Spring 5-1-2024

Diabetes & Dementia: A Health Study on the Risk Factors for Dementia in Individuals with Diabetes in the United States

Maria A. E. Adjini
Georgia State University

ABSTRACT

DIABETES & DEMENTIA: A HEALTH STUDY ON THE RISK FACTORS FOR DEMENTIA IN INDIVIDUALS WITH DIABETES IN THE UNITED STATES

By
Maria Afi Enyonam Adjini
DATE: April 27th, 2024

INTRODUCTION: Diabetes has been classified as one of the leading preventable risk factors for cognitive decline and further progression to dementia. Approximately 40% of all dementia cases can theoretically be prevented or at least delayed if certain risk factors in subjects with diabetes are eliminated. If risk factors for dementia in individuals with diabetes are targeted, it will lead to a decrease in the number of people with cognitive decline, and further reduce the prevalence of dementia in the coming years.

AIM: This study aims to investigate risk factors associated with cognitive decline in subjects with diabetes.

METHODS: The study analyzed data from the Behavioral Risk Factor Surveillance System using a sample of 1,913 individuals with diabetes. We determined the association between various risk factors such as gender, BMI, physical activity, race/ethnicity, marital status, satisfaction with life, inability to afford a doctor, and depressive disorder diagnosis in subjects with diabetes. Odds ratios from the multivariable logistic regression models were used to estimate the degree of association. Statistical significance was established using 95% confidence intervals or p-value < 0.05.

RESULTS: Regular physical activity (OR = 0.70, 95% CI: 0.52 – 0.94, P = 0.018) and satisfaction with life (OR = 0.70, 95% CI: 0.52 – 0.94, P = 0.018) were associated with reduced odds for dementia. Individuals with a depressive disorder and those 'unable to afford to see a doctor' had 1.59 and 1.97 higher odds of dementia than those who had no depression and could afford to see a doctor. Also, males had 7% reduced odds of dementia, and overweight or obese people had 1.35 higher odds for dementia. Moreover, non-Hispanic White individuals had higher odds of dementia compared to non-Hispanic Black and Hispanic individuals, and married people had reduced odds compared to divorced, 'never married,' and widowed people. Unemployed individuals and those earning good income had higher odds of dementia than individuals who were employed for wages or self-employed and individuals earning low income.

CONCLUSION: These findings are crucial in terms of public health and call for public health practitioners to be aware of risk factors for cognitive decline and dementia in diabetes patients. Public health interventions can help reduce the prevalence of cognitive decline in diabetes patients by promoting physical activity, improving diet, and encouraging cognitively stimulating activities such as reading and social engagement.

DIABETES & DEMENTIA: A HEALTH STUDY ON THE RISK FACTORS FOR DEMENTIA IN INDIVIDUALS WITH DIABETES IN THE UNITED STATES

by

MARIA AFI ENYONAM ADJINI

B.Sc., KWAME NKRUMAH UNIVERSITY OF SCIENCE & TECHNOLOGY

A Thesis Submitted to the Graduate Faculty
of Georgia State University in Partial Fulfillment
of the
Requirements for the Degree

MASTER OF PUBLIC HEALTH

ATLANTA, GEORGIA
30303

APPROVAL PAGE

DIABETES & DEMENTIA: A HEALTH STUDY ON THE ASSOCIATION, PREVALENCE, AND RISK FACTORS IN THE UNITED STATES

by

MARIA AFI ENYONAM ADJINI

Approved:

___Dr. Ike Okosun_____
Committee Chair

__Dr. Elizabeth Armstrong-Mensah_____
Committee Member

__April 27th, 2024__
Date

Acknowledgments

I am grateful to my committee members, Dr. Ike Okosun and Dr. Elizabeth Armstrong-Mensah for their guidance and support with this project. I appreciate my mother, Ms. Jane Kodo, for all her prayers and sacrifices, my sisters, Abigail Mokli and Christabel Adjini, for their support and prayers, my uncle, Kokou Degbe, for his immense support and guardianship, and my partner, Levi Kimbi, for always encouraging me and being my cheerleader. Ultimately, all praise goes to God Almighty, without whom I can do and achieve nothing. Glory to God.

Author's Statement Page

In presenting this thesis as a partial fulfillment of the requirements for an advanced degree from Georgia State University, I agree that the Library of the University shall make it available for inspection and circulation in accordance with its regulations governing materials of this type. I agree that permission to quote from, to copy from, or to publish this thesis may be granted by the author or, in his/her absence, by the professor under whose direction it was written, or in his/her absence, by the Associate Dean, School of Public Health. Such quoting, copying, or publishing must be solely for scholarly purposes and will not involve potential financial gain. It is understood that any copying from or publication of this dissertation that involves potential financial gain will not be allowed without written permission of the author.

___Maria A. E. Adjini___
Signature of Author

TABLE OF CONTENTS

List of Tables

List of Figures

1 INTRODUCTION

1.1 Background

Cognitive decline is a significant public health problem that is associated with a loss of ability to perform usual daily activities, chores, and social engagements, and it is a warning sign of dementia (Snead et al., 2022). In a 2014 statement issued by the World Dementia Council, diabetes was classified as one of the leading preventable risk factors related to cognitive decline and dementia (Bertram et al., 2016). Diabetes, pre-diabetes, and diabetic complications such as depression, hypertension, and metabolic syndrome enhance the progression of cognitive decline and result in all-cause dementia (Janoutova et al., 2022). The number of people with dementia is increasing in number worldwide. In 2019, 57.4 million people were living with this disease; by 2050, it is projected to rise to 152.8 million cases (Savalieff et al., 2022). Approximately 40% of dementia cases can be prevented or delayed if associated risk factors, including diabetes, are controlled (Rohr et al., 2022). Diabetes is associated with an increased risk for dementia. However, risk factors for individuals with both diabetes and cognitive decline are unclear (Savalieff et al., 2022). Cognitive decline among people with diabetes is a significant public health problem. Understanding the risk factors for dementia in individuals with diabetes may help in initiating interventions to decrease the number of people with cognitive decline and further reduce the prevalence of dementia. Though not clear, the relationship between diabetes and dementia is detectable in the similarities in terms of pathogenesis. The biological mechanisms for the development of dementia after a diabetes diagnosis are discussed in the next chapter. In this study, the term "cognitive decline" refers to the clinical manifestation of Alzheimer's disease and other forms of dementia. However, the

term "Dementia" will be used in discussing the potential association between Alzheimer's disease and diabetes. “Subjective cognitive decline” will be used in discussing data, analysis, and results, and "Alzheimer's disease" will be used in discussing biological mechanisms.

