7-16-2024

Association Between Psychological Distress and Diabetic Retinopathy Among U.S. Adults

Claret Ijeoma Onukogu
Walden University

Walden University

College of Health Sciences and Public Policy

This is to certify that the doctoral dissertation by

Claret Onukogu

has been found to be complete and satisfactory in all respects,
and that any and all revisions required by
the review committee have been made.

Review Committee
Dr. Srikanta Banerjee, Committee Chairperson, Public Health Faculty
Dr. Raymond Panas, Committee Member, Public Health Faculty

Chief Academic Officer and Provost
Sue Subocz, Ph.D.

Walden University
2024

Abstract

Association Between Psychological Distress and Diabetic Retinopathy Among U.S. Adults

by

Claret Onukogu

DBA, Walden University, 2018

MBA, South University, 2008

BS, Armstrong Atlantic State University, 2005

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

May 2024

Abstract

Diabetes can lead to diabetic retinopathy, an eye disease that causes damaged blood vessels and the growth of abnormal ones, leading to vision loss. The two stages of the disease are non-proliferative and proliferative diabetic retinopathy. In the non-proliferative stage, diabetics develop macular edema and ischemia with shortage of blood in the macula region of the eye, and the vision eventually becomes blurry. However, the proliferative stage is the advanced stage of the disease involves neovascularization and retinal detachment. The quantitative study employed the socioecological model as the theoretical framework to examine the relationship between psychological distress and diabetic retinopathy while considering gender. The aim was to determine the role of psychological distress in diabetic retinopathy after controlling for covariates such as age, educational level, and income among U.S. adults. The association between the independent variables, gender and psychological distress, and the dependent variable, diabetic retinopathy was explored. The National Health and Nutrition Examination Survey was used as the data source. There was no association between psychological distress, OR = 0.96 (CI 0.60-1.56, p = .84), and gender (OR = 1.65, p = .18), and diabetic retinopathy when controlling for covariates. Further research on patient education and regular screening for diabetic retinopathy in the United States for diabetic patients is necessary. Implications for positive and sustainable social change include providing new insights on ways understanding the pathophysiology of diabetes and diabetic retinopathy could lead to the improvement of psychological distress.

Association Between Psychological Distress and Diabetic Retinopathy

Among U.S. Adults

by

Claret Onukogu

DBA, Walden University, 2018

MBA, South University, 2008

BS, Armstrong Atlantic State University, 2005

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

May 2024

Dedication

I thank God for giving me the gift of intellect to complete my doctoral journey. I thank him for answering my countless prayers for the strength and means to move forward every step of the way during the tedious doctoral journey despite the challenges and obstacles that came my way. Thanks for being my pillar and backbone. I owe so much thanks to my mother, Catherine Ngozi Onukogu, for her unwavering love and support. Your zeal and enthusiasm towards my success inspire me to attain greater heights in my life. Your moral support and encouragements fueled my strengths towards completing my doctoral study. I love you.

Acknowledgments

I would like to offer special thanks and gratitude to my committee chair and mentor, Dr. Sri Banerjee, and his predecessors who also contributed to my success in this difficult journey. I would also like to acknowledge and thank my second committee member, Dr. German Gonzalez, and my methodologist, Dr. Raymond Panas, for their valuable suggestions, which contributed to the development and enrichment of my doctoral study. I am grateful for my university research reviewer (URR) for the invaluable contributions to the completion of my doctoral study. Thanks to Dr. Angela Prehn, the program director of the PhD in Public Health program at Walden University, for establishing a rewarding learning opportunity through this program. Thanks to other Walden University faculty who helped me along the way.

Table of Contents

Part 1: Overview

Introduction

Diabetes is the inability of the body to respond to or produce a hormone called insulin. According to the Centers for Disease Control and Prevention (CDC, 2020), out of the 37.3 million U.S. adults living with the disease, 1 in 5 of them is unaware that they have the condition. Diabetes occurs when the human body is unable to take glucose or sugar into its cells and convert it to energy. The body lacks the ability to adequately process and use sugar from food, which causes damage and consequences to the tissues and organs in the nerves, eyes, kidneys, and heart (CDC, 2021). It is the seventh leading cause of death, and the number one cause of adult blindness, lower-limb amputations, and kidney failure in the nation. Adults living with diabetes in the United States have more than doubled in the last 20 years (CDC, 2020). Diabetes leads to the accumulation of excess sugar in the bloodstream. During the process of digestion, the body breaks down food into various nutrients. It turns carbohydrates from food such as pasta, rice, and bread into glucose. With its presence in the bloodstream, it needs assistance from insulin to navigate to the body's cells, which build organs and tissues, which are its final destination (CDC, 2021).

The pancreas, an organ situated behind the stomach, makes the insulin hormone (National Institute of Diabetes and Digestive and Kidney Disease, n.d.). Insulin enables glucose to penetrate into the body's cells. Glucose provides energy for the proper functioning of the organs and tissues. The pancreas of individuals living with diabetes fails to make enough or any insulin. In some instances, it makes insulin, but the body's cells refuse to respond to the hormone and fail to use it as they should (CDC, 2020). The blood glucose level rises when glucose cannot get into the body's cells and stays in the bloodstream. The different types of diabetes include type 1 diabetes, type 2 diabetes, prediabetes, and gestational diabetes (CDC, 2021). The rare types of diabetes include drug- or chemical-induced diabetes, cystic-fibrosis-related diabetes, and monogenic diabetes syndromes (Cleveland Clinic, 2021).

Type 1 diabetes is caused by an autoimmune attack of the pancreas that causes the body to fight itself. In the pancreas, the insulin-producing cells are often destroyed. An estimated 0.55% of individuals in the United States are living with type 1 diabetes (CDC, 2020). Although type 1 diabetes develops mainly in young adults and children, individuals of any age can get the disease diagnosis. It has been best known as *juvenile diabetes* and referred to as *insulin-dependent diabetes* (CDC, 2020). Those living with the disease need daily intake of insulin. In type 2 diabetes, also called *insulin-resistant* or *adult-onset diabetes*, the body's cells do not have a normal response to insulin or the body fails to make enough insulin. It is the most common type of diabetes and often occurs in adults who are middle-aged or older. An estimated 90–95% of individuals living with diabetes have type 2 diabetes (CDC, 2020). *Prediabetes* occurs prior to the onset of type 2 diabetes. In prediabetes, blood glucose levels tend to be slightly elevated but not high enough to warrant a type 2 diabetes diagnosis (CDC, 2020). During pregnancy, *gestational diabetes* develops in some women and goes away after they give birth, but those women have a higher risk of type 2 diabetes diagnoses later in life. In the United States, more than 1 in 3 adults, 96 million, have prediabetes; more than 8 out of

10 of those individuals do not know that they are prediabetic (CDC, 2020). *Monogenic diabetes syndrome* is a rare form of inherited diabetes and entails maturity-onset diabetes and neonatal diabetes. *Cystic-fibrosis-related diabetes* is a type of diabetes that affects individuals living with cystic fibrosis (Cleveland Clinic, 2021). *Drug- or chemical-induced diabetes* occurs after organ transplant, the use of glucocorticoid steroids, or human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) treatment. *Diabetes insipidus* is a rare condition that affects the kidney and causes it to produce excess urine (Cleveland Clinic, 2021).

Diabetic retinopathy is common in people living with diabetes. Diabetes tends to cause eye problems, with diabetic retinopathy being the most common. Eye problems resulting from diabetes can lead to blindness or vision loss. In working-age adults living in the United States, retinopathy is the most common cause of blindness (Regeneron Pharmaceuticals, 2021). The risk of developing diabetic retinopathy along with its complications, such as diabetic macular edema, tends to increase the longer people live with the disease. Although diabetic retinopathy affects the eyes, its symptoms might not show until later in life. Even though their vision might seem normal, people with diabetes need to visit ophthalmologists or optometrists for annual eye exams. The only way to determine whether an individual has diabetic retinopathy is through eye examination during a doctor’s visit. By performing dilated eye exams, optical coherence tomography, fluorescein angiography, fundus photographs, eye pressure, and distance vision exams, eye care professionals can detect signs of retinopathy and commence treatment immediately to avoid further damage (Regeneron Pharmaceuticals, 2021). Based on their findings of what is happening inside the eyes, they can suggest necessary actions to patients. If patients prioritize eye care, potential treatments, routine monitoring, and early detection can make a difference in their eye health. Diabetic retinopathy progresses in two stages: proliferative diabetic retinopathy (PDR) and nonproliferative diabetic retinopathy (NPDR), which varies from mild to moderate to severe (Regeneron Pharmaceuticals, 2021).

Ophthalmologists and optometrists use the imaging method *optical coherence tomography (OCT)* to obtain a picture of the retina, which is located at the back of the eye. They create the picture through a measurement of the amount of a dim red light reflecting off the retina. The test is often instrumental in capturing the images of the eyes of individuals living with conditions such as retinopathy and glaucoma. OCT measures the thickness of the retina's nerve layer. It is evaluated as a new way of following, testing, and measuring the response to treatment and the recovery of patients living with eye diseases. In the process of performing OCT, patients place their chins on the machine and stare into a lens with nothing touching their eyes. The scan takes a few minutes for each eye. If eye doctors have not performed the exam, they ask participants to undergo a bedside neurological exam and vision testing that involves the reading of an eye chart. The total time required to perform OCT is 45 minutes. Although some patients notice temporary eye dryness and fatigue, there are usually no anticipated health risks associated with OCT (Cleveland Clinic, 2022).

Fluorescein angiography (FA) is a procedure that involves ophthalmologists using a special camera to capture images of the retina; they are able to use the pictures to get a clearer view of the structures in the back of the eye, such as blood vessels (Porter, 2022). FA is useful in finding and diagnosing eye problems such as ocular melanoma, macular pucker, macular degeneration, diabetic retinopathy, macular edema, and vein blockage in the eye called branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO; Porter, 2022). *Ocular melanoma* is a type of eye cancer. *Macular pucker* comprises of the accumulation of fluid behind the eye that causes a wrinkle in the retina. *Diabetic retinopathy* is an abnormality or damage in the blood vessels of the eye because of diabetes. *Macular edema* is retinal swelling that leads to distorted vision. *Macular degeneration* is characterized by a problem in the retina because of damages to its part called the macula. Ophthalmologists and optometrists use FA to focus on treatment areas and to monitor changes in eye diseases. The procedure is usually carried out in the doctor’s office and it lasts less than 30 minutes. To widen or dilate the pupil, the ophthalmologist or their assistants administer eye drops into the patient’s eyes. They inject fluorescein, a yellowish-colored dye, into a vein, usually in the arm. In about 10–15 seconds, the dye circulates in the body and eventually travels to the blood vessels in the eye causing them to shine bright. A special camera captures the dye passing through the retina. Ophthalmologists examine the pictures to identify abnormalities and areas that need treatment. Light sensitivity and blurry vision are the effect of dilating eye drops, and they can linger for several hours. Patients need to use sunglasses to protect the eyes and ensure that someone drives them home after the procedure because it is not safe for them to do so. There are some risks and side effects associated with FA. Objects may seem tinted or dark when patients look at them. The side effects usually fade after a few minutes. The skin may turn slightly yellow because the dye spreads to the veins in the body, but it returns to normal after a few hours. The urine may look dark yellow or orange for up to 24 hours.

Individuals living with diabetic retinopathy at the different stages are at a risk for developing diabetic macular edema as a serious complication. For NPDR, excess sugar levels begin to affect small blood vessels at the back of the eye during the early stages of diabetic retinopathy; that part of the eye is the retina (Regeneron Pharmaceuticals, 2021). It detects light and transports signals to the brain to interpret as images. Initially, there might not be changes in vision, but there could be a gradual progression of the NPDR from mild to moderate and severe (Regeneron Pharmaceuticals, 2021). Such an occurrence is a result of swollen blood vessels and leaky fluids that prevent the retina from receiving nutrients or oxygen. There may not be any vision changes at that point, and the individual might not notice any warning signs. Without treatments administered to slow down NPDR, other changes and bleeding may occur, and symptoms such as increased floaters in the eyes, difficulty with reading, and blurriness surrounding the edges of vision may become noticeable. Floaters in the eyes can also be a sign of other eye conditions that do not relate to diabetes (Regeneron Pharmaceuticals, 2021).

Following the changes that NPDR causes, as a response, the body produces *vascular endothelial growth factor (VEGF)* in the PDR stage (Regeneron Pharmaceuticals, 2021). The substance enables abnormal new blood vessel growths in the retina in an attempt to get its needed blood flow. Abnormal blood vessels are easily damaged and fragile, and they contribute to leakage and swelling in the eyes. The advanced stage of diabetic retinopathy is known as proliferative diabetic retinopathy, and it is a result of the rapid increase or proliferation of the new blood vessels (Regeneron Pharmaceuticals, 2021). At this stage, individuals may experience visual symptoms such as dark spots or blurry vision. PDR is a serious eye condition that could lead to vision loss. There are treatment options to assist in possibly reversing or slowing down some of the damage in the eyes. Normally, there is no retina blood vessel swelling or leaky fluid. During the stage of mild nonproliferative diabetic retinopathy, small bulges tend to appear in the walls of the retina's blood vessels even though there are no visual symptoms. In the moderate nonproliferative diabetic retinopathy stage, there is some swelling and leakage of the blood vessels. Some blood vessels may resemble beads on a string because they are taking an uneven shape (Regeneron Pharmaceuticals, 2021). Usually, no visual symptoms exist during this stage. In the severe nonproliferative diabetic retinopathy stage, more blood leaks into the retina. There could be blockages of blood vessels that supply nutrients and oxygen to the eyes. The body signals for help by indicating the need for the growth of new blood vessels. There may be visual symptoms at this stage. At the proliferative diabetic retinopathy stage, the retina grows fragile, and new blood vessels bleed into the eyes and reveal symptoms such as dark spots. There may be permanent vision loss (Regeneron Pharmaceuticals, 2021).

There are an estimated 2.2 billion visually impaired individuals worldwide (Demmin & Silverstein, 2020). The projection of the number rising is evident because of the rise in average lifespans. Factors such as diabetic retinopathy and age-related vision loss contribute to the causes of vision impairment. Vision loss can lead to serious disability, and it is associated with concurrent medical issues, reduced quality of life, economic burden, and mental health issues (Demmin & Silverstein, 2020). It is imperative to examine the mental and psychological health outcomes of people with diabetic retinopathy and the treatments for the visually impaired. Substantial data indicate that there are elevated rates of anxiety and depression in people with visual impairments such as diabetic retinopathy. Those who belong to a lower socioeconomic status could face an increased risk for mental and psychological health problems. There are limitations in existing psychosocial interventions geared towards the improvement of mental and psychological well-being for people who are visually impaired. For improved outcomes, there is a need for a better understanding of the mechanisms linking poor psychological or mental health and visual impairment such as diabetic retinopathy (Demmin & Silverstein, 2020). The development of additional effective interventions and the expansion of accessibility of services necessary for the improvement of the detection and treatment of psychological and mental health problems in the diabetic retinopathy population are important.

Background

This section describes articles pertaining to diabetes mellitus, diabetic retinopathy, and psychological distress. The searched keywords were *diabetes mellitus, type 1 diabetes*, *type 2 diabetes*, *gestational diabetes*, *retinopathy*, *gender*, and *psychological distress*. EBSCOhost was beneficial in searching various databases to gather scholarly books and peer-reviewed articles published between 2015 and 2023. The searched journals included articles on health, science, and medicine.

