not found in the file than the person was assumed alive.[113, 117] Briefly, this linkage was conducted by the NCHS and was done by a probabilistic match of information from participants aged 17 years or older in NHANES III with information from the National Death Index through December 31, 2000 to determine mortality status. More detail about the matching on mortality conducted by NCHS can be found elsewhere.[113, 117] Verification of correct matches was also conducted by NCHS staff. The underlying causes of death were based on the *International Classification of Diseases (ICD), 9th and 10th Revision Clinical Modification* and were grouped by the NCHS staff into a standard list of 113 death categories. The CVD mortality variable was defined based on the ICD-10 variable for CVD mortality, and coded as: 1) yes, and 2) no. The yes category corresponds to ICD-10 deaths codes: I10-I13, I20-I25, I44-I49, I50, I60-I69, and

I70-I78.[113, 117] The no category corresponds to anyone who died from another cause.

Person-years of follow-up is included as a variable in the NHANES III linked mortality

data file and were calculated by NCHS staff by subtracting the NHANES III examination

date (as listed in the NHANES III data file) from the date of follow-up (when the death

status was ascertained).

Desire to lose weight: This was a categorical variable based on the question

"Would you like to weigh less, about the same, or more." For the purposes of the present

analyses, this variable was defined as: 1) less, and 2) about the same or more (reference

group).

Employment status: This was a categorical variable based on the question "Did

you work last week (at a job or business)?" This variable was defined as: 1) yes, and 2)

no (reference group).

Numbers of hours worked: This was a numeric variable expressed in hours, based

on the question "How many hours did you work last week at all jobs or businesses?"

Along with using this variable as a numeric variable, it was also categorized into three

categories: 1) 1-20 hours (to include those with part-time or less), 2) 21-40 (to include

those with more than a part-time and inclusive of full-time, and 3) 41+ (to include those

considered generally to be working overtime). These categories were partially based on

the definitions of part-time, full-time, and over-time employment based on federal labor

laws, particularly over-time work which is defined as more than 40 hours by the Bureau

of Labor Statistics.[118, 119]

Number of missed work days (absenteeism): This was a variable expressed in days

based on the question "During the past 12 months, about how many days did you miss

work at a job or business because of an illness or injury (do not include maternity leave)?

Type of occupation: This was a categorical variable based on the NCHS industry codes.[120] This variable was collapsed into four NCHS occupational groups: 1) white collar, 2) blue collar, 3) service, and 4) farm worker, as done in previous studies.[121]

Smoking status: This was a categorical variable created from several variables to have the following categories: 1) non-smoker with undetectable cotinine (reference group), 2) non-smoker with detectable cotinine, and 3) smoker. For this study, smoking status was defined as a combination of self-report and serum cotinine levels. Current smokers were participants who answered yes to the question "Do you smoke cigarettes now?", and/or with serum cotinine levels >15 ng/mL.[122] Participants who answered yes to the question "Does anyone who lives [with you] smoke cigarettes, cigars, or pipes anywhere inside this home?" and/or had had a serum cotinine level at or above the level of detection but below $\leq$ 15 ng/ml, and reported not being current smokers were categorized as being exposed to secondhand smoke. Non-exposed non-smokers were participants who reported being former smokers or never smoking, no reported home secondhand smoke, and had cotinine levels below the detection limit. The detection limit for NHANES III and NHANES 1999-2000 surveys was 0.035 ng/ml, while for NHANES 2001-2004 it was 0.015 ng/ml.[123, 124]

Potential confounding variables

Confounding variables that were tested included the following:

Sex was a categorical variable defined as: 1) female (reference group), 2) male.

Age group in years was a continuous variable that was also categorized as

follows: 1) 20-44 (reference group), 2) 45-64, and 3) 65 or more. Most analyses used the categorized variable in order to be consistent with the other continuous variables that were categorized, such as body mass index.

Race/ethnicity was a categorical variable defined as: 1) non-Hispanic White (reference group), 2) non-Hispanic Black, 3) Hispanic, and 4) other.

Educational level was a categorical variable defined as: 1) less than high school (reference group), 2) high school graduate or equivalent, and 3) > high school.

Marital status was a categorical variable defined as: 1) not married (reference group), and 2) married/with partner. The not married category included responses of single, divorced, and widowed, while the married category included living with partner.

Alcohol consumer was a categorical variable created based on the question "In your entire life did you drink at least 12 drinks of any type of alcoholic beverage?". It was defined as: 1) no, and 2) yes. This question was the only question related to alcohol that was used because of the large number of missing data for the other alcohol-related questions that exist in the NHANES data files.

Insurance status was a categorical variable defined as: 1) uninsured (reference group), and 2) insured.

Physical activity (PA) level was a categorical variable defined as 1) vigorous, 2) moderate, and 3) none (reference group). "Vigorous" was a response of yes to the question: "Over the past 30 days did you do any vigorous PA for at least 10 minutes that caused heavy sweating, or large increases in breathing or heart rate?. "Moderate" was a response of yes to the question "Over the past 30 days did you do any moderate PA for at least 10 minutes that caused heavy sweating, or large increases in breathing or heart

rate?" but no to the question of vigorous physical activity. A response of "no" to both the vigorous or moderate physical activity questions was defined as none. [Note: Although NHANES has other questions related to PA, these were the ones that where consistently asked from 1999-2004 and contained the least missing data.

Measured BMI group (kg/m^2) was continuous variable that was redefined into a categorical variable as: 1) BMI < 25 (reference group), 2) BMI 25-29.9, and 3) BMI $\geq$30.

Take insulin was a dichotomous variable based on the self report of currently taking insulin defined as: 1) yes take insulin, and 2) do not take insulin (reference group).

Take anti-diabetic pills was a dichotomous variable based on self-report of taking diabetic pills defined as: 1) yes take diabetic pills, and 2) do not take diabetic pills (reference group).

Duration of diabetes was a numeric variable expressed in number of years based on the variable for age of diabetes diagnosis and the variable for age.

Hypertension diagnosis was a categorical variable defined as: 1) no (reference), and 2) yes.

Total cholesterol (milligrams (mg)/deciliter(dl) was a continuous variable expressed in mg/dl.

Albumin/creatinine ratio was a continuous variable based on a formula using two other variables: urinary albumin divided by urinary creatinine.

Percent (%) carbs in diet was a continuous variable representing the percent of calories in the diet that came from carbohydrates and was based on a formula using two separate questions in the nutrition file of NHANES: the number of total calories in the diet and the number of calories from carbohydrates consumed (derived based on grams of

carbohydrates consumed in the previous day; a 24 hour diet recall).

Cancer history was a created as a dichotomous variable based on the following two questions: "Has a doctor ever told you had skin cancer?" and "Has a doctor ever told you had other cancer?" A response of yes to either of the questions was defined as: 1) yes, while a response of no to both question was defined as 2) no (reference group).

History of stroke or heart failure was a dichotomous variable based on the following two questions: "Has a doctor ever told you had a stroke" and "Has a doctor ever told you had congestive heart failure." A response of yes to either question was defined as 1) yes, while a response of no to both questions was defined as 2) no (reference group).

Presence of asthma was a dichotomous variable based on the questions: "has a doctor ever told you had asthma" and "do you still have asthma?" A response of yes to both was defined as 1) yes, while a response of no to these two questions was defined as 2) no (reference group).

Sample weight variables

Each sampled person has a sampling weight providing unbiased national estimates. NHANES surveys use an unequal selection probability design. It is particularly important to know the weights when analyzing NHANES data because the NHANES oversamples some subgroups that may be of greater public health interest (e.g. African Americans). Weights are created by calculating a base weight (the reciprocal of the final probability of selection at each stage), then adjusting for non-response, and finally adjusting for post-stratification.[28]

Sample weight variables are calculated by the NCHS in two-year increments. For the continuous NHANES 1999-2002, a sample weight variable was created by NCHS (based on population estimates by the Bureau of the Census before the 2000 Decennial Census counts prior to public release), and can be obtained from the demographic data files for both cycles.[28] The variable name for the weight variable depends on the type of data that are being investigated in the analysis and what data exists for the individuals in the study. Only one weight variable is typed in the command line in the STATA software for the analyses, and this weight variable is the one for the data file with a smaller sample size. For example, the questionnaire data files are those that have data on questions asked to participants while the laboratory files are those files that have data on blood or urine samples drawn from participants. Since it is more feasible and inexpensive to ask only questions in person rather than collect urine and blood samples, not all individuals have laboratory data. If one is interested in data from the laboratory file and an individual exist in both the questionnaire and laboratory files, then the weight variable for the laboratory file would be used.

As detailed in the NCHS documentation,[28] each survey participant has several weights given differences in overall response rates to different survey components (e.g. home interview versus physical examination or laboratory specimen collection) as well as differences in population estimates provided from the Bureau of the Census for each given year. When using the NHANES III data file, we used the NCHS weight variable labeled wtpfhx6, which is the weight variable to be used for survey participants who had not only in-person interview data but also examination and laboratory data.[125]

Because we analyzed pooled NHANES data across years 1999 to 2004, we created a 6-year sample weight variable for these analyses. In addition, we also created a 4-year sample weight for analyses involving data from survey years 2001-2004. These variables had to be created since NHANES data files only contain 2-year sample weights and a 4 year sample weight for NHANES 1999-2004. The 6-year (1999-2004) sample weight variable was created as follows: 1) the 4-year sample weight variable created by NCHS staff for participants sampled from 1999-2002 (labeled by NCHS as MEC4YR) was downloaded, 2) the 2-year sample weight created by NCHS staff for participants sampled from 2003-2004 (labeled by NCHS as MEC2YR) was downloaded, 3) a new variable was created based on the multiplication of the MEC4YR variable by 2/3 if the participant was sampled from the 1999-2000 or the 2001-2002 survey years data file and multiplication by 1/3 if the participant was sampled from the 2003-2004 survey years data file. The multiplication by 2/3 was done for participants sampled from 1999-2002 because they are contributing 2/3 of the total 6 years of weights while the multiplication by 1/3 was done for participants sampled from 2003-2004 because they are contributing only 1/3 of the total 6 years of weights. The 2001-2004 weight variable was created by dividing the weight from the 2001-2002 or the 2003-2004 by half, depending on which of the two 2-year survey cycles the person was sampled in.

Primary sampling units (PSU) and strata variables:

The NHANES uses various methods and survey software to calculate sampling errors, which is used to determine the reliability of the statistics performed. These variables, however, are not disclosed to the public. Variances thus need to be calculated

based on masked variance units (MVUs). Variance units are based on strata and PSU variables. The NCHS created these PSU and strata variables and has them available in all NHANES data files. These variables are labeled sdmvpsu and sdmvstra for the NHANES 1999 to 2004 cycles, and sdppsu6 and sdpstra6 for NHANES III. Both PSU and strata variables are used to provide appropriate adjustment in all statistical models for the complex sample design of the NHANES.

Data management and preparation

The public-use NHANES data files were downloaded from the NCHS website (http://www.cdc.gov/nchs/nhanes.htm). The consistency of variable labels across all cycle years was checked; variable labels were changed if needed. Data files were then appended. Certain variables were redefined in order to allow for appendage. In order to determine the extent of missing data, the presence of outliers (by looking at extreme values outside the upper or lower quartiles in boxplots) , and any non-normality issues, frequency distributions were performed for discrete variables, and mean, standard deviation, and range for continuous variables were checked. Normality plots were also done. Transformations were not performed. Extreme outliers were not found.

Missing data

In addition to variables that are naturally defined as missing because they were left blank, values that were defined as "don't know" were redefined as missing and excluded from the analyses. Following the NCHS rule for missing data, if a variable had less than <10% missing data, that variable was used. However, if there was more missing

data for a variable, sample characteristics were compared in terms of demographic variables (e.g. age, sex, race/ethnicity) to determine if there were any nonrandom missing data pattern that may indicate selection bias. If there were no differences in demographic characteristics, then an imputation method was proposed to be used to replace missing values. In the present analyses however, none of the variables used had more than 10% missing data (responses of "don't know" or left blank) and therefore imputation method not used. Variables that were omitted in the analyses were those that were asked of only a small portion of survey participants. The variables omitted from the analyses included variables related to the frequency and duration of physical activity and variables related to the frequency and the number of alcohol beverages consumed.

Model criteria and strategy

The purpose or goal of the present study was to test the proposed hypotheses derived from the research questions. Because for the first research question there was a relatively small sample and in order to avoid an over-parameterized model,[126, 127] parsimonious models (i.e. models with less variables) that would best explain the relationship between the main independent (predictor) variables and the outcome variable while controlling for potential confounders were sought. In general, the more variables added to a model, the more significant the model is or the better fit of the model; at the same time, this may lead to confusion in the interpretation of the findings and to complex interactions.[126, 127 128] In this study, model evaluation was not based on the overall fit or model significance, but rather the inclusion of the most important variables that if were otherwise omitted could lead to a type I error (false positive).[126, 127 128]

This method of model evaluation allowed for a parsimonious model with mainly important and clinically relevant variables and ease of interpretation of findings. Variables were added in a step-wise fashion (i.e. one at a time) with the main independent variable added first. At each time a variable was added, any changes in the coefficients and the p-value of the main independent variables as well as other covariates of interest in the model were noted; changes of 20-25% of the coefficients were considered meaningful.[126] Thus, the assessment of the interactions and/or confounding was possible using this approach. The approach used in the present analyses is not the same as stepwise modeling. This stepwise modeling approach is mainly concerned with the inclusion of variables that are statistically significant.[126, 127]

Variables that were candidates for inclusion in the models were those that were pre-determined based on the literature to have clinical significance and/or that were significant at the 0.20 alpha level in univariable analyses. The 0.20 alpha level was chosen in order to allow for inclusion of variables that were perhaps clinically significant but not statistically significant at a stricter 0.05 alpha level; the age group, race/ethnicity, and sex variables were automatically included in all models regardless of statistical significance.[126, 127]

However, since a parsimonious model was sought and because by definition a confounder has to be associated with both the main predictor variable and the outcome variable, only variables associated with both were used in the multivariable regression analyses (either logistic, multinomial, or Poisson models). For example, since occupational group was one of the potentially new factors of interest which was associated with glycemic control at the univariable level, variables associated with both

occupational group and with glycemic control at the univariable level were included in the multivariable logistic regression model as well as were age group, sex, and race/ethnicity.

Interaction terms

Several potential interactions were tested based on other studies that found them to be important.[36, 41, 55, 129, 130] The following interactions were tested for each hypothesis:

Hypotheses 1a-1d:

- o 'age group'*sex
- o 'age group'*race/ethnicity
- o race/ethnicity*education
- o race/ethnicity*sex
- o physical activity*sex
- o occupation*marital status
- o desire to lose weight*sex.

Hypotheses 2a-2c:

- o 'age group'*sex
- o 'age group'*race/ethnicity
- o race/ethnicity*education
- o race/ethnicity*sex,
- o 'suboptimal glycemic control'*sex'
- o 'borderline glycemic control'*sex
- o 'poor glycemic control'*sex.

Hypotheses 3a-3b:

- o 'age group'*sex

- o age group*race/ethnicity

- o race/ethnicity*sex

- o sex*education,

- o 'suboptimal glycemic control'*sex'

- o 'borderline glycemic control'*sex

- o 'poor glycemic control'*sex, and sex*'BMI category'

Only statistically significant interactions at the 0.05 alpha level were included in the adjusted models or discussed in the results sections for each hypothesis.

Statistical analyses

All analyses were conducted using STATA 10.0 statistical software (College Station, TX, USA) because of its ability to adjust for the complex sample survey design of the NHANES. The type I error was set at 0.05, and an observed statistic was deemed statistically significant if the association was at or below the alpha 0.05 level. Several statistical analyses were performed after the preliminary analyses. Preliminary analyses included assessing if the assumptions to perform the regression analyses were met. For example, before performing multivariable logistic regression analyses, the linearity in the residuals was assessed using residual versus predicted plots and scatter plots, for each predictor variable. The assumption of independence and randomness was checked by looking at any patterns in the residuals. Nevertheless, independence and randomness are

more likely because this was a cross-sectional study (except for the mortality analyses) with a multi-stage complex sampling frame that includes a random selection of participants at the first stage of sampling. The proportionality assumption for Cox proportional hazard analyses was also assessed. The SVYSET and SVY commands in STATA, for indicating survey analyses, take into account the complex survey sample, and were used for all univariable and multivariable regression analyses.

In general, first descriptive statistics and other preliminary analyses such as chi-square tests were performed.[131] Chi-square tests were done in order to evaluate if there were statistically significant differences in the percentage of the outcome variables based on the independent variable. In addition, cross-tabulations allowed for the assessment of any cell sizes of less than 5 that could possibly lead to unstable regression estimates or prevent regression models to run properly. Second, univariable regression analyses were performed in order to evaluate the un-adjusted relationship (e.g. odds ratio or hazards rate) between the outcome variable and each independent variable. Third, multivariable regression analyses were performed with only clinically and/or statistically significant covariates included in the final models while controlling for potential confounders.[127] Dummy variables were automatically created by STATA for categorical variables when performing regression analyses. However, when testing interactions, dummy variables were created manually (e.g. a variable with 4 categories would have 3 dummy variables, each dummy variable as 0 vs. 1).

Where the literature suggested the need for stratified analyses (e.g. sex-specific analyses) or the use of variables in a different fashion (e.g. numerical versus categorical) or using different categorization, analyses in addition to the ones proposed were also

conducted. Moreover, mediation tests, such as the Sobel test,[132] were also performed to help explain the association (or indirect effect) between the main independent variable being tested and the outcome variable. The indirect effect of the mediator is the product of path "a" (the estimate of the independent variable predicting the mediator) and "b" (the estimate of the mediator predicting the dependent variable). This test is conducted by first determining the standard error of the indirect effect, dividing the estimate of the path "ab" with the standard error of the indirect effect; a Z test is then used comparing this ratio with a critical value for a given alpha level.[132] Statistical analyses for each hypothesis derived from the different research questions are described below.

Hypothesis 1a

It was hypothesized that individuals with type 2 diabetes who worked more hours were more likely to have suboptimal, borderline, and/or poor glycemic control, after controlling for potential confounders.

Hypothesis 1b

It was hypothesized that individuals with type 2 diabetes who had occupations which are known for having stricter or demanding time schedules (i.e. service workers and blue collar workers relative to white collar workers) were more likely to have suboptimal, borderline, and/or poor glycemic control, after controlling for potential confounders.

Hypothesis 1c:

It was hypothesized that individuals with type 2 diabetes who were exposed to secondhand smoke that were self-reported non-smokers were more likely to have suboptimal, borderline, and/or poor glycemic control compared to non-smokers not exposed to secondhand smoke, after controlling for potential confounders.

Hypothesis 1d:

It was hypothesized that individuals with type 2 diabetes who desired to lose weight were more likely to have suboptimal, borderline, and/or poor glycemic control, after controlling for potential confounders.

The NHANES 1999-2004 merged data file was used to test hypotheses 1a-1d using the sample of adults classified with type 2 diabetes. Only the employed sample, based on self-report of being employed, was used when testing the association between glycemic control and occupation and work hours. However, when using the desire to lose weight and the secondhand smoke exposure as independent variables, the full sample (i.e. regardless of employment) was used.

Chi-square tests were first conducted cross-tabulating the independent variables separately with each of the three measures of glycemic control status (i.e. suboptimal, borderline, and poor glycemic control). For the independent variables that were continuous, t tests were conducted instead of chi-square tests; these variables had normal distributions. After these preliminary analyses, univariable and multivariable logistic regression analyses were performed since the dependent variables were each dichotomous variables. The LOGISTIC command in STATA was used. The dependent variables were suboptimal, borderline, and poor glycemic control (0 if no, 1 if yes).

Hypothesis 2a

It was hypothesized that individuals with type 2 diabetes who had suboptimal, borderline, and poor glycemic control would be more likely to have poor health-related quality of life (HRQOL) (i.e. poor self reported general health, more days with poor mental and physical health, and more days of inactivity in the past 30 days), after controlling for potential confounders.

The NHANES 2001-2004 data were used to test hypothesis 2a, using the sample of adults classified with type 2 diabetes. Chi-square tests were first conducted cross-tabulating separately the four HRQOL measures with the three variables for glycemic control status. Univariable analyses for the general health variable were performed since it was a dichotomous variable. Univariable and multivariable multinomial (polychotomous) logistic regressions were then performed for dependent variables for number of days of poor mental health, poor physical health, and limited activity since these dependent variables are each categorical with three levels. The MLOGIT command in STATA was used, which does not assume ordering of the dependent variable categories. The dependent variables are the four HRQOL measures [1) general health, 2) days of poor mental health, 3) days of poor physical health, and 4) days of limited activity due to poor health in the past 30 days]). For the general health variable, 'excellent health, very good, and good' was the reference group, and it was compared to a response of 'fair or poor health'. For the 'days or poor mental health' and 'days of poor physical health' variables, '0 days with poor health' was the reference group, and it was compared to '1-13 days of poor health' and '$\geq$14 days of poor health'. Similarly, for the

'days with limited activity' variable, '0 days with inactivity' was the reference group, and it was compared to '1-13 days of inactivity' and '≥14 days of inactivity'.

Hypothesis 2b

It was hypothesized that individuals with type 2 diabetes who had suboptimal, borderline, and poor glycemic control would have a greater number of missed work days in the past 12 months, after controlling for potential confounders.