1.2 Biological Mechanisms

Alzheimer's disease is the most common form of dementia, developing from an accumulation of amyloid-β peptide senile plaques and neurofibrillary tangles (NFTs) of tau, a protein responsible for generating microtubules that provide organization within cells—their accumulation results in a gradual decline in memory, thinking, and social skills. There are two clinical subtypes of the disease: familial and sporadic. Familial Alzheimer's disease is caused by mutations in any one of three genes involved in amyloid-β production; amyloid-protein precursor (APP), presenilin-1 (PSEN1), or presenilin-2 (PSEN2), and sporadic Alzheimer's disease is multi-factorial, caused by a combination of genetic, epigenetic, and lifestyle factors. Sporadic Alzheimer's disease (sAD) is the most common type of AD, accounting for approximately 98% of cases, and usually occurs in the latter years of an individual's life (D. Baglietto-Vargas et al., 2016; Cater & Holter, 2022). Elderly individuals with sAD usually suffer from a variety of comorbidities, and one of the most prevalent is diabetes. Diabetes is associated with structural and functional changes in the nervous system, and structural changes usually occur as a reduction in hippocampus and cortex volume. Functionally, these areas are involved in learning and memory formation, and therefore, once damaged or affected by diabetes, there will be disruptions in these functions in the brain, and susceptibility to Alzheimer's disease increases (Baglietto-Vargas et al., 2016)

Despite the controversy on the actual mechanisms explaining diabetes as a risk factor for dementia, The Lancet Commission on dementia prevention, intervention, and care has recognized diabetes as a well-established risk factor for dementia due to the shared pathogenetic factors between type 2 diabetes and AD. The association between reduced glucose metabolism and the onset of mild cognitive decline has been known for an extended period and was determined as so vital that Alzheimer's disease has been referred to as type 3 diabetes (Baglietto-Vargas et al., 2016). The principal suggested mechanisms are hyperglycemia, tau phosphorylation, and impaired insulin signaling (Salas & Strooper, 2018).

1.2.1 Impaired insulin signaling

Although the mechanisms of insulin action are unclear, it was initially believed that insulin was not involved in the physiology of the brain. However, insulin and insulin receptors are present in the brain, particularly in the hippocampus, cortex, and thalamus, and play a key role in normal brain function by regulating metabolic homeostasis and increasing glucose metabolism in brain regions important for learning and memory (Baglietto-Vargas et al., 2016). Insulin deficiency and insulin receptor activity are the major causes of type 1 and type 2 diabetes, respectively, and defects in insulin signaling lead to hyperinsulinemia and hypercholesterolemia. Both conditions will lead to an increase in the production of amyloid and tau proteins, and these play a significant role in the development of Alzheimer's disease. Other effects of insulin malfunctioning on brain cells are depression, anxiety, and other influences on an individual's emotions. This is possible because insulin receptors are present in the brain's limbic region, where emotions are obtained. Another possibility is that insulin modulates brain

serotonergic neurons, affecting their transmission and resulting in the development of depression (Cater & Holter, 2022).

1.2.2 Tau Phosphorylation

The abnormal accumulation of tau proteins, a hallmark of Alzheimer's disease, is a result of excessive phosphorylation and glycosylation. Both animal models and human patients have shown that diabetes contributes to this aberrant tau modification. Notably, preclinical studies on animal models with type 1 or type 2 diabetes have demonstrated an increase in tau phosphorylation compared to normal animals. These findings suggest a link between insulin, insulin signaling, and the regulation of tau phosphorylation, implying that insulin signaling abnormalities could potentially lead to tau pathogenesis (Baglietto-Vargas et al., 2016).

1.2.3 Hyperglycemia

Individuals with elevated blood glucose have been shown to progress from mild cognitive decline to Alzheimer's disease. Advanced glycation end-products (AGEs) are formed due to glycation reactions from abnormal glucose metabolism and are formed as a normal part of the aging process. However, when an individual has diabetes, accumulation of AGEs occurs at a faster rate, and these glycation end-products are associated with amyloid plaques and NFTs (Baglietto-Vargas et al., 2016).