1. Lien et al. (2017) and Emani et al. (2018) described the self-management of type 2 diabetes and the perceptions of adopters versus nonadopters of a patient portal pertaining to the application of diffusion of innovation theory.
2. Ansari et al. (2016) and Vitger et al. (2017) further described the management of type 2 diabetes and the involvement of family preferences and challenges as they relate to the management of the disease.
3. Torpy et al. (2007) and the National Institutes of Health (NIH, 2019) emphasized that retinopathy is disease of the retina and the different types of the disease entail small retinal blood vessels. The symptoms include blindness, floating spots in the vision, and blurry vision. The treatment of the disease includes surgery, laser treatment, and medicine.
4. McLachlan and Gale (2018) emphasized that the characteristics of psychological distress include emotional suffering linked to the inability to handle demands of daily activities and stressors. The difficulties associated with the identification and the failure to provide effective care for the condition could cause frustrations for health professionals and patients.

High blood sugar resulting from diabetes causes diabetic retinopathy. Excessive sugar in the blood could damage the retina, which is the part of the eye that transmits signals to the brain, after detecting light, through the optic nerve. The blood vessels in the body could become damaged because of diabetes mellitus. When blood sugar causes blockage to the blood vessels that lead to the retina, resulting in fluid leakage or bleeding, it damages the eyes. To compensate for the blocked blood vessels, new blood vessels that do not function properly start to grow in the eyes. Those new blood vessels can easily bleed or leak (Torpy et al., 2007). A prediabetic diagnosis means that the blood sugar is high, but not high enough to qualify for a type 2 diabetes diagnosis. Certain problems can arise from high blood sugar, such as damage to the nerves, kidney, blood vessels, skin, heart, brain, and eyes (Dansinger, 2020). The disease can affect sleep, hearing, and pregnancy and lead to depression (Dansinger, 2020). Depending on the distress severity range, psychological distress could lead to diseases such as chronic obstructive pulmonary disease, cardiovascular disease, arthritis, and diabetes (McLachlan & Gale, 2018).

Overview of the Manuscripts

Out of the 34.2 million adults living with diabetes in the United States, 1 in 5 of them is unaware that they have the disease (CDC, 2020). The number of individuals diagnosed with diabetes has more than doubled in the last 20 years (CDC, 2020). Diabetes mellitus (DM) is a disorder that prevents the body from a normal response to or sufficient production of insulin, which leads to abnormally high blood glucose levels (CDC, 2020). The three types of diabetes are type 1, type 2, and gestational diabetes, which can occur during pregnancy. A possible cause of type 1 diabetes is that the body may mistakenly attack itself, causing an autoimmune reaction and stopping the production of insulin (CDC, 2020). People with type 2 diabetes have a pancreas that cannot produce sufficient amounts of insulin and their bodies lack the ability to efficiently use the produced insulin for the body to maintain a normal glucose level (American Diabetes Association, 2020). People with diabetes could develop an eye disease called retinopathy characterized by an increased blood sugar level that may damage the retina, leading to the swelling and leakage of the blood vessels (Boyd & Gregori, 2020). Attitudes, beliefs, feelings, and thoughts can affect individual health. Untreated mental health issues could worsen diabetes, and the problems associated with the disease could worsen mental health issues (Boyd & Gregori, 2020). The general public health problem is the association between psychological distress and diabetic retinopathy after controlling for covariates such as age, educational level, and income. The specific public health problem is determining the role of gender predisposition in psychological distress and diabetic retinopathy, which could fill a public health knowledge gap contributing to population health planning and implementation, after controlling for covariates such as age, educational level, and income.

Purpose

The purpose of this quantitative study was to investigate the relationship between psychological distress and diabetic retinopathy while considering gender. I examined the association between the independent variables, gender and psychological distress, and the dependent variable, diabetic retinopathy. For the study, I used a nationally representative dataset, such as The National Health and Nutrition Examination Survey (NHANES), to analyze data. The study is unique because it explored the gap in the literature about the under-researched area of the likelihood of gender modifying the effect of psychological distress on diabetic retinopathy.

Framework (Conceptual or Theoretical)

The social-ecological model enabled the understanding of the relationship between psychological distress and diabetic retinopathy. It assisted in evaluating the interplay between societal, community, relationship, and individual factors; and enabled the exposure of the factors that place individuals at risk for psychological distress and diabetic retinopathy (CDC, 2021). In the socioecological model, factors on one level often influence those on another level. The model provided some clarity on the different factors pertaining to the dependent and independent variables. The individual level of the model includes the personal history and biological factors increasing the likelihood of developing diabetic retinopathy and psychological distress. Those factors include income, education, and age. On an individual level, prevention strategies could result in the promotion of behaviors, beliefs, and attitudes that could prevent psychological distress and diabetic retinopathy. The second level of the model, relationship, emphasizes the close relationships that could increase the risk of diabetic retinopathy and psychological distress (CDC, 2021). People's closest family members, partners, and social circle peers tend to impact their experiences and influence or contribute to their behaviors (CDC, 2021). At the relationship level, strategies for the prevention of psychological distress and diabetic retinopathy could involve the promotion of positive peer programs for strengthening communications, family-focused prevention, and mentoring programs, and the promotion of healthy relationships and problem-solving skills. The third level is the community, it explores the neighborhood, workplaces, and schools where people form social relationships, and those settings might contribute to psychological distress associated with diabetic retinopathy. The prevention strategies involve the improvement of the social and physical environment in settings where individuals play, work, learn, and live (CDC, 2021). The community level of the model also addresses residential instability and poverty. The fourth level pertains to societal factors that may encourage the creation of an environment that inhibits or encourages psychological distress (CDC, 2021). The factors entail cultural and social norms that support behaviors that might lead to psychological distress and diabetic retinopathy. Societal factors also include social, educational, economic, and health policies that assist in the maintenance of social or economic inequalities in various sects of society. Prevention strategies at the societal level include efforts geared towards societal norm promotions that would foster employment and educational opportunities, financial security in the household, and additional policies influencing structural determinants of health (CDC, 2021).

Weight loss is important for the management of diabetes mellitus. The reduction of carbohydrates could reduce fat and inflammation linked to insulin resistance (Curry, 2020). Losing weight usually leads to positive changes in the body. Managing diabetes requires dedication and determination from people living with the disease to improve their health by living a healthy lifestyle through dieting and exercising (Doheny, 2020). Although their pharmacists, diabetes educators, nutritionists, eye doctors, foot doctors, and primary care physicians can assist them, managing the disease is tough for diabetics and it is a challenge that requires them to change their regular way of life and routine (CDC, 2019). Checking their blood sugars regularly, maintaining a targeted cholesterol level and blood pressure, taking their oral and injectable medications to prevent complications, being active, and eating healthy requires work and perseverance. The social-ecological model was the most suitable framework for the study because it depicts the influence of various determinants of behaviors and enables a better understanding of them as they pertain to psychological distress and diabetic retinopathy (CDC, 2021). Evaluating the range or level of psychological distress as it relates to diabetes mellitus involves the investigation of the mediating roles of health behaviors. Diabetics would have to go through relative advantage by seeing that the new way of life would be better than their regular or current lifestyles. They would have to check the consistency of the new behavior with their needs, values, and experiences. They would need to evaluate the complexity or the level of difficulty of the changes, experiment with the new way of life to determine which routines they can commit to, and observe the extent to which the lifestyle changes provide tangible results.

Research Questions and Hypotheses

Manuscript 1

Specific Problem

The specific public health problem is determining the role of psychological distress in diabetic retinopathy, which would fill a public health knowledge gap contributing to population health planning and implementation, after controlling for covariates such as age, educational level, and income.

Research Question 1 (Diabetic Retinopathy)

What is the association between Psychological Distress and Diabetic Retinopathy among U.S. Adults after controlling for age, educational level, and income?

Null hypothesis (H_01): There is no association between psychological distress and diabetic retinopathy among U.S. Adults after controlling for age, educational level, and income.

Alternative hypothesis (H_a1): There is an association between psychological distress and diabetic retinopathy among U.S. Adults after controlling for age, educational level, and income.

Nature of Study and Design

The study is quantitative in nature. Quantitative research methods rely on the quantities of responses instead of the emotional insights of qualitative studies. Because quantitative research designs deal with closed-ended questions that involve a list of answers, it is more efficient than qualitative studies and reduces time consumption by eliminating the process of coding large amounts of open-ended answers (Winston-Salem State University, n.d.). The aim of the study was to understand the relationship between diabetic retinopathy and psychological distress while considering gender. I used a cross-sectional design based on secondary data analysis to address the research question in this study. The design was beneficial in exploring the relationship between psychological distress and diabetic retinopathy among the adult African-American population in the United States while considering the role of the covariates age, educational level, and income. My role as the researcher was as a quantitative researcher. A quantitative researcher analyzes and organizes data for the identification of causal relationships among variables. They use unstructured and structured data to gain deep insights into research topics of interest (Allen, 2017). The study design is cross-sectional which means that it is observational. The justification for the use of the study design is that it enables the researcher to measure the exposures and outcomes of the participants at the same time (Setia, 2016). Compared to cohort studies, which involve the selection of participants based on the status of exposure, and case-control studies which entail the selection of participants based on outcome statuses, cross-sectional studies involve the selection of participants using the study's exclusion and inclusion criteria (Setia, 2016). After the selection of the study participants, the researcher follows the study and conducts an assessment of the outcomes and exposures. Cross-sectional designs are appropriate for the assessment of disease prevalence in clinical-based samples and for population-based surveys; cross-sectional study design can be inexpensive and conducted faster (Setia, 2016). The design enables researchers to estimate odds ratios, which would lead to the examination of the association between the outcomes and exposures of the study (Setia, 2016).

Sources of Data

The study involves the examination of secondary data obtained from websites such as the United States Diabetes Surveillance System (USDSS) from the Centers for Disease Control and Prevention (CDC) and the Diabetes Report Card to gather and analyze data about diabetes mellitus. It also involves data from the study participants who completed the diabetes questionnaire from the University of North Carolina Campus Health (UNC, n.d.). I extracted the data for the independent and dependent variables from the 2020 datasets retrieved from the USDSS and the CDC websites to evaluate the association between diabetic retinopathy and psychological distress among U.S. adults.

The secondary data sources enabled me to gather some analytical and descriptive data pertaining to diabetic retinopathy. The datasets are in the public domain and reproducible and there is no need to acquire special permission to gain access to them. To reduce risks and biases and increase validity in the study, I examined whether the observed effects on the dependent variable relate to the independent variables and not because of the confounding variables. I examined the possibility of generating the results beyond the study population and observed how well the research instrument measured the studied construct. The internal validity was minimal based on the use of the multistage probability sampling technique used for the datasets.

Manuscript 2

Specific Problem

The specific public health problem is determining the role of gender in diabetic retinopathy, which fills a public health knowledge gap contributing to population health planning and implementation, after controlling for covariates such as age, educational level, and income.

Research Question 2 (Gender)

What is the association between gender and diabetic retinopathy after controlling for age, educational level, and income?

Null hypothesis ($H_0$2): There is no association between gender and diabetic retinopathy after controlling for age, educational level, and income.

Alternative hypothesis (H_a2): There is an association between gender and diabetic retinopathy after controlling for age, educational level, and income.

Nature of Study and Design

The study is quantitative in nature. By exploring numeric patterns, quantitative research involves the use of a set of assumptions, techniques, and strategies to study psychological processes. It involves the gathering of data that are sometimes intrinsically quantitative or numerically imposed. It is a dominant research framework that deals with closed-ended questions. Compared to qualitative research, it was more efficient and reduced time consumption because it did not involve the coding of a large number of open-ended answers (Winston-Salem State University, n.d.). The purpose of the study was to gain an understanding of the relationship between diabetic retinopathy and psychological distress while considering gender. I used a cross-sectional design based on secondary data analysis to address the research question in this study. The design explored the relationship between gender and diabetic retinopathy among the adult African-American population in the United States while considering the role of the covariates age, educational level, and income. My role as the researcher was as a quantitative researcher. Quantitative researchers focus on organizing and analyzing data to identify causal relationships among variables. They blend structured and unstructured data to gain deep insights into research topics of interest (Allen, 2017). The study design is cross-sectional which means that it is observational. With the use of the cross-sectional study design, researchers can measure the exposures and outcomes of the participants at the same time (Setia, 2016). Compared to cohort studies that involve participant selection based on the status of exposure, and case-control studies with the selection of participants that depends on outcome statuses, cross-sectional studies entail the selection of participants with the inclusion and exclusion criteria of the study (Setia, 2016). Following study participant selections, researchers follow the study and conduct assessments of outcomes and exposures. For population-based surveys and clinical-based samples, cross-sectional designs are appropriate for the assessment of the prevalence of diseases; they can be inexpensive and conducted faster (Setia, 2016). With a cross-sectional design, researchers can estimate odds ratios that would lead to the examination of the association between the outcomes and exposures of the study (Setia, 2016).

Sources of Data

The study involves the examination of secondary data obtained from websites such as the United States Diabetes Surveillance System (USDSS) from the Centers for Disease Control and Prevention (CDC) and the Diabetes Report Card to gather and analyze data about diabetes mellitus. It also involves data from the study participants who completed the diabetes questionnaire from the University of North Carolina Campus Health (UNC, n.d.). I extracted the data for the independent and dependent variables from the 2020 datasets retrieved from the USDSS and the CDC websites to evaluate the association between diabetic retinopathy and psychological distress among U.S. adults. The secondary data sources enabled me to gather some analytical and descriptive data pertaining to diabetic retinopathy. The datasets are in the public domain and reproducible and there is no need to acquire special permission to gain access to them. To reduce risks and biases and increase validity in the study, I examined whether the observed effects on the dependent variable relate to the independent variables and not because of the confounding variables. I examined the possibility of generating the results beyond the study population and observed how well the research instrument measured the studied construct. The internal validity was minimal based on the use of the multistage probability sampling technique used for the datasets.

Manuscript 3

Specific Problem

The specific public health problem is determining the role of gender-related psychological distress in diabetic-related retinopathy, which fills a public health knowledge gap contributing to population health planning and implementation, after controlling for covariates such as age, educational level, and income.

Research Question 3 (Gender-Related Psychological Distress)

Does gender modify the effect of psychological distress on diabetes-related retinopathy after controlling for age, educational level, and income?

Null hypothesis ($H_0$3): Gender does not modify the effect of psychological distress on diabetes-related retinopathy after controlling for age, educational level, and income.

Alternative hypothesis (H_a3): Gender modifies the effect of psychological distress on diabetes-related retinopathy after controlling for age, educational level, and income.