The NHANES 1999-2004 data were analyzed using the sample of adults classified with type 2 diabetes. Univariable and multivariable Zero Inflated Poisson (ZIP) regression analyses were performed since the dependent variable, missed work days, was a count variable associated with rare events. The variable missed work days also showed over-dispersion (i.e., the mean was larger than the variance, with dispersion index or variance-to-mean ratio [VMR]) of 126) and excess zeros (over 50% were zero). Zero-inflated Poisson (ZIP) regression models were used because, unlike traditional Poisson regression, this analytic approach is robust even in the presence excess zeros and over-dispersions.[133, 134] The ZIP regression protocol was used for these analyses because STATA is capable of incorporating adjustments for the NHANES complex sample survey design.[133, 134]

Hypothesis 2c

It was hypothesized that individuals with type 2 diabetes who had suboptimal, borderline, and poor glycemic control would be less likely to be employed, after controlling for confounders.

The NHANES 1999-2004 merged data file was used to test hypothesis 2c, using all adults classified with type 2 diabetes. Chi-square tests were first conducted, cross-tabulating employment status and the three glycemic control variables separately. Univariable and multivariable logistic regression analyses were then performed since the dependent variable was a dichotomous variable, employed [1) yes, 2) no (reference group)]. The LOGISTIC command in STATA was used.

Hypotheses 3a

It was hypothesized that individuals with type 2 diabetes who had suboptimal, borderline, and poor glycemic control would have a greater risk of all-cause mortality, after controlling for potential confounders.

The NHANES III (1988-1994) data file was used to test hypothesis 3a, using all adults classified with type 2 diabetes. Cox proportional hazards regression analyses were performed since the dependent variable was time to death (the event of interest) and the death indicator was defined as 1 if the person died, and 0 if otherwise (event-free or censored). The STCOX command in STATA was used.

Hypotheses 3b

It was hypothesized that individuals with type 2 diabetes who had suboptimal, borderline, and poor glycemic control would have a greater CVD mortality risk, after controlling for potential confounders.

The NHANES III (1988-1994) data file was used to test hypothesis 3a, using all adults classified with type 2 diabetes. Cox proportional hazards regression analyses were

performed since the dependent variable was time to death (the event of interest) and the

death indicator was defined as 1 if the person died, and 0 if otherwise (event-free or

censored). The STCOX command in STATA was used.

CHAPTER IV.

RESULTS

<u>Overview</u>

All statistical analyses for the present study are described for adults with type 2

diabetes and were conducted using weighted statistics and using STATA software 10.0.

Table 1 provides a summary of the STATA commands used in this study. Descriptive

statistics for all NHANES datasets used are shown first. For ease of presentation (e.g. to

avoid very long tables) descriptive tables and tables of preliminary analyses (e.g. cross-

tabulations) are generally divided into the following sections: 1) demographics, 2)

potentially new risk factors, and 3) health indicators and behaviors. Following these

tables, the main results (i.e., multivariable regression models) are presented based on the

research question and hypothesis tested. Results are divided into sections based on the

outcome variable. For example, for hypotheses 1a-1d, 2a, and 3a-3b, the results are

shown based on the glycemic control variable used (i.e. suboptimal, borderline, or poor

glycemic control). For research question 2a, the results are shown based on the variable

for HRQOL used (i.e. self-reported general health, poor mental or physical health, and

days of inactivity). The results for each hypothesis are embedded in the section for that

hypothesis. A summary of results for each research question is also included at the end of

the results for that research question.

Table 1. List of key STATA commands used in the present study	
STATA Command	Purpose
svy	Indicates analyses of surveys, weighted analyses
svyset	Sets all future STATA commands to be using weighted analyses of survey data
svy: tab	For cross-tabulations of weighted analyses of survey data
stset	Sets all future STATA commands to be using weighted mortality analyses of survey data. For example the following commands were written in STATA: svyset sdmvpsu [pweight=mec6yr], strata (sdmvstra)
svy: mean	For means of weighted analyses of survey data
svy: reg	For univariable and multivariable regression analyses of weighted analyses of survey data
svy: logistic	For univariable and multivariable logistic regression analyses of weighted analyses of survey data
st cox	For Cox-proportional analyses of weighted analyses of survey data
svy: mlogit	For multinomial logistic regression analyses of weighted analyses of survey data
svy: zip	For Zero Inflated Poisson (ZIP) regression analyses of weighted analyses of survey data
pweight	Indicates that a weight will be used in the analyses, precedes the weight variable used
sdmvpsu	Indicates that a psu variable is being used in the analyses
strata	Indicates that a strata variable will be used in the analyses, precedes the strata variable used
xi:	Indicates that categorical variables will be used in the analyses and tells STATA to automatically create dummy variables for the categorical variables. For example the following commands were written in STATA: xi: svy, subpop (if adultdiabetic): logistic suboptimala1c i.workhours
i.	Must precede the categorical independent variable being used and indicates that the variable should be made into dummy variables automatically (i.e. not manually) by STATA software
subpop	Indicates that the analyses will only be using a subsample of the entire date set file and usually follows the "svy" command

<u>General characteristics of study sample</u>

The general characteristics of the study sample for all NHANES data files are described in Tables 2a-2d. A total of 1273 individuals classified as type 2 diabetics aged 20 years or older who participated in the NHANES surveys anytime from 1999-2004 were included in the study. Of these, 384 (28.5%) were employed (at a job or business in the prior week). In the 2001-2004 NHANES survey period, there were a total of 827 individuals classified as type 2 diabetes, aged 20 years or older, while there were a total of 1381 individuals with type 2 diabetes, aged 20 years and older, who participated in NHANES III (1988-1994) and who had mortality data available. There was a fairly equal representation of males and females across all NHANES.

The mean age across all NHANES data files ranged from 53 (in the employed NHANES 1999-2004 sample) to 65 (in the NHANES III sample). The mean duration of diabetes ranged from 8.7 years (employed NHANES 1999-2004 sample) to 13.2 years (NHANES 2001-2004 sample). Furthermore, over half of the study sample had at least a high school education irrespective of survey period. The sample had a slightly greater percentage of individuals who were married or living with a partner versus single, divorced or widowed across all survey periods. The majority of the sample across all NHANES survey periods was overweight or obese (79.3 to 85.2%). In the NHANES 1999-2004, among all adults with type 2 diabetes, there were 671 (52.7%) with suboptimal glycemic control (HbA1c $\geq$7), 449 (42.7%) with borderline glycemic control (i.e. 7$\geq$ HbA1c < 9), and 222 (17.4%) with poor glycemic control (HbA1c $\geq$9). In the employed NHANES 1999-2004 sample, there were 216 (58.5%) adults with suboptimal glycemic control, 134 (46.7%) with borderline glycemic control, and 82 (22.2%) with

poor glycemic control. In the NHANES 2001-2004, there were 423 (48.0%) adults with

suboptimal glycemic control, 289 (38.7%) with borderline glycemic control, and 134

(15.2%) had poor glycemic control. In the NHANES III data file, there were 507 (43.2%)

adults with suboptimal glycemic control, 204 (23.4%) with borderline glycemic control,

and 303 (25.8%) with poor glycemic control. There were a total of 600 (43.5%) deaths

from 1986 to 2000 among adults with type 2 diabetes sampled in NHANES from 1986-

2000. Of these deaths, 315 (52.5%) were due to cardiovascular disease.

Table 2a. Demographic characteristics among individuals classified with type 2 diabetes, 20+ years of age, NHANES III (1988-1994) and NHANES 1999-2004

	NHANES[a]			
	All Adults			**Employed Adults**
	1988-1994 (n=1381)	**2001-2004 (n=921)**	**1999-2004 (n=1348)**	**1999-2004 (n=384)**
Characteristic	**Frequency (Percent)**	**Frequency (Percent)**	**Frequency (Percent)**	**Frequency (Percent)**
Sex				
Female	755 (54.7)	459 (49.8)	678 (50.3)	157 (40.9)
Male	626 (45.3)	462 (50.2)	670 (49.7)	227 (59.1)
Age group				
20-44	124 (9.0)	91 (9.9)	128 (9.5)	86 (22.4)
45-64	483 (35.0)	356 (38.7)	522 (38.7)	241 (62.8)
65+	774 (56.1)	474 (51.5)	698 (51.8)	57 (14.8)
Race/ethnicity				
Non-Hispanic White	563 (40.8)	387 (42.0)	513 (38.1)	132 (34.4)
Non-Hispanic Black	365 (26.4)	208 (22.6)	326 (24.2)	101 (26.3)
Hispanic	402 (29.1)	287 (31.2)	454 (33.7)	134 (34.9)
Other	51 (3.7)	39 (4.2)	55 (4.1)	17 (4.4)
Education^				
< HS	861 (63.1)	397 (43.2)	657 (48.8)	128 (33.3)
HS	287 (21.0)	201 (21.9)	277 (20.6)	85 (22.1)
> HS	216 (15.8)	322 (35.0)	412 (30.6)	171 (44.5)
Marital status				
Not married/divorced/widowed	547 (39.8)	335 (36.4)	477 (36.6)	99 (26.9)
Married/living with partner	829 (60.3)	586 (63.6)	826 (63.4)	269 (73.1)

Table 2a (continue)

	All Adults			Employed Adults
	1988-1994 (n=1381)	2001-2004 (n=921)	1999-2004 (n=1348)	1999-2004 (n=384)
	Frequency (Percent)	Frequency (Percent)	Frequency (Percent)	Frequency (Percent)
Employment status				
Unemployed	--	656 (71.3)	963 (71.5)	---
Employed	--	264 (28.7)	384 (28.5)	---
Insurance status				
Uninsured	--	91 (10.0)	150 (11.3)	73 (19.3)
Insured	--	823 (90.0)	1,182 (88.7)	306 (80.7)

[a]Sample sizes do not always equal column totals due to missing data.

^ HS=High School

Table 2b. Presence of potentially new risk factors among individuals classified with type 2 diabetes, 20+ years of age, NHANES III (1988-1994) and NHANES 1999-2004

	NHANES[a]			
	All Adults			Employed Adults
	1988-1994 (n=1381)	2001-2004 (n=921)	1999-2004 (n=1348)	1999-2004 (n=384)
Characteristic	Frequency (Percent)	Frequency (Percent)	Frequency (Percent)	Frequency (Percent)
Smoking and secondhand smoke (SHS) exposure				
Non-Smoker & no SHS exposure	185 (15.8)	187 (21.4)	357 (28.5)	77 (21.0)
Non-Smoker with SHS exposure	685 (58.3)	485 (55.5)	629 (50.2)	195 (53.3)
Smoker	306 (26.0)	202 (23.1)	267 (21.3)	94 (25.7)
Weight desirability				
Stay the same or gain weight	---	326 (35.4)	498 (37.0)	113 (29.4)
Lose weight	---	595 (64.6)	849 (63.0)	271 (70.6)
Hours worked				
0-20 hours	---	---	---	54 (14.8)
21-40 hours	---	---	---	188 (51.5)
41+ hours	---	---	---	123 (33.7)
Occupational group				
White collar worker	---	---	---	177 (46.2)
Service worker	---	---	---	78 (20.3)
Farm worker	---	---	---	10 (2.6)
Blue collar worker	---	---	---	118 (30.8)

[a]Sample sizes do not always equal column totals due to missing data.

Table 2c. Presence of glycemic control group characteristics among individuals classified with type 2 diabetes, 20+ years of age, NHANES III (1988-1994) and NHANES 1999-2004

| | NHANES[a] | | | |
| | All Adults | | | Employed Adults |
Characteristic	1988-1994 (n=1381) Frequency (Percent)	2001-2004 (n=921) Frequency (Percent)	1999-2004 (n=1348) Frequency (Percent)	1999-2004 (n=384) Frequency (Percent)
Suboptimal glycemic control[b]				
No	666 (56.8)	458 (52.0)	602 (47.3)	153 (41.5)
Yes	507 (43.2)	423 (48.0)	671 (52.7)	216 (58.5)
Borderline glycemic control[c]				
No	666 (76.6)	458 (61.3)	602 (57.3)	153 (53.3)
Yes	204 (23.4)	289 (38.7)	449 (42.7)	134 (46.7)
Poor glycemic control[d]				
No	870 (74.2)	747 (84.8)	1051 (82.6)	287 (77.8)
Yes	303 (25.8)	134 (15.2)	222 (17.4)	82 (22.2)

[a]Sample sizes do not always equal column totals due to missing data.
[b]An individual is said to have suboptimal glycemic control if she or he has an HbA1c of $\geq$ 7.0%.
[c]An individual is said to have suboptimal glycemic control if she or he has an HbA1c 7-8.9%. In these analyses, individuals with an HbA1c $\geq$9.0% are excluded from the analyses.
[d]An individual is said to have suboptimal glycemic control if she or he has an HbA1c $\geq$9.0%.

Table 2d. Categorical health indicators and behavioral characteristics among individuals classified with type 2 diabetes, 20+ years of age, NHANES III (1988-1994) and NHANES 1999-2004

| | NHANES[a] | | | |
| | All Adults | | | Employed Adults |
Characteristic	1988-1994 (n=1381) Frequency (Percent)	2001-2004 (n=921) Frequency (Percent)	1999-2004 (n=1348) Frequency (Percent)	1999-2004 (n=384) Frequency (Percent)
History of cardiovascular disease				
No	---	662 (71.9)	937 (69.5)	338 (88.0)
Yes	---	259 (28.1)	411 (30.5)	46 (12.0)
Cancer diagnosis				
No	1225 (88.7)	---	---	---
Yes	156 (11.3)	---	---	-
Alcohol Use				
No	--	370 (42.8)	136 (36.7)	555 (44.0)
Yes	--	494 (57.2)	235 (63.3)	707 (56.0)
Physical activity				
None	---	418 (51.8)	634 (54.3)	170 (45.2)
Moderate	---	270 (33.5)	355 (30.4)	115 (30.6)
Vigorous	---	119 (14.8)	178 (15.3)	91 (24.2)
Take anti-diabetic Pills				
No	690 (50.2)	254 (27.7)	375 (27.9)	114 (29.7)
Yes	685 (49.8)	664 (72.3)	969 (72.1)	270 (70.3)

Table 2d (continue)

	All Adults			Employed Adults
	1988-1994 (n=1381)	2001-2004 (n=921)	1999-2004 (n=1348)	1999-2004 (n=384)
	Frequency (Percent)	Frequency (Percent)	Frequency (Percent)	Frequency (Percent)
Take insulin				
No	972 (70.4)	727 (78.9)	1052 (78.1)	323 (84.1)
Yes	408 (29.6)	194 (21.1)	295 (21.9)	61 (15.9)
Table 2d (continue)				
Family history of diabetes				
No	---	218 (24.5)	331 (25.3)	60 (15.9)
Yes	---	672 (75.5)	976 (74.7)	316 (84.0)
Hypertension diagnosis				
No	596 (43.3)	297 (32.3)	419 (31.2)	169 (44.0)
Yes	782 (56.8)	624 (67.8)	929 (68.9)	215 (55.0)
BMI category				
Normal/under weight	253 (20.7)	143 (16.5)	210 (16.6)	55 (14.8)
Overweight	475 (38.9)	299 (34.6)	442 (34.9)	128 (34.3)
Obese	494 (40.4)	423 (48.9)	616 (48.6)	190 (50.9)

[a]Sample sizes do not always equal column totals due to missing data.

Table 2e. Numerical health indicators and behavioral characteristics among individuals classified with type 2 diabetes, 20+ years of age, NHANES III (1988-1994) and NHANES 1999-2004

	NHANES[a]			
	All Adults			Employed Adults
	1988-1994 (n=1381)	2001-2004 (n=921)	1999-2004 (n=1348)	1999-2004 (n=384)
Characteristic	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)
Diabetes duration (years)	10.61 (9.6)	13.19 (15.0)	12.79 (14.3)	8.57 (10.4)
Total cholesterol (mg/dl)	---	199.77 (47.8)	200.27 (47.1)	201.64 (44.6)
Albumin/Creatinine Ratio	---	20.34 (95.9)	25.17 (110.2)	21.23 (136.9)
Percent calories from carbohydrates	---	49.44 (12.1)	49.51 (12. 2)	47.73 (12.2)

[a]Sample sizes do not always equal column totals due to missing data.

<u>Potentially new risk factors and glycemic control</u>

The first research question was whether the work hours, the type of occupation, secondhand smoke exposure, and the desire to lose weight were associated with suboptimal, borderline, and poor glycemic control among individuals with type 2 diabetes who were 20 years of age or older. It was hypothesized that individuals who worked greater number of hours (i.e. 20-40 hours or more than 40 hours relative to less than 20 hours), had occupations which are known for having stringent or demanding time schedules (i.e. service worker and blue collar workers relative to white collar workers), were exposed to secondhand smoke, and desired to lose weight were more likely to have suboptimal and/or poor glycemic control, after for potential confounders.

The associations between categorical independent variables involved in hypothesis 1a-1d and suboptimal, borderline poor, and poor glycemic control among the employed sample of adults with type 2 diabetes are tabulated and the significance of the chi-square statistics are presented in Tables 3a-3c. In addition, the means of numerical independent variables involved in hypothesis 1a-1d and significance of the t-test statistics are presented in Table 3d. Furthermore, univariable logistic regression analyses for suboptimal, borderline, and poor glycemic control among the employed sample of adults with type 2 diabetes are presented in Table 4a-4c. Odds ratios are presented along with 95% confidence intervals and the corresponding p values. P values are shown only for tables 4a-4d since p values at the 0.20 alpha level in the univariable analyses were used to determine which variables were to be included in subsequent multivariable analyses.

Table 3a. Cross-tabulations[†] of demographic variables with suboptimal (HbA1c $\geq$ 7.0%), borderline (HbA1c $\geq$ 7.0-8.9%), and poor (HbA1c $\geq$ 9.0%) glycemic control, employed adults classified with type 2 diabetes, NHANES 1999-2004

	Glycemic Control*					
	Suboptimal**		Borderline**		Poor**	
	N (%)		N (%)		N (%)	
	No	Yes	No	Yes	No	Yes
Sex						
Male	93 (46.2)	131(53.8)	93(58.1)	77 (41.9)	170(77.0)	54 (23.0)
Female	60 (49.5)	85 (50.5)	60 (60.0)	57 (40.0)	117(85.3)	28 (14.7)
Age group						
20-44	29 (42.6)	51 (57.4)	29 (58.8)	27 (41.2)	56 (72.4)	24 (27.6)
45-64	93 (47.7)	140(52.3)	93 (59.0)	85 (41.0)	178(80.7)	55 (19.3)
65+	31 (58.5)	25 (41.5)	31 (60.7)	22 (39.3)	53 (96.4)	3 (3.6)
Race/ethnicity						
Non-Hispanic White	**72 (55.7)**	**56 (44.3)**	72 (65.3)	39 (34.7)	**111(85.3)**	**17 (14.7)**
Non-Hispanic Black	**29 (30.7)**	**63 (69.3)**	29 (44.2)	36 (55.9)	**65 (69.5)**	**27 (30.5)**
Hispanic	**46 (40.1)**	**87 (59.9)**	46 (57.6)	52 (42.4)	**98 (69.6)**	**35 (30.4)**
Other	**6 (30.0)**	**10 (70.0)**	6 (36.6)	7 (63.6)	**13 (82.2)**	**3 (17.8)**
Education^						
< HS	**39 (33.5)**	**86 (66.5)**	39 (46.6)	49 (53.4)	88 (72.0)	37 (28.0)
HS	**40 (51.5)**	**40 (48.5)**	40 (65.0)	26 (35.0)	66 (79.3)	14 (20.7)
> HS	**74 (50.9)**	**90 (49.1)**	74 (60.8)	59 (39.2)	133(83.7)	31 (16.3)
Marital status						
Not married	109(47.7)	152(52.3)	109(57.8)	94 (42.2)	203(82.5)	58 (17.5)
Married/living with partner	38 (45.8)	54 (54.2)	38 (61.7)	34 (38.3)	72 (74.3)	20 (25.7)
Insurance Status						
Uninsured	32 (46.1)	40 (53.9)	32 (76.6)	120(57.8)	48 (60.1)	24 (39.9)
Insured	120(48.2)	172(51.8)	16 (23.4)	115(42.2)	235(83.3)	57 (16.7)

*row percentages=100, percentages do not reflect sample size in each cell due to weighted analyses.
** Statistically significant differences at the 0.05 level appear in bold.
[†]Designed based Pearson statistics performed to account for complex survey design.
^ HS=High School

Table 3b. Cross-tabulations[†] of potentially new risk factors variables with suboptimal (HbA1c $\geq$ 7.0%), borderline (HbA1c $\geq$ 7.0-8.9%), and poor (HbA1c $\geq$ 9.0%) glycemic control, Employed adults classified with type 2 diabetes, NHANES 1999-2004

	Glycemic Control*					
	Suboptimal**		Borderline**		Poor**	
	N (%)		N (%)		N (%)	
	No	Yes	No	Yes	No	Yes
Smoking and Secondhand smoke (SHS) exposure						
None smoker/& no SHS	30 (48.4)	47 (51.6)	30 (57.0)	31 (43.0)	61 (88.0)	16 (15.0)
Non-smoker with SHS	81 (47.3)	111(52.7)	81 (60.0)	67 (40.0)	148 (78.9)	44 (21.1)

	Glycemic Control*					
	Suboptimal**		Suboptimal**		Suboptimal**	
	N (%)		N (%)		N (%)	
	No	Yes	No	Yes	No	Yes
Smoker	38 (45.1)	53 (54.9)	38 (57.1)	34 (43.0)	72 (79.0)	19 (21.0)
Weight Desirability						
Stay the same or gain weight	48 (57.6)	36 (42.4)	48 (57.6)	36 (42.4)	84 (76.3)	27 (23.7)
Lose weight	105 (59.8)	98 (40.2)	105(59.8)	98 (40.3)	203 (81.5)	55 (18.5)
Hours of worked group						
0-20 hours	26 (61.50	26 (38.5)	26 (68.3)	19 (31.7)	45 (90.0)	7 (10.0)
21-40 hours	74 (49.8)	106(50.2)	74 (62.4)	62 (37.6)	136 (79.7)	44 (20.3)
41+ hours	44 (38.6)	75 (61.4)	44 (50.8)	47 (49.2)	91 (76.0)	28 (24.0)
Occupational group						
White collar worker	75 (53.1)	91 (46.9)	75 (62.2)	61 (37.8)	**136 (85.5)**	**30 (14.6)**
Service worker	28 (42.5)	46 (57.5)	28 (52.1)	31 (47.9)	**59 (81.7)**	**15 (18.3)**
Farm worker	1 (4.9)	9 (95.1)	1 (12.5)	6 (87.5)	**7 (38.9)**	**3 (61.1)**
Blue collar worker	48 (41.5)	70 (58.6)	48 (58.0)	36 (42.0)	**84 (71.5)**	**34 (28.5)**

*row percentages=100, percentages do not reflect sample size in each cell due to weighted analyses.
** Statistically significant differences at the 0.05 level appear in bold.
[†]Designed based Pearson statistics performed to account for complex survey design.