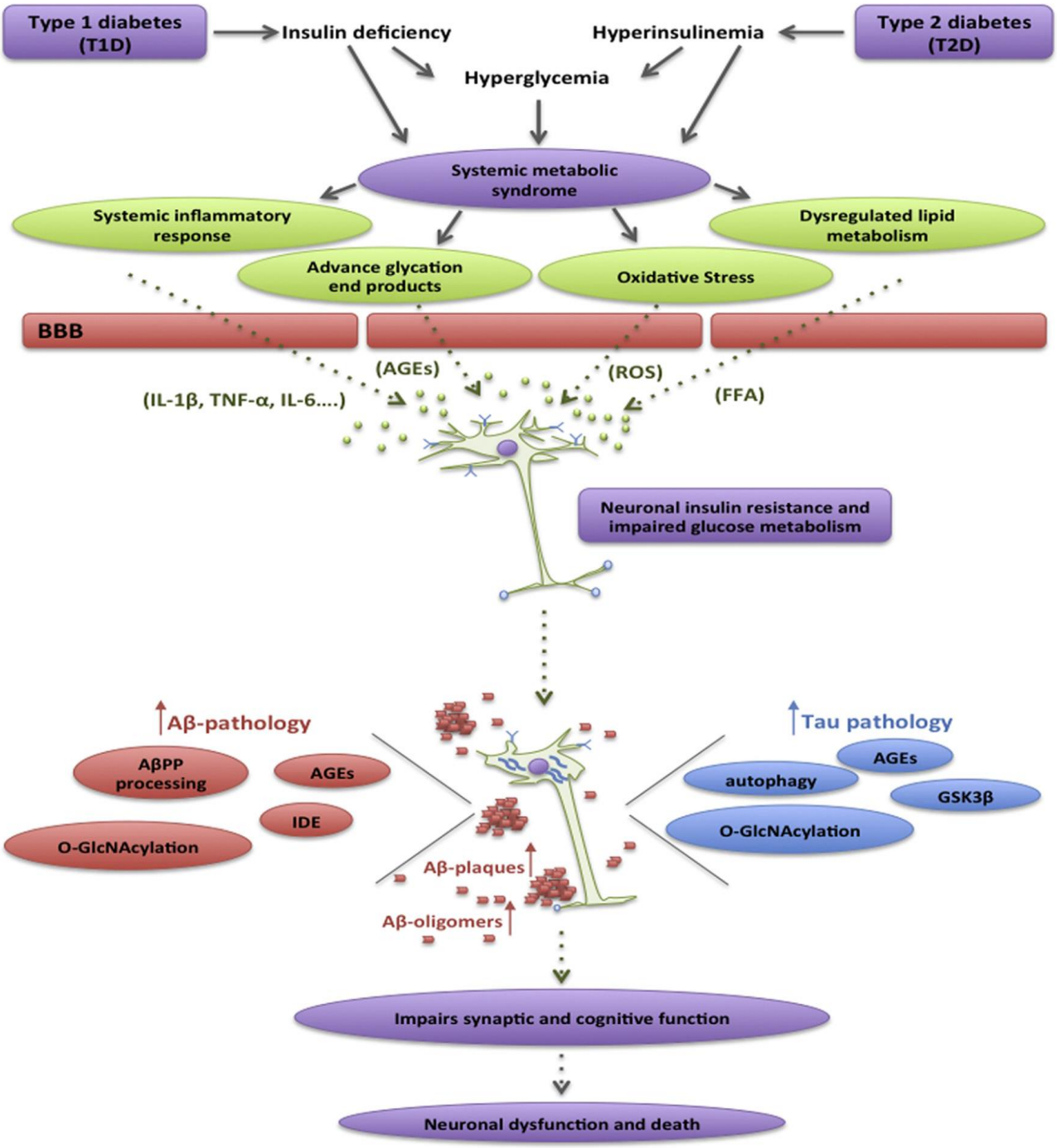

Figure 1 gives an outline of how diabetes causes the development of Alzheimer's disease. The major mechanisms involved are insulin resistance and the creation of advanced glycation end-products. These lead to the accumulation of amyloid and tau proteins, which in turn lead to cognitive decline and cell death.

1.3 At-Risk Population

Individuals who have both diabetes and dementia are more likely to be female, have low education, low income, and spend less time doing physical activity. Two-thirds of Alzheimer's disease patients are women. Women with diabetes are at a higher risk of developing Alzheimer's disease than women without diabetes, and they are 1.5 times more likely to experience Alzheimer's disease than men. The reason for this may be that gestational diabetes is associated with higher risks of cognitive decline and diabetes mellitus later in life. Early onset of menopause is also linked to a higher risk of cognitive decline, elevated risk of diabetes, and dementia. All these factors increase the risk of developing diabetes and Alzheimer's disease in women.

White people with diabetes are 2.85 times more likely to develop all-cause dementia (Zhou et al., 2023). Being married and having high social engagement and support are associated with better mental and physical health. On the other hand, divorced or widowed individuals, as well as those with no or inadequate social engagement, are at risk of several health outcomes, including diabetes, cognitive decline, and other chronic diseases (Beydoun et al., 2022).

2 LITERATURE REVIEW

In this section, literature related to the link between diabetes and dementia, as well as the various variables that will be examined in this study are presented. These variables include physical activity, socioeconomic status, lifestyle factors, psychological factors, and healthcare accessibility. The purpose of the literature review is to provide a clear understanding of the factors, other than pathogenesis and biological mechanisms, that may lead to dementia in people with diabetes.

2.1 Physical Activity & Obesity

Obesity is characterized by excess body fat amounting to a body mass index over 30. Diet and exercise affect mood and neurocognition and are significant determinants of the risk of obesity, diabetes, dementia, and many other chronic conditions. High caloric intake and a lack of physical activity enhance obesity in individuals (Espeland et al., 2018). Animal models demonstrate that obesity alters brain structure and function and is associated with high cognitive decline and elevated risk for dementia. There is also some evidence that proves that individuals with pre-diabetes or Type 2 diabetes can target the disease with frequent physical activity and reduce the development of dementia (Selman et al., 2022). The Finnish Diabetes Prevention Study provided results from a project involving middle-aged individuals with impaired glucose that showed that after a decade of regular physical activity, they had improved cognitive performance (Lehtisalo et al., 2016).

2.2 Socioeconomic Status & Lifestyle Factors

Social determinants of health significantly affect an individual's health status. Socioeconomic factors such as income, education, and race are strong determinants of cognitive function.

These determinants play out via different mechanisms; individuals with high education attainment generally have better cognitive status and maintain normal functioning longer than individuals with low education attainment (Beydoun et al., 2022). The English Longitudinal Study of the Aged (ELSA) demonstrated that participants with low income and low education had a higher dementia risk than their counterparts with higher income and education (Rohr et al., 2022). Persons with high educational status are less likely to have lower stress levels from financial issues concerning unstable housing and paying bills, allowing them to engage in more cognition-stimulating activities like leisure reading and other creative avenues. They are also more likely to receive timely medical attention due to the ability to afford frequent medical check-ups (Bodryzlova et al., 2022). Diabetic patients who have a high education status and a good income are more likely to manage diabetes and reduce their odds of developing cognitive decline than individuals who have low education and low income.