Nature of Study and Design

The study is quantitative in nature. Although they are both important for acquiring knowledge, during the collection and analysis of data, quantitative research deals with statistics and numbers pertaining to the quantities of responses compared to qualitative research which deals with words, meanings, and emotions. Through the development of hypotheses and specific questions, quantitative researchers can answer research questions through the identification and processing of relevant datasets. To form conclusions, they must blend unstructured and structured data and perform statistical analyses. Because quantitative research designs deal with closed-ended questions that involve a list of answers and the drawing of conclusions based on mathematical and logical rationale from processed data, it tends to be more efficient than qualitative studies and reduces time consumption because it does not involve the process of coding large amounts of open-ended answers (Winston-Salem State University, n.d.). The goal of the study was to understand the relationship between diabetic retinopathy and psychological distress while considering gender. I used a cross-sectional design based on secondary data analysis to address the research question in this study. The design explored the relationship between psychological distress and diabetic-related retinopathy among the adult population in the United States while considering the role of gender and the covariates age, educational level, and income. My role as the researcher was as a quantitative researcher. A quantitative researcher uses an advanced knowledge of statistics and probability to process data in mathematical format, identify trends and patterns in datasets, formulate hypotheses, and implement actionable solutions to the research questions (Allen, 2017). The study design is cross-sectional and it is observational. The study design is appropriate because it enabled the measurement of the exposures and outcomes of the participants at the same time (Setia, 2016). Compared to cohort studies that entail the selection of participants based on the status of exposure, and case-control studies involving participant selection based on outcome statuses, with cross-sectional studies, the selection of participants is based on the study's inclusion and exclusion criteria (Setia, 2016). The researcher follows the study and conducts an assessment of the outcomes and exposures after the selection of the study participants. In clinical-based samples and population-based surveys, cross-sectional designs are appropriate for the assessment of disease prevalence and they can be inexpensive and conducted faster (Setia, 2016). With the design, researchers can estimate odds ratios, which lead to the examination of the association between the outcomes and exposures of the study (Setia, 2016).

Sources of Data

The study involved the examination of secondary data obtained from websites such as the United States Diabetes Surveillance System (USDSS) from the Centers for Disease Control and Prevention (CDC) and the Diabetes Report Card to gather and analyze data about diabetes mellitus. It also involved data from the study participants who completed the diabetes questionnaire from the University of North Carolina Campus Health (UNC, n.d.). I extracted the data for the independent and dependent variables from the 2020 datasets retrieved from the USDSS and the CDC websites to evaluate the association between diabetic retinopathy and psychological distress among U.S. adults. The secondary data sources enabled me to gather some analytical and descriptive data pertaining to diabetic retinopathy. The datasets are in the public domain and reproducible and there is no need to acquire special permission to gain access to them. To reduce risks and biases and increase the validity of the study, I examined whether the observed effects on the dependent variable relate to the independent variables and not because of the confounding variables. I examined the possibility of generating the results beyond the study population and observed how well the research instrument measured the studied construct. The internal validity was minimal based on the use of the multistage probability sampling technique used for the datasets.

Limitations, Challenges, and/or Barriers

With the use of secondary data in the study, a possible challenge was the fees involved in the acquisition of data, from websites with no affiliation to the CDC, and a need to sign a partner agreement to gain access to some important data. The recruitment of participants who might not be willing to share their personal health information could have been a potential barrier to the collection of data for the study.

Significance

The study aimed to determine the relationship between psychological distress and diabetic retinopathy while considering the role of gender. The findings of the study contribute to positive social change because they provide new insights pertaining to ways that the improvement of the pathophysiology of diabetes and diabetic retinopathy could lead to the improvement of psychological distress. The study findings could facilitate the implementation of national policies geared towards the empowerment or assistance of individual adherence to healthier lifestyles leading to the prevention of diabetes mellitus and diabetic retinopathy. The study findings could also encourage individuals with the disease to seek additional information and enroll in classes for diabetes education. It might encourage additional research on diabetes-related laser eye surgery, intraocular drug therapy for vision improvement, and neuro-degeneration. Stakeholder-sponsored grants could become available to provide funding for educational promotions through the media pertaining to diabetic retinopathy and psychological distress. Population health planning and implementation are important in the public health field and public health practitioners of all sizes, types, specialties, and expertise must possess such competencies. With the investment of financial incentives in the monitoring of care continuum and preventative services, the results of the study could enable public health organizations and practitioners that are proactive in population health planning and implementation to reach their goals (Romero, 2016). The development and deployment of population health management programs can be a daunting task particularly with healthcare organizations working with limited budget and staff. Properly managing patients who have chronic diseases, such as diabetes, limited access to healthcare, and a high tendency of frequent visits to the hospital would require healthcare providers to change their workflow. The results of the study could enable healthcare professionals to tackle some of the challenges they face when they develop new population health management programs and strive to achieve success in a fast-evolving healthcare industry (Romero, 2016).

Summary

When the human body lacks the ability to convert sugar or glucose into energy in its cells, diabetes occurs. In such conditions, the body is unable to properly process and use sugar from food which might lead to damaged organs and tissues in the heart, kidneys, eyes, and nerves (CDC, 2021). Excess sugar accumulates in the bloodstream. The body usually breaks down nutrients from food during the digestion process. It converts carbohydrates from food such as bread, rice, and pasta into glucose which needs assistance from insulin in the bloodstream to travel to its destination in the body's cells that build tissues and organs (CDC, 2021). An organ behind the stomach, the pancreas, produces the insulin hormone (National Institute of Diabetes and Digestive and Kidney Disease, n.d.). With insulin, glucose is able to penetrate the body's cells. By providing energy, glucose enables the body's tissues and organs to function properly.

The body attacks itself with Type 1 diabetes which is an auto-immune disease. The insulin-producing cells in the pancreas are usually destroyed. Type 2 diabetes is also called insulin-resistant or adult-onset diabetes. The body's cells often lack a normal response to insulin and might not make enough of the hormone. It is the most common type of diabetes and it usually occurs in middle-aged adults or older. Prediabetes happens before the onset of type 2 diabetes from a slight elevation of the blood sugar (CDC, 2020). In some women, gestational diabetes develops during pregnancy and goes away after childbirth (Cleveland Clinic, 2021).

In people living with diabetes, diabetic retinopathy is common. Vision loss and blindness could be the consequences of eye problems resulting from diabetes. Diabetes is the most common cause of blindness in working-age adults living in the United States (Regeneron Pharmaceuticals, 2021). The symptoms of diabetic retinopathy might not be noticeable until later in life. Even with normal vision, individuals with diabetes need to visit optometrists or ophthalmologists for yearly eye exams (Regeneron Pharmaceuticals, 2021). The progression of diabetic retinopathy is in two stages which include proliferative diabetic retinopathy (PDR) and nonproliferative diabetic retinopathy

(NPDR) which differs from mild, to moderate to severe (Regeneron Pharmaceuticals, 2021). Those living with diabetic retinopathy are at risk for the development of diabetic macular edema. Lack of treatments administered to slow down the progression of NPDR might lead to other changes and bleeding. Symptoms such as blurriness around the edges of vision, difficulty with reading, and increased floaters in the eyes may occur. Proliferative diabetic retinopathy is the advanced stage of diabetic retinopathy characterized by the rapid increase or proliferation of new blood vessels (Regeneron Pharmaceuticals, 2021).

Age-related vision loss and diabetic retinopathy contribute to the causes of vision impairment in individuals worldwide. Vision loss is associated with mental health and medical issues, reduced quality of life, and economic burden, and can lead to serious disability (Demmin & Silverstein, 2020). It is important to examine the psychological and mental health outcomes of individuals with diabetic retinopathy and the treatments for the visually impaired. Substantial data shows an increase in the rates of depression and anxiety in those living with visual impairments such as diabetic retinopathy. There could be an increased risk for psychological and mental health problems for people who belong to a lower socioeconomic status. Limitations exist in psychosocial interventions for the improvement of psychological and mental well-being for individuals who are visually impaired. There is a need for a better understanding of the mechanisms that are associated with visual impairment such as diabetic retinopathy and poor mental or psychological health (Demmin & Silverstein, 2020). It is important to develop additional effective interventions and expand the accessibility of services necessary for the improvement of the detection and treatment of psychological and mental health problems in the diabetic retinopathy population.

This section described articles related to psychological distress, diabetic retinopathy, and diabetes mellitus. The searched keywords were gender and psychological distress, retinopathy, gestational diabetes, type 2 diabetes, type 1 diabetes, and diabetes mellitus. EBSCOhost was valuable in searching different databases and gathering peer-reviewed articles and scholarly books published between 2015 and 2023. The searched journals focused on articles on health, science, and medicine. The general public health problem is the association between psychological distress and diabetic retinopathy after controlling for covariates such as age, educational level, and income. The specific public health problem is determining the role of gender predisposition to psychological distress and diabetic retinopathy, which fills a public health knowledge gap contributing to population health planning and implementation, after controlling for covariates such as age, educational level, and income.

The purpose of this quantitative study was to investigate the relationship between psychological distress and diabetic retinopathy while considering gender. I studied the association between the independent variables, gender and psychological distress, and the dependent variable, diabetic retinopathy. I used a nationally representative dataset, such as The National Health and Nutrition Examination Survey (NHANES), to analyze data for the study. The study is distinctive because it explored the gap in the literature related to the under-researched area of the likelihood of gender modifying the effect of psychological distress on diabetic retinopathy.

The social-ecological model facilitated the understanding of the relationship between psychological distress and diabetic retinopathy. It assists in examining the interplay between community, societal relationships, and individual factors; and leads to the exposure of the factors that contribute to people being at risk for psychological distress and diabetic retinopathy (CDC, 2021). Using the socioecological model for the study provided some clarification on the factors, such as income, education, and age related to the dependent and independent variables. The social-ecological model was the most appropriate framework for the study because it outlined the influence of different determinants of behaviors which led to a better understanding of them as they relate to psychological distress and diabetic retinopathy (CDC, 2021).

For manuscript one, the specific public health problem is determining the role of psychological distress in diabetic retinopathy, which fills a public health knowledge gap contributing to population health planning and implementation, after controlling for covariates such as age, educational level, and income. The research question is: What is the association between Psychological Distress and Diabetic Retinopathy among U.S. Adults after controlling for age, educational level, and income? The study is quantitative in nature. A cross-sectional design based on secondary data analysis was suitable for addressing the research question in this study. While considering the role of the covariates age, educational level, and income, the design explored the relationship between psychological distress and diabetic retinopathy among the adult population in the United States. With data obtained from websites such as the United States Diabetes Surveillance System (USDSS) from the Centers for Disease Control and Prevention

(CDC) and the Diabetes Report Card, the study entailed secondary data examination and analysis about diabetes mellitus.

For manuscript two, the specific public health problem is determining the role of gender in diabetic retinopathy, which fills a public health knowledge gap contributing to population health planning and implementation, after controlling for covariates such as age, educational level, and income. The research question is: What is the association between gender and diabetic retinopathy after controlling for age, educational level, and income? The study is quantitative in nature. The purpose of the study was to gain an understanding of the relationship between diabetic retinopathy and psychological distress while considering gender. Using a cross-sectional design based on secondary data analysis to address the research question in this study facilitated the exploration of the relationship between gender and diabetic retinopathy among the adult African-American population in the United States while considering the role of the covariates age, educational level, and income.

The study involved the examination of secondary data from websites such as the United States Diabetes Surveillance System (USDSS) from the Centers for Disease Control and Prevention (CDC) and the Diabetes Report Card to gather and analyze data about diabetes mellitus. It also involved data from the study participants who completed the diabetes questionnaire from the University of North Carolina Campus Health (UNC, n.d.).

For manuscript three, the specific public health problem is determining the role of gender-related psychological distress in diabetic-related retinopathy, which fills a public health knowledge gap contributing to population health planning and implementation, after controlling for covariates such as age, educational level, and income. The research question is: Does gender modify the effect of psychological distress on diabetes-related retinopathy after controlling for age, educational level, and income? The study is quantitative in nature. The goal of the study was to understand the relationship between diabetic retinopathy and psychological distress while considering gender. Using a cross-sectional design based on secondary data analysis for addressing the research question in this study was beneficial in exploring the relationship between psychological distress and diabetic-related retinopathy among the adult African-American population in the United States while considering the role of gender and the covariates age, educational level, and income.

The study involved the examination of secondary data obtained from websites such as the United States Diabetes Surveillance System (USDSS) from the Centers for Disease Control and Prevention (CDC) and the Diabetes Report Card to gather and analyze data about diabetes mellitus. It also included data from the study participants who completed the diabetes questionnaire from the University of North Carolina Campus Health (UNC, n.d.). A possible challenge associated with using secondary data in the study was the fees attached to the acquisition of data, from websites with no affiliation to the CDC, and the need to sign a partner agreement for access to some important data. The findings of the study contributed to positive social change because it provided new information related to ways that the improvement of the pathophysiology of diabetes and diabetic retinopathy could lead to the improvement of psychological distress. The study findings could be instrumental to the implementation of national policies encouraging the assistance or empowerment of adherence to healthier lifestyles leading to diabetes mellitus and diabetic retinopathy prevention.

Literature Review

Diabetic retinopathy is an eye condition prevalent in people living with diabetes. It can lead to blindness and vision loss and affects the blood vessels in the light-sensitive area of the tissue in the back of the eye called the retina. It is imperative for diabetic individuals to get annual comprehensive dilated eye exams. At the initial stage, diabetic retinopathy might not have symptoms, but early detection can lead to proactive steps taken toward vision protection. People can delay or prevent vision loss if they manage diabetes by taking medications, eating healthy, and staying physically active. For individuals living with diabetes, the most common cause of vision loss is diabetic retinopathy. Individuals with diabetes are also susceptible to developing other eye conditions such as open-angle glaucoma and cataracts. It not only makes them two to five times more likely to develop cataracts but also at a younger age. The disease almost doubles the risks of an open-angle glaucoma diagnosis (Kovoor et al., 2022; Li et al., 2022; Lien & Jiang, 2017; Mahs et al., 2022; National Institutes of Health, 2019).

During its early stages, there are usually no symptoms of diabetic retinopathy. Some individuals notice occasional changes in their vision when they experience difficulties seeing far objects and reading. Bleeding from the blood vessels in the retina pours into the gel-like fluids in the eyes called the vitreous in the later stages of diabetic retinopathy. When it occurs, individuals with the disease might see floating dark streaks, like cobwebs, and spots in their eyes. Although the spots might eventually clear, it is advisable to seek treatment immediately. Failure to do so might lead to recurring bleeding, scarring, and worsening of the condition. It is common for diabetic retinopathy to result in other serious eye conditions such as neovascular glaucoma and diabetic macular edema (DME). Glaucoma comprises of a group of eye diseases that could lead to vision loss and blindness. As time progresses, 1 in 15 individuals living with diabetes becomes diagnosed with DME. The condition occurs when blood vessels in the retina discharge fluid into the area needed for central and sharp vision leading to blurriness. In terms of neovascular glaucoma, diabetic retinopathy can lead to the abnormal growth of blood vessels out of the retina, obstructing the draining of fluid out of the eyes. Diabetic retinopathy could also cause scars to appear in the back of the eye pulling the retina away from the eye and resulting in a tractional retinal detachment (Parthasharathi et al., 2022; Poly et al., 2023; Porter, 2022; Prasad et al., 2023; Qiao et al., 2020; Qummar et al., 2019; Regeneron Pharmaceuticals, 2021; Rezazadeh-Gavgani et al., 2023).