Table 3c. Cross-tabulations[†] of health indicators and behaviors variables with suboptimal (HbA1c $\geq$ 7.0%), borderline (HbA1c $\geq$ 7.0-8.9%), and poor (HbA1c $\geq$ 9.0%) glycemic control, employed adults classified with type 2 diabetes, NHANES 1999-2004

	Glycemic Control*					
	Suboptimal**		Borderline**		Poor**	
	N (%)		N (%)		N (%)	
	No	Yes	No	Yes	No	Yes
History of CVD						
No	132(47.2)	192(52.8)	132(60.1)	117(39.9)	249(78.5)	75 (21.5)
Yes	21 (49.0)	24 (51.0)	21 (53.9)	17 (46.1)	38 (91.0)	7 (9.0)
Alcohol Use						
No	49 (42.8)	78 (57.3)	49 (50.7)	51 (49.3)	100(84.4)	27 (15.6)
Yes	101(49.7)	131(50.3)	101(63.3)	81 (36.7)	182(78.5)	50 (21.5)
Physical activity						
None	63 (44.8)	101(55.2)	63 (59.6)	61 (40.4)	124(75.2)	40 (24.8)
Moderate	46 (47.4)	64 (52.6)	46 (54.6)	44 (45.4)	90 (86.8)	20 (13.2)
Vigorous	39 (48.9)	48 (51.1)	39 (60.7)	29 (39.3)	68 (80.6)	19 (19.4)
Take anti-diabetic pills						
No	**62 (57.9)**	**50 (42.1)**	**62 (74)**	**91 (52.6)**	90 (78.3)	22 (21.7)
Yes	**91 (42.6)**	**166(57.4)**	**28 (26)**	**106(47.4)**	197(81.0)	60 (19.0)

Table 3c (continue)

	Glycemic Control*					
	Suboptimal**		Suboptimal**		Suboptimal**	
	N (%)		N (%)		N (%)	
	No	Yes	No	Yes	No	Yes
Take insulin						
No	**140(50.8)**	**171(49.2)**	**140(62.2)**	**107(37.8)**	**247(81.7)**	**64 (18.3)**
Yes	**13 (27.5)**	**45 (72.5)**	**13 (39.0)**	**27 (61.0)**	**40 (70.7)**	**18 (29.3)**
Family history of diabetes						
No	33 (59.4)	26 (40.6)	33 (70.1)	19 (29.9)	52 (84.7)	7 (15.4)
Yes	116(45.4)	186(54.6)	116(56.4)	114(43.6)	230(80.4)	72 (19.6)
Hypertension diagnosis						
No	62 (45.0)	101(55.0)	62 (55.6)	62 (44.4)	124(80.9)	39 (19.1)
Yes	91 (49.6)	115(50.4)	91 (62.5)	72 (37.5)	163(79.4)	43 (20.6)
BMI category						
Normal/under weight	22 (34.7)	33 (65.3)	**22 (49.9)**	**17 (50.1)**	39 (69.5)	16 (30.5)
Overweight	53 (54.1)	71 (45.9)	**53 (71.8)**	**42 (28.2)**	95 (75.4)	29 (24.6)
Obese	75 (46.3)	108(53.7)	**75 (54.7)**	**72 (45.3)**	147(84.7)	36 (15.3)

*row percentages=100, percentages do not reflect sample size in each cell due to weighted analyses.
** Statistically significant differences at the 0.05 level appear in bold.
†Designed based Pearson statistics performed to account for complex survey design.

Table 3d. Mean comparisons for numerical variables with suboptimal (HbA1c $\geq$ 7.0%), borderline (HbA1c $\geq$ 7.0-8.9%), and poor (HbA1c $\geq$ 9.0%) glycemic control, employed adults classified with type 2 diabetes, NHANES 1999-2004

	Glycemic Control*					
	Suboptimal		Borderline		Poor	
Characteristic	Mean (SE)		Mean (SE)		Mean (SE)	
	No	Yes	No	Yes	No	Yes
Diabetes duration	7.07	8.13	7.07	8.22	7.55	8.0
(years)	(1.07)	(0.78)	(1.07)	(1.14)	(0.90)	(0.86)
Total cholesterol (mg/dl)	**197.0**	**211.0**	197.2	198.4	**197.69**	**232.01**
	(6.29)	**(5.02)**	(3.01)	(5.15)	**(2.79)**	**(8.76)**
Albumin/Creatinine	**2.98**	**15.60**	**2.98**	**13.98**	**7.42**	**18.21**
Ratio	**(0.67)**	**(4.87)**	**(0.67)**	**(7.14)**	**(2.91)**	**(5.45)**
Percent calories from	0.47	0.45	0.47	0.46	0.47	0.44
carbohydrates	(0.01)	(0.01)	(0.01)	(0.012)	(0.01)	(0.02)

* Statistically significant differences at the 0.05 level appear in bold.

Table 4a. Univariable logistic regression. Relationships between demographic characteristics with suboptimal (HbA1c $\geq$ 7.0%), borderline (HbA1c $\geq$ 7.0-8.9%), and poor (HbA1c $\geq$ 9.0%) glycemic control, employed adults classified with type 2 diabetes, NHANES 1999-2004

	Glycemic Control		
	Suboptimal	Borderline	Poor
Characteristic	Odds Ratio (95% Confidence Interval), p value	Odds Ratio (95% Confidence Interval), p value	Odds Ratio (95% Confidence Interval), p value
Sex			
Female	1.00	1.00	1.00
Male	1.14 (0.60-2.17), 0.68	0.92 (0.49-1.74), 0.80	1.73 (0.87-3.44), 0.12
Age group			
20-44	1.00	1.00	1.00
45-64	0.81 (0.38-1.76),0.60	0.99 (0.41-2.37), 0.98	0.63 (0.26-1.50), 0.29
65+	0.530 (0.21-1.30), 0.16	0.93 (0.37-2.33), 0.87	0.10 (0.02-0.66), 0.02
Race/ethnicity			
Non-Hispanic White	1.00	1.00	1.00
Non-Hispanic Black	2.84 (1.56-5.17), 0.00	2.37 (1.26-4.49), 0.01	2.55 (1.13-5.7), 0.03
Hispanic	1.88 (1.11-3.12) 0.02	1.38 (0.87-2.20), 0.17	2.54 (1.08-5.97), 0.03
Other	2.94 (0.74-11.64) 0.12	3.28 (0.73-14.72), 0.12	1.26 (0.39-4.06), 0.69
Education[^]			
< HS	1.00	1.00	1.00
HS	0.47 (0.22-1.04),0 .06	0.47 (0.20-1.11), 0.08	1.67 (0.30-1.52), 0.33
> HS	0.49 (0.28-0.84), 0.01	0.56 (0.30-1.01), 0.08	0.50 (0.28-0.89), 0.02
Marital status			
Not married	1.00	1.00	1.00
Married/living with partner	1.08 (0.60-1.93), 0.79	0.85 (0.44-1.65), 0.62	1.64 (0.88-3.04), 0.12
Insurance status			
Uninsured	1.00	1.00	1.00
Insured	0.28 (0.15-0.53), 0.00	2.40 (1.19-4.79), 0.02	0.30 (0.14-0.64), 0.00

[^] HS=high school

Table 4b. Univariable logistic regression. Relationship between potentially new risk factors with suboptimal (HbA1c $\geq$ 7.0%), borderline (HbA1c $\geq$ 7.0-8.9%), and poor (HbA1c $\geq$ 9.0%) glycemic control, employed adults classified with type 2 diabetes, NHANES 1999-2004

	Glycemic Control		
	Suboptimal	Borderline	Poor
Characteristic	Odds Ratio (95% Confidence Interval), p value	Odds Ratio (95% Confidence Interval), p value	Odds Ratio (95% Confidence Interval), p value
Smoking and secondhand smoke (SHS) exposure			
None smoker/& no SHS	1.00	1.00	1.00

Table 4b (continue)

| | Glycemic Control | | |
| | Suboptimal | Borderline | Poor |
	Odds Ratio (95% Confidence Interval), p value	Odds Ratio (95% Confidence Interval), p value	Odds Ratio (95% Confidence Interval), p value
Non-smoker with SHS exposure	1.05 (0.45-2.38), 0.92	1.72 (0.27-11.01), 0.56	1.51 (0.58-3.92), 0.39
Smoker	1.14 (0.45-2.93), 0.77	0.70 (0.288-1.68), 0.41	1.50 (0.52-4.37), 0.45
Weight desirability			
Stay the same or gain weight	1.00	1.00	1.00
Lose weight	0.83 (0.44-1.56), 0.55	0.91 (0.46-1.83), 0.80	0.73 (0.33-1.62), 0.43
Hours of worked group			
0-20 hours	1.00	1.00	1.00
21-40 hours	1.61 (0.77-3.38), 0.20	1.30 (0.52-3.26), 0.57	2.28 (0.59-8.78), 0.22
41+ hours	2.54 (1.24-5.22), 0.01	2.10 (0.93-4.68), 0.07	2.84 (0.72-11.18), 0.13
Occupational group			
White collar worker	1.00	1.00	1.00
Service worker	1.52 (0.77-3.04), 0.89	1.51 (0.67-3.38), 3.57	1.31 (0.49-3.51), 0.58
Farm worker	22.07(2.47-202.11),0.01	11.45 (1.17-112.09), 0.03	9.21 (1.66-51.09), 0.01
Blue collar worker	1.60 (0.85-3.01), 0.14	1.19 (0.57-2.47), 0.64	2.34 (1.05-5.21), 0.04

Table 4c. Univariable logistic regression. Health indicators and behaviors factors associated suboptimal (HbA1c $\geq$ 7.0%), borderline (HbA1c $\geq$ 7.0-8.9%), and poor (HbA1c $\geq$ 9.0%) glycemic control employed adults classified with type 2 diabetes, NHANES 1999-2004

| | Glycemic Control | | |
| | Suboptimal | Borderline | Poor |
Characteristic	Odds Ratio (95% Confidence Interval), p value	Odds Ratio (95% Confidence Interval), p value	Odds Ratio (95% Confidence Interval), p value
CVD history			
No	1.00	1.00	1.00
Yes	0.93 (0.40-2.16), 0.86	1.29 (0.52-3.23), 0.58	0.36 (0.12-1.08), 0.07
Alcohol use			
No	1.00	1.00	1.00
Yes	1.35 (0.96-1.90), 0.08	0.60 (0.32-1.17), 0.10	1.48 (0.82-2.66), 0.19
Physical activity			
None	1.00	1.00	1.00
Moderate	0.90 (0.46-1.77),0.76	1.23(0.59-2.55), 0.58	0.46 (0.22-0.99), 0.05
Vigorous	0.85 (0.45-1.62), 0.61	0.96 (0.47-1.94), 0.90	0.73 (0.32-1.64), 0.44

Table 4c (continue)

| | Glycemic Control | | |
| | Suboptimal | Borderline | Poor |
	Odds Ratio (95% Confidence Interval), p value	Odds Ratio (95% Confidence Interval), p value	Odds Ratio (95% Confidence Interval), p value
Take anti-diabetic pills			
No	1.00	1.00	1.00
Yes	1.17 (0.69-1.97), 0.55	2.57 (1.39-4.72), 0.00	0.85 (0.39-1.81), 0.66
Take insulin			
No	1.00	1.00	1.00
Yes	2.07 (1.34-3.21), 0.00	2.57 (1.12-5.88), 0.03	1.85 (0.85-4.05), 0.12
Family history of diabetes			
Yes	1.30 (0.78-2.14),0.31	1.61 (1.13-2.27), 0.01	1.34 (0.47-3.83), 0.66
Hypertension diagnosis			
No	1.00	1.00	1.00
Yes	0.85 (0.55-1.30), 0.44	0.75 (0.41-1.38), 0.35	1.10 (0.54-2.23), 0.78
BMI category			
Normal/under weight	1.00	1.00	1.00
Overweight	0.45 (0.17-1.22), 0.11	0.39 (0.15-1.01), 0.05	0.74 (0.26-2.11), 0.57
Obese	0.62 (0.27-1.40), 0.24	0.82 (0.34-1.98), 0.66	0.42 (0.16-1.04), 0.06
Diabetes duration (years)	0.99 (0.98-1.00), 0.25	1.01 (0.98-1.04), 0.41	1.01 (0.98-1.03), 0.72
Total cholesterol (mg/dl)	1.02 (1.00-1.02), 0.00	1.00 (0.99-1.00),0.83	1.02 (1.01-1.03), 0.00
Albumin/Creatinine Ratio	1.00 (1.00-1.00), 0.05	1.00 (1.00-1.02), 0.11	1.00(0.98-1.01), 0.35
% calories from carbohydrates	0.36 (0.03-3.96), 0.40	0.64 (0.05-8.08), 0.73	0.15 (0.01-2.53), 0.18

Suboptimal glycemic control

Among the employed sample, individuals with type 2 diabetes who worked

greater than 40 hours relative to those who worked 20 hours or less had greater odds for

suboptimal (HbA1c $\geq$7) glycemic control (Odds Ratio, OR,= 2.54 [95% confidence

interval, CI, = 1.24-5.22]) (Tables 4a-c). In addition, farm workers were more likely than

white collar workers to have suboptimal glycemic control (OR=22.07 [CI=2.40-202.11]).

Other factors associated with suboptimal glycemic control at the 0.20 alpha level (the

level for determining potential confounders) included: taking insulin (OR=2.70 [p

<0.001]), being 65 years of age or older relative to 20-44 years of age (OR=0.53 [p=0.016), being insured (0.28 [p<0.001]), being non-Hispanic Black (OR=2.37 [p=0.01]), Hispanic (OR 1.38 [p=0.17]), being of 'other' race (OR=2.94 [p=0.12]), and being overweight (OR=0.39 [p=0.05]). The other independent variables of interest for research question 1 (i.e. secondhand smoke exposure and desire to lose weight) were not statistically associated with suboptimal glycemic control at the 0.20 alpha level among all adults of the sample (i.e., regardless of employment status).

Multivariable model development: For the model to assess the relationship between work hours and suboptimal glycemic control, variables were entered in this logistic regression model in the following order: 1) work hours, 2) sex, 3) age group, 4) race/ethnicity, 5) occupation, 6) education, 7) insurance status, 8) taking insulin, and 9) BMI category.

These variables were added because they have shown clinical significance in the literature[30-39] and were statistically associated with work characteristics and glycemic control in the present study (see for example tables 4a-4d).
The order for the model was based on adding variables that had the greatest magnitude in the association with glycemic control in the univariable model. Only the variables statistically associated with both work hours and glycemic control and that had clinical significance were entered in the model. There were no notable difference (i.e. change of 20% or greater in coefficients or p values) in the direction of the estimates (odds ratios) and the p values for each category of the work hours variable and the other covariates in the models at each step in the mode building procedure.

The final multivariable logistic regression model assessing the relationship between suboptimal glycemic control, work hours, and occupation among employed adults with type 2 diabetes using NHANES 1999-2004 data are presented in Table 5. Individuals aged 20 years or older with type 2 diabetes working greater than 40 hours were more likely to have suboptimal glycemic control compared to those working 1-20 hours (OR= 5.03 [CI=1.37-18.42]), after controlling for sex, age group, race/ethnicity, occupation, education, insurance, taking insulin, and BMI category. Although not statistically significant at the 0.05 alpha level, individuals working 21-40 hours also had greater odds for suboptimal glycemic control compared to those working 20 hours or less (OR=1.91 [CI= 0.72-5.07]). In addition, farm workers were more likely to have suboptimal glycemic control relative to white collar workers (OR=28.2 [CI=1.96-403.3]).

Table 5. Multivariable logistic regression. Relationship between suboptimal glycemic control and work characteristics among employed adults with type 2 diabetes, NHANES 1999-2004

Characteristic	Odds Ratio	95% Confidence Interval
Work hours		
1-20 hours	1.00	
21-40 hours	1.91	0.72- 5.07
41+ hours	**5.03**	**1.37-18.42**
Sex		
Male	1.00	
Female	0.92	0.35-2.44
Age group (yrs)		
20-44	1.00	
45-64	0.89	0.39- 2.02
65+	0.94	0.36-2.45
Race/Ethnicity		
Non-Hispanic White	1.00	
Non-Hispanic Black	**3.36**	**1.49-7.58**
Hispanic	2.10	0.91-4.81
Other	4.24	0.91-19.79
Occupation		
White collar worker	1.00	
Service worker	1.18	0.51- 2.72
Farm worker	**28.2**	**1.96- 403.3**

Table 5 (continue)

Characteristic	Odds Ratio	95% Confidence Interval
Blue Collar worker	0.77	0.37-1.62
Education^		
<HS	1.00	
HS	0.53	0.20-1.40
>HS	0.61	0.29-1.29
Have insurance		
No	1.00	
Yes	0.87	0.35- 2.12
Taking insulin		
No	1.00	
Yes	**3.97**	**1.45-10.89**
BMI category		
Under/normal weight	1.00	
Overweight	0.48	0.16-1.48
Obese	0.79	0.34-1.82

^ HS=High School

Borderline glycemic control

Among the employed sample, univariable analyses indicated that individuals with type 2 diabetes who worked greater than 40 hours relative to those who worked 20 hours or less had greater odds for borderline glycemic control (OR=2.09 [CI=0.93-4.68]) (Table 4a-c). Although not statistically significant at the 0.20 alpha level (the level for determining potential confounders), employed individuals with type 2 diabetes who worked 21-40 hours were more likely than those who worked less than 20 hours (OR=1.30 [CI=0.52-3.26]) to have borderline glycemic control. In addition, the type of occupation was marginally associated with borderline glycemic control at the 0.20 alpha level (the level for determining potential confounders). Specifically, farm workers were also more likely than white collar workers to have borderline glycemic control (OR=11.25 [p=0.03]). Other factors associated with greater odds of borderline glycemic control at the 0.20 alpha level included: being a non-Hispanic Black (OR=2.37 [p=0.01]), Hispanic (OR=1.38 [p=0.17]), or of other race/ethnic background (3.28 [p=0.12]) relative

to non-Hispanic whites, taking diabetic pills (OR=2.57 [p=<0.001]), taking insulin (OR=2.57 [p=0.03]), and having family history of diabetes (OR=1.61 [p=0.01]).

The other 2 main independent variables of interest for research question 1 (i.e., secondhand smoke exposure and desire to lose weight) were not statistically associated with borderline glycemic control at the 0.20 alpha level among all adults or the employed sample.

Multivariable model development: For the model to assess the relationship between work hours, occupation, and borderline glycemic control, the order of how the variables were entered in this logistic regression model was as follows: 1) work hours category, 2) sex, 3) age group, 4), race/ethnicity, 5) occupation, 6) education, 7) insurance status, 8) taking insulin, and 9) BMI category. These variables were added because they have shown clinical significance in the literature[30-39] and were statistically associated with work characteristics and glycemic control in the present study (see for example tables 4a-4d). The order for the model was based on adding variables that had the greatest magnitude in the association with glycemic control in the univariable model. Only the variables statistically associated with both work hours and glycemic control and that had clinical significance were entered in the model.

When sex, age group, race/ethnicity, occupation, education, and insurance status were added in the model, the direction of the estimates (odds ratios) for each category of the work hours variable and the corresponding p values remained relatively unchanged except that the work hours variable category of 41+ hours became statistically significant when sex was added. When the variable 'taking insulin' was added, the odds ratio for the category for '21-40 work hours' and '41+ work hours' doubled. When the BMI category

and hypertension diagnosis were added, the direction of the estimates and the p values for

the work hours and the covariates (i.e., sex, age group, race/ethnicity, occupation,

education, and insurance status) remained relatively unchanged.

The final multivariable logistic regression model assessing the relationship

between borderline glycemic control, work hours, and occupation among employed

adults with type 2 diabetes using adjusting for confounders is presented in Table 6.

Individuals aged 20 years or older with type 2 diabetes working over 40 hours were more

likely to have borderline glycemic control compared to those working 1-20 hours

(OR=7.19 [CI= 1.88-27.45]), after controlling for sex, age group, race/ethnicity,

occupation, education, insurance, taking insulin, and BMI category.