2.3 Social Isolation & Psychological Factors

Active participation in social and leisure activities protects normal cognitive functioning and decreases memory problems. Social isolation increases long-term stress from apparent or perceived social threats and a lack of social engagement and comfort. It is associated with many other chronic diseases, such as hypertension, depression, anxiety, and increased dementia risk. A study found that aerobic physical activities done alone did not seem to have any cognitive benefits in 754 healthy older adults (Shafighi et al., 2023). The finding highlights the need for consistent social engagement for cognitive stimulation and better physical and mental health. Being married increases social engagement and support and greatly benefits an individual's health and well-being. Various studies comparing married and divorced individuals indicate that

married people have better mental and physical health, and divorced, widowed, and unmarried people have cardiovascular health issues and risks of inflammation. Married people have access to economic resources that are unavailable to people outside of this status due to multiple income sources and the combining of wealth in the union (Liu et al., 2019). Companionship on a level of intimacy, such as may be available in marriage, is crucial, especially in the older years, and is protective in keeping mental health stable, managing diabetes, preventing depression, and ultimately reducing the risk of developing dementia.

A Maastricht Study showed that men who live alone had higher odds of a Type 2 diabetes diagnosis and further developed cognitive decline and dementia. Another essential factor to be considered regarding social engagement is an individual's work life. A large portion of adult life is spent in the workplace, and activity and colleagues there represent a significant part of cognitive stimulation. When a person retires, all this activity ceases abruptly, and if there is a lack of social activity outside of this environment, it might take a toll on a person's mental health. Results of various studies confirm that an individual's retirement usually coincides with the fastest decline of their memory and general cognition (Sundstrom, 2020). Depression is one of the outcomes that occur because of social isolation, and it doubles the risk for dementia. Comorbid with diabetes, dementia increases the risk for further health complications, including mortality (Katon et al., 2015).

2.4 Gender Differences

The at-risk population for diabetes and the association with dementia show multiple differences in their effects on gender. In a study performed to observe differences in gender for dementia, it was found that women and men with diabetes are at 120% and 70%, respectively,

higher odds of developing vascular dementia compared to healthy individuals, and women were 19% more affected compared to men (Jash et al., 2020). There could be several reasons for these differences. Women with diabetes usually ingest meals highly saturated in trans-fat and are less likely to exercise compared to men. Hence, they have a higher likelihood of being obese and developing comorbidities. Biological differences such as pregnancy, birth control, menopause, and female hormones make women more susceptible to negative emotions and stress factors and, therefore, more predisposed to obesity and complications from it (Selman et al., 2022). A comparison of social isolation scores revealed that many women had high isolation scores. Women are usually more emotionally attached to their social connections than men and are more reliant on them. After the death of a spouse, men are more likely to remarry or get a new partner than women (Read et al., 2020). These are a few mechanisms that make women much more likely to demonstrate more significant cognitive decline.

3. METHODS

3.1 Source of Data

Data from the Behavioral Risk Factor Surveillance System (BRFSS) survey for the year 2022 was used for this study. The BRFSS is a system of telephone surveys for collecting health-related data on chronic health conditions and health-risk behaviors among US residents. The survey is conducted annually for more than 400,000 adults and is the largest health survey system in the world. The survey comprises modules with various standard questions to collect prevalence data for preventive health practices (CDC, BRFSS, 2024). Data is available for public use and includes cross-sectional data on individuals with diabetes and subjective cognitive decline. A detailed description of the BRFSS, including data collection methods, is published on the CDC BRFSS website and has been published by others (https://www.cdc.gov/brfss/annual_data/annual_2022.html).

3.2 Variables and the study population

The study is designed to include a diverse range of American adults with diabetes (18 years and older), encompassing non-Hispanic Blacks, non-Hispanic Whites, and Hispanics. The eligibility criteria also extend to all participants with information on physical activity, diabetes status, marital status, income, employment status, cognitive decline, race/ethnicity status, and depressive disorder status, ensuring a comprehensive and representative sample.

Data on physical activity was collected in the BRFSS using the question, 'During the past month, other than your regular job, did you participate in any physical activities or exercises?'. Diabetes status was determined by asking the question, 'Ever told you had diabetes?', and

participants were grouped based on their answer choice, 'yes' or 'no.' Marital status was determined using the BRFSS question, 'Are you married, divorced, widowed, separated, never married, or a member of an unmarried couple?' and participants had to select one of the options. This study used four values for this variable: 'married,' 'divorced,' 'widowed,' and 'never married.' Participants were grouped into income categories by asking the question, 'Is your annual household income from all sources..?' and had various income levels for selection (< $10,000, <$15,000, <$20,000, < $25,000, <$35,000, <$50,000, <$75,000, <$100,000, <$150,000, <$200,000, and $200,000 or more). Six sub-categories were combined: <$10,000, <$15,000, <$20,000, <$25,000, <$35,000, and <$50,000 to create one sub-category (<$50,000). Two sub-categories were combined, <$75,000 and <$100,000, to create one sub-category ($50,000 - $100,000). Two sub-categories were combined, <$150,000 and <$200,000, to create one sub-category ($150,000 - $200,000). Four categories were generated: <$50,000, $50,000 - $100,000, <$150,000 - $200,000, and $200,000 or more. Employment status was determined using the BRFSS question, 'Are you currently employed for wages, self-employed, out of work for 1 year or more, out of work for less than 1 year, a homemaker, a student, retired, or unable to work?'. The ‘employment status’ variable values used for the study were 'employed for wages', 'self-employed,' 'retired,' and 'unable to work.' Cognitive decline was measured by asking the question, 'As a result of confusion and memory loss, how often do you need assistance with these day-to-day activities?' and the options provided were 'always,' 'usually,' 'sometimes,' 'rarely,' 'never,' and 'don't know/not sure.' The question was modified to 'As a result of confusion and memory, do you need assistance with day-to-day activities?', and values were combined to create new answer categories. 'Always' and 'Usually' were combined to

create 'Yes,' and 'Rarely' and 'Never' were combined to create 'No.' Medical affordability, satisfaction with life, and depressive disorder status were determined by asking the questions, 'Was there a time in the past 12 months when you needed to see a doctor but could not because you could not afford it?' 'Are you satisfied with life?', and '(Ever told (you had) a depressive disorder (including depression, major depression, dysthymia, or minor depression)?) respectively. Participants were grouped by answer choice; 'yes' or 'no' for all three questions. Race/Ethnicity categories selected for the study were non-Hispanic Black, non-Hispanic White, and Hispanic, and Gender categories were male and female. All variables and corresponding questions for data collection are summarized in Table 1 below:

Table 1: Study Variables and BRFSS-associated Questions

VARIABLES	QUESTIONS
Physical Activity	During the past month, other than your regular job, did you participate in any physical activities or exercises?
BMI	Are you overweight or obese?
Diabetes	Ever told you had diabetes?
Marital Status	Are you: (marital status)?
Income	Is your annual household income from all sources: (with options for income)?
Employment	(Are you currently…? (with options for employment)
Cognitive decline	As a result of confusion and memory loss, do you need assistance with day-to-day activities?
“Could not afford to see a doctor”	Was there a time in the past 12 months when you needed to see a doctor but could not because you could not afford it?
Depressive disorder	(Ever told) (you had) a depressive disorder (including depression, major depression, dysthymia, or minor depression)?
Gender	Are you male or female?
Race/Ethnicity	Race/Ethnicity categories

3.3 Disease Measures and Definitions

The dependent variable of the study was subjective cognitive decline. Subjective cognitive decline was defined as having answered 'yes' to the question, 'As a result of confusion or memory loss, do you need assistance with day-to-day activities?' (CDC, Alzheimer's Disease and Healthy Aging, 2019). Other terms used for this outcome in the study include 'Alzheimer's disease' and 'dementia.' The primary independent variable for the study was diabetes. Diabetes was defined as answering 'yes' to the question, 'Ever told you have diabetes?'. Other covariates for this study include physical activity, BMI, gender, employment status, income, race/ethnicity, education, marital status, satisfaction with life, and depressive disorder. Medical affordability was defined using the question, 'Was there a time in the past 12 months when you needed to see a doctor but could not because you could not afford it?' Participants who answered 'no' were classified as unable to afford medical care.

3.4 Statistical Analysis

BRFSS data was downloaded using the SAS Transport Format and imported into SPSS for analysis. We compared individuals with diabetes and subjective cognitive decline and individuals with diabetes and no subjective cognitive decline. Pearson's chi-square test was used to ascertain statistically significant differences between study variables (physical activity, BMI, gender, employment status, income, race/ethnicity, education, marital status, satisfaction with life, and depressive disorder) and subjective cognitive decline. Multivariate logistic regression analysis was performed to predict the association between the above independent variables and the odds of subjective cognitive decline in subjects with diabetes. Statistical significance was determined by p-values less than 0.05 or 95% confidence intervals.

4 RESULTS

4.1 Basic characteristics of the study population

The total number of all diabetic individuals was 61,158, out of which 1,913 were selected for assessments upon meeting eligibility criteria and after eliminating missing or duplicate data values. The working data set for assessments constituted 53% female, 47% male, and 13.7% diabetic individuals out of 445,132 cases. Table 2 below summarizes all the studied demographic variables stratified by gender. As shown in Table 2, there were statistically significant differences between males and females eligible for this study. Out of the total number of obese subjects, 51.8% of them are female and 48.2% are male. The proportion of females who are retired or unable to work is 56.1% and 59.1%, respectively, compared to 43.9% and 40.9% of males. A greater proportion of individuals earning $150,000 or more are males, while individuals earning less than $100,000 are primarily female.

Table 2: Demographic characteristics of the study population

Variables	Values	Male n (%)	Female n (%)	Total	P-Value
AGE	18 - 24	9905 (36.8)	17038 (63.2)	26943	<.001
	25 - 34	17505 (36.6)	30335 (63.4)	47840	
	35 – 44	21438 (36.2)	37736 (63.4)	59174	
	45 – 54	25929 (38.7)	41055 (61.3)	66984	
	55 – 64	36878 (44.6)	45862 (55.4)	82740	
	65 or older	97583 (60.4)	63868 (39.6)	161451	
BMI	Underweight	2373 (35.0)	4405 (65.0)	6778	<.001
	Normal Weight	48765 (41.7)	68211 (58.3)	116976	
	Obese	63881 (48.2)	68696 (51.8)	132577	
RACE-ETHNICITY	White only, NH	150432 (46.9)	169989 (53.1)	320421	<.001
	Black only, NH	14477 (40.8)	20969 (59.2)	35446	
	Asian only, NH	7137 (53.5)	6210 (46.5)	13347	
	Hispanic	20276 (47.2)	22641 (52.8)	42917	
EDUCATION	Did not graduate high school	12083 (50.3)	12928 (49.7)	26011	<.001
	Graduated high school	54054 (49.6)	54936 (50.4)	108990	
	Attended college or technical school	53452 (44.4)	66800 (55.6)	120252	
	Graduated from college or technical school	87352 (46.6)	100144 (53.4)	187496	
EMPLOYMENT STATUS	Employed for wages	94748 (50.9)	91256 (49.1)	186004	<.001
	Self-employed	23500 (60.6)	15268 (39.4)	38768	
	Retired	60214 (43.9)	76869 (56.1)	137083	
	Unable to work	10924 (40.9)	15813 (59.1)	26737	
INCOME LEVEL	Less than $50, 000	62128 (42.8)	83012 (57.2)	145140	<.001
	$50,000 - $100,000	53063 (49.3)	54521 (50.7)	107584	
	$150,000 - $200,000	39241 (53.8)	33642 (46.2)	72883	
	$200,000 or more	13836 (58.9)	9642 (41.1)	349085	
URBAN/RURAL STATUS	Urban counties	179815 (47.2)	200917 (52.8)	380732	<.001
	Rural counties	25398 (46.2)	29594 (52.9)	54992	