People with any type of diabetes, such as type 1, type 2, and gestational diabetes are at risk for diabetic retinopathy. The longer they have diabetes, the higher the likelihood of them developing diabetic retinopathy. However, through the proper management or control of diabetes, those individuals can lower their risks of developing diabetic retinopathy. Women who develop gestational diabetes during pregnancy and those with the disease before pregnancy tend to have a higher risk of getting a diabetic retinopathy diagnosis. It is imperative for them to get an immediate comprehensive dilated eye exam. Pregnant women need to ask their doctors if it is necessary to get additional eye exams (Hewage et al., 2020; Madhuri & Srilakshmi, 2019; Muche et al., 2020; Muhwava et al., 2019).

The high blood sugar associated with diabetes leads to diabetic retinopathy. Excess sugar in the blood can cause a damaged retina, a part of the eye detecting light and sending signals to the brain through a nerve at the back of the eye called the optic nerve. Diabetes severs blood vessels in the body. Damages become noticeable when sugar blocks small blood vessels extending to the retina, resulting in the leakage of blood or fluid. To replace the blocked blood vessels, the eye grows new ones that are ineffective and can easily bleed or leak. Through dilated eye exams, doctors detect diabetic retinopathy. The exam is often painless and simple as the doctor administers some eye drops that would widen or dilate the pupil making it easier to check for eye problems such as diabetic retinopathy. Early eye exams, for people living with diabetes, geared towards the detection of diabetic retinopathy can result in early treatment to prevent blindness and further damage. When eye doctors detect severe diabetic macular edema or diabetic retinopathy, they might perform a fluorescein angiogram test which gives them a clear picture of the blood vessels in the retina. The best way to prevent diabetic retinopathy is by managing diabetes and keeping a healthy blood sugar range. They can maintain a healthy lifestyle through a healthy and balanced diet, physical activity, and adherence to doctor’s instructions for diabetes medicines and insulin. A special lab test called an A1C test will show if a diabetes treatment plan is working. The test depicts the level of average blood sugar in a 3-month timeframe. People living with diabetes can work with their doctors to set a personal A1C goal, and if met, can assist in managing or preventing diabetic retinopathy (Porter, 2022; Romero, 2016; Ruamviboonsuk et al., 2022; Saadane et al., 2023; Setia, 2016; Teo et al., 2020).

Having high cholesterol or high blood pressure with diabetes can increase the risk of diabetic retinopathy and controlling these factors can lower the risk of vision loss. In terms of the treatment for diabetic macular edema and diabetic retinopathy, eye doctors keep track of the eye during the early stages of diabetic retinopathy. Every 2 to 4 months, some individuals living with diabetic retinopathy might require comprehensive dilated eye exams. It is important to begin immediate treatment in the later stages of the disease particularly if there are noticeable changes in vision. Although treatment might not reverse damage to the vision, it can stop it from worsening. Taking control of cholesterol levels, blood pressure, and diabetes is also important. Injections, laser treatments, and eye surgery are beneficial in managing the disease (Grzybowski et al., 2020; Li, F., Wang et al., 2022; National Institutes of Health, 2019; Regeneron Pharmaceuticals, 2021; Torpy et al., 2007).

In terms of injections, there are some medicines that can reverse or slow down diabetic retinopathy called anti-VEGF. Corticosteroids may also have such effects. Eye doctors follow certain procedures when administering injections in the eye. To make it more comfortable during the injection, they place numbing medicine in the eye, clean the eye to prevent infections and use a small needle to administer the medicine. After the injection, patients may need to apply antibiotic eye drops to prevent infection. The treatment usually does not change the vision immediately and most individuals can return to work and to their normal daily activities after the procedure. People living with DME or diabetic retinopathy often have VEGF, a protein that facilitates swelling in a portion of the retina called the macula and blood vessel leakage. Anti-VEGF drugs inhibit the protein and improve vision. The most common anti-VEGF drugs are Eylea/ Afilibercept, Lucentis/ Ranibizumab, and Avastin/ Bevacizumab. Many individuals who get the anti-VEGF injections need to repeat the process at least once a month during the first 3 months. With time, their need to get the injections lessens. While some individuals need to continue taking the injections for their vision protection, others eventually stop the procedure. Corticosteroids reduce swelling in the macula and lead to a clearer vision. Doctors can administer corticosteroids as injections or eye drops. They can also implant a special device in the eye that regularly disburses small doses of medicine occasionally. With the implant, people could stop getting the monthly injections. The most common corticosteroids are lluvien/ Fluocinolone Acetonide for long-term and Ozurdex/ Dexamethasone for short-term. An increased risk of glaucoma and cataracts is associated with corticosteroids. To check the signs of these problems, individuals getting corticosteroid injections for DME need regular eye exams (Tymchenko et al., 2020; University of North Carolina, n.d.; Vitger et al., 2017; Vujosevic et al., 2020; Wang et al., 2020; Zheng et al., 2023; Zhou et al., 2023).

In an attempt to reduce retinal swelling, eye doctors often use laser treatments to stop leakage or shrink blood vessels. If there is excessive retinal bleeding and scarring in the eyes, eye doctors could recommend a surgery known as vitrectomy. In terms of the latest research on diabetic macular edema and diabetic retinopathy, scientists are conducting studies on effective ways to prevent, locate, and treat vision loss in individuals with diabetes. A team from the National Institutes of Health is studying whether fenofibrate, a medicine for cholesterol, can halt the worsening of diabetic retinopathy (Ansari et al., 2022; Antonetti et al., 2021; Atwany et al., 2022; Boyd & Gregori, 2020; Cleveland Clinic, 2022; Curry, 2020).

Part 2: Manuscripts

The Association Between Psychological Distress and Diabetic Retinopathy Among U.S. Adults After Controlling for Age, Educational Level, and Income

Claret Onukogu

Walden University

Doctoral Study

Outlet for Manuscript

The *American Journal of Public Health* (AJPH) is ideal for this manuscript's publication because of its dedication to publicizing original work pertaining to program evaluations, research methods, and research in the public health field. Its mission of advancing public health education, practice, policy, and research makes it a suitable outlet to publish data on the association between psychological distress and diabetic retinopathy among U.S. adults after controlling for age, educational level, and income.

Abstract

Diabetes could lead to diabetic retinopathy, an eye disease that causes damaged blood vessels and the growth of abnormal ones. The disease could cause vision loss because high blood sugar levels damage retinal blood vessels. The two stages of the disease are nonproliferative and proliferative diabetic retinopathy. In the nonproliferative stage, diabetics develop macular edema from retinal swelling and macular ischemia with a shortage of blood in the macula region of the eye, and the vision eventually becomes blurry. The proliferative is the advanced stage of the disease when the retina grows new blood vessels and diabetics may experience a detached retina. The quantitative study employed the socioecological model as the theoretical framework to examine the relationship between psychological distress and diabetic retinopathy while considering gender. The aim was to determine the role of psychological distress in diabetic retinopathy after controlling for covariates such as age, educational level, and income. The study examined the association between the independent variables, psychological distress, and the dependent variable, diabetic retinopathy. For the study, a nationally representative dataset, The National Health and Nutrition Examination Survey (NHANES), was used to analyze data. There was no association between psychological distress and diabetic retinopathy among U.S. adults when controlling for education level, income, and age. The results of the study have implications for positive social change and fill a public health knowledge gap, contributing to population health planning and implementation. Further research on patient education and regular screening for diabetic retinopathy in the United States for diabetic patients is necessary.

Introduction

A common microvascular complication associated with diabetes is diabetic retinopathy, which can cause blindness. The main risk factors of diabetic retinopathy are longer duration of diabetes, hypertension, dyslipidemia, and hyperglycemia (Ansari et al., 2022; Antonetti et al., 2021). After years of suffering from type 1, type 2, or gestational diabetes, individuals can develop diabetic retinopathy. Its diagnosis is based on the severity and presence of objective clinical signs that include the appearance of tortuous, superfluous, and new blood vessels, intraretinal microvascular abnormalities or venous beading, cotton wool spots, intraretinal hemorrhages, and microaneurysms (Aziz et al., 2023; Boyd & Gregori, 2020; Farooq et al., 2022; Grzybowski et al., 2020). The different stages of diabetic retinopathy are proliferative diabetic retinopathy (PDR), severe nonproliferative diabetic retinopathy, moderate nonproliferative diabetic retinopathy, and mild nonproliferative diabetic retinopathy (NPDR). Visual functioning and visual acuity are often not affected in moderate and mild nonproliferative diabetic retinopathy stages, but as the disease progresses to PDR or NPDR, visual impairment, leading to difficulty with mobility, driving, and daily tasks, could occur (Kang & Yang, 2020; Li et al., 2022; National Institutes of Health, 2019; Poly et al., 2023).

A range of emotional and social issues are linked to visual impairment resulting from ocular conditions; almost one-third of individuals living with visual impairment report clinically significant symptoms of depression. Compared to their sighted counterparts, working-aged adults with visual impairment report worse quality of life, social functioning, and mental health; because individuals with vision-threatening diabetic retinopathy have diabetes and visual impairment, it is safe to hypothesize that their experienced emotional and social strain is considerable (Li et al., 2022; Rezazadeh-Gavgani et al., 2023). Compared to their psychologically healthy counterparts, people with diabetes or visual impairment who have psychosocial problems experience significantly reduced quality of life and levels of functioning. The reduction in functionality can result in a negative downward spiral involving a decreased adherence to healthcare appointments and advice, increased strain on social support systems and family functionality, increased progression and development of diabetic retinopathy, and worsened diabetes control resulting in more psychosocial stress (American Diabetes Association, 2018; Fenwick et al., 2011; Kang & Yang, 2020; Kowluru, 2023; McLachlan & Gale, 2018).

Because of a combination of threatened or actual visual impairment and the stress of diabetes that individuals with diabetic retinopathy experience, those individuals may become prone to the cycle, which has several implications for patient health, healthcare costs, clinical outcomes, and disease management. With the escalation of diabetes worldwide, it is important to understand the emotional and social effects of complications, such as diabetic retinopathy, linked to diabetes. Although there is compelling evidence of the impact of diabetic retinopathy and related vision loss on the quantitative measurements of visual functionality, such as limitations in the activities of mobility and daily living, there are no systematic reviews of the evidence pertaining to traits beyond disability such as the social and emotional health consequences of diabetic retinopathy (Allen, 2017; National Institutes of Health, 2019; Parthasharathi et al., 2022;

Poly et al., 2023; Qiao et al., 2020). It is vital information that would lead to targeted and effective interventions being valuable in the avoidance of possible detrimental implications of diabetic retinopathy. The understanding of the individuals with the likelihood of being affected, when they might be affected, and the underlying mechanisms of the associations means that at critical time points, the populations at risk could be targeted. For example, with an increased understanding of the social implications linked to diabetic retinopathy, there could be an offering of better services such as family counseling, social networking advice, financial support, and work support to those in need of them. The information is vital in equipping healthcare workers who want to provide better assistance to their patients and to policy planners for budgeting future healthcare expenditures (Atwany et al., 2022; Romero, 2016; Ruamviboonsuk et al., 2022; Saadane et al., 2023; Setia, 2016). Healthcare providers need to be knowledgeable about the current quantitative and qualitative evidence pertaining to the emotional and social impacts of diabetic retinopathy. The negative social impacts of diabetic retinopathy include social isolation and affect leisure and hobbies; social life; personal relationships such as friendships, spousal relationships, family relationships, and work relationships; work productivity; community positions and social networks; role maintenance in the family; and income and financial security. The emotional impact of diabetic retinopathy encompasses all emotional reactions to threatened or actual vision loss such as vulnerability, fear, low self-esteem, stress, worthlessness, helplessness, anger, uncertainty, dependence, loss of confidence, guilt, worry, demoralization, mental health disorders such as anxiety and depression (Bora et al., 2021; Torpy et al., 2007;

Tymchenko et al., 2020; Vujosevic et al., 2020). Researchers need to focus on the identification of directions for future research, limitations of the nature of current evidence, and the potential and need for improved outcome measures for the provision of meaningful and valid measurement of the emotional and social impact of diabetic retinopathy.

There are negative emotions associated with diabetic retinopathy that include stress, anxiety, vulnerability, worthlessness, worry, difficulty coping, demoralization, vulnerability, frustration, loss of self-esteem and confidence, a feeling of being burdensome, feelings of hostility and inferiority, irritation, awkwardness, loss of independence, guilt, mood swings, anger, depression, and fear. There is also anxiety and fear related to the use of photocoagulation as a treatment for diabetic retinopathy (Centers for Disease Control and Prevention, 2021; Vujosevic et al., 2020; Zheng et al., 2023; Zhou et al., 2023). There is a significant association between emotional well-being and diabetic retinopathy. The relationship between diabetic retinopathy and depression is statistically significant and consistent when examining the association between diabetic retinopathy and depressive symptoms. The link between anxiety, psychiatric symptomology, distress, low self-esteem, worry, fear, emotional instability, phobic anxiety, somatization, stress, and anxiety is evident (Ansari et al., 2022; Centers for Disease Control and Prevention, 2020; Dai et al., 2021). Studies have confirmed the triggering of a spectrum of emotions from diabetic retinopathy-related vision loss such as issues of self-perception, sadness, anger, and fear. The link between diabetic retinopathy and clinical depression is real, but it is important to understand that other emotional reactions could be equally detrimental to the emotional function of individuals (Centers for Disease Control and Prevention, 2021; Demmin & Silverstein, 2020). The quantitative studies conducted on the topic tend to be limited by their small sample and cross-sectional design. Obtaining meaningful comparisons of results is often difficult because of the range of outcome measures used. The consistency in findings can be ambiguous, and the various large gaps in knowledge suggest that for the provision of a better understanding of the emotional and social implications of diabetic retinopathy, more compelling designed studies are necessary in the future. Before the efficacy of new treatment modalities, interventions, and policies can be fully informed, it is important to have substantive high-quality research to systematically investigate the extent of, type of, and factors linked with the emotional and social impacts of diabetic retinopathy on individuals (Centers for Disease Control and Prevention, 2020; McLachlan & Gale, 2018; National Institute of Diabetes and Digestive and Kidney Diseases, n.d.; National Institutes of Health, 2019). The absence of appropriate outcome measures for the precise and accurate assessment of the emotional and social impact of diabetic retinopathy could hinder future research. The issue is often highlighted in the analysis of the psychosocial impact of visual impairment on working-aged adults, and it is a barrier to overcome. Despite the availability of several vision-specific patient-reported outcome measures, most of them have barely any content related to economic impact and health concerns, or social and emotional issues; instead, they focus mainly on symptoms and mobility, and activity limitations.

With the use of a traditional psychometric approach, many quality-of-life outcome measures have gone through minimal validation. Many researchers depend on subjective reports on the quality of life derived from the perspective of patients through patient-reported outcome measures; in a situation where the outcome measure is suboptimal in validity or in content, researchers cannot be confident that the received results are accurate or meaningful. They are usually of limited use for informing policy, interventions, or clinicians. It is problematic to use only the traditional psychometric test to validate outcome measures because it has various erroneous assumptions (Cleveland Clinic, 2021; Fenwick et al., 2011; Hayati et al., 2023; International Diabetes Federation, 2022). When subjected to modern psychometric methods, many ophthalmological scales function suboptimally.