Table 6. Multivariable logistic regression. Relationship between borderline (HbA1c 7-8.9%) glycemic control and work characteristics among employed adults with type 2 diabetes, NHANES 1999-2004

Characteristic	Odds Ratio	95% Confidence Interval
Work hours		
1-20 hours	1.00	
21-40 hours	2.39	0.82-6.90
41+ hours	**7.19**	**1.88-27.45**
Sex		
Male	1.00	
Female	1.03	0.37-2.83
Age group (yrs)		
20-44	1.00	
45-64	1.04	0.43-2.57
65+	1.90	0.59-6.12
Race/Ethnicity		
Non-Hispanic White	1.00	
Non-Hispanic Black	**2.93**	**1.16-7.38**
Hispanic	1.95	0.90-4.24
Other	4.99	0.83- 29.90
Occupation		
White collar worker	1.00	
Service worker	1.47	0.56-3.83
Farm worker	13.30	0.51-347.65
Blue Collar worker	0.71	0.28-1.83
Education		
<HS	1.00	

Table 6 (continue)

Characteristic	Odds Ratio	95% Confidence Interval
HS	0.36	0.10-1.29
>HS	0.56	0.22-1.43
Have insurance		
No		
Yes	2.67	0.98-7.27
Taking insulin		
No	1.00	
Yes	**3.35**	**1.13-9.88**
BMI category		
Under/normal weight	1.00	
Overweight	0.35	0.12-1.07
Obese	1.04	0.38- 2.81

^ HS=High School

Of the interactions that were tested for the borderline glycemic control variable, only 'desire to lose weight'*race/ethnicity and 'desire to lose weight'*sex were significant. Individuals who wanted to lose weight and were of other race were significantly less likely to have borderline glycemic control compared to individuals who did not want to lose weight and were white (OR=0.23 [CI=0.06-0.95]). Females who wanted to lose weight were more likely to have borderline glycemic control compared to males who did not want to lose weight (OR=2.17 [CI=1.18-4.02]). The addition of these interactions in the model did not appreciably alter the OR estimates for the 'desire to lose weight' variable or the work hours or occupation variables in the logistic regression model. Therefore the interaction variable was not included in the final model shown in Table 6.

Poor glycemic control

At the 0.20 alpha level, among the employed sample, individuals with type 2 diabetes who were farm workers or blue collar workers were more likely to have poor glycemic control relative to white collar workers (OR=9.21 [CI=1.66-51.09]) and

(OR=2.35 [CI=1.06-5.21]), respectively (Table 2). Other factors associated with greater

odds of poor glycemic control included at the 0.20 alpha level included: being a non-

Hispanic Black (OR=2.55 [p=0.03]), and Hispanic (OR=2.54 [p=0.03]) relative to non-

Hispanic whites. Factors that were inversely related to poor glycemic control included

having more than a high school education compared to having less than a high school

education (OR=0.50 [p=0.03]), being 65 years of age or older relative to those aged 20-

44 years (OR=0.10 [p=0.02]), and having insurance (0.30 [p<0.01). The other 3 main

independent variables of interest for research question (i.e. work hours category,

secondhand smoke exposure and desire to lose weight) were not statistically associated

with poor glycemic control at the 0.20 alpha level among all adults or the employed

sample.

Multivariable model development: For the model to assess the relationship

between occupation and poor glycemic control, the order of how the variables were

entered in this logistic regression model was as follows: 1) occupation, 2) sex, 3) age

group, 4) race/ethnicity, 5) work hours category, 6) education, 7) insurance status, 8)

taking insulin, and 9) BMI category.

These variables were added because they have shown clinical significance in the

literature[30-39] and because they were statistically associated with work characteristics and

glycemic control in the present study (see for example tables 4a-4d).

The order for the model was based on adding variables that had the greatest magnitude in

the association with glycemic control in the univariable model. Only the variables

statistically associated with both work hours and glycemic control and that had clinical

significance were entered in the model. When age group, race/ethnicity, and work hours,

education, insurance, taking insulin, and BMI category were added, the direction of the

estimates and the p values for the occupation and the other covariates remained relatively

unchanged.

The final multivariable logistic regression model assessing the relationship

between poor glycemic control, occupation, and work hours among employed adults with

type 2 diabetes using NHANES 1999-2004 data are presented in Table 7. Among

individuals aged 20 years or older with type 2 diabetes and after adjusting for potential

confounders such as sex, age group, race/ethnicity, work hours category, education,

insurance, taking insulin, and BMI category, there was no statistically significant

relationship between poor glycemic control and being a farm worker (OR=9.93 [CI=0.94-

105.21]).

Table 7. Multivariable logistic regression. Relationship between poor glycemic control (HbA1c $\geq$ 9.0%) and work characteristics among employed adults with type 2 diabetes, NHANES 1999-2004

Characteristic	Odds Ratio	95% Confidence Interval
Work hours		
1-20 hours	1.00	
21-40 hours	1.32	0.30- 5.93
41+ hours	1.88	0.37-9.44
Sex		
Male	1.00	
Female	0.68	0.32-1.46
Age group (yrs)		
20-44	1.00	
45-64	0.58	0.24-1.38
65+	**0.10**	**0.02- 0.73**
Race/Ethnicity		
NH White	1.00	
NH Black	**3.18**	**1.24-8.15**
Hispanic	2.02	0.70-5.86
Other	1.51	0.42-5.35
Occupation		
White collar	1.00	
Service	0.89	0.29-2.72
Farm worker	9.93	0.94-105.21
Blue Collar	1.20	0.43-3.34

Table 7 (continue)

Characteristic	Odds Ratio	95% Confidence Interval
Education^		
<HS	1.00	
HS	1.21	0.41-3.63
>HS	0.78	0.34 -1.82
Have insurance		
No		
Yes	**0.37**	**0.15-0.91**
Taking insulin		
No		
Yes	2.21	1.10-4.84
BMI category		
Under/normal weight	1.00	
Overweight	0.77	0.27-2.24
Obese	0.42	0.16-1.10

^ HS=High School

The Sobel test for mediation was used to test for the indirect effect of work hours on suboptimal and borderline glycemic control through the number of visits to a healthcare provider. This test was not statistically significant for suboptimal or borderline glycemic control (test statistic 1.294, [p=0.195] and 0.744 [p=0.456]) or for the indirect effect of farm worker occupation on suboptimal glycemic control (test statistic 1.817, [p=0.069]).

Summary of results of research question 1

In summary, it was found that diabetics working greater than 40 hours per week, relative to those working 1-20 hours per week, had greater odds of having suboptimal and borderline glycemic control, after adjusting for potential confounders. Farm workers, relative to white collar workers, were also at greater odds for suboptimal glycemic control, after adjusting for potential confounders. In addition, being a non-Hispanic Black, compared to non-Hispanic white, and taking insulin as opposed to not taking

insulin, were risk factors for suboptimal, borderline, and poor glycemic control. However, secondhand smoke exposure among non-smokers and desire to lose weight were not found to be statistically significant with glycemic control.

The association between glycemic control and HRQOL

Part of the second research question in this study was whether suboptimal, borderline, and poor glycemic control were associated with HRQOL measures indicative of poor health (i.e., greater days of poor physical and mental health and inactivity and poor self-reported general health). It was hypothesized that suboptimal, borderline, and poor glycemic control would be inversely associated with all four HRQOL measures, after controlling for potential confounders.

Cross-tabulations for each of the four HRQOL measures and each of the three glycemic control variables and the corresponding chi-square test statistics are shown in Table 8. The univariable multinomial regression analyses for number days of poor mental health, physical health and activity limitation are presented in Table 9. The univariable analyses for the self-reported general health variable are reported separately (i.e., not in Table 9) because it is a dichotomous variable requiring logistic regression as opposed to the other HRQOL variables that require multinomial logistic regression due to the three categories for each variable.

Table 8. Cross-tabulations[†] of health related quality of life variables and suboptimal (HbA1c $\geq$ 7.0%), borderline (HbA1c $\geq$ 7.0-8.9%), and poor (HbA1c $\geq$ 9.0%) glycemic control, adults classified with type 2 diabetes, NHANES 1999-2004

	Glycemic Control*					
	Suboptimal**		Borderline**		Poor**	
	N (%)		N (%)		N (%)	
	No	Yes	No	Yes	No	Yes
Self-rated health						
Fair/poor	227(56.3)	200(43.7)	227(65.2)	139(34.8)	366 (84.3)	75 (15.7)
Good/very good/excellent	213 (57.1	198(42.9)	213(65.4)	133(34.6)	346 (84.0)	77 (16.0)
Days of poor mental health						
0	**287(54.5)**	**273(45.5)**	287(58.9)	188 63.1)	**475 (84.4)**	**98 (15.6)**
1-13	**102(67.0)**	**63 (33.0)**	102(74.3)	44 (25.7)	**146 (86.5)**	**24 (13.6)**
14-30	**69 (49.0)**	**87 (51.0)**	69 (59.5)	57(40.5))	**126 (72.6)**	**52 (27.4)**
Days of poor physical health						
0	244(58.5)	213(41.9)	244(54.5)	137(45.8)	381 (82.5)	88 (17.5)
1-13	100(52.8)	104(47.2)	100(58.9)	77 (28.8)	177 (86.8)	34 (13.2)
14-30	114(62.5)	106(46.0)	114(23.1)	75 (37.5)	189 (77.6)	52 (22.4)
Days of inactivity						
0	340(56.5)	313(43.5)	340(73.5)	21(34.3)	**555 (83.6)**	**116(16.4)**
1-13	56 (55.0)	51 (45.1)	56 (12.6)	36 (40.0)	**92 (86.8)**	**21 (13.2)**
14-30	62 (53.7)	59 (46.3)	62 (13.9)	38 (14.0)	**100 (72.5)**	**37 (27.4)**

*row percentages=100, percentages do not reflect sample size in each cell due to weighted analyses.
** Statistically significant differences at the 0.05 level appear in bold.
[†]Designed based Pearson statistics performed to account for complex survey design.

<u>Self-rated general health</u>

As shown in the cross-tabulations distributions (table.8), self-rated health groups did not differ significantly with respect to suboptimal, borderline, and poor glycemic control. In addition, in the univariable logistic regression models, neither suboptimal glycemic control (OR=0.97 [CI=0.67-1.40]), borderline (OR=0.99 [CI=0.67-1.47]), or poor glycemic control (OR=1.02 [CI=0.62-1.67]), were associated with fair/poor self-rated general health (versus excellent, very good, or good health) among adults with type 2 diabetes sampled from 2001-2004.

Days of poor mental health in the past 30 days

As shown in the cross-tabulations (table 8), the proportions of suboptimal, borderline, and poor glycemic control were significantly different among poor mental health groups. In the univariable models, suboptimal, and poor glycemic control were each associated with greater number of days of poor mental health days among adults with type 2 diabetes who were 20 years of age or older sample in NHANES 2001-2004 (table 9). Specifically, suboptimal glycemic control (OR=0.59 [CI=0.38-0.92]) was associated with lower odds of having 1-13 days of poor mental health versus '0 days of poor mental health in the past 30 days. However, poor glycemic control was associated with greater odds of having 14 days or more versus 0 days of poor health in the past 30 days (OR=2.04 [CI=1.34-3.11]). In addition, borderline glycemic control was marginally associated with 1-13 days of poor mental health (OR=0.59 [CI=0.36-1.00). Since there was marginal significance for the relationship between borderline glycemic control and poor mental health, further multinomial logistic regression analyses were conducted adjusting for potential confounders.

Table 9. Multinomial logistic regression. Relationship between days of poor physical and mental health and activity limitation among adults with type 2 diabetes with suboptimal (HbA1c $\geq$ 7.0%), borderline (HbA1c $\geq$ 7.0-8.9%), and poor (HbA1c $\geq$ 9.0%) glycemic control, NHANES 2001-2004

	Days of					
	Poor Physical Health		Poor Mental Health		Limited Activity	
	1-13 days	>= 14 days	1-13 days	>= 14 days	1-13 days	>= 14 days
Characteristic	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Suboptimal glycemic control						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	1.18 (0.84-1.66)	1.23 (0.78-1.95)	**0.59 (0.89-0.92)**	1.25 (0.89-1.74)	1.06 (0.63-1.78)	1.12 (0.65-1.93)

Table 9 (continue)

	Days of					
	Poor Physical Health		Poor Mental Health		Limited Activity	
	1-13 days	>= 14 days	1-13 days	>= 14 days	1-13 days	>= 14 days
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Borderline						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	1.53 (1.00-2.34)	1.31 (0.89-1.92)	0.59 (0.36-1.00)	1.17 (0.77-1.76)	1.28 (0.75-2.18)	1.05 (0.60-1.82)
Poor						
No	1.00	1.00	1.00	1.00	1.00	1.00
Yes	0.72 (0.40-1.32)	1.36 (0.81-2.29)	0.85 (0.48-1.52)	**2.04 (1.34-3.11)**	0.78 (0.42-1.43)	**1.93 (1.01-3.70)**

Note: 0 days of poor physical, mental health or activity limitation is the reference category.

Multivariable model development: For the models built to assess the relationship between number of days of poor physical health and all of the three glycemic control variables, the variables were entered in this multinomial logistic regression model in the following order: 1) sex, 2) age group, 3) race/ethnicity, 4) education, 5) employment status, 6) insurance status, and 7) taking insulin. The order for the model was based on adding variables that had the greatest magnitude in the association with glycemic control in the univariable model. Only the variables statistically associated with both day of poor physical health and glycemic control and that had clinical significance were entered in the model. There were no meaningful changes in the direction, strength or significance of the odds ratio of the glycemic control variables or the other covariates added at each point that a covariate was entered.

Table 10 shows the final multivariable multinomial logistic regression model for the relationship between suboptimal glycemic control and poor mental health. Adults with type 2 diabetes who had suboptimal glycemic control were less likely to have ≥ 1-13

days versus 0 days of poor mental health compared to those with good glycemic control

(OR=0.50 [CI=0.30-0.83]), after controlling for sex, age group, race/ethnicity, education,

insurance, employment status and taking insulin.

Table 10. Multinomial logistic regression. Relationship between suboptimal glycemic control (HbA1c ≥7.0%) and days with poor mental health among adults with type 2 diabetes, NHANES 2001-2004

| | Days of poor mental health | | | |
| | 1-13 days | | ≥14 days | |
Characteristics	OR	95% CI	OR	95% CI
Suboptimal glycemic control				
No	1.00		1.00	
Yes	**0.50**	**0.30-0.83**	1.03	0.67-1.60
Sex				
Male	1.00		1.00	
Female	1.07	0.69-1.67	1.53	0.86-2.72
Age group (yrs)				
20-44	1.00		1.00	
45-64	1.29	0.65-2.55	0.90	0.41-2.01
65+	0.49	0.20-1.19	**0.20**	**0.08-0.47**
Race/Ethnicity				
NH White	1.00		1.00	
NH Black	0.98	0.57-1.67	**0.69**	**0.38-1.24**
Hispanic	1.22	0.61-2.46	**0.43**	**0.22-0.84**
Other	0.36	0.18-1.11	0.65	0.21-2.03
Education^				
<HS	1.00		1.00	
HS	1.23	0.63-2.38	0.74	0.35-1.56
>HS	1.40	0.77-2.53	**0.43**	**0.24-0.75**
Employed				
No				
Yes	0.79	0.49-1.28	0.39	0.24-0.65
Have insurance				
No	1.00		1.00	
Taking Insulin				
No	1.00		1.00	
Yes	1.62	0.78-3.39	**2.07**	**1.14-3.76**

Note: 0 days of poor physical, mental health or activity limitation is the reference category.
  ^ HS=High School

Table 11 shows the final multivariable multinomial logistic regression model for

the relationship between borderline glycemic control and poor mental health. Adults with

type 2 diabetes who had borderline glycemic control were less likely to have ≥ 1-13 days

versus 0 days of poor mental health (OR=0.55 [CI=0.31-0.98]), after controlling for

potential confounders.

Table 11. Multinomial logistic regression. Relationship between borderline glycemic control (HbA1c 7-8.9%) and days with poor mental health among adults with type 2 diabetes, NHANES 2001-2004

| | Days of poor mental health | | | |
| | 1-13 days | | ≥14 days | |
Characteristic	OR	(95% CI)	OR	(95% CI)
Borderline glycemic control				
No	1.00		1.00	
Yes	**0.55**	**0.31-0.98**	1.00	0.60-1.67
Sex				
Male	1.00		1.00	
Female	1.30	0.78-2.16	1.62	0.92-2.88
Age group (yrs)				
20-44	1.00		1.00	
45-64	1.13	0.55-2.32	0.74	0.32-1.73
65+	0.42	0.16-1.13	**0.17**	**0.07-0.44**
Race/Ethnicity				
NH White	1.00		1.00	
NH Black	0.89	0.52-1.52	0.75	0.38-1.48
Hispanic	1.70	0.84-3.43	0.52	0.24-1.14
Other	0.39	0.13-1.14	0.63	0.19-2.10
Education^				
<HS	1.00		1.00	
HS	1.27	0.61-2.61	0.84	0.43-1.64
>HS	1.54	0.82-2.92	**0.51**	**0.29-0.92**
Employed				
No	1.00		1.00	
Yes	0.73	0.43-1.26	**0.41**	**0.21-0.80**
Have insurance				
No	1.00		1.00	
Yes	0.94	0.36-2.48	2.18	0.89-5.36
Taking insulin				
No				
Yes	1.43	0.59-3.48	**1.94**	**1.01-3.74**

Note: 0 days of poor physical, mental health or activity limitation is the reference category.
^ HS=High School

Table 12 shows the final multivariable multinomial logistic regression model for

the relationship between poor glycemic control and number of days of poor mental

health. Adults with type 2 diabetes who had poor glycemic control were more likely to

have ≥ 14 days versus 0 days of poor mental health compared to those with good

glycemic control (OR=1.73 [CI=1.14-2.64]), after controlling for sex, age group,

race/ethnicity, education, insurance, employment status and taking insulin. Although not

statistically significant but similar to results using the other glycemic control variables,

adults with poor glycemic control were less likely to have 1-13 days (versus 0 days) of

poor mental health compared to those with good glycemic control.

Table 12. Multinomial logistic regression. Relationship between poor glycemic control (HbA1c $\geq$ 9.0%) and days with poor mental health among adults with type 2 diabetes, NHANES 2001-2004

| | Days of poor mental health | | | |
| | 1-13 days | | >= 14 days | |
Characteristic	OR	(95% CI)	OR	(95% CI)
Poor glycemic control				
No	1.00		1.00	
Yes	0.69	0.38-1.26	**1.73**	**1.14-2.64**
Sex				
Male	1.00		1.00	
Female	1.08	0.71-1.64	**1.65**	**1.03-2.65**
Age group (yrs)				
20-44	1.00		1.00	
45-64	1.25	0.62-2.53	0.72	0.38-1.37
65+	0.50	0.21-1.16	**0.69**	**0.08-0.36**
Race/Ethnicity				
NH White	1.00		1.00	
NH Black	0.90	0.55-1.46	0.69	0.40-1.19
Hispanic	1.24	0.64-2.42	**0.46**	**0.24-0.90**
Other	**0.30**	**0.10-0.93**	0.66	0.24-1.81
Education^				
<HS	1.00		1.00	
HS	1.22	0.61-2.45	0.66	0.33-1.32
>HS	1.64	0.90-3.00	**0.44**	**0.25-0.76**
Employed				
No				
Yes	0.77	0.48-1.25	**0.41**	**0.25-0.69**
Have insurance				
No	1.00		1.00	
Yes	0.91	0.39-2.10	1.54	0.70-3.39
Taking insulin				
No	1.00		1.00	
Yes	1.37	0.68-2.79	2.32	1.51-3.58

Note: 0 days of poor physical, mental health or activity limitation is the reference category.
^ HS=High School

Days of poor physical health in the past 30 days

     As shown in the cross-tabulations (table 8), the proportions of days of poor physical health were not statistically significantly different among the various glycemic control groups. In addition, in univariable models, neither suboptimal nor poor glycemic control was associated with number of days with poor physical health (table 9). However, borderline glycemic control was marginally associated with poor physical health at the 0.20 alpha level. Specifically, borderline glycemic control was associated with greater odds of having 1-13 days of poor physical health versus 0 days of poor physical health in the past 30 days (OR=1.53 [CI=1.00-2.34]), p= 0.05). Since there was marginal significance for borderline glycemic control, further multinomial logistic regression analyses were conducted adjusting for potential confounders.

     Multivariable model development: For the model to assess the relationship between the number of days of poor physical health and borderline glycemic control, the variables were entered in this multinomial logistic regression model in the following order: 1) sex, 2) age group, 3) race/ethnicity 4) education, 5) employment status, 6) insurance status, and 7) taking insulin. The order for the model was based on adding variables that had the greatest magnitude in the association with glycemic control in the univariable model. Only the variables statistically associated with both number of days of poor physical health and glycemic control and that had clinical significance were entered in the model. There were no meaningful changes in the direction, strength or significance of the odds ratio for the borderline glycemic control variable or the other covariates added at each point a covariate was entered.

Table 13 shows the final multivariable multinomial logistic regression model
assessing the relationship between borderline glycemic control and number of days of
poor physical health. Adults with type 2 diabetes who had borderline glycemic control
were statistically more likely to have 1-13 days versus 0 days of poor physical health
compared to those with good control (OR=1.59 [CI=1.03-2.45]); the relationship was
however not statistically significant for having at least 14 days of poor physical health
(OR=1.30 [CI=0.81-2.07]), after controlling for sex, age group, race/ethnicity, education,
insurance, employment status, and taking insulin. Being employed was protective against
having ≥ 14 days versus 0 days of poor physical health (OR=0.30 [CI=0.16-0.57]).