Table 3 displays the distribution of study variables based on cognitive status. Except for BMI, all study variables showed statistically significant differences. The distribution of study variables varied depending on cognitive status ($p>0.05$). A higher proportion of females (38.4%) showed

cognitive decline compared to males (30.4%). Among individuals with cognitive decline, 50.8% could not afford medical consultation, while 32% could afford it. Also, 28.4% of individuals who were satisfied with their lives had cognitive decline, and 71.6% did not. Among individuals who regularly engage in physical activity, 27.5% have cognitive decline, while 72.5% do not. In contrast, 41.7% of individuals who do not regularly engage in physical activity have cognitive decline, while 58.3% do not.

TABLE 3: Distribution of study characteristics by cognitive decline status

Variables	Categories	Cognitive Decline		P-Value
		Yes n (%)	No n (%)	
Gender	Male Female	284 (30.4) 376 (38.4)	651 (69.6) 602 (61.6)	<.001
BMI (Overweight or Obese)	Yes No	539 (34.7) 86 (31.9)	1015 (65.3) 184 (68.1)	.365
Physical Activity	Yes No	264 (27.5) 393 (41.7)	697 (72.5) 550 (58.3)	<.001
Employment Status	Employed for wages Self-employed Retired Unable to work	44 (19.0) 18 (24.0) 308 (31.0) 243 (51.2)	188 (81.0) 57 (76.0) 685 (69.0) 232 (48.8)	<.001
Income	Less than $50,000 $50,000 - $100,000 $100,000 - $200,000 $200,000 or more	411 (39.1) 80 (24.5) 23 (17.0) 1 (5.3)	640 (60.9) 247 (75.5) 112 (83) 18 (94.7)	<.001
Race/Ethnicity	White only, non-Hispanic Black, non-Hispanic Hispanic	446 (30.7) 96 (47.1) 55 (49.5)	1008 (69.3) 108 (52.9) 56 (50.5)	<.001
Education	Did not graduate high school Graduated high school Attended College/Tech School Graduated from College/Tech School	89 (45.4) 221 (37.9) 212 (36.2) 135 (24.9)	107 (54.6) 362 (62.1) 373 (63.8) 408 (75.1)	<.001
Could not afford to see a doctor	Yes No	121 (50.8) 531 (32.0)	117 (49.2) 1129 (68.0)	<.001
Marital Status	Married Divorced Widowed Separated Never married	257 (31.8) 163 (39.3) 133 (32.6) 26 (46.4) 60 (33.9)	551 (68.2) 252 (60.7) 275 (67.4) 30 (53.6) 117 (66.1)	0.027
Satisfaction with life	Yes No	357 (28.4) 161 (53.5)	898 (71.6) 140 (46.5)	<.001
Depressive disorder	Yes No	401 (44.3) 251 (25.3)	505 (55.7) 740 (74.7)	<.001

4.2 Results of Multivariate Logistic Regression Analysis

The result of multivariate logistic regression analysis of the association of selected independent variables and cognitive decline, adjusting for confounders, is shown in Table 4. Participants who exercise regularly had 30% reduced odds (OR = 0.70, 95% CI: 0.52 – 0.94, p = 0.018) of cognitive decline compared to individuals who do not exercise regularly. Participants who reported being satisfied with life reported 52% reduced odds (OR = 0.48, 95% CI: 0.33 – 0.71, p<.001) of cognitive decline than for individuals who were dissatisfied with life. Individuals who reported their inability to afford a doctor had 1.97 higher odds (OR = 1.97, 95% CI: 1.57 – 3.79, p<.001) of cognitive decline than those who could afford a doctor. Also, subjects with diagnosed depressive disorder had significantly higher odds (OR = 1.59, 95% CI: 1.16 – 2.17, p<.001) of cognitive decline than individuals without a depressive disorder diagnosis.

Male gender was associated with 7% reduced odds (OR = 0.93, 95% CI: 0.69 – 1.24, p = 0.235) of cognitive decline compared to female gender. It was noted that individuals who were overweight or obese had 1.35 higher odds (OR = 1.35, 95% CI: 0.86 – 2.04, p = 0.195) of cognitive decline than individuals who were normal weight or underweight. Other variables that were positively associated with cognitive decline were marital status (Divorced; OR = 1.74, 95% CI: 1.14 – 2.65, p = 0.011), (Never married; OR = 2.07, 95% CI: 1.19 – 3.58, p = 0.010), (Widowed; OR = 1.30, 95% CI: 0.89 – 1.91, p = 0.181). Compared to employed participants, self-employed participants had a 64% decreased odds of cognitive decline (OR = 0.36, 95% CI: 0.15 – 0.87, p = 0.024), retired participants had 47% decreased odds of cognitive decline (OR = 0.53, 95% CI: 0.30 – 0.92, p = 0.023), and participants who are unable to work had a 68% decreased odds of cognitive decline (OR = 0.32, 95% CI: 0.18 – 0.58, p<.001).

Compared to non-Hispanic White individuals, non-Hispanic Black individuals were associated with 50% decreased odds of cognitive decline (OR = 0.50, 95% CI: 0.32 – 0.77, p = 0.002), and Hispanic individuals were associated with 29% decreased odds of cognitive decline (OR = 0.71, 95% CI: 0.38 – 1.33, p = 0.290).

Finally, compared to individuals earning <$50,000, those earning $50,000 - $100,000 had 1.96 higher odds of cognitive decline (OR = 1.96, 95% CI: 1.30 – 2.97, p = 0.001), individuals earning <$150, 000 - $200,000 had 2.58 higher odds of cognitive decline, (OR = 2.58, 95% CI: 1.31 – 5.01, p = 0.006), and individuals earning $200,000 had 3.36 higher odds of cognitive decline (OR = 3.36, 95% CI: 0.40 – 28.39, p = 0.266).