The traditional psychometric test scores all items equally and assumes that they are of equal difficulty, but modern psychometric theory has proven it to be incorrect. For instance, Rasch analysis highlights that it is easier to drive during the day than to drive at night; if participants report slight difficulties with the former, it does not equate with difficulty with the latter. The traditional psychometric erroneously assumes that changes between categories, such as extreme difficulty, some difficulty, and no difficulty, are uniform and that the allocated values can be added to obtain an overall score, and it depicts validity in the measurement of the underlying latent trait (Cleveland Clinic, 2022; Fenwick et al., 2011; Jiwani et al., 2022). The total score is treated as an interval and not simply an ordinal scale. The traditional psychometric test lacks unidimensionality or strong indicators of scale. Cronbach's alpha is the most commonly reported statistic that shows scale reliability. Through local dependence of items and redundancy, Cronbach's alpha can be inflated artificially. Because they contain limited items, paper-based questionnaires can fail in the optimal targeting of participant ability levels across the severity of disease spectrum. Researchers have addressed several issues linked with the traditional psychometric test through modern psychometric methodologies such as Rasch analysis. Using the same interval scale, Rasch analysis calibrates person ability and item difficulty. It also adheres to strict criteria that a scale must satisfy before providing a valid and unidimensional measurement. The second-generation approach still has some of the limitations of restricted and static scales. By using techniques that include item banking and computer adaptive testing (CAT), the third-generation approach bypasses the limitations of using paper-pencil questionnaires (DiaGundluru, 2022; Fenwick et al., 2011; Lauffenburger et al., 2020; Li et al., 2022).

In terms of hormonal imbalance and cardio-metabolic differences in men and women, there is often an androgen deficiency in men and an excess in women. A balanced proportion of androgens and estrogens plays a significant role in the maintenance of sexual function, body composition, and energy metabolism. Androgens and estrogens influence the bidimensional modulation of lipid homeostasis and glucose by sex hormones and their receptor activation in peripheral and central target in men and women. Higher androgen levels in women lead to increased visceral fat (VAT) and body weight (Forrester et al., 2020; Kautzky-Willer et al., 2016; Kautzy-Willer et al., 2019; Kovoor et al., 2022; Kowluru et al., 2023). The same dynamics occur in female-to-male transsexuals. Lower levels of testosterone in men and higher levels in women could lead to incident diabetes. Excess androgen in the female body indicates the presence of polycystic ovary syndrome (PCOS) and an increased risk of higher cardiometabolic levels, type 2 diabetes, and hyperinsulinemia related to obesity (Kautzky-Willer et al., 2016). Genes are associated with the prevalence of metabolic disorder in females and males. Impaired glucose metabolism and PCOS are linked with obesity. Fathers of women with PCOS might have secretory pancreatic β-cell defects and higher risks of fasting dysglycemia compared to the mothers. For those women, maternal heritability has a higher impact on fasting dysglycemia. Diabetic or obese males tend to have a higher likelihood of late hypogonadism onset, higher prevalence of erectile dysfunction, and low testosterone levels. Obese or overweight males have heightened aromatization from androgens to estrogens, stopping the secretion of gonadotropin through the activation of estrogen receptor from the hypothalamus that promotes hypogonadism. The aromatization to β-estradiol from testosterone influences energy homeostasis. In males, a higher ratio of testosterone to estrogen facilitates visceral obesity, and the deficiency of androgen increases VAT (Doheny, 2020; Gadekallu et al., 2020; Kautzky-Willer et al., 2016; Lien & Jiang, 2017).

Whether the deficiency of testosterone leads to metabolic derangement or the levels of testosterone reduce because of aging, researchers are working towards fully understanding and getting further clarification on the changes in body composition, illnesses, or reverse causality. In hypogonadal diabetic males, the improvement of insulin sensitivity and hyperglycemia can improve through testosterone replacement therapy. Between sexes, the prevalence of prediabetic categories is different leading to clinical implications with women developing impaired glucose tolerance (IGT) and men showing impaired fasting glucose. Impaired early insulin secretion and increased hepatic glucose output are characteristics of impaired fasting glucose (Alperet et al., 2019; Ansari et al., 2016; International Diabetes Federation, 2023; Lauffenburger et al., 2020). IGT occurs mainly because of peripheral insulin resistance. IGT could be a better predictor of diabetes progression with the risk of mortality relating strongly to a rise in cardiovascular risk. It could explain why the criterion of the World Health Organization, which includes IGT status, appears to be more acceptable than other metabolic syndrome (MetS) definitions in predicting cardiovascular disease (CVD) and diabetes in women (Kautzky-Willer et al., 2016). It further shows that it is important to perform oral glucose tolerance tests when screening for IGT, particularly in women.

Psychosocial risk factors and stress entail behavioral, environmental, and economic components. These factors could influence the overall risk of diabetes differently between women and men and they are usually interrelated. In developed countries, when assessed by income, position, and educational level, socioeconomic status is associated with the prevalence of type 2 diabetes and obesity (Alperet et al., 2019; Ansari et al., 2016; Atlanta Diabetes Association, 2020). After controlling for physical activity and obesity in women, there seems to be a persisting association between self-reported diabetes, low education, and income. There tends to be a strong association between abdominal obesity, socioeconomic status, and physical activity in women. With occupational evaluation, low socioeconomic status relates to IGT risk in men excluding other confounders. Based on confirmed metaanalysis of cohort and case-control studies, an important risk factor for type 2 diabetes in men and women is low socioeconomic status. With consideration for the individual socioeconomic status variables, such as food insecurity, and lower household income, there tends to be a higher risk of diabetes in women and not men (Centers for Disease Control and Prevention, 2019; Curry, 2020; Emani et al., 2018; Kautzky-Willer et al., 2016). Researchers could assess the cumulative risk effect for adult body mass index (BMI) and childhood socioeconomic status from fathers' education or occupation as a predictor of incident diabetes, particularly in women. When compared to men with low socioeconomic status, high levels of stress factors, smoking, energy intake, and physical inactivity increase neuroendocrine perturbations in women (Lauffenburger et al., 2020; Li et al., 2020). Women tend to have more sensitivity to sociocontextual predictors such as income, education, and occupation for future risk of developing diabetes (Mahs et al., 2022). It may be as a result of behavioral and environmental mechanisms. There is an opportunity for further research for the clarification of the complex issue.

In terms of the adverse effects of cardiometabolic impact of occupational stress, sleep disturbance, and psychosocial stress, women are more vulnerable than men. Greater responsibilities and housework in the family could contribute to sustained stress levels and conflicting demands for females. Gender roles and discrimination could further exacerbate environmental psychosocial stress and stress responses, particularly in women. In terms of allostatic load, the imbalance between overexposure to environmental stress and the ability to adapt to environmental demands increases the risk of cardiometabolic diseases through immune, autonomic, and neuroendocrine mediators

(Mamo et al., 2019; Mikkola et al., 2020; Teo et al., 2020). In terms of work stress and sleep deprivation, women face a greater negative impact from post-traumatic stress disorders than men. They also have a higher risk of suffering from insomnia. Impaired qualities of sleep, short sleep duration, and sleep loss correlate with impaired glucose metabolism (IGM) related to insulin resistance and obesity (Kautzky-Willer et al., 2016; Kang & Yang, 2020; Vitger et al., 2017). There is a close link between the incidence of hypertension and less than 5 hours of sleep (Kautzky-Willer et al., 2016). Sleep deprivation causes detrimental cardiovascular issues. Difficulties maintaining or initiating sleep and short sleep are associated with higher risks of diabetes. Sleep deprivation could lead to increased fat and food intake. Based on higher daily caloric intake, particularly at night, males are more susceptible to weight gain. Different results exist pertaining to gender and sex differences as they relate to the impact of work stress, shift work, and coping. The differences could be attributed to the negative effects of testosterone secretion as it pertains to the changes in the circadian timing system (Curry, 2020; Kautzy-Willer et al., 2019; Winston-Salem State University, n.d.).

Job strains are linked to higher risks of diabetes in women, particularly those experiencing high job demand, lack of control, and low emotional support. Stress-induced diabetes could be attributable to biological risk factors and obesity with the mediating effects of low socioeconomic status and employment grade. Individuals with job strain have higher risks of developing type II diabetes despite sex differences, and traditional risk factors (Kautzy-Willer et al., 2019; Kowluru, 2023). The results of the gender and sex differences in the work-stress-diabetes risk interrelationship can be controversial. The explanation for the result is the differences in occupational groups, interindividual shift work tolerance, differences in the opportunities for recovery from work stress between women and men, and specific definitions of job strains. Work-related circadin misalignment, the individual chronotype, and rotating shift work could regulate the risk of diabetes in the workforce. The incidence of type 2 diabetes increased in early chronotypes with work during the night shift and length of shift work exposure (Kautzy-Willer et al., 2019; Kowluru, 2023; Wang et al., 2020). Late chronotypes pose the most risk with a daytime work schedule. There is a sex-specific link between the incidence of type 2 diabetes and night work exposure which could be stronger in women after adjusting confounders such as obesity. The evening chronotype could be more common in younger women and could be associated with sleep duration, lifestyle, sex dimorphism, and metabolic diseases. The evening chronotype also relates to a 2-fold higher risk of MetS in women and a 3-fold higher risk of type 2 diabetes in men (Kautzy-Willer et al., 2016; Kautzy-Willer et al., 2019). Compared to females with more visceral fat mass, late chronotype is associated with less lean mass in males. Independent of sleep loss, circadian misalignment increases inflammatory parameters, diabetes risk, and insulin resistance. In women and men, misalignment between social rhythms and the circadian clock and between gender-dependent social timing and sex-dependent biological factors, such as body composition, impacts the pathogenesis of diabetes (Kautzy-Willer et al., 2019; Lien & Jiang, 2017). There is a need for further research to investigate the complex sex-dimorphic associations between diabetes, work stress, and sleep. The research could assist in the implementation of sex-specific prevention programs in certain groups of shift workers. In the pathogenesis of psychiatric disorders, such as depression, and in cardiometabolic disease, excess Hypothalamus Pituitary-Adrenal (HPA) axis reactivity is often identified (Kautzy-Willer et al., 2019).

The hypothalamus coordinates important endocrine and metabolic processes and the autonomous nervous system. It also regulates energy homeostasis and food intake. Compared to males, females have more estrogen-proopiomelanocortin (POMC) which is an anorexigenic prohormone that the pituitary gland and hypothalamus synthesize (Kautzy-Willer et al., 2016; Kautzy-Willer et al., 2019). It leads to α-melanocyte-stimulating hormone and adrenocorticotropic hormone (ACTH) that influences energy expenditure and appetite. Proopiomelanocortin neurons express leptin and insulin receptors. Glucocorticosteroids play vital roles in hepatic insulin resistance, lipolysis in fatty tissue, adipogenesis, and possible sex differences pertaining to basal or stress-induced activity of the HPA axis. Cortisone converts to cortisol through the actions of 11β-hydroxysteroid dehydrogenase type 1 and causes an increase in the local levels of glucocorticoid in the adipose tissue and liver especially in visceral fat (VAT). Women tend to have higher cortisol and ACTH sensitivity which are lower in younger women who also have lower circadian variations (Kautzy-Willer et al., 2016; Kautzy-Willer et al., 2019; Porter, 2022). However, these factors remain the same in postmenopausal women and their male counterparts of comparable age. Estrogen may increase corticosterone levels and ACTH release. On the hypothalamus-pituitary-adrenal (HPA) axis stress response, androgens have inhibitory effects. There is an increase in cortisol release during acute stress challenges, especially for women with abdominal obesity.

Compared to men, adrenal response to ACTH is usually higher in postmenopausal women and healthy young women (Kautzy-Willer et al., 2019; Muhwava et al., 2019). In patients with type 2 diabetes mellitus, the sex differences usually do not apply. When compared with controls, diabetic men often have higher levels of peak cortisol. Studies have shown an association between vascular endothelial nitric oxide (NO) system activation and stress levels in women (Kautzy-Willer et al., 2019; Muhwava et al., 2019). Also, the thickness of the carotid intima media could indicate cardiovascular dysfunction in women induced through stress.

Hyperinsulinemia or insulin resistance relates to sex hormonal imbalance and neuroendocrine pathways. Sex hormones and the Hypothalamus Pituitary-Adrenal (HPA) axis often interact through the impairment of stress responses which leads to visceral obesity phenotype enhancement and metabolic abnormalities (Alperet et al., 2019; Lauffenburger et al., 2020). Acute stress results in immune system changes, inflammatory cytokine release, renin-angiotensin system activation, increased release of glucocorticoid from the adrenal glands combined with sympathetic arousal responsible for fight-or-flee responses during danger (Kautzy-Willer et al., 2019; Porter, 2022). It results in the establishment of a vicious cycle where chronic stress leads to disturbed energy homeostasis and feeding behavioral patterns which results in insulin resistance and the accumulation of visceral fat (VAT) that sympathetic overactivity aggravates further. In men, the deficiency of testosterone aggravates MetS through hyperinsulinemia and obesity that in turn suppresses the production of testicular androgen. Excessive androgen, which relates to increases in HPA activity, in obese women, causes unfavorable cardiometabolic effects. Orexigenic anxiolytic neuropeptide Y (NPY) and ghrelin increases with stress and contributes to emotional eating which fosters the relationship between stress, obesity, and diabetes and plays a greater role in women (Kautzy-Willer et al., 2019). Stress impacts food reward and increases the likelihood of individuals craving energy-dense food.

Compared to men, women have a higher vulnerability to stress-related weight gain and women have a lower hunger-suppressing ability. Women are at a higher risk of having diseases associated with dysfunctional HPA because they have higher HPA sensitivity. Dysfunctional HPA relates to psychiatric disorders, such as major anxiety and depression, and eating pathologies. The diagnoses are more common in diabetic or obese women than in men. Depression may cause disruption in HPA axis which could lead to increases, possibly in a sex-specific manner, in inflammatory cytokines, catecholamines, and cortisol (Kautzy-Willer et al., 2019). There could be an unfavorable influence of depression on physical activity, dietary intake, and lifestyle which in turn further aggravates obesity and diabetes. Sleep disturbance or sleep loss links to desynchronized circadian rhythm and rotating shift work and through the stimulation of similar neuroendocrine pathways, it could induce glucose intolerance. The interaction of the circadian clock system circuits and metabolic elements involves the regulation of sleep-wake cycle through the central pacemaker neurons of the suprachiasmatic nucleus influencing the feeding schedule and behavioral rhythm. Peripheral clocks at the pancreas, fat, muscle, and liver are also regulated. Genetic studies have indicated possible links between the signaling of melatonin in the pancreas, glucose metabolism regulation, and the circadian clocks. Melatonin is the hormone responsible for midnight chronobiotic peak (Kautzy-Willer et al., 2019; Saadane et al., 2023). Reduction in the release of the hormone during shift work contributes to glucose intolerance and the deterioration of insulin resistance. Elderly women and depressed individuals tend to have lower levels of melatonin. The misalignment of the circadian cycle is linked to adjustments in the secretion of leptin and cortisol as they relate to feeding-fasting and wake-sleep cycles causing heightened aggravation of glucose deregulation and energy homeostasis. A sex-dimorphic hypothalamic melanocortin system influences sex-different behavior. In the regulation of glucose and energy metabolism, POMC peptides are involved. Decreases in protein and anorexigenic neuropeptide POMC genes are linked to energy intake increase. Leptin receptors in the hypothalamic arcuate nucleus, in the POMC neurons, depict important sexual differences. To a great extent, leptin receptors influence glucose metabolism, and females have a greater lipid distribution influence (Kautzy-Willer et al., 2019; Qummar et al., 2019; Regeneron Pharmaceuticals, 2021).