Table 13. Multinomial logistic regression. Relationship between borderline glycemic control (HbA1c 7-8.9%) and days with poor physical health among adults with type 2 diabetes, NHANES 2001-2004

| | Days of poor physical health | | | |
| | 1-13 days | | ≥14 days | |
Characteristic	OR	(95% CI)	OR	(95% CI)
Borderline glycemic control				
No	1.00		1.00	
Yes	**1.59**	**1.03-2.45**	1.30	0.81-2.07
Sex				
Male	1.00		1.00	
Female	**1.58**	**1.09-2.29**	1.46	0.98-2.16
Age group (yrs)				
20-44	1.00		1.00	
45-64	0.91	0.39-2.11	1.14	0.55-2.37
65+	**0.30**	**0.14-0.63**	**0.44**	**0.21-0.94**
Race/Ethnicity				
NH White	1.00		1.00	
NH Black	0.92	0.47-1.80	1.14	0.62-2.09
Hispanic	0.81	0.30-2.15	**0.44**	**0.21-0.92**
Other	1.05	0.43-2.55	0.74	0.26-2.11
Education^				
<HS	1.00		1.00	
HS	1.38	0.77-2.48	0.72	0.36-1.43
>HS	1.69	0.98-2.91	0.53	0.27-1.01
Employed				
No				
Yes	**0.44**	**0.24-0.80**	0.30	0.16-0.57

Table 13 (continue)

Characteristic	1-13 days		≥14 days	
	OR	(95% CI)	OR	(95% CI)
Have insurance				
No	1.00		1.00	
Yes	0.69	0.28-1.70	1.30	0.59-2.79
Taking insulin				
No	1.00		1.00	
Yes	1.83	0.85-3.96	1.44	0.73-2.85

Note: 0 days of poor physical, mental health or activity limitation is the reference category.
^ HS=High School

Days of inactivity due to poor health in the past 30 days

As shown in the cross-tabulations (table 8) proportions of suboptimal, borderline, or poor glycemic control were not significantly different among days of inactivity groups. In univariable models, while suboptimal or borderline glycemic control was not associated with number of inactivity days, poor glycemic control was. Specifically, among adults with type 2 diabetes, those with poor glycemic control were more likely to have ≥ 14 days versus 0 days of inactivity (OR=1.93 [CI=1.01-3.70]) (table 9).

Multivariable model development: For the model to assess the relationship between number of days of inactivity and poor glycemic control the order of how variables were entered in this multinomial logistic regression model was as follows: 1) sex, 2) age group, 3) race/ethnicity, 4) education, 5) employment status, 6) insurance status, and 7) taking insulin. The order for the model was based on adding variables that had the greatest magnitude in the association with glycemic control in the univariable model. Only the variables statistically associated with both inactivity days and glycemic control and that had clinical significance were entered in the model.

Table 14 shows the final multivariable multinomial logistic regression model assessing the relationship between number of days of inactivity and poor glycemic

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control. Adults with type 2 diabetes who had poor glycemic control were more likely to have ≥ 14 days versus 0 days of inactivity compared to those with good control (OR=2.00 [CI=1.07-3.76]), after controlling for sex, age group, race/ethnicity, education, insurance, employment status, and taking insulin. Among the confounders, being Hispanic was inversely associated with having ≥ 14 days versus 0 days of poor physical health (OR=0.32 [CI=0.14-0.71]).

Table 14. Multinomial logistic regression. Relationship between poor glycemic control (HbA1c ≥ 9.0%) and inactivity days among adults with type 2 diabetes, NHANES 2001-2004

	Days of inactivity			
	1-13 days		≥ 14 days	
Characteristic	OR	(95% CI)	OR	(95% CI)
Poor glycemic control				
No	1.00		1.00	
Yes	0.71	0.35-1.43	**2.00**	**1.07-3.76**
Sex				
Male	1.00		1.00	
Female	1.63	0.89-2.97	1.31	0.81-2.14
Age group (yrs)				
20-44	1.00		1.00	
45-64	0.58	0.26-1.29	0.77	0.32-1.85
65+	**0.22**	**0.07-0.66**	**0.22**	**0.09-0.53**
Race/Ethnicity				
NH White	1.00		1.00	
NH Black	1.03	0.56-1.92	0.72	0.33-1.61
Hispanic	**0.35**	**0.17-0.74**	**0.32**	**0.14-0.71**
Other	0.7	0.24-2.12	0.88	0.36-2.14
Education^				
<HS	1.00		1.00	
HS	0.81	0.43-1.50	**0.35**	**0.15-0.86**
>HS	0.73	0.31-1.69	**0.38**	**0.17-0.85**
Employed				
No				
Yes	0.52	0.22-1.21	**0.22**	**0.10-0.45**
Have insurance				
No	1.00		1.00	
Yes	1.61	0.58-4.50	**4.01**	**1.56-10.28**
Taking insulin				
No	1.00		1.00	
Yes	1.83	0.99-3.34	1.68	0.86-3.26

Note: 0 days of poor physical, mental health or activity limitation is the reference category.
^ HS=High School

Missed work days and glycemic control

Part of the second research question in this study was to examine whether suboptimal, borderline, and poor glycemic control were associated with greater number of missed work days in the past 12 months among workers with type 2 diabetes. It was hypothesized that suboptimal, borderline, and poor glycemic control was associated with greater number of missed work days in the past 12 months, after controlling for potential confounders. Neither suboptimal (beta coefficient -0.50 [-1.23, -0.23]), borderline glycemic control, or poor glycemic control (beta coefficient -0.39 [-0.98, -0.21]), were associated with number of missed work days.

Employment and glycemic control

Part of the second research question in this study was whether suboptimal, borderline, and poor glycemic control was associated with employment among adults with type 2 diabetes. It was hypothesized that suboptimal, borderline, and poor glycemic control was inversely associated with employment, after controlling for potential confounders.

Cross-tabulations of employment and glycemic control and the corresponding Chi-square test statistics are shown in table 15. The proportions of employed versus unemployed did not vary by glycemic control groups. In univariable logistic regression, neither suboptimal glycemic control (OR=1.22 [CI=0.88-1.70]) nor borderline glycemic control (OR=1.05 [CI=0.75-1.48]) were significantly associated with employment. However, poor glycemic control was significantly associated with employment status (OR=1.62 [CI=1.05-2.53]).

Table 15. Cross-tabulations[†] of health related quality of life variables and suboptimal (HbA1c $\geq$ 7.0%), borderline (HbA1c $\geq$ 7.0-8.9%), and poor (HbA1c $\geq$ 9.0%) glycemic control among adults classified with type 2 diabetes, NHANES 1999-2004

	Glycemic Control*					
	Suboptimal**		Borderline**		Poor**	
	N (%)		N (%)		N (%)	
	No	Yes	No	Yes	No	Yes
Employed						
No	449 (52.5)	454 (47.6)	449 (60.4)	314 (39.6)	**763 (86.8)**	**140 (13.2)**
Yes	153 (47.4)	216 (52.6)	153 (59.2)	134 (40.8)	**287 (80.1)**	**82 (19.9)**

*row percentages=100, percentages do not reflect sample size in each cell due to weighted analyses.
** Statistically significant differences at the 0.05 level appear in bold.
[†]Designed based Pearson statistics performed to account for complex survey design.

Multivariable model development: For the model assessing the relationship between employment status and poor glycemic control the variables were added in the model as follows: 1) poor glycemic control, 2) sex, 3) age group, 4) race/ethnicity, 5) education, 6) insurance, 7) taking insulin, and 8) CVD status. The order for the model was based on adding variables that had the greatest magnitude in the association with glycemic control in the univariable model. Only the variables statistically associated with both employment and glycemic control and that had clinical significance were entered in the model. When age group was added in the model, the estimate for poor glycemic control changed direction, but was no longer statistically significant (0.98 [0.61-1.57]); there were no sex differences. When race/ethnicity was added, the direction of the estimates and the p values for the variables in the model remained relatively unchanged except that the direction for poor glycemic control changed (OR=1.02 [CI=0.65-1.63]). Sequential addition of the other covariates (i.e. education, insurance status, taking insulin, and CVD status) did not result in any meaningful changes in the direction or significance of the estimates for poor glycemic control or the other covariates.

Table 16 displays the final multivariable logistic regression model for the relationship between employment status and poor glycemic control. In the final adjusted model, although the results were not significant, adults with type 2 diabetes who had poor glycemic control were slightly more likely to be employed (OR=1.10 [CI=0.70-1.73]).

Sex specific analyses were also conducted. Females with poor glycemic control were less likely to be employed (OR=0.84 [CI=0.39-1.79], while males with poor glycemic control were more likely to be employed (OR=1.55 [CI=0.76-3.18]).

Table 16. Multivariable logistic regression. Relationship between employment status and poor glycemic control (HbA1c $\geq$9%) among adults with type 2 diabetes, NHANES 1999-2004

Characteristic	Odds Ratio	95% Confidence Interval
Poor glycemic control		
Employment		
No	1.00	
Yes	1.10	0.70-1.73
Sex		
Male	1.00	
Female	**0.42**	**0.29-0.62**
Age group (yrs)		
20-44	1.00	
45-64	**0.44**	**0.22-0.87**
65+	**0.05**	**0.03-0.09**
Race/Ethnicity		
NH White	1.00	
NH Black	0.88	0.52-1.48
Hispanic	1.08	0.54-2.17
Other	0.77	0.37-1.57
Education^		
<HS	1.00	
HS	**2.10**	**1.20-3.68**
>HS	**2.46**	**1.50-4.02**
CVD history		
No	1.00	
Yes	0.46	0.29-0.74
Taking insulin		
No	1.00	
Yes	0.63	0.38-1.03
Have insurance		
No	1.00	
Yes	1.12	0.68-1.85

^ HS=High School

Summary of results of research question 2

In summary, it was found that the odds having 1-13 days of poor mental health were greater among those having suboptimal and borderline glycemic control. Individuals with poor glycemic control were more likely to report at least 14 days of poor mental health as well as inactivity in the past 30 days. In addition, greater odds for having 1-13 days of poor physical health in the past 30 days were reported among those with borderline glycemic control. However, the other measures of overall health and well-being, such as self-rated general health, missed work in the past 30 days and employment status, were not statistically associated with having suboptimal, borderline, or poor glycemic control, after controlling for potential confounders.

Glycemic control and all-cause mortality risk

Part of the third research question was whether suboptimal, borderline, and poor glycemic control were associated with greater all-cause mortality risk among US adults with type 2 diabetes, controlling for potential confounders. It was hypothesized that individuals with suboptimal, borderline, and poor glycemic control would have greater all-cause mortality risk.

Cross-tabulations of all-cause mortality and participant characteristics including glycemic control along with the corresponding chi-square test statistics are shown in table 17. In un-adjusted Cox proportional hazards models, neither suboptimal (HR=1.22 [CI=0.95-1.58]), borderline (HR=1.28 [CI=0.98-1.68]), or poor glycemic control (HR=1.03 [CI=0.98-1.57]) were associated with greater likelihood of all-cause mortality among adults with type 2 diabetes (Table 18). Factors associated with all-cause mortality

in un-adjusted analyses included being greater than 65 years of age (HR=6.01 [CI=2.36-15.61]), being Hispanic (HR 0.59 [0.44-0.78]), being married or living with a partner (HR=1.75 [CI=1.29-2.36]), cancer history (HR=1.58 [CI=1.05-2.38]), being obese (HR= 0.54 [CI=0.37-0.78]), taking insulin (HR=0.59 [CI=0.41-0.85]), and being a high school graduate (HR=0.66 [CI=0.49-0.91]) or having more than a high school education (HR=0.57 [CI=0.37-0.88]) (Table 18). Since age is an important predictor of death, and because we wanted to assess the possibility of confounders, age and other variables were included in the adjusted model.

The covariates included in the adjusted models for each of the glycemic control variables were entered in the following order: 1) age group, 2) sex, 3) race/ethnicity, 4) education, 5) BMI category, 6) duration of diabetes, 7) cancer history, and 8) hypertension diagnosis. However, there were no differences in the association between the glycemic control variables and mortality risk after each covariate was sequentially added to the model. There were also no changes in the hazard ratios of the other covariates as each variable was added in the model.

Table 17. Cross-tabulations[†] of cause of death with participant characteristics, adults classified with type 2 diabetes, NHANES 1986-1994 and NHANES III mortality linked data file

	Cause of Death			
	All-cause		Cardiovascular	
	N (%)		N (%)	
	No	Yes	No	Yes
Suboptimal glycemic control				
No	296 (67.6)	210 (32.4)	96 (42.2)	114 (57.8)
Yes	402 (63.5)	264 (36.5)	137 (52.3)	127 (47.7)

Table 17 (continue)

	Cause of Death			
	All-cause		Cardiovascular	
	N (%)		N (%)	
	No	Yes	No	Yes
Borderline glycemic control				
No	296 (67.60	210 (32.4)	96 (42.2)	114 (57.8)
Yes	214 (62.1)	149 (37.9)	77 (56.2)	72 (43.8)
Poor glycemic control				
No	510 (65.3)	359 (34.7)	173(48.5)	186 (51.5)
Yes	188 (65.4)	115 (34.6)	60 46.6)	55 (53.4)
Sex				
Male	321 (66.4)	304 (33.6)	**140(42.6)**	**164 (57.4)**
Female	458 (64.2)	296 (35.8)	**145(52.9)**	**151 (47.1)**
Age group				
20-44	**114 (87.7)**	**10 (12.3)**	8 (69.0)	2 (31.0)
45-64	**355 (79.9)**	**127 (20.1)**	72 (54.1)	55 (45.9)
65+	**310 (44.2)**	**463 (55.8)**	205(45.1)	258 (54.9)
Race/ethnicity				
Non-Hispanic White	**261 (63.4)**	**301 (36.6)**	127(46.5)	174 (53.5)
Non-Hispanic Black	**212 (63.5)**	**153 (36.5)**	84 (58.6)	69 (41.4)
Hispanic	**267 (76.9)**	**134 (23.1)**	70 (58.5)	64 (41.5)
Other	**39 (81.5)**	**12 (18.5)**	4 (36.3)	8 (63.7)
Education^				
< HS	**465 (57.8)**	**395 (42.2)**	183(48.6)	212 (51.4)
HS	**178 (69.4)**	**109 (30.6)**	56 (49.5)	53 (50.5)
>HS	**130 (74.4)**	**85 (26.0)**	39 (45.4)	46 (54.6)
Marital status				
Not married	**506 (70.8)**	**322 (29.2)**	145(42.7)	177 (57.3)
Married/living with partner	**270 (55.0)**	**276 (45.0)**	139(55.2)	137 (44.8)
Hypertension diagnosis				
No	357 (66.6)	238 (33.4)	114(49.7)	124 (50.4)
Yes	422 (64.2)	359 (35.8)	170(47.1)	189 (52.9)
Cancer history				
No	**718 (67.0)**	**505 (33.0)**	234(45.6)	271 (54.4)
Yes	**61 (53.9)**	**95 (46.1)**	51 (60.7)	44 (39.2)
Take insulin				
No	**197 (55.2)**	**211 (44.8)**	132(46.5)	158 (53.5)
Yes	**581 (68.8)**	**389 (31.2)**	153(52.3)	153 (47.7)
BMI category				
Normal/under weight	**122 (53.4)**	**131 (46.6)**	65 (49.3)	66 (50.7)
Overweight	**266 (64.5)**	**208 (35.5)**	94 (41.8)	114 (58.2)
Obese	**334 (70.6)**	**159 (39.4)**	86 (54.0)	73 (46.0)

*row percentages=100, percentages do not reflect sample size in each cell due to weighted analyses.
** Statistically significant differences at the 0.05 level appear in bold.
†Designed based Pearson statistics performed to account for complex survey design.
^ HS=High School

Table 18. Un-adjusted Cox proportional hazards model. Factors associated with all-cause and cardiovascular mortality risk among adults with type 2 diabetes, NHANES III

	Cause of Death			
	All-cause		Cardiovascular	
	Hazards Ratio	95% Confidence Interval	Hazards Ratio	95% Confidence Interval
Suboptimal glycemic control				
No	1.00		1.00	
Yes	1.22	0.95-1.58	1.04	0.75-1.44
Borderline glycemic control				
No	1.00		1.00	
Yes	1.28	0.98-1.68	1.00	0.68-1.49
Poor glycemic control				
No	1.00		1.00	
Yes	1.03	0.98-1.57	1.09	0.54-2.19
Sex				
Male	1.00		1.00	
Female	1.06	0.82-1.38	0.91	0.67-1.23
Age group				
20-44	1.00		1.00	
45-64	1.57	0.63-3.94	2.14	0.34-13.19
65+	**6.01**	**2.36-15.61**	**10.56**	**1.77-63.21**
Race/ethnicity				
Non-Hispanic White	1.00		1.00	
Non-Hispanic Black	1.04	0.80-1.35	0.81	0.58-1.12
Hispanic	**0.59**	**0.44-0.78**	**0.47**	**0.29-0.77**
Other	0.53	0.21-1.37	0.63	0.19-2.15
Education^				
< HS	1.00		1.00	
HS	**0.66**	**0.49-0.91**	**0.57**	**0.39-0.83**
> HS	**0.57**	**0.37-0.88**	**0.66**	**0.44-0.99**
Marital status				
Not married	1.00		1.00	
Married/living with partner	**1.75**	**1.29-2.36**	1.40	0.91-2.16
Hypertension diagnosis				
No	1.00		1.00	
Yes	1.05	0.77-1.42	1.08	0.74-1.58
Cancer history				
No	1.00		1.00	
Yes	**1.58**	**1.05-2.38**	1.14	0.71-1.85
Take insulin				
No	1.00		1.00	
Yes	**0.59**	**0.41-0.85**	0.67	0.41-1.09
Duration of diabetes	**1.03**	**1.02-1.04**	**1.03**	**1.01-1.04**
BMI category				
Normal/under weight	1.00		1.00	
Overweight	0.70	0.47-1.04	0.80	0.51-1.24
Obese	**0.54**	**0.37-0.78**	**0.47**	**0.28-0.79**

^ HS=High School

Suboptimal glycemic control

The adjusted Cox proportional hazards model for the relationship between suboptimal glycemic control and all-cause mortality risk for a participants is presented in Table 19. Suboptimal glycemic control was not statistically associated with all-cause mortality risk among adults with type 2 diabetes (HR=1.24 [CI=0.99-1.56]).

Table 19. Adjusted Cox proportional hazards model. Relationship between suboptimal glycemic control and all-cause mortality risk among adults with type 2 diabetes, NHANES III

Characteristic	Hazards Ratio	95% Confidence Interval
Suboptimal glycemic control		
No	1.00	
Yes	1.24	0.99-1.56
Age group (yrs)		
20-44	1.00	
45-64	1.75	0.61-4.99
65+	**5.66**	**202-15.82**
Sex		
Male	1.00	
Female	0.90	0.68-1.18
Race/Ethnicity		
NH White	1.00	
NH Black	1.05	0.77-1.43
Hispanic	**0.62**	**0.48-0.80**
Other	0.63	0.24-1.63
Education^		
<HS	1.00	
HS	**0.69**	**0.49-0.97**
>HS	**0.63**	**0.45-0.88**
BMI category		
Under/normal weight	1.00	
Overweight	**0.67**	**0.45-0.99**
Obese	**0.65**	**0.45-0.94**
Duration of diabetes (yrs)	1.01	0.99-1.02
Hypertension diagnosis		
No	1.00	
Yes	1.07	0.80-1.42
Cancer history		
No	1.00	
Yes	1.21	0.79-1.86

^ HS=High School

Borderline glycemic control

The adjusted Cox proportional hazards model for the relationship between borderline glycemic control and all-cause mortality risk is presented in Table 20. Borderline glycemic control was not statistically associated with all-cause mortality risk among adults with type 2 diabetes in un-stratified analyses (HR=1.20 [CI=0.94-1.53]) or in the stratified analyses (HR=1.02 [CI=0.61-1.71] and HR=1.21 [CI=0.78-2.86]) for males and females, respectively.

Table 20. Adjusted Cox proportional hazards model. Relationship between borderline glycemic control and all-cause mortality risk among adults with type 2 diabetes, NHANES III

Characteristic	Hazards Ratio	95% Confidence Interval
Borderline Glycemic control		
No	1.00	
Yes	1.20	0.94-1.53
Age group (yrs)		
20-44	1.00	
45-64	1.11	0.37-3.35
65+	**3.69**	**1.25-10.87**
Sex		
Male	1.00	
Female	0.96	0.71-1.30
Race/Ethnicity		
NH White	1.00	
NH Black	1.02	0.71-1.48
Hispanic	**0.59**	**0.39-0.88**
Other	0.46	0.16-1.34
Education^		
<HS	1.00	
HS	**0.77**	**0.54-1.09**
>HS	**0.60**	**0.39-0.93**
BMI category		
Under/normal weight	1.00	
Overweight	0.70	0.45-1.08
Obese	**0.70**	**0.44-0.98**
Duration of diabetes (yrs)	1.01	1.00-1.02
Hypertension diagnosis		
No	1.00	
Yes	1.16	0.88-1.54
Cancer history		
No	1.00	
Yes	1.18	0.77-1.81

^ HS=High School

Poor glycemic control

The adjusted Cox proportional hazards model for the relationship between poor glycemic control and all-cause mortality risk is presented in Table 21. Poor glycemic control was not statistically associated with all-cause mortality risk (HR=1.24 [CI=0.79-1.95]). Of note, addition of the interaction term of BMI category and sex did not change the results in the in the adjusted model nor was it statistically significant when added in the model.