TABLE 4: Multivariate Logistic Regression of factors associated with cognitive decline in subjects with diabetes

Variables	Categories	Odds Ratio	95% CI	P-Value
Gender	Male Female	0.93 1.00	0.69 – 1.24 Ref	0.235
BMI	Yes No	1.00 1.35	Ref 0.86 – 2.04	0.195
Physical Activity	Yes No	0.70 Ref	0.52 – 0.94 Ref	0.018
Could not afford to see a doctor	Yes No	1.97 1.00	1.57 - 3.79 Ref	<.001
Satisfaction with life	Yes No	0.48 1.00	0.33 – 0.71 Ref	<.001
Depressive disorder	Yes No	1.59 1.00	1.16 – 2.17 Ref	<.001
Employment Status	Employed for wages Self-employed Retired Unable to work	1.00 0.36 0.53 0.32	Ref 0.15 – 0.87 0.30 – 0.92 0.18 – 0.58	<.001 0.024 0.023 <.001
Income Level	<$50,000 $50,000 - $100,000 <$150,000 - $200,000 $200,000 or more	1.00 1.96 2.58 3.36	Ref 1.30 – 2.97 1.31 – 5.01 0.40 – 28.39	0.002 0.001 0.006 0.266
Race/Ethnicity	Non-Hispanic, White Non-Hispanic, Black Hispanic	1.00 0.50 0.71	Ref 0.32 – 0.77 0.38 – 1.33	0.005 0.002 0.290
Marital Status	Married Widowed Divorced Never married	1.00 1.30 1.74 2.07	Ref 0.89 – 1.91 1.14 – 2.65 1.19 – 3.58	0.016 0.181 0.011 0.010

5 DISCUSSION

5.1 Interpretations of Findings

The premise of this study was to shed light on the relationship between diabetes and cognitive decline. The analysis shows that there is a significant effect of physical activity, healthcare affordability, satisfaction with life, and depression diagnosis on the development of dementia in individuals with diabetes. This study is necessary to understand and develop target intervention strategies to cater to these individuals and reduce dementia prevalence resulting from diabetes (Rohr et al., 2022). Study results show that subjects with diabetes who engage in physical activity have 30% more protection from developing subjective cognitive decline than those who do not exercise regularly. This finding is consistent with results from The Finnish Diabetes Prevention Study, which reported similar findings. It is also confirmed by a study which revealed that individuals with pre-diabetes can reduce the likelihood of developing Type 2 diabetes and pre-diabetes with frequent physical activity (Selman et al., 2022). Espeland et al., 2018, report that diet is associated with a high risk for obesity, diabetes, and dementia. The study results show that similarly, individuals who are obese or overweight are 1.35 times more likely to develop dementia than individuals who are not. However, this result was insignificant.

This study showed that individuals with diabetes who are unable to afford a doctor are 1.97 times more likely to develop dementia than those who can afford one. In addition to this, the study demonstrated that individuals who are employed and earn a high income are more likely to develop dementia than individuals who are unemployed or retired and earn a low income. These results are inconsistent with the literature reviewed. Rohr et al., 2022 report findings from the English Longitudinal Study of the Aged, which demonstrates that individuals

with low income have a higher dementia risk than their counterparts with high income. Bodryzlova et al., 2022 also highlight that they are more likely to receive timely medical attention due to their ability to afford frequent check-ups. A diabetes diagnosis in conjunction with a depressive disorder makes an individual 1.59 times more likely to develop dementia than an individual who has a diabetes diagnosis only. A study by Katon et al., 2015 supports findings by reporting that depression has been shown to double the risks for dementia, and when it is comorbid with diabetes, it further increases this risk.

Selman et al., 2022 highlight biological reasons for differences in dementia for males and females. Their report shows that women are 1.5 times more likely to have dementia than men. Results from this study align with the literature; males are 7% protected from dementia. However, these results are not statistically significant.

Zhou et al., 2023 report that White people with diabetes are 2.85 times more likely to develop dementia than non-Hispanic Black people with diabetes. This study similarly shows that non-Hispanic Black and Hispanic individuals are 50% and 29% more protected from dementia than non-Hispanic White individuals. Results for marital status in this report demonstrate that divorced and 'never married' individuals are more likely to develop dementia than married individuals. This finding is consistent with the literature comparing social isolation scores for men and women, clarifying that women have higher social isolation scores than men. All these results are consistent with the literature.

There are a few possibilities as to why retired and unable-to-work individuals would be protected from dementia compared to employed individuals. Individuals who are employed could experience stress and burnout from their workload. They could also be engaged in shift

work, which consists of irregular hours, especially at night, disrupting the normal circadian rhythm. A cohort of 2,764 men aged 65 years and older revealed that disrupted sleep was positively associated with cognitive decline after 3.4 years of follow-up (Lee et al., 2023). Employment and income are closely connected factors; therefore, if shift work and multiple jobs are the source of income for such individuals accounted for, it would make sense that it would be the case that an increase in odds of developing dementia will be observed for individuals earning high income.

5.2 Strengths, Limitations, and Future Research

The main strength of the BRFSS survey is that it consists of a large sample size and is nationally representative compared to other national datasets. It has also undergone many improvements over the years of administering the survey. The limitations of this study were that it had a cross-sectional design, and therefore, causation cannot be inferred; it only involved the association between exposure and outcome. All data was collected via self-report, which may be subject to difficulty in remembering the frequency of behaviors. Most of the data had to be excluded due to the refusal to respond. This has the potential to cause bias in the results. There may also be selection bias, given that households without telephones could not have been contacted. Further studies should be performed with primary data to assess individuals via laboratory tests instead of self-reporting. Variables such as employment status and income should be considered in addition to more specific details concerning types of jobs and avenues of income to determine what exact factor needs to be addressed to ensure appropriate interventions are implemented.