Females are more sensitive to anorectic effects when injected with leptin than males who are more sensitive to injected insulin. Females, after an ovariectomy, exhibit greater central insulin and lower leptin sensitivity that could be restored through estrogen administration. The proposed mechanism behind the reduction of female insulin sensitivity is as a result of brain estrogen signaling, possibly mediated through the effects of estrogen on Estrogen Receptor Alpha (ERα) in different hypothalamus regions (Kautzy-Willer et al., 2016; Kautzy-Willer et al., 2019). The effects are involved in body weight regulation. After estrogen administration, the effects of the hormone in the brain with insulin sensitivity and leptin alterations could be verified in males. The effects apply to younger males and females with low gonadal hormone levels and are linked to anorexigenic effects of intranasal insulin with reductions in total food intake and meal frequency with comparable changes in gene expression in the hypothalamus. The anorexigenic central nervous insulin effects could potentially serve as therapeutic interventions for the treatment of childhood obesity in males and females (Kautzy-Willer et al., 2016; Kautzy-Willer et al., 2019; Mamo, 2019). The impairment of the central insulin action through binge drinking is similar to some extent in females and males. The cause could be protein kinase B phosphorylation in the hypothalamus and a decrease in insulin receptor with expression of down-regulating components and increased inflammation of insulin signaling cascade. After binge drinking, glucose tolerance is disrupted more in females than in males. The secondary effects of hypothalamic insulin resistance are the effects of hepatic and adipose insulin (Kautzy-Willer et al., 2016; Kautzy-Willer et al., 2019; Mamo, 2019).

Increased food intake in females could be a result of the inactivation of the brain insulin receptor. The bodies of both sexes can show increased insulin resistance, leptin, body fat, impaired reproduction, and triglyceride levels. In insulin-resistant obese individuals with reduced physical activity and increased appetite, the POMC function restoration within 5-hydroxytryptamine 2c receptor containing cells leads to induced sex differences in energy balance (Kautzy-Willer et al., 2016; Kautzy-Willer et al., 2019; Mamo, 2019). With improved insulin sensitivity and food intake, females tend to be physically inactive with higher fat mass and low total energy expenditure. It may lead to implications for antiobesity treatment because the target of new drugs is on main regulators of energy balance, and the restoration of impaired function of the POMC neuron. In terms of sex differences in insulin signaling, leptin and insulin are critical in body weight and energy metabolism regulation through peripheral and central effects. In men, intranasal insulin decreases leptin levels and the feeling of hunger and reduces fat mass which, in the male brain, confirms higher sensitivity to catabolic insulin action (Kautzy-Willer et al., 2016; Kautzy-Willer et al., 2019; Mamo, 2019). In both sexes, the application of intranasal insulin reduces the circulation of free fatty acid concentrations and suppresses systemic lipolysis, independent of leptin or blood insulin concentrations, mediated through insulin signaling in the central nervous system (Kautzy-Willer et al., 2016). There might be new treatment options in the future that target glucose homeostasis and energy metabolism central regulation. Further research could focus on the compulsoriness of possible sexual dimorphism.

There are sex differences pertaining to frequent comorbidities and major diabetic complications. Considering cardiovascular complications across different ages, diabetes leads to the attenuation of the female biological advantage. Psychosocial stress or symptom presentation, differences in experience and reproductive factors play roles in the unfavorable diabetic situation in women. The present comorbidities seen in the early phase of type 2 diabetes mellitus are inflammation, greater cardiometabolic load, and depression. Later diagnosis of the disease in women tends to contribute to the persistence of discrepancies in the cardiovascular complications between women and men. There are sex differences related to different risk factors for myocardial infarction (MI) which include hypertension, diabetes, high alcohol intake, and low physical activity are stronger MI predictors in females than males (Kautzy-Willer et al., 2019).

Individuals who are newly diagnosed with diabetes and do not have clinical cardiovascular diseases tend to have increased media thickness in their carotid arteries and higher atherosclerosis. Besides age, males have stronger associations with carotid plaques than females. Compared to nondiabetic females, newly diagnosed diabetic women have a higher prevalence of carotid atherosclerosis. Diabetes increases the risk of cardiovascular disease and reduces the protective effect of the female sex to a higher extent than in males. The presence of visceral adiposity and MetS predicts the development of cardiovascular disease mainly through IGM in women and independent of diabetes in men (McLachlan & Gale, 2018; Mikkola et al., 2020). Although many environmental and biological factors play roles in diabetic women having excess risk, further research is needed to fully understand the phenomenon. Physiologically, there are beneficial effects on cardiovascular wall properties associated with female sex hormones. Considering the modification of the effects of beneficial hemodynamic estrogen through complex interactions between estrogen signaling and insulin, diabetes dramatically impairs endothelial response in women than in males. There is an adverse modification of the activity and balance of expression of estrogen receptors (ERs) through hyperglycemia which leads to the observation of increases in endothelin-1 and oxidative stress (Kautzy-Willer et al., 2019; McLachlan & Gale, 2018; Mikkola et al., 2020). It results in the reduction of endothelium-dependent relaxation and nitric oxide (NO) production through insulin signaling and further promotion of platelet aggregation and vasoconstriction.

In diabetic females, mesenteric arteries have more abnormal vascular responses that manifest through a rise in endothelial nitric oxide synthase and increased impairment of acetylcholine-induced relaxation. There could be a relative endothelium-derived relaxing factor reduction with more reliance on the expression of nitric oxide. Female arteries could be predisposed to vascular injury with the modulations of vascular reactivity in cases of diabetes. The antiproliferative effects of estrogen on vascular smooth muscle cells are restrained through hyperglycemia. Under normoglycemic conditions, these actions are mediated through the selective activation of estrogen receptor alpha (ERα). Simultaneous Estrogen receptor beta (ERβ) activation counterbalances beneficial effects which leads to the loss of estrogen effects that are protective, and in mainly diabetic women, it causes cardiovascular diseases and proinflammatory environment that accelerates atherosclerotic processes. It might potentially serve as a therapeutic pathway (Kautzy-Willer et al., 2019; McLachlan & Gale, 2018; Mikkola et al., 2020).

In young males, the mutations of ERα are linked to early atherosclerosis and insulin resistance. The effect of sex hormones on endothelin-1 expression is indisputable in humans with increasing androgen and decreasing estrogen plasma levels that are verifiable in female to male and male to female transsexuals. In men, there are sex differences in the density of endothelin receptor and higher binding capacity. Middle aged males have increased receptor mediated vasoconstrictor tone that may be an added contributor to the lower risk of cardiovascular conditions in normoglycemic women (Kautzky-Willer et al., 2019; McLachlan & Gale, 2018). Endothelin-1 expression is increased in diabetic cells. In diabetic females, there is a higher endothelin-1 mediated vasoconstriction in mesenteric artery rings. Diabetes induced cardiac remodeling is more evident in females at an earlier stage than in males and it is measured through prooxidant and prohypertrophic gene expression and also cardiomyocyte size (Kautzky-Willer et al., 2019). Compared with diabetic men, women with type 2 diabetes mellitus have higher cardiovascular risk. In terms of in-vitro sex differences in fibrin structure functionality, with prolonged fibrinolysis and denser fibrin clots, diabetic women have higher prothrombotic fibrin profile that is evident through increased maximum clot formation, absorbance, and lysis time. Even after making adjustments for higher fibrinogen and plasminogen activator inhibitor 1, found in women, the results remain the same (Kautzky-Willer et al., 2019). In diabetic women, further aggravations include lower high-density lipoprotein (HDL)-cholesterol levels and increasing waist circumferences (WCR) and BMI levels.

In men, increased atherothrombotic risk is related to worse glycemic control. At higher ages, increased fibrinolysis is evident in men and the possible explanation could be decreases in Plasminogen activator inhibitor-1 (PAI-1) levels that occur with increasing age. Peripheral arterial occlusive disease, smoking, low glomerular filtration rate, and renal impairment in both sexes, measured through ankle brachial index, are associated with the increased risk of atherothrombosis in type 2 diabetes (Kautzky-Willer et al., 2019; Mikkola et al., 2020). A significant relation is found in men with ischemic heart disease. For women with type 2 diabetes mellitus, sex-specific findings implicate an increased risk of atherothrombosis which could potentially have clinical consequences.

With a more aggressive antithrombotic therapy in higher risk groups and diabetic women, an individualized therapy strategy might be necessary, but a more cautious approach is important to reduce the risk of bleeding from increased fibrinolysis (Kautzky-Willer et al., 2019; Mikkola et al., 2020). In terms of arteriogenesis in individuals with occluded or stenotic coronary vessels, type 2 diabetes mellitus and sex are independent risk factors for poor development of collateral vessel in chronic total occlusion in individuals with severe coronary artery stenosis. After menopause, the decline in estrogen levels could be the underlying cause of women having worse outcomes. Estrogen loss negatively influences angiogenesis. Estrogen therapy induces microvascular and collateral remodeling (Kautzky-Willer et al., 2019; Mikkola et al., 2020; Romero, 2016).

In the human heart, there is glucose metabolism, but in the diabetic heart, the energy supply through glucose is disturbed. There seems to be a substantial influence of sex on glucose utilization in diabetic and obese individuals. Generally, female hearts use lipids and male hearts prefer more glucose. Compared with men, there is a reduced intramyocardial glucose metabolism or kinetics, which entails fractional glucose uptake, in diabetic women. The reduction of glycolysis, glucose synthesis, and glucose oxidation is more evident in men with reduction in levels of normal-weight, obese, and individuals with type 2 diabetes mellitus (De Ritter et al., 2020; Kautzky-Willer et al., 2016). Prior tolerance (IGT). In diabetic patients, preclinical diabetic cardiomyopathy is common and the only independent predictor of left ventricular (LV) hypertrophy is the female sex. Preclinical diabetic cardiomyopathy is linked to higher mortality and adverse cardiac outcomes. Independent and important risk factors for heart failure are diabetes, hypertension, and obesity, which in women more than men, could result in adverse impairment of myocardial metabolism. There is a positive association between heart failure, BMI, and type 2 diabetes mellitus (De Ritter et al., 2020; International Diabetes Federation, 2022; Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019; Lien & Jiang, 2017; Magne et al., 2020). At a younger age, because of cardiovascular diseases, men tend to suffer from heart failure more often. They also have a higher likelihood of developing myocardial dilatation compared to women who tend to suffer preserved ejection fraction and hypertrophic cardiomyopathy with diastolic heart failure.

Diabetes has an independent relationship with nonischemic diabetic cardiomyopathy. Analysis of heart failure would indicate that women suffer more from diabetes than men including individuals with preserved and reduced ejection fraction. Some women with nonischemic etiology have survival benefits but diabetes heightens the risk of mortality related to females and it modifies the association between deaths and sex regardless of reduced or preserved LV function. Diabetes reduces the value of the protective effects of the female sex as it pertains to the progression of cardiomyopathy, which is a condition like CVD, even though the main underlying mechanism lacks clarity (De Ritter et al., 2020; Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019; Lien & Jiang, 2017). Aside from lipotoxicity, there are other molecular mechanisms involved such as intramyocardial inflammation, mitochondrial dysfunction, sex-hormone related myocardial calcium handling, metabolic stress response through altered insulin signaling or female-specific cardiac glycogen handling, reninangiotensin system involvement, and oxidative stress. Through interactions, the mechanisms can impede cardiac functioning and result in cardiomyocyte injury. Sex differences are often evident in adrenergic response to physical activity with profound higher effects in women leading to variations in hypertrophic action and lipid metabolism (Mahs et al., 2022; Mamo et al., 2019; McLachlan & Gale, 2018). An opportunity for further research would be to breach the knowledge gap associated with sex dimorphism in human diabetic cardiomyopathy.

At an earlier age, men tend to develop diabetic foot syndrome and often experience amputations of the lower extremity. Compared with females, socioeconomic status and gender interactions impact males the most. The highest disparity is between women in the highest and men in the lowest socioeconomic class (Mahs et al., 2022; Mamo et al., 2019; McLachlan & Gale, 2018). For higher risk of foot ulceration, the positive predictors are longer type 2 diabetes mellitus duration, missing of a pedal pulse, negative results of the monofilament test, male sex, and previous ulcerations. When conducting assessments of the populations without previous history of amputation or ulceration, the higher risk for men is often not observed. There are sex-specific differences in peripheral arterial disease risk factors for patients with type 2 diabetes mellitus. Independent risk factors for disease progression in men are systolic blood pressure, BMI, and age, for women, they are insulin therapy, uric acid levels, and age. The long-term predictors of death are renal insufficiency, peripheral arterial disease, and male sex (Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019; Lien & Jiang, 2017; Mahs et al., 2022; Mamo et al., 2019; McLachlan & Gale, 2018). Researchers should focus on conducting studies pertaining to the exploration of pathophysiological mechanisms and sex dimorphism in humans. They could also explore sex-specific differences and whether sex-specific background influences disease progression.

Compared to women, men undergo dialysis therapy more often and they show faster diabetic nephropathy progression. During chronic dialysis treatment, diabetic women have higher risks of mortality than diabetic men. There is a clear interaction between diabetes and sex that leads to an excessive mortality rate in diabetic women. Sex differences in insulin-resistant patients and organ damage is linked to reduced pulse wave velocity, higher vascular plaques, increased intima-media thickness progression, and increased renal and vascular damage in women compared to men. It is particularly pronounced in women living with type 2 diabetes mellitus. Women over the age of 60 with type 2 diabetes mellitus after their first renal replacement therapy have higher risk of mortality (Gomulka & Ruta, 2023; Grzybowski et al., 2020; Hayati et al., 2023; Jiwani et al., 2022). In the younger population, the difference is not evident. During the first four years after dialysis, there is an increase in mortality rate for diabetic women living with end-stage renal disease. To a higher extent, older women tend to be affected the most. In women younger than 55 years of age and living with advanced renal disease, excess mortality is higher than it is in men (Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019). Increased risk of death stemming from different causes, including cardiovascular problems, are obvious at older age and in milder cases of renal disease for women living with diabetes and experiencing further deterioration because of worsening glycemic control. Greater oxidative stress and higher inflammation in diabetic women with end-stage renal disease, and modifiable gender differences in accessibility to and modalities of treatment, explain excess mortality in diabetic women. There is a faster progression of renal impairment in nondiabetic males. There are more negative effects of androgens on blood pressure, glycemic control, vascular and endothelial response to thromboxane, nitric oxide, or endothelial-1. Researchers could examine the effects of sex hormones on renal and systematic hemodynamic parameters, renal medullary blood flow, renal cortical flow, and mean arterial pressure in diabetic females and males. Endogenous androgen withdrawal is associated with the effects of nitric oxide production, that tends to be higher in the absence of testosterone, and the endothelial B receptor that could be influenced by testosterone and lead to vasoconstriction. Androgen blockade could have possible renal-protective effects in hypertensive females and males treated with anti-androgens (Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019; Kang & Yang, 2020; Madhuri & Srilakshmi, 2019; Magne et al., 2020).