Table 21. Adjusted Cox proportional hazards model. Relationship between poor glycemic control and all-cause mortality risk among adults with type 2 diabetes, NHANES III

Characteristic	Hazards Ratio	95% Confidence Interval
Poor glycemic control		
No	1.00	
Yes	1.24	0.79-1.96
Age group (yrs)		
20-44	1.00	
45-64	1.81	0.62-5.20
65+	**5.89**	**2.10-16.54**
Sex		
Male	1.00	
Female	0.89	0.68-1.17
Race/Ethnicity		
NH White	1.00	
NH Black	1.03	0.77-1.41
Hispanic	**0.63**	**0.49-0.81**
Other	0.62	0.24-1.58
Education^		
< HS	1.00	
HS	**0.71**	**0.50-0.99**
> HS	**0.63**	**0.45-0.89**
BMI category		
Under/normal weight	1.00	
Overweight	0.67	0.45-1.00
Obese	**0.64**	**0.44-0.93**
Duration of diabetes (yrs)	1.01	0.99-1.02
Hypertension diagnosis		
No	1.00	
Yes	1.06	0.79-1.42
Cancer history		
No	1.00	
Yes	1.19	0.76-1.85

^ HS=High School

Sex-specific analyses were also conducted. In the sex-specific analyses, suboptimal glycemic control was not associated with all-cause mortality among males (HR=1.19 [CI=0.80-1.77.]) nor females (HR=1.19 [CI=0.77-1.83]). In addition, there were no statistically significant relationship between all-cause mortality risk and borderline glycemic control among males (HR=1.02 [CI=0.61-1.71]) nor females (HR=1.21 [CI=0.78-2.86]). In addition, all-cause mortality risk was not associated with poor glycemic control among males (HR=1.45 [CI=0.88-2.39] nor females (HR=1.09 [CI=0.59-2.00]). Furthermore, when using the continuous variable of HbA1c values as the independent variables, levels of HbA1c were not found to be statistically significantly associated with all-cause mortality (HR=1.06 [CI=0.98-1.15]). However, when stratifying by sex, a statistically significant association with all-cause mortality risk was found for males (HR=1.14 [CI=1.02-1.28]) but not for females (HR=1.05 [CI=0.94-1.16]) in multivariable analyses. There was no statistically significant relationship between HbA1c values and CVD mortality risk. Sex-specific analyses for CVD mortality were not possible due to the few CVD deaths.

Further analyses were also conducted using different HbA1c cut-offs. Specifically, the thresholds of 6.5% and 6.0% we used. Diabetic individuals with a HbA1c of less than 6.0% or 6.5% had a statistically significant lower mortality risk (HR 0.69 [0.48-99] and 0.72 [0.57-0.92], respectively) compared to individuals with greater values, even after adjusting for potential confounders. The HbA1c threshold of 6.5% was used since it is a cut-off used by AACE for suboptimal glycemic control.[13] Additional hazard analyses were conducted among four diabetic groups. Specifically, these groups were the following: 1) 65 years of age or older (n=620), 2) 65 years of age or older and

taking insulin only (n=169), 3) 65 years of age or older, taking insulin only, 4) 65 years of age or older and being diagnosed with hypertension (n-344), 5) taking insulin only (n=332), and 6) being diagnosed with hypertension (n=644). Among these diabetic groups, statistically significant relationships between strict glycemic control and all-cause mortality risk were not found. Specifically, diabetics 65 years of age or older with an HbA1c of less than 6.5% had a mortality risk of 0.73 [CI=0.48-1.12]; diabetics 65 years of age or older and taking insulin only with a HbA1c of less than 6.5% had a mortality risk of 1.05 [CI=0.37-3.00]; diabetics 65 years of age or older and taking insulin only and diagnosed with hypertension with an HbA1c of less than 6.5% had a mortality risk of 1.41 [CI=0.51-3.88]; 4) diabetics 65 years of age or older and diagnosed with hypertension with an HbA1c of less than 6.5% had a mortality risk of 0.87 [CI=0.64-1.22]); 5) diabetics taking insulin only with an HbA1c of less than 6.5% had a mortality risk of 0.95 [CI=0.46-1.97]; and 6) diabetics diagnosed with hypertension and with an HbA1c of less than 6.5% had mortality risk of 0.84 [CI=0.52-1.36].

Glycemic control and cardiovascular mortality risk

Part of the third research question of this study was whether suboptimal, borderline, and poor glycemic control were associated with greater cardiovascular mortality risk among US adults with type 2 diabetes, after controlling for potential confounders. It was hypothesized that individuals with suboptimal, borderline, and poor glycemic control would have greater cardiovascular mortality risk.

Cross-tabulations of cardiovascular mortality and participant characteristics including glycemic control along with the corresponding chi-square test statistics are

shown in the table 17. In un-adjusted Cox proportional hazards models, neither

suboptimal (HR=1.04 [CI=0.75-1.44]), borderline (HR=1.0 [CI=0.68-1.49]), or poor

glycemic control (HR=1.09 [CI=0.54-2.19]) were associated with greater likelihood of

cardiovascular mortality among adults with type 2 diabetes (Table 18). To be consistent

with the hazard models for all-cause mortality, adjusted hazards models were also

performed with the same variables added in the model except for cancer diagnosis.

However, there were no differences in the association between the glycemic control

variables and CVD mortality risk after a covariate was added in the model.

Suboptimal glycemic control

      The adjusted Cox proportional hazards model for the relationship between

suboptimal glycemic control and CVD mortality risk is presented in Table 22.

Suboptimal glycemic control was not statistically associated with CVD mortality risk

among adults with type 2 diabetes (HR=1.06 [CI=0.75-1.51]).

Table 22. Adjusted Cox proportional hazards model. Relationship between suboptimal glycemic control (HbA1c $\geq$7.0%) and CVD mortality risk among adults with type 2 diabetes, NHANES III

Characteristic	Hazards Ratio	95% Confidence Interval
Suboptimal glycemic control		
No	1.00	
Yes	1.06	0.75-1.51
Age group (yrs)		
20-44	1.00	
45-64	1.69	0.26-10.84
65+	**6.92**	**1.12-42.69**
Sex		
Male	1.00	
Female	0.77	0.51-1.18
Race/Ethnicity		
NH White	1.00	
NH Black	0.78	0.53-1.16

Table 22 (continue)

Characteristic	Hazards Ratio	95% Confidence Interval
Hispanic	**0.49**	**0.29-0.83**
Other	**0.86**	**0.29-2.57**
Education		
<HS	1.00	
HS	0.64	0.40-1.05
>HS	0.63	0.40-1.00
BMI category		
Under/normal weight		
Overweight	0.74	0.40-1.13
Obese	**0.57**	**0.36-0.89**
Duration of diabetes (yrs)	1.01	0.99-1.02
Hypertension diagnosis		
No	1.00	
Yes	1.14	0.76-1.72

Borderline glycemic control

The adjusted Cox proportional hazards model for the relationship between

borderline glycemic control and CVD mortality risk is presented in Table 23. Borderline

glycemic control was not statistically associated with CVD mortality risk among adults

with type 2 diabetes (HR=0.91 [CI=0.62-1.33]).

Table 23. Adjusted Cox proportional hazards model. Relationship between borderline glycemic control and CVD mortality risk among adults with type 2 diabetes, NHANES III

Characteristic	Hazards Ratio	95% Confidence Interval
Borderline glycemic control		
No	1.00	
Yes	0.91	0.62-1.33
Age group (yrs)		
20-44	1.00	
45-64	1.10	0.17-7.33
65+	4.30	0.73-25.34
Sex		
Male	1.00	
Female	0.77	0.48-1.24
Race/Ethnicity		
NH White	1.00	
NH Black	0.72	0.45-1.17
Hispanic	0.50	0.25-1.01
Other	0.48	0.12-2.08

Table 23 (continue)

Characteristic	Hazards Ratio	95% Confidence Interval
Education^		
<HS	1.00	
HS	0.79	0.47-1.35
>HS	0.62	0.33-1.16
BMI category		
Under/normal weight	1.00	
Overweight	0.80	0.49-1.29
Obese	0.60	0.34-1.04
Duration of diabetes (yrs)	1.01	0.99-1.03
Hypertension diagnosis		
No	1.00	
Yes	1.19	0.75-1.90

^ HS=High School

Poor glycemic control

The adjusted Cox proportional hazards model for the relationship between poor

glycemic control and CVD mortality risk is presented in Table 24. Poor glycemic control

was not statistically associated with CVD mortality risk in un-stratified analyses

(HR=1.38 [CI=0.67-2.82]).

**Table 24. Adjusted Cox proportional hazards model. Relationship between poor
glycemic control and CVD mortality risk among adults with type 2 diabetes,
NHANES III**

Characteristic	Hazards Ratio	95% Confidence Interval
Poor glycemic control		
No	1.00	
Yes	1.38	0.67-2.82
Age group (yrs)		
20-44	1.00	
45-64	1.76	0.27-11.22
65+	**7.25**	**1.14-45.90**
Sex		
Male	1.00	
Female	0.76	0.50-1.16
Race/Ethnicity		
NH White	1.00	
NH Black	0.77	0.52-1.15
Hispanic	**0.49**	**0.30-0.81**
Other	0.87	0.29-2.59
Education^		
<HS	1.00	

Table 24 (continue)

Characteristic	Hazards Ratio	95% Confidence Interval
HS	0.65	0.41-1.06
>HS	0.64	0.40-1.01
BMI category		
Under/normal weight	1.00	
Overweight	0.75	0.48-1.15
Obese	**0.56**	**0.36-0.89**
Duration of diabetes (yrs)	1.01	0.99-1.02
Hypertension diagnosis		
No	1.00	
Yes	1.13	0.75-1.72

^ HS=High School

Summary of results of research question 3

In summary, it was found that neither all-cause nor CVD mortality risk was statistically associated with having suboptimal, borderline, or poor glycemic control, after controlling for potential confounders. However, when HbA1c was used as a continuous variable, males with greater HbA1c values were found to have greater all-cause mortality risk. In addition, lower all-cause mortality risk was found among individuals with an HbA1c of less than 6.5%. Stratification by diabetic groups did not result in any statically significant relationships although the hazard ratios were in some cases in opposite directions.

CHAPTER V.

DISCUSSION

Overview

In diabetes management, although glycemic control is one of the main outcomes for determining treatment prognosis, it continues to be inadequate in the US diabetic population, with about half not having good control.[27] Not being able to reach glycemic control, despite adherence to diabetes management recommendations, can lead to frustration, indifference, and unwillingness to continue treatment.[135] In the present study we attempted to assess both risk factors for suboptimal, borderline, and poor glycemic control as well as its outcomes with the expectation of gaining knowledge of why there may continue to be a high prevalence of suboptimal and poor glycemic control among adults with diabetes despite medical awareness of their importance.

Potentially new risk factors and glycemic control

There has been much research into the possible determinants of glycemic control. Most studies have repeatedly focused on demographic risk factors such as race-ethnicity[37] as well as characteristics specific to diabetes such as duration of diabetes and type of diabetes treatment.[35, 136] From the review of the literature of suboptimal and poor glycemic control, it appears that other potential risk factors for suboptimal and poor glycemic control may exist. For example, although it is not surprising the lack of adherence to diabetes treatment is shown to be associated with poor glycemic control,[39] reasons for this incompliance are not entirely known. Possible reasons for the incompliance and consequent poor glycemic control may include a diabetic's fear of

weight gain. It may also be that there are barriers in the diabetic's environment preventing them from being compliant to diabetic treatment advice, such as lack of time to take medication or eat regularly because of inflexible work schedules. Furthermore, although an association between diabetes complications and glycemic control and smoking has been found, [60-64] a factor closely associated, secondhand smoke exposure, has not been fully investigated.

Glycemic control and work hours

Work constitutes an important part of most adult lives and sometimes is even a culprit of ill health. Long work hours has been implicated as a risk factor for poor health, including increased risk of mortality,[137, 138] increased accidents,[139] cardiovascular disease,[140-142] greater unhealthy behaviors such as alcohol consumption,[143] increased smoking,[144] and less participation in physical activity.[145] Thus, it is possible that glycemic control is also affected by having long hours of work.

Most research studies on the effects of long work hours on diabetes and glycemic control have been based on non-US populations.[146, 147] However, the consequences of long work hours should be of particular concern for American workers given that they report some of the highest number of work hours among industrialized countries.[147] In fact, the amount of overtime in the US has increased since the 1970's. [148, 149 147] Among 15 industrialized nations in the world, in 2003 the US ranked as the fourth highest in average annual work hours, preceded only by Thailand, Hong Kong, and South Korea.[150] Meanwhile, the European Union does not allow more than 48 hours per work week, and Japan does not permit more than 100 hours of overtime per month. Yet in the US, only

certain occupations (e.g. transport workers and medical residents)[151] have restricted work hours by law, and there are regulations regarding the amount to be paid for overtime work but not limiting the number of overtime hours.[152]

In the present study we sought to understand the relationship between work hours and glycemic control. We found that among adults with type 2 diabetes who worked greater than 40 hours (about 34% of the sample) relative to those that worked 1-20 hours were at least 7 times as likely to have suboptimal or borderline glycemic control.

Although research has shown a relationship between work hours and cardiovascular disease,[140-142] there is limited research specifically looking at its relationship with diabetes or glycemic control. Thus, the findings from the present study cannot be adequately compared to other studies. However, our findings are in agreement with studies in which individuals have reported irregular work hours and inflexible work schedule as a barrier to proper diabetes management.[44, 45]

There are several reasons why working a greater number of hours may be associated with worse glycemic control. First, the reason for suboptimal glycemic control among those working long work hours may be simply related to the lack of time (i.e. time scarcity) to properly manage diabetes. For example, workers may not have enough time to check blood glucose levels or eat regularly or at scheduled time intervals.[153, 154] In a study in the Netherlands, a higher work load was perceived as a barrier to proper diabetes management, particularly insulin injection, in both type 1 and type 2 diabetes patients.[153] Time scarcity has been associated with an increased risk of obesity and of making poor food choices.[154] Weight gain and obesity, both risk factors for type 2 diabetes, have also been found to be greater among individuals working long hours.[144] In addition, time

scarcity is one of the barriers noted to be associated with the lack of adherence to a diabetic regimen or treatment.[155] Furthermore, lack of time because of greater work hours may also interfere with important diabetes management activities outside of work such as getting medical care or visiting a diabetes healthcare provider or educator. For example, it has been shown that individuals who work a full-time or even a part-time job (as opposed to being unemployed or retired) are more likely to discontinue going to diabetes self-management education programs.[156-158] In addition, lack of time has been associated with self-reported inability to visit dieticians.[159, 160]

Second, longer work hours may result in suboptimal glycemic control due to greater job stress or strain as a result of working greater hours. Job strain has been linked to higher HbA1c levels among employed individuals without diabetes in non-US studies,[42, 46, 47] while stress management programs have been associated with improved glycemic control.[161] Although the biological mechanism is not well understood, stress may affect glycemic control via behaviors and neurohumoral pathways such as the counter-regulatory hormones,[162, 163] and glycemic control may be related to the allostatic load or body's way of adjusting to long-term stress.[164] Poor glycemic control could also be in part due to the release of catecholamine and stress hormones (such as cortisol), which have been linked with increased cardiovascular risk factors.[165, 166] The elevated stress levels could also result in negative behavioral habits, such as increased eating, in order to cope with such stress. In fact, weight gain and obesity have been found to be the highest among individuals reporting high job strain.[167]

Third, it is possible that greater work hours may lead to worse glycemic control due to a greater propensity of late night eating since the time of day that meals are

consumed has been reported to affect insulin levels and to increase glucose intolerance.[168] Nevertheless, greater research is needed to understand the mechanism behind the relationship between long work hours and suboptimal glycemic control among adult with diabetes.

Glycemic control and farm workers

With regards to our findings about farm workers being more likely to have suboptimal glycemic control compared to white collar workers, there are very few if any studies that have investigated the association between glycemic control and being a farm worker to compare to. There are several possible explanations to our findings nonetheless. For example, it may be possible that farm workers, compared to white collar workers, may have less knowledge about diabetes self-management,[169] have inflexible work schedules,[170] and be more likely to have unhealthy eating behaviors;[171] all factors that may be responsible for poor glycemic control. For example, unhealthy diets are said to be greater among workers with high workloads,[172] low status jobs,[173] low control at work,[174] and among workers with lower education and income [175, 176] all characteristics that may be more predominant among farm workers. Moreover, other factors such as social isolation, lack of social support, and depression,[177] [178, 179]among farm workers may explain their higher likelihood of poor glycemic control. For example, a study of farm workers with diabetes found that over 66% reported themselves as being depressed and were greatly concerned about the long-term consequences of diabetes.[171] In addition, stress may be higher in farm workers compared to white collar workers and may be contributing to the worse glycemic control in this group. Farm workers may be stressed

due to not knowing for how long they will be employed (fear of being unemployed), working strenuous hours, being away from the family, fear of being deported or discriminated against and exploited.[171] This fear of losing their job may make the worker more hesitant to ask for time off and therefore be less able to access healthcare[180] and routinely get diabetes care including getting their HbA1c checked and getting physician advice about diabetes.[181]

We could not assess the relationship between the above mentioned potential mediators of the relationship between work hours or farm worker occupation and glycemic control. This is because the data were not available in NHANES, except for the number of visits to a healthcare professional in the last 12 months. Nevertheless, the mediation test with that variable was not significant suggesting that the number of visits to a healthcare professional in the last 12 months does not explain the relationship between work hours or farm worker occupation and suboptimal/poor glycemic control.

Glycemic control and desire to lose weight

Research has shown that one of the barriers to adherence to diabetes treatment regimen is the fear of weight gain commonly associated with treatment regimens such as taking insulin.[66-72] Furthermore, adolescents with diabetes perceiving themselves as overweight have reported poor glycemic control.[73] Thus, it may be that individuals that want to lose weight are less likely to be adherent to treatment regimens and consequently have suboptimal or poor glycemic control. However, the association between glycemic control and weight desirability among adults with diabetes has been understudied.

In the present study, a statistically significant association between glycemic control and desire to lose weight was not found. This finding is in agreement with a study among adolescents with both type 1 and type 2 diabetes that found that trying to lose weight or worrying about one's weight was not associated with poor glycemic control, although perception of being overweight was.[73] Nevertheless, the null finding could also be a reflection of the two possible directions of the association between glycemic control and weight desirability. As the literature review indicated and as hypothesized, it is possible that individuals who wanted to lose weight and who knew of the possible consequences of tighter glycemic control such as weight gain,[182-186] would be less likely to have suboptimal or poor glycemic control because of the lack of adherence to treatment. A typical recommendation in diabetes management is weight loss if the person is overweight or obese.[187] Thus, it is also possible that those individuals who wanted to lose weight would adhere more to diabetes management advice and would therefore be more likely to have good glycemic control. Thus, it is possible that the null finding in the present study is a factor of having two types of individuals, those not adherent to diabetes management treatment due to fear of weight gain, and those adherent to diabetes management treatment due to wanting to lose weight and already understanding the detrimental effects of being overweight on diabetes prognosis.

There may also be other factors into play in the relationship between desire to lose weight and glycemic control. For example, among adolescents, research has shown that unhealthy weight loss practices is associated with poor glycemic control among females but not among males.[73] Given the potential differences in the relationship between glycemic control and dieting behavior by sex, we tested the interaction between desire to

lose weight and sex. We also conducted sex-specific analyses but did not find any statistically significant results. Therefore, more research is needed to understand the association between desire to lose weight and glycemic control.

Glycemic control and secondhand smoke exposure

Studies have shown a relationship between smoking and glycemic control[63, 64] as well as diabetes complications that are often a result of poor glycemic control.[61, 62] Research on the various effects of SHS exposure on health outcomes aside from respiratory function is also mounting. Studies have recently documented the potential effects of SHS on cardiovascular disease,[188, 189] glucose intolerance and diabetes incidence.[43, 65, 190-192] Given the literature, it is plausible that SHS affects glycemic control as well.

We assessed the association between glycemic control and SHS among adults with type 2 diabetes but did not find a statistically significant relationship. Our results cannot be adequately compared to other studies since there are very few if any studies assessing the relationship between glycemic control and SHS exposure. Nevertheless, the lack of statistical significance may also be a result of lack of power. It may also be that our definition of SHS exposure did not properly capture individuals with SHS exposure due to the short half-life of detectable serum cotinine levels,[193] not knowing how long individuals were exposed to secondhand smoke, the absence of self-reported exposure to smoke in other settings (e.g., restaurants, bars, or motor vehicles), and potential misclassification of smoking and SHS exposure status.[124] Because of this potential misclassification, analyses were also done using cotinine as a continuous variable among

individuals who reported not being current smokers but no statistically significant relationship was found with this measure of SHS either. Therefore, because of the possibility of error in defining smoking and SHS exposure groups, the uncertainty of the accuracy of the measure for SHS exposure (which may explain the lack of statistical significance), and because other studies have suggested that SHS effects glycemic control,[42, 64] further research is needed to fully understand the relationship between SHS exposure and glycemic control among US adults with type 2 diabetes.

Glycemic control and health related quality of life

Quality of life measures have been gaining interest in the medical and public health professions over the past years. In the late 1960's to early 1970's, HRQOL was mentioned approximately 40 times in the medical literature while in the late 1980's to early 1990's it was mentioned approximately 10,000 times.[194]

The HRQOL measures may indicate how an individual views his or her health. This self-reflection of health status has been suggested to be a better indicator or ill health and good predictor of mortality.[195] The determinants of how a person's self-perceived health may be based on an array of factors such as family history and other risk factors, medical history, and psychological orientation (i.e., optimism or pessimism).[195] Furthermore, based on the premise of the "self-regulation theory", one's perception about the seriousness of one's illness does affect how one's disease is managed.[196]

How HbA1c affects everyday activities may be important given that individuals may perform certain self-management tasks as a result of short-term benefits such as lack of negative symptoms that may accompany poor glycemic control.[77, 197] Social activities

such as gatherings with friends are among the activities that may be affected by poor glycemic control because of fear of embarrassment from having the manifestation of hypoglycemia or hyperglycemia symptoms in public. An individual may be more likely to adhere to diabetes treatment if she or he knows that by following their physician's advice about proper diet for glycemic control, their respective risk of hypoglycemia or hyperglycemia may be lowered. In fact, among adults with diabetes, knowledge of HbA1c levels has been noted as an important factor determining how a patient rates his or her health, particularly physical functioning, mobility, and satisfaction with physical health and family life.[198] In addition, among adults with diabetes, barriers for lack of compliance have been noted to include lack of symptoms[155] and the belief that having diabetes is not serious.[199] Patients with diabetes have stated that managing their diabetes is associated with an impaired ability to engage in activities with their family and friends.[200] Thus, bringing awareness of how poor glycemic control affects everyday life may lead to better treatment compliance.