5.3 Conclusion

According to this study, individuals with diabetes who experience cognitive decline are more likely to be female, have lower income, spend little or no time doing physical activity, are dissatisfied with life, and are socially isolated. These individuals with diabetes are also more prone to having a depressive disorder and infrequent health check-ups. These findings are crucial in terms of public health and call for public health practitioners to be aware of risk factors for cognitive decline and dementia in diabetes patients. Public health interventions can help reduce the prevalence of cognitive decline in diabetes patients by promoting physical activity, improving diet, and encouraging cognitively stimulating activities such as reading and social engagement.

REFERENCES

Baglietto-Vargas, D., Shi, J., Yaeger, D. M., Ager, R., & LaFerla, F. M. (2016). Diabetes and Alzheimer's disease crosstalk. Neuroscience & Biobehavioral Reviews, 64, 272-287. (Moranet et al., 2013; Roberts et al., 2014)

Bertram, S., Brixius, K., & Brinkmann, C. (2016). Exercise for the diabetic brain: how physical training may help prevent dementia and Alzheimer's disease in T2DM patients. Endocrine, 53, 350-363.

Beydoun, M. A., Beydoun, H. A., Banerjee, S., Weiss, J., Evans, M. K., & Zonderman, A. B. (2022). Pathways explaining racial/ethnic and socioeconomic disparities in incident all-cause dementia among older US adults across income groups. Translational Psychiatry, 12(1), 478.

Bodryzlova, Y., Kim, A., Michaud, X., Andre, C., Belanger, E., & Moullec, G. (2023). Social class and the risk of dementia: A systematic review and meta-analysis of the prospective longitudinal studies. Scandinavian journal of public health, 51(8), 1122-1135.

Čater, M., & Hölter, S. M. (2022). A pathophysiological intersection of diabetes and Alzheimer's disease. International journal of molecular sciences, 23(19), 11562.

Centers for Disease Control and Prevention. (2024, January 9). CDC - BRFSS. Centers for Disease Control and Prevention. https://www.cdc.gov/brfss/index.html

Espeland, M. A., Small, D. M., & Stoeckel, L. E. (2018). Diet, obesity, and physical inactivity: linking diabetes and dementia. In Type 2 diabetes and dementia (pp. 117-141). Academic Press.

Janoutová, J., Machaczka, O., Zatloukalová, A., & Janout, V. (2022). Is Alzheimer's disease a type 3 diabetes? A review. Cent. Eur. J. Public Health, 30, 139-143.

Jash, K., Gondaliya, P., Kirave, P., Kulkarni, B., Sunkaria, A., & Kalia, K. (2020). Cognitive dysfunction: a growing link between diabetes and Alzheimer's disease. Drug development research, 81(2), 144-164.

Katon, W., Pedersen, H. S., Ribe, A. R., Fenger-Grøn, M., Davydow, D., Waldorff, F. B., & Vestergaard, M. (2015). Effect of depression and diabetes mellitus on the risk for dementia: a national population-based cohort study. JAMA psychiatry, 72(6), 612-619.

Lee, K. W., Yang, C. C., Chen, C. H., Hung, C. H., & Chuang, H. Y. (2023). Shift work is significantly and positively associated with dementia: A meta-analysis study. Frontiers in Public Health, 11, 998464.

Lehtisalo, J., Ngandu, T., Valve, P., Antikainen, R., Laatikainen, T., Strandberg, T., ... & Lindström, J. (2017). Nutrient intake and dietary changes during a 2-year multi-domain lifestyle intervention among older adults: secondary analysis of the Finnish Geriatric Intervention Study

to Prevent Cognitive Impairment and Disability (FINGER) randomised controlled trial. British journal of nutrition, 118(4), 291-302.

Liu, H., Zhang, Z., Choi, S. W., & Langa, K. M. (2020). Marital status and dementia: Evidence from the Health and Retirement Study. The Journals of Gerontology: Series B, 75(8), 1783-1795.

Read, S., Comas-Herrera, A., & Grundy, E. (2020). Social isolation and memory decline in later-life. The Journals of Gerontology: Series B, 75(2), 367-376.

Röhr, S., Pabst, A., Baber, R., Engel, C., Glaesmer, H., Hinz, A., ... & Riedel-Heller, S. G. (2022). Social determinants and lifestyle factors for brain health: implications for risk reduction of cognitive decline and dementia. Scientific Reports, 12(1), 12965.

Salas, I. H., & De Strooper, B. (2019). Diabetes and Alzheimer's disease: a link not as simple as it seems. Neurochemical Research, 44(6), 1271-1278.

Savelieff, M. G., Chen, K. S., Elzinga, S. E., & Feldman, E. L. (2022). Diabetes and dementia: Clinical perspective, innovation, knowledge gaps. Journal of diabetes and its complications, 36(11), 108333. https://doi.org/10.1016/j.jdiacomp.2022.108333

Selman, A., Burns, S., Reddy, A. P., Culberson, J., & Reddy, P. H. (2022). The role of obesity and diabetes in dementia. International journal of molecular sciences, 23(16), 9267.

Shafighi, K., Villeneuve, S., Rosa Neto, P., Badhwar, A., Poirier, J., Sharma, V., ... & Bzdok, D. (2023). Social isolation is linked to classical risk factors of Alzheimer's disease-related dementias. Plos one, 18(2), e0280471.

Snead, R., Dumenci, L., & Jones, R. M. (2022). A latent class analysis of cognitive decline in US adults, BRFSS 2015-2020. BMC Public Health, 22(1), 1560.

Sundström, A., Rönnlund, M., & Josefsson, M. (2020). A nationwide Swedish study of age at retirement and dementia risk. International journal of geriatric psychiatry, 35(10), 1243-1249.

Zhou, C., Dong, C., Xie, Z., Hao, W., Fu, C., Sun, H., & Zhu, D. (2023). Sex-specific associations between diabetes and dementia: the role of age at onset of disease, insulin use and complications. Biology of sex Differences, 14(1), 9.