Among individuals living with type 2 diabetes mellitus, there is a higher risk of renal disease and proteinuria in women compared to men. In terms of differences in sex-specific gene polymorphism, diabetic women with angiotensin-converting enzyme (ACE) D allele are at a higher risk for developing diabetic nephropathy compared to diabetic men. Sex dimorphism in endothelial function plays a role in patients living with type 2 diabetes mellitus. Females have reduced renal oxidative stress and more nitric oxide than their male counterparts which could have protective effects on the exacerbation of diabetic renal impairment (Gomulka & Ruta, 2023; Grzybowski et al., 2020; Hayati et al., 2023; Jiwani et al., 2022; Kautzky-Willer et al., 2019). The key differences between women and men are the sex hormones. Estrogens protect women and hinder nondiabetic renal disease progression before menopause. The protection is alleviated in diabetic individuals. Testosterone increases nondiabetic chronic renal disease development. Changes in sex hormone levels and reduced testosterone levels accelerate diabetic nephropathy development and depict the importance of sex hormones in pathophysiologic mechanisms linked to disease progression (National Institutes of Health, 2019); Parthasharathi et al., 2022; Poly et al., 2023).

The sex of an individual is a fundamental biological factor that contributes to the regulation of health homeostasis and leads to the vulnerability to cardiometabolic risk factors and also the management, clinical picture, and manifestation of type 2 diabetes mellitus. In a sex-specific way, the severity of diabetes-related comorbidities is different particularly renal and cardiovascular disease (Romero, 2016; Saadane et al., 2023; University of North Carolina, n.d.). Psychosocial factors impact coping, progression, and the development of diabetes in a gender-dimorphic way. It is important to consider sexual function and reproductive factors. Special attention is necessary for the care of diabetic pregnancy because it is a vulnerable phase tied to the health of offspring especially in a sex-specific way. Hyperglycemic parents tend to have diabetic offspring which contributes further to an increase of the type 2 diabetes pandemic. In a balanced manner, biomedical clinical and basic research in the field of endocrinology would be beneficial to men and women. In personalized treatment in modern medicine, healthcare professionals should consider differences in biological factors such as neurohumoral pathways, sex hormones, genetic predisposition, and the environmental and behavioral differences between women and men (Hewage et al., 2020; Muche et al., 2020; Muhwava et al., 2019; Zhang et al., 2020).

Methods

I tested the relationship between psychological distress and diabetic retinopathy among adults in the United States while controlling for age, educational level, and income, through a retrospective, quasi experimental study and using descriptive data analysis, multivariate logistic regression of secondary data, and bivariate analysis using chi-square test of independence and include the statistical information at the end of this section. I set the significance level for the complex samples logistic regression and chi-squared analysis at 0.05. I measured the individual level variable, sex, as having two levels which are female and male. The geographic location or places of residence covered in the study were grouped in districts found in various parts of the United States. I measured age at the individual level based on the Medical Subject Headings (MeSH) for adults which are (age 19-44 years), Middle Aged (age 45-64 years), Aged (age 65-79 years), and Aged 80 and above. I used already collected data on the population level through reputable agencies. I transformed the data into nominal data in the order of low, medium, and high depending on the tertiles of the range of data. Some variables were measured at the population level within different districts and by years depending on the data collection method. Education was ranked based on the highest level attained and grouped in the categories of no education, primary (1-some high school education), secondary (2- high school graduate), tertiary (3- some college education) levels measured at a population level. The categories of no education were in measurements of low, medium, and high. The category of less than secondary education was in low, medium, and high categories. Secondary education was in low, medium, and high categories. Tertiary education was low, medium, and high.

NHANES has variables for depression and psychological distress measurement. The Patient Health Questionnaire (PHQ-9) measures how often individuals experience the following problems: Feeling down, depressed, or hopeless; little pleasure or interest in doing things; having little energy or feeling tired; sleeping too much or trouble staying or falling asleep; feeling bad about oneself or that they are failures or that they have let themselves or their families down; overeating or poor appetite; speaking or moving too slow to the noticeability of others or being so restless or fidgety and moving around more than usual; or thoughts of being better off hurting oneself or dying (CDC, 2017). The responses are measured in days and in categories such as Not at all (0), Several days (1), More than half days (2), and Nearly every day (3). For each checked off problem on the PHQ-9 patient depression questionnaire, respondents indicate how the problems made it difficult for them to do their work, perform duties at home, or get along with other individuals. The categories of their responses are: Not difficult at all; Somewhat difficult; Very difficult; and Extremely difficult. Checks of at least four on the list indicate a depressive disorder. Major depressive disorders have at least five affirmative responses in the very difficult and the extremely difficult categories and also in the several days category for the thoughts of death or hurting oneself section. The total scores correspond with the severity of depression are as follows: Minimal depression (1-4), Mild depression (5-9), Moderate depression (10-14), Moderately severe depression (15-19), and Severe depression (20-27; Stanford.edu, n.d.).

The chosen study design was the most practical because of the existence of large datasets of relevant information, the reduction of the study time, and the elimination of one-on-one interactions with patients, and the inclusion of variables at the population and individual levels. Assessment of the data would be through the Centers for Disease Control and Prevention website (CDC). I obtained ethical approval from Walden University.

Results

Complex Samples—Logistic Regression

What is the association between Psychological Distress and Diabetic Retinopathy among U.S. Adults after controlling for age, educational level, and income?

The weighted population size is 16639717.14. The valid number of people included within the analysis is 468 and the number represents the weighted population size.

Table 1

Frequency and Percentage of Each of the Variables Within the Model

Variable	Frequency	Percentage/Mean
Diabetic retinopathy	3,199,802	20.7%
Education level		
Some high school	2,650,510	15.9%
High school graduate	5,683,292	34.2%
Some college	8,305,914	49.9%
Age (mean)	--	60.9
Family poverty-income-ratio (mean)	--	2.87

Table 2

Odds Ratio of Each of the Variables Within the Model

Variable	Odds ratio	95% confidence interval	*p*-value
Age (continuous)	0.99	0.96–1.02	0.30
Poverty-income-ratio (continuous)	1.202	0.91–1.60	0.17
Education			0.95
Some high school	1.18	0.37–3.75	
High school graduate	0.96	0.44–2.10	
Some college	Reference category	Reference category	
Psychological distress	0.96	0.60–1.56	0.87

The result indicates that there is no association between psychological distress and diabetic retinopathy. The odds ratio of 0.96 (CI 0.60-1.56) denotes strong evidence to fail to reject the null hypothesis. There is no association (p=0.87) between psychological distress and diabetic retinopathy among U.S.

adults after controlling for age, educational level, and income.

The result shows that there is no association between education level and diabetic retinopathy. The odds ratio of 1.18 (CI 0.37-3.75) denotes strong evidence for the null hypothesis being true and it is not rejected.

The odds ratio of 0.96 (CI 0.44-2.10) denotes strong evidence to fail to reject the null hypothesis. There is no association between those who had some high school education, those that are high school graduates, and people with some college education developing diabetic retinopathy. The result shows that there is no association between psychological distress and diabetic retinopathy among U.S. adults after controlling for age, educational level, and income.

The result indicates that there is no association between age and diabetic retinopathy. The odds ratio of 0.99 (CI 0.96-1.02) denotes strong evidence to fail to reject the null hypothesis. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for age.

The result indicates that there is no association between income and diabetic retinopathy. The odds ratio of 1.20 denotes strong evidence to fail to reject the null hypothesis. The result shows that there is no statistically significant association between psychological distress and diabetic retinopathy when controlling for income.

Discussion

A p-value of 0.87 shows that there is no association between psychological distress and diabetic retinopathy among U.S. adults after controlling for age, educational level, and income. The odds ratio of 0.96 (CI 0.60-1.56) denotes strong evidence to fail to reject the null hypothesis. The result shows that although the literature on the topic indicated a link between psychosocial functioning and diabetic macular edema (DME) or diabetic retinopathy, there is uncertainty behind the direction and extent of the association. Psychosocial functioning entails social and emotional factors that relate to depression, vision-specific distress, anxiety, depressive disorder, social and emotional well-being, and diabetes-specific distress (Beaser et al., 2018; Khoo et al., 2019; Patel et al., 2022). In adults, the leading causes of vision loss are DME and diabetic retinopathy. A worldwide estimate of one-third of individuals living with diabetes show signs of diabetic retinopathy. One in ten of those individuals develop clinically significant macular edema (CSME), proliferative diabetic retinopathy (PDR), or nonproliferative diabetic retinopathy (NPDR), and vision-threatening diabetic retinopathy (Beaser et al., 2018; Khoo et al., 2019; Patel et al., 2022).

The impact of DME and DR on quality of life, mobility, and independence, and on vision-specific functioning, such as driving and reading, especially in the VTDR stage, is detrimental and profound. Some studies show a significant association between psychological distress and complications of diabetes and a correlation between depressive symptoms and diabetic retinopathy. Others show an independent association between poor emotional well-being, visual loss, and diabetic retinopathy. Some quantitative studies emphasize the association between poor psychosocial outcomes and diabetic retinopathy. Depression could be associated with the incidence and presence of diabetic retinopathy. Many pathophysiological mechanisms, such as increases in circulating cytokines, glucose and insulin resistance alteration, and dysregulation of hypothalamic-pituitary-adrenal (HPA) axis, could play contributory roles in the pathogenesis of diabetic retinopathy (Ansari et al., 2022; Beaser et al., 2018; Khoo et al., 2019; Patel et al., 2022). The interaction shows a probable bi-directional relationship between psychosocial functioning and diabetic retinopathy.

The odds ratios of 1.18 (CI 0.37-3.75) and 0.96 (CI 0.44-2.10) indicate that there is no association between educational level and diabetic retinopathy after controlling for age and income, and denotes strong evidence for the null hypothesis being true. The results show that there is no association between those who had some high school education, those who are high school graduates, and people with some college education developing diabetic retinopathy. They also indicate that there is no association between psychological distress and diabetic retinopathy when controlling for education. To limit and prevent the progression or development of diabetic retinopathy, it is necessary to have a coordinated management strategy which includes early diagnosis of the disease, glycemic control, and regular screening of the diabetic retinopathy risk factors. Preventive care would entail comprehensive ancillary tests, patient education, and dilated eye exams implemented through a multidisciplinary team that comprises retina specialists, ophthalmologists, and primary diabetes care providers such as diabetologists, endocrinologists, and primary care providers. Despite the dissemination of the guideline recommendations for regular patient education and screening, many individuals with diabetes do not receive the ophthalmological care needed for the prevention of blindness and visual impairment (Ansari et al., 2016; Ansari et al., 2022; Beaser et al., 2018; Khoo et al., 2019; Patel et al., 2022). Patient-focused education could have an impact on patient self-efficacy and knowledge as they relate to the management and prevention of diabetic retinopathy. Online education could assist in changing patient practice, competence, and knowledge. An effective tool for building patient awareness and knowledge about diabetic retinopathy and for motivating patients to take actions towards diabetic retinopathy self-care is patient education (Ansari et al., 2016; Beaser et al., 2018; Patel et al., 2022).

The odds ratio of 0.99 (CI 0.96-1.02) denotes strong evidence to fail to reject the null hypothesis. The result indicates that there is no association between age and diabetic retinopathy. It shows that there is no association between psychological distress and diabetic retinopathy when controlling for age. The duration of diabetes mellitus is associated with the severity of diabetic retinopathy. Considering the significant increase in human lifespan and the aging population, diabetic retinopathy has become devastating to healthcare systems and individuals. Although aging plays a significant role in the onset of age-related diseases, its indirect or direct effects on the development of diabetic retinopathy are understudied (Alperet et al., 2019; Ansari et al., 2016; Li et al., 2023). Some studies emphasize that the development of diabetic retinopathy and age-related degeneration have similar risk factors which explains the prevalence of increased visual impairment and diabetic retinopathy in the aging population.

There is no association between income and diabetic retinopathy based on the odds ratio of 1.20 which denotes strong evidence to fail to reject the null hypothesis. The result shows that there is no statistically significant association between psychological distress and diabetic retinopathy when controlling for income. In working-aged people living with diabetes, diabetic retinopathy is the leading cause of blindness. Diabetes-related health outcomes and diabetic retinopathy disproportionately affect minority and underserved populations in the United States. Racial disparities and those associated with the social determinants of health, such as education, healthcare access, geography, and socioeconomic status play roles in the screening and prevalence of diabetic retinopathy (American Diabetes Association, 2018; Ansari et al., 2016; Beaser et al., 2018; Patel et al., 2022).

Limitations

The study has some limitations. The lack of patient education and regular screening for diabetic retinopathy leads to the inability of many individuals living with diabetes in the United States not receive ophthalmological care needed for the prevention of visual impairment and blindness. The educational and screening factors and those lacking ophthalmological care were not controlled in the study because of the constraints of data availability and sample size. Factors such as lack of effective communication and lack of care by healthcare providers regarding patients, and the extent of diabetic retinopathy progression were not controlled in the study. Nonbinary and transgender respondents were not controlled for in the study because the sample size was not large enough for this category of respondents.

Implications

The study has implications for social change and the practice and discipline of public health as a profession. It provides new insights into ways that the improvement of the pathophysiology of diabetes and diabetic retinopathy could lead to the improvement of psychological distress. The study findings could facilitate the implementation of national policies focused on the empowerment or assistance of individual adherence to healthier lifestyles leading to the prevention of diabetes mellitus and diabetic retinopathy. The findings could also encourage individuals with the disease to enroll in classes for diabetes education and to seek additional information. The study would increase the awareness and importance of preventative care in public health practice and profession through evidence-based screenings and patient education. It could create a sense of urgency around the need for a coordinated management strategy which includes early diagnosis of diabetes, glycemic control, and regular screening of the diabetic retinopathy risk factors. Preventive care would entail dilated eye exam, comprehensive ancillary tests, and patient education implemented through a multidisciplinary team that comprises ophthalmologists, retina specialists, and primary diabetes care providers such as diabetologists, endocrinologists, and primary care providers. The study might encourage additional research on diabetes-related laser eye surgery, intraocular drug therapy for vision improvement, and neuro-degeneration.

The study findings could facilitate stakeholder-sponsored grants when seeking funding for educational promotions pertaining to diabetic retinopathy and psychological distress. It could also provide information for population health planning and implementation in the public health field and for public health practitioners of all types, sizes, specialties, and expertise. With the investment of financial incentives in preventative services and the monitoring of care continuum, the results of the study could enable public health organizations and practitioners that are proactive in population health planning and implementation to reach their goals (Romero, 2016). Healthcare organizations working with limited staff and budgets on the development and deployment of population health management programs, particularly on diabetes and diabetic retinopathy, could use the findings of the study. Healthcare providers could use the information from this study to change their workflow to enable them to properly manage patients with chronic diseases, such as diabetes, and other issues such as limited access to healthcare, and a high tendency of frequent visits to the hospital.

The results of the study could enable healthcare professionals to tackle some of the challenges they face when developing health programs and enable them to strive in achieving success in a fast-evolving healthcare industry (Romero, 2016). The study findings could be instrumental to the implementation of national policies encouraging the assistance or empowerment of adherence to healthier lifestyles leading to diabetes mellitus and the prevention of diabetic retinopathy.