Diabetes is a disease that requires self-management behaviors to improve treatment prognosis. The adherence to treatment and the positive self-management behaviors may be influenced by symptoms and physiologic changes due to the diabetes disease, which may take years develop or be physiological manifested.[200] Thus, understanding the impact of good management practices on day-to-day activities and well-being may lead to better adherence and ultimately improved glycemic control.

There have been studies assessing the relationship between glycemic control and quality of life, but these have been contradictory and/or are not based on nationally-representative US population.[83-88, 201, 202] Thus, we attempted to assess the relationship

between glycemic control and HRQOL. We found that these relationships were not the same for all HRQOL indicators. Specifically, we observed a statistically significant relationship between poor glycemic control and number of days with poor mental health and inactivity. However, poor glycemic control was not associated with number of days of poor physical health or poor self-reported general health.

Our findings are in agreement with the literature which has shown that suboptimal and/or poor glycemic control is not related to all aspects of health in the same fashion.[83-88] These studies have however defined quality of life based on SF-36 scores, the validated instrument with 36 questions about perceived health status and number of disability days. This instrument is considered the gold standard for evaluating overall health including physical and mental health. [78]

For example, one study of patients from community health clinics in California followed for one year showed a slight inverse relationship (-0.21 regression) between HbA1c levels and SF-36 Mental composite scores (higher score indicating better mental health). [83] However, in that same study[83] no significant relationship was observed with the SF-36 Physical Composite Score. In another study of diabetic adult patients from a Veterans Affairs Health Care system, perceived poor health (as indicated by SF-36 scores) was associated higher HbA1c levels but mental health was not associated.[85] Other studies have not found any significant relationship between overall quality of life and glycemic control.[81, 201, 202] For example, in a study of non-insulin diabetic patients of a Veteran's clinic in North Carolina, HbA1c levels and HRQOL assessed using SF-36 were not correlated.[202]

Glycemic control and self-reported general health, physical health, and activity limitation

A statistically significant relationship between self-reported general health and glycemic control was not found in our study, which is not surprising given the inconsistent findings in previous studies. For example, in a double-blind randomized controlled trial of adults with type 2 diabetes, the treatment group with more strict diabetes treatment regimen (aimed at improving glycemic control) reported better self-perceived general health and improved cognitive functioning.[102] However, other studies have not found a statistically significant relationship between self-reported general health and quality of life.[88]

We also did not observe a statistically significant relationship between glycemic control and number of days of poor physical health. This is in contradiction to research that has suggested poor glycemic control to be associated with poor physical health given the greater likelihood of diabetes complications that cause chronic pain such as neuropathy among diabetic adults with poor glycemic control.[194] Nevertheless, we cannot compare our findings to other studies due to the lack of studies specifically investigating the relationship between glycemic control and number of days of poor physical health.

We did, however, find a statistically significant relationship between days of limited activity and glycemic control. Specifically, those with poor glycemic control were more likely to have ≥14 days of inactivity (versus 0 days) but were less likely to have 1-13 days (versus 0 days). These findings are inconsistent with the literature on disability and diabetes and glycemic control.[94, 100] For example, a study using data from the Midlife Development in the United States Survey among adults between the ages of 25 and 54 years, noted diabetics to have an average of 3.6 impairment days per month although

diabetes ranked lower than other conditions such as cancer, ulcer, heart disease, and generalized anxiety disorder in terms of the number of impairment days per month.[94] Studies specifically investigating the relationship between self-reported activity limitation and glycemic control were not found however.

A potential reason for the lack of statistically significant associations between days of poor physical health and days of inactivity and glycemic control could be due to the categorization of these variables, as these are somewhat arbitrary categories used in previous studies.[115, 116] The application of categories for these variables could have also accounted for the differences in the directions of the estimates for days of poor mental health. Since the numerical variables of number of days of poor physical health, number of days of poor mental health, and days of inactivity showed over-dispersion and excess zeros, ZIP analyses were conducted as opposed to traditional linear regression analyses. The ZIP analyses showed no statistically significant relationships between number of days of poor mental or physical health or inactivity with glycemic control. Therefore, further research may be needed, with perhaps better measures, to establish is there is a relationship between number of days of poor health and inactivity and glycemic control among US adults with type 2 diabetes.

Glycemic control and mental health

In the present study suboptimal and borderline glycemic control was associated with lower odds for having 1-13 days of poor mental health (versus 0 days). These findings suggest that individuals with suboptimal glycemic control rather than good glycemic control have better mental health. Thus, there may be a level of distress or

mental discomfort associated with having to maintain very low HbA1c levels among adults with type 2 diabetes. Our findings are in agreement with studies that have found that tight or strict glycemic control (e.g. HbA1c levels of less than or equal to 6.5%) is associated with poor quality of life measures of mental health and physical health.[198, 203, 204] One of the reasons why those individuals with tight glycemic control rate their health as poorer may be due to greater episodes of hypoglycemia when HbA1c levels are lower,[198, 205, 206] which can range from 2 to 4 episodes per year among those type 2 diabetics trying to manage their diabetes. For example, the Diabetes Control and Complications Trial (DCCT) study showed that strict glycemic control increases the chances of severe hypoglycemia.[206] Hypoglycemia may cause psychological symptoms such as displeasure, feelings of anger, and fatigue[207] as well as more visible physiologic symptoms such as poor coordination, nausea, drowsiness, shaking and sweating.[208, 209] Researchers have also suggested a curvilinear relationship between HbA1c levels and quality of life likely due to the negative aspects of either the intricate treatment regimen and/or the greater episodes of hypoglycemia due to tight glycemic control.[79]

In addition to the symptoms of hypoglycemia, the greater days of reported poor mental health may be due to the sometimes overwhelming chore of diabetes self-management. The diabetes regimen can be mentally taxing since it may require drastic dietary changes, and the re-scheduling of activities (due to, for example, having to take medications or insulin injections at certain times of the day or having to eat regularly).[39] Furthermore, these lifestyle changes in everyday activities may make others annoyed which may then result in conflict between the individual with diabetes and his/her friends, family and co-workers. This conflict may be a contributor to the mental stress

that adults with diabetes often report.[194] Finally, the fear of hypoglycemic events due to such strict glycemic control, particularly in social settings, may place an additional level of emotional distress to the individual with diabetes.[194] There are no known studies however investigating the relationship between fear of hypoglycemia and glycemic control among adults with type 2 diabetes. As hypothesized however, poor glycemic control (i.e. HbA1c $\geq$9) was found to be associated with having greater days of poor mental health. There are several potential explanations for our findings. One is that the negative symptoms associated with hyperglycemia (i.e. increased thirst, urination, and weight loss, as well as fatigue, drowsiness, depression) [210]are higher when the person has their blood glucose levels out of control, thereby leading to reduced feelings of well-being and consequently report of poor mental heath.[80, 211]

On the other hand, it may be that these individuals with diabetes have poor glycemic control because they are depressed and are in poor mental health to begin with. This scenario is very likely given the high prevalence of depression among adults with diabetes, with data suggesting that as many as 9-27% of the diabetes population may experience depression.[212, 213] Thus, it is possible that depression preceded poor glycemic control in our study sample. These individuals with depression may be having poor glycemic control due to being more likely to be non-adherent to treatment regimens.[214] Individuals with poor mental health may be in denial of their condition and therefore not follow diabetes management steps thereby leading to further poor glycemic control.[215] In addition, for a percentage of hard to treat individuals with type 2 diabetes, particularly those newly diagnosed, the lack of reaching good glycemic control levels despite taking measures may lead to feelings of disappointment despair, emotional distress, and

consequently poor self-reported mental health. [39, 194, 216] Thus there may be a "negative reinforcing cycle" in which lack of attainment of good glycemic control despite good efforts leads to emotional distress, and the emotional distress leads to lack of encouragement and hope and consequently lack of adherence to treatment, which further leads to even worse glycemic control.[39] Finally, there may be biological mechanisms for the relationship between depression and glycemic control. For, example it has been suggested that decreases in serotonin and cortisol due to depression may increase fasting glucose levels.[217] More research is need in this area however.

Although we did not find a statistically significant interaction between sex and number of days with poor mental health, to be consistent with the literature suggesting a relationship[218, 219, 220 221] we conducted sex-specific analyses for the relationship between poor glycemic control and poor mental health. In sex-specific analyses, we found that among females with type 2 diabetes, poor glycemic control was associated with lower odds for having 1-13 days (versus 0 days) of poor mental health while among males, poor glycemic control was associated with greater odds of 1-13 days (versus 0 days) of poor mental health. Our findings are in agreement with studies that have shown that among women, poor glycemic control is associated with poor overall quality of life (i.e., not specifically mental or physical health).[218, 219] Furthermore, in a Netherlands study, there was an observed positive association between depression and poor glycemic control among women but not among men.[220] This association may be greater among women because of the lower estrogen levels as women become older.[221] In fact, a study found that estrogen replacement therapy was associated with improvement in glycemic control.[221] In addition, depression has been associated with changes in estrogen levels.[222]

However, one study found depression to be associated with higher HbA1c levels in men but not in women.[223] Thus, the contradictory study findings suggests that further research is needed to truly understand the sex differences in the relationship between depression and poor mental health and glycemic control.

Finally, to further investigate why there was a difference in the direction of the estimate for the relationship between poor mental heath and glycemic control, multinomial logistic regression analyses for poor mental heath were repeated using collapsing zero to 5 days of poor mental health into one category. The results, however, did not reveal any difference whether having zero days as one category by itself or grouping it with 1-5 days.

Workforce participation and glycemic control

In addition to morbidity outcomes and HRQOL including self report of well-being, workforce participation is another measure of the effect of ill health and the overall burden of disease. Two commonly used measures of workforce participation are employment status and missed work or absenteeism. Research has shown that adults with diabetes are less likely to be employed and more likely to miss work,[57, 97-99, 201, 224-226] particularly if they have complications from diabetes.[94, 100, 101, 227-229] This may be due to diabetes being a health condition unlike many others that requires self-management in order to improve disease prognosis, reduce the risk of complications, and increase overall quality of life.[230] Individuals with diabetes usually need to follow strict dietary regimens as well as medication regimens that require medication (such as insulin injections) to be followed in a scheduled manner. These regimens may thus need to be implemented

during work hours, which may appear burdensome to both the employee and the employer. Such frustration and inability or unwillingness to properly accommodate the employee may lead to unemployment. In turn, the lack of proper diabetes management and consequently poor glycemic control and related symptoms may result in greater absenteeism from work.

Since poor glycemic control is a factor that greatly increases the chance of diabetes complications, it is more likely that glycemic control is associated with unemployment and missed work. In the present study the relationship between employment status, missed work days, and glycemic control was assessed.

Glycemic control and missed work

In the present study, a statistically significant relationship between glycemic control and missed work days in the previous month was not found. The null finding in the present study could be due to two reasons.

First, there may not be a relationship between glycemic control and missed work, since there are contradictory findings in the literature. Similar to the present study, some studies have not found a statistically significant relationship. For example, in a cross-sectional study of adults with diabetes referred to a diabetes program (the Control Diabetes Services Program) from several centers in the US, there was marginally statistically association between an HbA1c level of $\geq$ 8% and self-reported days lost from work or school during the previous year, after controlling for confounders.[104] However, in that study,[104] an HbA1c of 8-10% was not statistically associated with days lost from work or school during the previous year. Furthermore, HbA1c levels of 7-8%, HbA1c 8-

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10%, or HbA1c of $\geq$10% was associated with having greater than five days of missed work in the previous month or with difficultly accomplishing work tasks among adults with diabetes enrolled in health maintenance organization in the US.[227] However, other studies have found a statistically significant relationship. In a cross-sectional of patients with diabetes from Michigan, having an HbA1c of 8-8.9% was associated with greater probability of missing at least one hour of work using probit models. However, a statistically significant relationship was not found for HbA1c levels of 7.0-7.99% or greater than 9.0%.[103] Furthermore, in that study,[103] missed work was based on hours missed from work in only the last 4 weeks, which may not be accurate estimation of the habitual missed work due to glycemic control issues.

Second, literature on absenteeism related to health, or sickness absence, has suggested that absenteeism is not a factor that is solely determined by the presence of a medical condition, but rather based on different factors such as an individual's perception of his/her health and symptoms related to disease, attitudes related to work and missing work, job demands and accommodations at work, job strain, and other factors.[231] Thus, it is possible for example that some of these individuals with diabetes are resistant to missing work regardless of how ill they feel from being in poor glycemic control.[232]

Glycemic control and unemployment

In the present study we did not observe a statistically significant relationship between glycemic control and employment status. Our findings are in disagreement with the sparse studies assessing the relationship between glycemic control and employment status. In a study of health maintenance organization enrollees with diabetes, HbA1c

levels of $\geq 10\%$ were associated with greater disability and unemployment.[227] Furthermore, in a double-blind randomized controlled trial of adults with type 2 diabetes the treatment group with more restrictive diabetes treatment regimen were less likely to report losing their jobs during the follow-up period.[102]

There are several potential reasons for the lack of a statistically significant relationship between employment and glycemic control. First, there is the potential of misclassification of employment given that employment is based on working in the prior week. Thus the person would be considered unemployed when in fact they were employed. Second, it is possible that unemployment (or employment) is a result of other factors not related to health. For example adults 65 years of age or older may be more likely to unemployed because of retirement and not necessarily due to their level of glycemic control. However, when analyses were repeated removing those 65 years and older, there were no statistically significant relationships between glycemic control and employment status in those less than 65 years of age or 65 years of age or older. Third and lastly, there may be the potential for healthy worker effect bias. If healthy worker effect bias is present, then the true association between employment and glycemic control would be masked given that those employed are generally in better health than those not employed.

Although no statistically significant interactions were found, since the literature suggests that there may be differences in employment due to sex[129], sex-specific analyses were conducted. When the full model was stratified by sex, the results remained non-statistically significant but the direction of the association was different for males and females.

Mortality and glycemic control

It is well established that individuals with diabetes are at an increased risk of death compared to individuals without. The mortality rate ratio of the mortality rates comparing individuals with diabetes versus those without has been shown to range from 1.5 among individuals age 65-74 years of age to 3.6 among individuals 25-44 years of age.[233] Not surprisingly, diabetes is the sixth leading cause of death based on the most current national death statistics with a death rate of 23.3 per 100,000 US population according to CDC 2006 data.[6, 234] One of the proposed reasons for the higher mortality risk is poor glycemic control among individuals with diabetes since poor glycemic control is associated with increased diabetes complications.[10]

Several studies have assessed the relationship between glycemic control and all-cause and cause-specific mortality risk, although these have led to conflicting findings, particularly when analyses were sex-specific analyses, and/or based on non nationally representative sample of adults with diabetes, specifically type 2 diabetes.[105-107] The only nationally representative study assessing glycemic control among adults with type 2 diabetes that was recently published found that there was a curvilinear relationship between HbA1c levels and all-cause and CVD mortality risk.[235] However, that study [235] did not assess the relationship between mortality risk glycemic control among diabetic groups such as those that may be in presumably worse health (e.g. older, insulin taking type 2 diabetics, or those with hypertension) and therefore be at greater risk of complications from very strict glycemic control. In addition, that study [235] did not address the potential impact of confounding by depression in the relationship between glycemic control and mortality risk. Assessing the role of depression in mortality risk is important

given it has been associated with increased mortality risk among adults with diabetes.[236] In addition, depression has been associated with poor glycemic control, [214, 223]plus we found poor glycemic control to be associated with number of days of poor mental health.

In this study we assessed the effect of suboptimal, borderline, and poor glycemic control on all-cause and CVD mortality risk. We found that neither suboptimal, borderline, or poor glycemic control was significantly associated with increased all-cause or CVD mortality risk, after adjusting for several potential confounders. Nevertheless, the results did show an effect in the hypothesized direction, with higher non-statistically significant mortality hazards due to suboptimal or poor glycemic control.

Since the literature suggests that there are differences in mortality by sex[130] and because there was an interaction between BMI category and sex, sex-specific adjusted hazards models were also undertaken. Even in sex-specific analyses, non-statistically significant relationships were found between the mortality risk and the dichotomous variables for glycemic control.

In order to be consistent with the studies on mortality risk and glycemic control, we also used the HbA1c measure as a continuous variable,[106-108] but no statistically significant relationship was found, except for when stratifying the results by sex, with statistically significant results found for males only. This finding suggest that perhaps the benefits in life expectancy due to improved glycemic control may be more pronounced in males rather than females, however more research in this area is needed.

We did not find that depression was associated with any of the glycemic control groups nor was it associated with increased mortality risk. Therefore, it was not believed to be a potential confounder in the relationship between glycemic control and all-cause

mortality risk and thus was not added in the final hazard models. Indeed, adding depression in the hazard models did not result in any change in the association between all-cause mortality and glycemic control.

Although we hypothesized that suboptimal, borderline, and poor glycemic control would be associated with greater odds of mortality, the findings are not surprising given the contradictory findings in previous studies. Among studies that have looked at all-cause mortality only, a statistically significant relationship with inadequate glycemic control has been observed. For example, poor glycemic control has been associated with all-cause mortality among advanced chronic kidney disease (CKD) and dialysis patients.[105] In a study of patients undergoing maintenance hemodialysis, greater HbA1c values predicted a greater risk of all-cause and cardiovascular mortality among adults with diabetes after three years of follow-up, after adjusting for confounders such as demographics, malnutrition and anemia.[107] In a prospective study of individuals primarily without diabetes in the United Kingdom to assess the relationship between HbA1c values and all-cause mortality and CVD mortality after a 6 year follow-up,[108] it was shown for every 1% increase in HbA1c level, the all-cause and CVD mortality risk increased in a dose response fashion. However this study[108] did not control for family history of diabetes or CVD and other potential confounders.

One study, however, did not find a statistically significant relationship between glycemic control and both all-cause mortality or CVD mortality risk.[106] In a study using data from the Modification of Diet and Renal Disease (MDRD) study, a randomized controlled study of non-diabetics with CKD, a 1% increase in HbA1c was associated with a greater risk of all cause mortality, but the association with CVD mortality was not

significant, after approximately a 7-11 year follow-up period.[106] However, in this study, the incidence of diabetes was not established, a factor which could have distorted the results. Moreover, most of the studies investigating the relationship between diabetes management measures (e.g., fasting blood glucose, HbA1c value) and CVD events including mortality risk has been primarily in men.[108-110, 237]

In addition to studies on the effect of suboptimal and poor glycemic control on mortality risk, there has been recent attention to the effects of more strict thresholds for glycemic control on mortality.[238-240] Strict glycemic control is generally considered an HbA1c value of less than or equal to 6.5% and is often reached by intensive diabetes management, for example with treatment with sulfonylurea or insulin and with the goal of reducing their fasting plasma glucose concentration to less than 108 mg/dl. Such intensive treatment has been associated with reductions in the incidence of nephropathy, neuropathy, and retinopathy complications by as much as 27%[241] and has been shown to lead to increases in life expectancy, with a slight increase in complications due to longer survival time.[241] However, negative health outcomes due to strict glycemic control, such as increased mortality risk, have also been reported. For example, in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study, individuals in the strict glycemic control arm, who achieved on average an HbA1c of 6.4%, had greater deaths (n=257) compared to the group not in the strict glycemic control (with average HbA1c of 7.0-7.95) (n=203 deaths) event after four years of follow-up.[242] This translates into a 1.4% death rate per year for the strict glycemic control arm versus 1.1% death rate per year for the control group.[242] This unexpected result in the ACCORD study resulted in termination of the trial and suggested that very strict glycemic control among certain

individuals with type 2 diabetes is harmful to health.[242] However, the findings of this trial should be interpreted with caution since the participants were perhaps more representative of the diabetics with worse health given that most had elevated HbA1c (average of 8.2 at baseline), had greater length of diabetes duration, were smokers, had high cholesterol and high blood pressure and were obese; these factors could have increased the mortality risk.[242] Nevertheless, continued debate exists as to whether strict glycemic control is beneficial in terms of decreasing mortality risk to all individuals, or whether for some more chronically-ill individuals, intensive treatment can cause more harm than good.

Given the recent controversy and remaining questions as to which threshold of glycemic control is most beneficial for improving overall health and reducing mortality risk,[238-240] we performed additional analyses using stricter thresholds for glycemic control. We found that indeed having an HbA1c value of less than 6.5% was protective against all-cause mortality among adults with type 2 diabetes. These results are in agreement with studies among hemodialysis patients.[107]

The literature also suggests that strict glycemic control may be particularly harmful to certain diabetic groups such as the older (and therefore likely more frail), those taking insulin only, and/or those with comorbid conditions such as hypertension, as implied by results of the ACCORD study.[242] However, analyses conducted stratifying by diabetic groups did not show statistically significant differences associations between mortality risk and glycemic control, although the hazard ratios were sometimes in the opposite directions, suggesting possible moderation. Given the differences in direction of the relationship between all-cause mortality risk and strict glycemic control, the results

suggest that the effect of strict glycemic control on mortality risk may depend on the age, gravity of diabetes condition (i.e. whether dependent on insulin or not), and the presence of other comorbid conditions. Greater research is needed in this area however since these results were not statistically significant.

Thus, our findings suggest that strict glycemic control may indeed be beneficial in increasing survival among adults with type 2 diabetes after a 6 to 12 year follow-up, assuming glycemic control remained relatively constant through the follow-up period. These findings would be therefore in disagreement with recent findings from the ACCORD study.[242] Differences in diabetic populations in the ACCORD study and the present study could account for the different findings related to mortality risk from strict glycemic control.

Strengths and limitations

This study has both strengths and limitations. A limitation of this study was its cross-sectional design, which does not allow for the establishment of causal relationships. However, the information gained from this research can generate hypotheses that could be tested in future analytical studies using for example cohort and prospective designs.

In addition, the individual's diabetes status and duration of diabetes were based on self-reported information. However, self report of diabetes has been found to be fairly accurate when compared to medical criteria, with overall agreement of 96.3% (sensitivity of 85.2% and specificity of 98.3%).[243] In addition, whether the individual had type 1 or type 2 diabetes is not truly known as individuals were only asked about diagnosis of diabetes in general not whether their diabetes was type 1 or type 2. The definition for

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type 2 diabetes that was used in the present study was modeled after definitions used in several studies in which diagnosis of diabetes after the age of 30 was considered type 2 diabetes.[30, 244, 245] However, since type 2 diabetes has been shown to be increasingly diagnosed in much younger age groups,[246] there is the potential for misclassification with the definition that was used that assumes that individuals diagnosed before the age of 30 have type 1 diabetes.

Also, glycemic control was based on only one HbA1c reading leaving the possibility of measurement error of glycemic control. However, the possibility of measurement error is minimal given that the NCHS HbA1c laboratory protocol includes strict quality control procedures to limit measurement error.[114] Specifically, a subset of laboratory specimens of HbA1c are randomly selected and replicated to test the validity of the measurements. The coefficient of variation of these specimens of range from 0.90-2.54%,[114] thereby showing high accuracy of the measurements retested. In addition, research using NHANES III data has shown low variability and high sensitivity of HbA1c measurements repeated after a two week period in an subset of individuals from NHANES, with a within-person coefficient of variation of 3.6%.[247] Thus, not only do the HbA1c measurements in NHANES data appear to be relatively free of measurement error due to for example faulty equipment or laboratory procedures. In addition, an individual's level of glycemic control as determined from HbA1c tests do not appear to vary much even if taken within a few weeks apart. Nonetheless, given the cross-sectional design of the study and that a diabetic's degree of glycemic control may vary from a time point to another (e.g. year to year) and that the consequences of unhealthy lifestyles or environments (e.g. arduous working conditions) may take months or years to be

manifested physiologically, the exact nature of the relationship between glycemic control, work characteristics and mental health may not be ascertained from this study.

Furthermore, although the likelihood of these to alter results are minimal, there may be some factors affecting the HbA1c reading that could lead to erroneous results such as hemoglobin disorders, erythrocyte mass and plasma volume, renal disorders, liver or cardiac function problems, anemia, and menstruation.[248, 249] There is also the possibility of recall-bias, for example for hours of missed work in the past 12 months and self-report of age of diagnosis, although studies have shown that age of diagnosis of some diseases is reliable.[250]

Furthermore, our findings may be skewed due to the healthy worker effect bias, which says that individuals tend to be in better health than non-employed individuals, or those working more hours are in better health than those putting fewer hours at work. If such bias is present in this study, then our results would be attenuated and the association between suboptimal/poor glycemic control and long work hours is even stronger than what the study showed. In other words, one would expect those working 1-20 hours to be in worse glycemic control than those working greater than 20 hours, yet we found the opposite relationship. In addition, we did not find a statistically significant association between employment status and glycemic control. Thus, a healthy worker effect bias is somewhat unlikely in the present study. Of note, only the analyses for hypothesis 1 and 2b using the work variables were based on the employed sample. The analyses for assessing the relationship between glycemic control and SHS, weight desirability, HRQOL, and mortality risk were done using both employed and unemployed individuals, with most analyses controlling for employment status.

Another limitation in the present study is that other possible determinants of glycemic control were not measured, such as patient adherence to medication dietary regimen,[251, 252] frequency of self blood glucose monitoring,[253] health literacy, [254, 255] diet [256, 257] and frequency of meals consumed per day and caloric beverages.[45] Psychological factors that may also be related to glycemic control were not assessed because these were not available in NHANES. These factors include stress,[258] depression,[214] beliefs regarding how serious the disease is.[259] It would have also been beneficial to know the length of diabetes management or treatment. The length of time the individuals have had either good or poor glycemic control is also not known. Yet, the length of time of glycemic control is important given that the risk of diabetic complications, morbidity and mortality may be dependent on this.[105] For example, in the DCCT study, renal improvements were evident after three years of good glycemic control.[206] In addition, the degree of hypoglycemic events in the individuals is not known, although hypoglycemia and fear of hypoglycemia is a barrier to good glycemic control,[208, 260, 261] particularly among those treated with insulin.[262] We may have also an unreliable measure of missed work in the present study. This absenteeism measure is based on self report of missed work in the past month, which may be subject to some recall bias. In addition, ideally missed work would be based on the missed work in the last three months, given that glycemic control is based in average glucose levels in the last three months. We also assume that missed work is directly due to poor glycemic control when in fact it could be related to other factors not related to health. For example, sickness absence has been reported to be due to a combination of personality factors such as "coping mechanism" [231] and "behavior of social inequity," [263] and burnout. [264] In addition, the use of ZIP

analyses could have possibly not captured the association between missed work days and glycemic control. However, categorization of the variable missed work days (as opposed to leaving it as a count variable) did not result in any statistically significant relationship between it and glycemic control groups either. All of these factors could have led to the null finding when assessing the relationship between missed work and glycemic control.

We also do not have data on depression for NHANES 1999-2004, yet it may partially explain the relationship between employment and glycemic control since depression has been linked with poor glycemic control[214] and with unemployment and disability.[227] In addition, reduced performance while at work due to ill health, in other words presenteeism, was not measured although it can be an additional indicator of the negative effects of poor glycemic control.

Furthermore, the NHANES utilized a generic instrument to measure quality of life that was used instead of a disease specific one, which can result in reduced sensitivity.[81] Although CDC's measure for HRQOL is a generic measure, therefore having the benefits of being able to be compared to findings from people living with other conditions,[77, 79] it might not be the most appropriate measure for diabetics. HRQOL scales that are more "illness-oriented" for diabetics include the Diabetes Quality of life Measure, the Diabetes Treatment Satisfaction Questionnaire, and the Problem Areas in Diabetes Questionnaire.[77, 79] These measures are better in that they can assess the impact of activities or experiences specific to diabetics, such as issues related to using pharmacological medication and diet.[79]

Another limitation is that mortality risk is only based on a 6-12 year follow up since NHANES III data was collected from 1988 to 1994 but the mortality linkage data

are up to 2000. However the psychological and physiologic effects of poor glycemic control may take longer to be manifested. There may also be some degree of misclassification of cause of death.[265] For example, a study comparing death certificates for coding of coronary heart disease as the underlying cause of death with cause of death judged by a panel of physicians showed that these death certificates have a sensitivity of 83.8%, with a 24.3% overrepresentation of coronary heart disease deaths.[265] Furthermore, level of glycemic control was only assessed at baseline in NHANES III and therefore level of glycemic control at time of death is not known, leading to potential misclassification. Finally, the small sample size of farm workers likely resulted in loss of precision of the estimates; this was evident in the widening of the confidence intervals as covariates were added in the regression models.

Despite these limitations, the present study has many strengths. The strengths of the present study included the use of data from a nationally representative sample of adults with type 2 diabetes, the availability of several potential confounders, the availability of a 6 to 12 year mortality follow-up of a nationally representative sample of adult with diabetes, the first known study to address the association between health related quality of life, workforce participation and glycemic control while adjusting for potential confounders, and the first study to assess the relationship between glycemic control and weight desirability, secondhand smoke, and work hours and type of occupation among US adults with diabetes.

CHAPTER VI.

CONCLUSION

The aims of the present study were to assess the relationship between four potentially new risk factors (number of hours worked per week, type of occupation, secondhand smoke exposure, and desire to lose weight) and suboptimal, borderline, and poor glycemic control using nationally representative secondary data (NHANES III and 1999-2004). We also investigated the consequences of suboptimal, borderline, and poor glycemic control in terms of HRQOL, employment status, absenteeism, and mortality.

Our findings suggest that the number of hours of work and possibly the type of occupation an adult with diabetes has does affect their level of glycemic control. However, whether the adult with diabetes is exposed to secondhand smoke or whether he or she wishes to lose weight may not have a significant bearing on their degree of glycemic control and further studies are needed to define these relationships accurately. In addition, we found that poor mental health to be among those with poor glycemic control yet better for those with suboptimal glycemic control. Furthermore, individuals with poor glycemic control may be more likely to have greater days of inactivity. Interestingly, although greater number of days of poor mental health and inactivity were reported among those with poor glycemic control, there was no statistically significant relationship between employment status and missed work days and glycemic control. Thus, our data suggest that individuals with poor glycemic control are attending work yet probably are not performing at their optimal level; in other words, there may be greater preseenteism among adults with poor glycemic control. Finally, our findings imply that

their may be a linear relationship between HbA1c levels and mortality risk among males. In addition, strict glycemic control appears to be protective of mortality after a 6 to 12 year follow-up among adults with diabetes, even after controlling for potential confounders including comorbidity, which contradicts recent reports.[242] These main findings from this study summarized in figure 2 (shown below).

Figure 2. A diagrammatic view of main study findings

Research Question 1:   **Research Questions 2 and 3:**
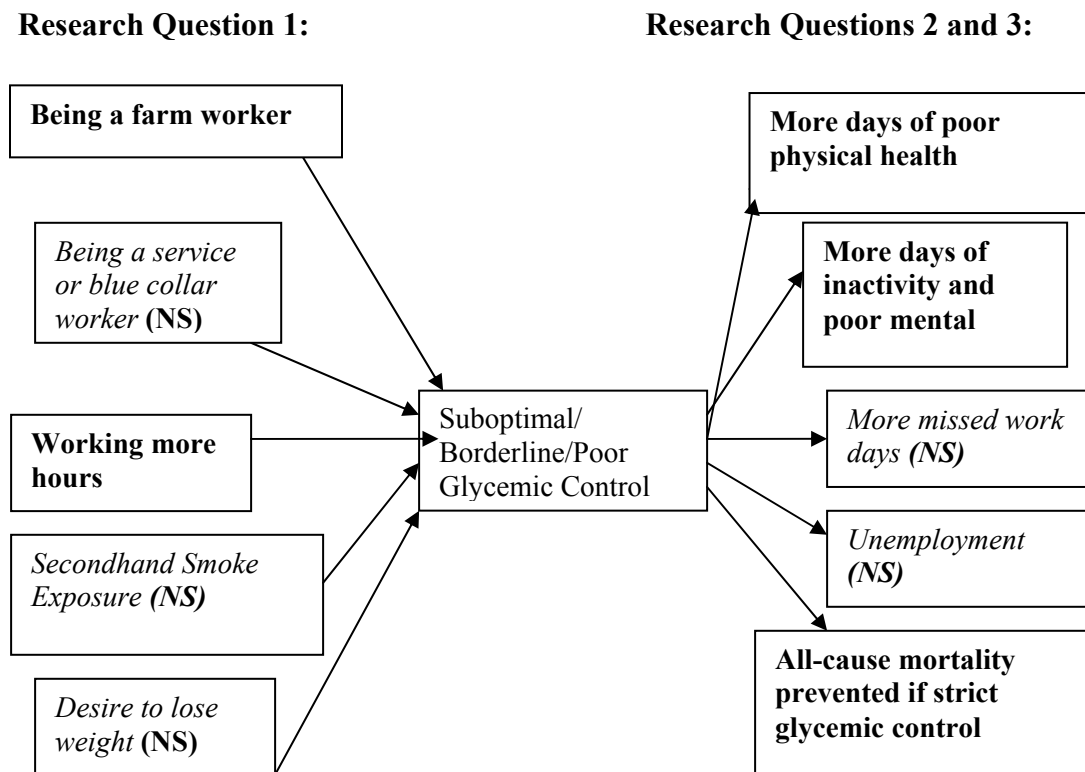
Note: NS=non-significant; statistically significant findings appear in bold.

Figure 3. A diagrammatic view of key recommendations for good glycemic control

Employer:
o Provide workplace accommodations such as greater breaks and flexible schedules.
o Provide workplace social support.
o Gain understanding of true work performance issues of diabetics.

Good glycemic control

Healthcare provider:
o Learn about the risk of poor metal health due to poor glycemic control; provide referral to mental health services if needed
o Discuss with patient reasons for lack of adherence if that is the reason for poor glycemic control.
o Educate the patient on how to manage diabetes at the workplace, discussing several medication options.
o Discuss with patient about the potential protective effects of strict glycemic control on mortality risk.

Patient:
o Communicate to both employer and healthcare provider about barriers related to work environment.
o Gain awareness of rights as employee and consequences of poor glycemic control in terms of QOL.

Public health professionals and researchers:
o Develop, implement, and evaluate workplace policies and prevention programs.
o Continue research to understand determinants of poor glycemic control as well as it consequences
o Disseminate research findings related to the known and novel risk factors of poor glycemic control.
o Educate employees on their roles in glycemic control.
o Provide employees information on potential workplace accommodations.

There are several implications and recommendations for employers, adults with diabetes and their primary healthcare providers, and public health advocates, professionals and researchers from our study findings. The key recommendations are presented in figure 3.

<u>Employers</u>

Given that work related factors appear to affect glycemic control, it is important to raise awareness among employers regarding issues that their employees with diabetes may have in terms of managing their diabetes. Employers should understand the benefits of having certain minor yet important workplace accommodations for their employees with diabetes. Such workplace accommodations, and as recommended by the American Diabetes Association,[266] may include healthier food choices at work, private places to check blood sugars or self-administer insulin, greater or more frequent breaks, more flexible work-schedules including the option to take time off to be able to visit their diabetes educator or health care provider, and even provision of diabetes educational materials and/or educational items or prevention programs on good overall health practices such as exercise and diet.[267]

Provision of workplace accommodations may be contingent on the workers with diabetes telling their employer of their illness. However, because of fear of work discrimination, the individual with diabetes may choose not to disclose their illness to the employer, even though such disclosure could result in employer support and workplace accommodations.[268, 269] In fact, compared to individuals with other chronic conditions, individuals with diabetes may be particularly less likely to disclose their medical status

for various reasons such as loss of job, rejection by co-workers and employer, and discrimination.[268] The employer may discriminate against an employee with diabetes due to the false perception that the employee cannot carry on a normal workload, may have reduced performance due to ill health, may have episodes of hypoglycemia or hyperglycemia that may lead to hazardous workplace situations, or the belief that these employees with diabetes may require costly special workplace accommodations. However, these reasons for discrimination are perhaps without merit. For example, studies have shown that individuals with diabetes perform well or even better in the job compared to individuals without diabetes.[224, 270] In addition, hypoglycemic events during work are unlikely[262, 271] and if they do occur, they typically do not result in any significant disruptions at work,[272] and are particularly less common among adults with type 2 diabetes.[208, 273] Thus, the notion that diabetes is an impediment in the workplace has to be rethought. However, as suggested from our findings, it may be that poor glycemic control, not necessarily diagnosis of diabetes, may results in poor work performance and productivity, given the reported greater days of inactivity. This further highlight's the importance of workplace policies and programs aimed at supporting effective diabetes management.

Furthermore, the importance of social support in the workplace needs to be underscored, since social support, especially among Hispanics, has resulted in improvements in diabetes management behavior.[177, 179] In addition, social support provided by *promotoras* (i.e. community health workers) for farm workers has also been associated with reduced HbA1c levels as well as greater participation in diabetes support groups.[171]

According to the American Diabetes Association, good diabetes control costs approximately \$24 a month, a much lower expense than the \$115 a month it would cost the employer in medical expenditures and loss in productivity to have diabetic workers in poor health, including those experiencing diabetic complications.[274] Thus, it may be cost-effective for employers to understand the important role they in the diabetes management of their employees diagnosed with diabetes. From an economic point of view that stipulates that individual earnings are a result of the individual's level of productivity,[275] inadequate diabetes management may result in lower income, which could further hinder the ability of the diabetic patient to purchase pharmacological agents or meals essential for proper diabetes management.

Individuals with diabetes and their healthcare providers

Given that long work hours or inflexible schedules are sometimes inevitable, certain accommodations should be considered for individuals with type 2 diabetes to make sure their blood glucose levels are normalized as much as possible. These accommodations may involve taking medications that have various duration of action or extended release properties based on work schedule. This may require keeping logs of the different work schedules and when each meal would be eaten, especially for workers with changing schedules.[276, 277] For insulin-taking individuals with inflexible work schedules, awareness of the implications of such work schedule is important so that when speaking with their health care provider, the employee may be able to ask the physician about this concern and what actions should be taken to mitigate such consequences; this may include switching to different diabetes medication options and dosing regimens.[278]

Moreover, because some patients may be fearful of hypoglycemic episodes, which may lead to lack of adherence to treatment regimens,[208, 272] patient education and strategies to prevent hypoglycemia is imperative. For example, the integration of coping strategies in order to provide the diabetic patient with a "sense of control" may be of great benefit in diabetes management programs.[208] Furthermore, it may be beneficial to have diabetes self-management programs, particularly among those that are fearful of hypoglycemia as a consequence of strict diabetes regimens, as these programs have been shown to reduce the risk of hypoglycemia.[279]

In addition, health care provider or diabetes educators should take into account barriers to healthy food choices for an individual with diabetes, particularly barriers due to work factors such as break times, work hours, and food availability and/or place to store/prepare foods.[280] Given that eating in a scheduled pattern or timely manner may not be feasible in certain occupations no matter how planned it is, it may be imperative to provide more tailored diabetes education. For example, one approach may be to educate how to adjust insulin based on the carbohydrate intake rather than carbohydrate intake based on insulin administration. A study among the Australian population showed that tailored eating program can result in benefits such as reduced HbA1c levels, minimal hypoglycemic episodes, and improved quality of life.[281]

Diabetes management has been associated with a degree of burden and consequently perceived worse quality of life[282] and techniques such as cognitive behavioral therapy, coping skills training, counseling, and patient empowerment programs have been found to be successful among individuals with diabetes.[283-285] Thus, the use of these techniques in diabetes management programs is recommended. These

strategies may help off-set the feelings of emotional distress among adults with diabetes and consequent risk of poor adherence and poor glycemic control.[286] However, since it has been suggested that primary health care providers may not know how to properly counsel a diabetic patient with poor mental health,[286] referrals to professionals in the psychology or mental health field is recommended.

Public health advocates and professionals

Given the association between glycemic control and work-related factors and the fact that much of a person's time is spent at work, the workplace should be an avenue in which to educate both employers and employees with diabetes about diabetes management. Workplace health programs have in fact been shown to be effective at improving health among employees.[287] Furthermore, increasing the prevalence of health promotion programs in the US is one of the goals of Healthy People 2010.[288] However, it is important that these worksite health promotion programs be available to all workers, which appears to not be the current situation. For example, one study found that non-professional, Black, and less educated workers were less likely to report having received any sort of health promotion in the worksite.[289] In addition, when these worksite health programs are available, certain workers, such as those workers receiving a higher salary and white collar workers appear more likely to participate than other workers.[290, 291] The lack of participation in these worksite programs may be in part due to the work schedule of these individuals.[292] Public health professionals should also work to address discrimination encountered by adults with diabetes that can hinder the proper management of diabetes.

To offset such discrimination, awareness of the rights of workers with diabetes and education of both the employers and employees should be required. This should entail proper education on the reality of living with diabetes as well as the legal terminology when speaking about individuals with chronic conditions including what the term "disability" means.[293] When individuals with diabetes argue that they need special accommodations, assuming these are considered "reasonable", the employers should provide them in accordance with the Americans with Disabilities Act (ADA).[267] However, since this act is based on individuals with more clear cut disabilities such as blindness, diabetes is often times not considered a hindering disability or covered by this act, and there is lack of clarity of the rights of adults with diabetes.[267, 293] Thus, changes to the ADA, such as clear statements regarding what constitutes a reasonable and justifiable accommodation for an adult with diabetes should be implemented.[267] Furthermore, policies such as insurance reimbursement of nutrition education services or free nutrition education among adults without insurance may prove to be beneficial since research has shown that adults with diabetes may not know the importance of nutrition and have been shown to not be compliant with visiting their dietitian; yet proper nutrition is key to diabetes management and improved patient prognosis.[159]

Future research

Further research is needed however to clearly understand the mechanisms involved in the relationships between work hours, the type of occupation, and glycemic control. Such studies would benefit from including surveys or questionnaires that ask about several work related characteristics, such as shift-work, night shift, number of

breaks, degree of flexibility to take time off from work, and usual tasks at work. In addition, studies on the relationship between presenteeism and glycemic control are needed. However this is contingent on the availability and feasibility of reliable measures of presenteeism.

Moreover, research is needed to understand the mechanisms involved in the relationship between poor mental health and glycemic control. Finally, prospective and longitudinal studies assessing the risk of mortality due to various degrees of glycemic control among a nationally representative sample of adults are needed. These studies would benefit from recording data on the number of hospitalizations, diabetes complications, changes in diabetes treatment, and episodes of hypo and hyperglycemia, as well as repeated measures of HbA1c tests.

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