Recommendations for Further Research

Within its limitations, the findings of this study highlight that with odds ratios of 1.18 (CI 0.37-3.75) and 0.96 (CI 0.44-2.10), there is no association between psychological distress and diabetic retinopathy while controlling for education levels, which includes some high school education, high school graduates, and some college, income, and age. Further research on patient education and regular screening for diabetic retinopathy in the United States for diabetic patients is necessary. Despite the recommended guidelines for patient education and frequent diabetic retinopathy screening, several diabetic individuals lack the proper ophthalmological care needed for visual impairment and blindness prevention. Researchers could explore the reasons for the gap in care such as lack of patient education, lack of care coordination between healthcare providers and patients, and lack of effective communication. The gaps could result in missed opportunities in the prevention of disease progression. There is a scarcity of published research pertaining to the possibility of education stimulating changes in knowledge and self-efficacy and leading to behavioral change.

Although a p-value of 0.87 shows that there is no association between psychological distress and diabetic retinopathy among U.S. adults, it is important to have a comprehensive understanding of the relationship between diabetic retinopathy and psychosocial outcomes for the development and implementation of effective interventions for diabetic patients. The odds ratio of 1.20 shows that there is no statistically significant association between psychological distress and diabetic retinopathy when controlling for income, but there is a need for further research on the study of the role socioeconomic status plays in the prevalence of diabetic retinopathy in the American population. Even though it could be a result of environmental and behavioral mechanisms, further research is important in determining the reason women tend to have more sensitivity to sociocontextual predictors, such as occupation, education, and income, for the risk of developing diabetes in the future (Mahs et al., 2022).

In men and women, there is often a misalignment between the circadian clock and social rhythms and between gender-dependent social timing and sex-dependent biological factors such as body composition that is associated with the pathogenesis of diabetes (Kautzy-Willer et al., 2019; Lien & Jiang, 2017). Researchers could conduct further research investigating the complexity of sex-dimorphic associations between sleep, work stress, and diabetes. The research findings could assist in implementing sex-specific prevention programs in some groups of shift workers. Compulsoriness of possible sexual dimorphism could be the focus of future studies. To gain a better understanding of the phenomenon, researchers should study the different biological and environmental factors associated with diabetic women having excess risks of cardiovascular disease. Sex differences are usually obvious in adrenergic responses to physical activity with higher effects in women that lead to variations in lipid metabolism and hypertrophic action (Mahs et al., 2022; Mamo et al., 2019; McLachlan & Gale, 2018). Researchers should endeavor to breach the knowledge gap pertaining to sex dimorphism in human diabetic cardiomyopathy. They should get clarification on the sex-specific dose-response relationships between the risk of type 2 diabetes mellitus and alcohol consumption and the underlying mechanisms. Further research to gain clarification on the relationship between birth weight, pregnancy-related stress, offspring HPA axis activity, and the impact of programming adult diseases in young women and men, is also important (Hewage et al., 2020; Madhuri & Srilakshmi, 2019; Muche et al., 2020; Muhwava et al., 2019). They should conduct research on the study of the role socioeconomic status plays in the prevalence of diabetic retinopathy in the American population. They should conduct reviews to identify the need for the improvement of outcome measures and obtaining valid and meaningful results of the social and emotional impact of diabetic retinopathy and possible directions of research pertaining to computer adaptive testing. It is important to explore the possibilities of education in stimulating changes in knowledge and self-efficacy in behavioral changes. Patient education activities could occur on demand, face-to-face, or online. To obtain optimal ophthalmological care, education could empower patients to act as their own advocates.

Conclusion

There is no association between psychological distress and diabetic retinopathy among U.S. adults when controlling for education level, income, and age. Considering the study's limitations, there is an uncertainty behind the direction and extent of the association between psychological distress and diabetic retinopathy. The senescence-associated secretory phenotype and the advanced glycation end products mechanisms are involved in the role of aging in the progression of diabetic retinopathy. Diabetic retinopathy and diabetic macular edema are the leading causes of vision loss in adults. Many individuals living with diabetes in the United States do not receive the necessary ophthalmological care for the prevention of visual impairment and blindness despite the recommended guidelines for the regular screening of diabetic retinopathy and patient education. There are various reasons for the gap in care such as the lack of care coordination between healthcare providers and patients, lack of patient education, and lack of effective communication (Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Patel et al., 2022). The gaps could result in missed opportunities in the prevention of disease progression. The rise of diabetes to epidemic proportions correlates with the increasing prevalence and incidence rates of diabetic retinopathy (Atwany et al., 2022;

Aziz et al., 2023; Beaser et al., 2018; Li et al., 2023). The impact of diabetic retinopathy and diabetic macular edema on mobility, independence, and vision-specific functioning such as reading and driving can be profound. Some studies show a significant association between psychological distress and complications of diabetes and a correlation between diabetic retinopathy and depressive symptoms and an independent association between visual loss, poor emotional well-being, and diabetic retinopathy (Beaser et al., 2018; Khoo et al., 2019; Patel et al., 2022). There is no association between those who had some high school education, those that are high school graduates, and people with some college education developing diabetic retinopathy. Preventive care for diabetic retinopathy and diabetic macular edema includes patient education, comprehensive ancillary tests, and dilated eye exams implemented through a multidisciplinary team that consists of ophthalmologists, retina specialists, and primary diabetes care providers such as endocrinologists, diabetologists, and primary care providers. It is important to have a coordinated management strategy that includes regular screening of the diabetic retinopathy risk factors, early diagnosis of the disease, and glycemic control, to limit and prevent the progression or development of diabetic retinopathy (Beaser et al., 2018; Khoo et al., 2019; Patel et al., 2022). The comprehensive understanding of the relationship between diabetic retinopathy and psychological outcomes is important for the development and implementation of effective interventions for diabetic patients.

References

Allen, M. (2017). Quantitative research. *The Sage Encyclopedia of Communication Research Methods*. https://dx.doi.org/10.4135/9781483381411.n476

Alperet, D. J., Rebello, S. A., Khoo, E. Y., Tay, Z., Seah, S. S., Tai, B., Tai, E., Emady-Azar, S., Chou, C. J., Darimont, C., Dam, R. M.V. (2019). The effect of coffee consumption on insulin sensitivity and other biological risk factors for type 2 diabetes: a randomized placebo-controlled trial. *The American Journal of Clinical Nutrition*, *111*(2), 448-458. https://doi.org/10.1093/ajcn/nqz306

American Diabetes Association. (2018). Economic costs of diabetes in the U.S. in 2017. Diabetes Care, 41 (4). Doi: 10.2337/dci18-0007

Ansari, R. M., Hosseinzadeh, H., & Zwar, N. (2016). A qualitative research on self-management of type 2 diabetes in middle-aged population of rural area of Pakistan. *International Education and Research Journal*, *2*(8), 62-65.

Ansari, P., Tabasumma, N., Snigdha, N. N., Siam, N. H., Panduru, R. V. N. R. S., Azam, S., Hannan, J. M. A., & Abdel-Wahab, Y. H. A. (2022). Diabetic retinopathy: An overview on mechanisms, pathophysiology and pharmacotherapy. *Diabetology, 3*, 159-175. https://doi.org/10.3390/diabetology3010011

Antonetti, D. A., Silva, P. S., & Stitt, A. W. (2021). Current understanding of the molecular and cellular pathology of diabetic retinopathy. *Nature Reviews Endocrinology, 17*, 195-206. https://doi.org/10.1038/s41574-020-00451-4

Atlanta Diabetes Association. (2020). Type 2 diabetes. *Endocrine Specialty Group*. https://atlantadiabetes.com/diabetes-care/type-2-diabetes/

Atwany, M. Z., Sahyoun, A. H., and Yaqub, M. (2022). Deep learning techniques for diabetic retinopathy classification: A survey. *IEEE Acess. 10*, 28642-28655. Doi: 10.1109/ACCESS.2022.3157632.

Aziz, T., Charoenlarpnopparut, C., & Mahapakulchai, S. (2023). Deep learning-based hemorrhage detection for diabetic retinopathy screening. *Scientific Reports, 13*(1), Article 1479. https://doi.org/10.1038/s41598-023-28680-3

Beaser, R.S., Turell, W.A., Howson, A. (2018). Strategies to improve prevention and management in diabetic retinopathy: Qualitative insights from mixed-methods study. *Diabetes Spectrum, 31*(1), 65-74. Doi: 10.2337/ds16-0043

Bora, A., Balasubramanian, S., Babenko, B., Virmani, S., Venugopalan, S., Mitani, A., Marinho, G., Cuadros, J., Ruamviboonsuk, P., Corrado, G., Peng, L., Webster, D., Varadarajan, A., Hammel, N., Liu, Y., & Bavishi, P. (2021). Predicting the risk of developing diabetic retinopathy using deep learning. *The Lancet Digital Health, 3*(1), e10-e19. https://doi.org/10.1016/S2589-7500(20)30250-8

Boyd, K., & Gregori, N. Z. (2020). What is diabetic retinopathy? *American Academy of Ophthalmology*. What Is diabetic retinopathy? - American Academy of Ophthalmology (aao.org)

Centers for Disease Control and Prevention. (2017). National health and nutrition examination survey (NHANES). 2015-2016 Data documentation, codebook, and frequencies. *Mental Health- Depression Screener (DPQ_1)*. NHANES 2015-2016: Mental Health - Depression Screener

Data Documentation, Codebook, and Frequencies (cdc.gov)

Centers for Disease Control and Prevention. (2019). Type 2 diabetes. *United States Department of Health and Human Services*. https://www.cdc.gov/diabetes/basics/type2.html

Centers for Disease Control and Prevention. (2021). The social-ecological model: a framework for prevention. violence prevention. *United States Department of Health and Human Services*. The Social-Ecological Model: A Framework for Prevention |Violence Prevention|Injury Center|CDC

Centers for Disease Control and Prevention. (2020). What is diabetes? *United States Department of Health and Human Services*. What is diabetes? | CDC

Centers for Disease Control and Prevention. (2021). *Diabetes*. Division of Diabetes Translation | CDC

Centers for Disease Control and Prevention. (2020). National diabetes statistics report 2020. Estimates of diabetes and its burden in the United States. *National Diabetes Statistics Report 2020*. (cdc.gov)

Cherchi, S., Gigante, A., Spanu, M. A., Contini, P., Meloni, G., Fois, M. A., Pistis, D., Pilosu, R. M., Lai, A., Ruin, S., Campesi, I., & Tonolo, G. (2020). Sex-gender differences in diabetic retinopathy. *Diabetology, 1*, 1-10. https://doi.org/10.3390/diabetology1010001

Cleveland Clinic. (2021). Diabetes: An overview. *100 Years of Cleveland Clinic*. Diabetes: Types, Risk Factors, Symptoms, Tests, Treatments & Prevention

(clevelandclinic.org)

Cleveland Clinic. (2022). Optical coherence tomography. *100 Years of Cleveland Clinic*. Diagnostics: Optical Coherence Tomography (clevelandclinic.org)

Curry, A. (2020). Fatty liver and type 2 diabetes. *University of Florida Diabetes Institute*. Fatty Liver and Type 2 Diabetes » Diabetes Institute » College of Medicine » University of Florida (ufl.edu)

Dai, L., Wu, L., Li, H., Cai, C., Wu, Q., Kong, H., Liu, R., Wang, X., Hou, X., Liu, Y., Long, X., Wen, Y., Lu, L., Shen, Y., Chen, Y., Shen, D., Yang, X., Zou, H., Sheng, B., & Jia, W. (2021). A deep learning system for detecting diabetic retinopathy across the disease spectrum. *Nature Communications, 12*(3242). https://doi.org/10.1038/s41467-021-23458-5

De Ritter, R., De Jong, M., Vos, R.C. (2020). Sex differences in the risk of vascular disease associated with diabetes. *Biology of Sex Differences*, *11* (1). https://doi.org/10.1186/s13293-019-0277-z

Demmin, D. L., & Silverstein, S. M. (2020). Visual impairment and mental health: Unmet needs and treatment options. *Journal of Clinical Ophthalmology, 14*, 4229-4251. https://doi.org/10.2147/OPTH.S258783

DiaGundluru, N., Rajput, D. S., Lakshmanna, K., Kaluri, R., Shorfuzzaman, M., Uddin, M., and Khan, M. A. R. (2022). Enhancement of detection of diabetic retinopathy using harris hawks optimization with deep learning model. *Computational Intelligence and Neuroscience*. *2022*. https://doi.org/10.1155/2022/8512469

Doheny, K. (2020). Pancreatic fat: Lifestyle habits count more than genetics.

Endocrineweb. Pancreatic Fat: Lifestyle Habits Count More Than Genetics (endocrineweb.com)

Emani, S., Peters, E., Desai, S., Karson, A. S. Lipsitz, S. R., LaRocca, R., Stone, J., Suric, V., Wald, J.S., Wheeler, A., Williams, D.H., & Bates, D.W. (2018). Perceptions of adopters versus non-adopters of a patient portal: an application of diffusion of innovation theory. *Journal of Innovation in Health Informatics, 25*(3), 149-157. http://dx.doi.org/10.14236/jhi.v25i3.991

Farooq, M. S., Arooj, A., Alroobaea, R., Baqasah, A. M., Singh, D., and Sardar, R. (2022). Untangling computer-aided diagnostic system for screening diabetic retinopathy based on deep learning techniques. *Sensors*, *22*(5), Article 1803. https://doi.org/10.3390/s22051803

Fenwick, E., Rees, G., Pesudovs, K., Dirani, M., Kawasaki, R., Wong, T. Y., and Lamoureux, E. (2011). Social and emotional impact of diabetic retinopathy: a review. *Clinical & Experimental Ophthalmology*. *40*(1), 27-38. https://doi.org/10.1111/j.1442-9071.2011.02599.x

Forrester, J. V., Kuffova, L., & Delibegovic, M. (2020). The role of inflammation in diabetic retinopathy. (2020). *Frontiers in Immunology, 11*. https://doi.org/10.3389/fimmu.2020.583687

Gadekallu, T. R., Khare, N., Bhattacharya, S., Singh, S., Maddikunta, P. K. R, & Srivastava, G. (2020). Deep neural networks to predict diabetic retinopathy. *Journal of Ambient Intelligence and Humanized Computing*. https://doi.org/10.1007/s12652-020-01963-7

Gomulka, K., Ruta, M. (2023). The role of inflammation and therapeutic concepts in diabetic retinopathy- a short review. *International Journal of Molecular Sciences. 24*(2). 1024. https://doi.org/10.3390/ijms24021024

Grzybowski, A., Brona, P., Lim, G., Ruamviboonsuk, P., Tan, G. S. W., Abramoff, M., and Ting, D. S. W. (2020). Artificial intelligence for diabetic retinopathy screening: A review. *Eye, 34*, 451-460. https://doi.org/10.1038/s41433-019-0566-0

Hayati, M., Muchtar, K., Roslidar, Maulina, N., Syamsuddin, I., Elwirehardja, G., N., Pardamean, B. (2023). Impact of CLAHE-based image enhancement for diabetic retinopathy classification through deep learning. Procedia *Computer Science*, *216*, 57-66. https://doi.org/10.1016/j.procs.2022.12.111

Hewage S, Audimulam J, Sullivan E, Chi C, Yew TW, Yoong J. (2020). Barriers to gestational diabetes management and preferred interventions for women with gestational diabetes in singapore: Mixed methods study. *JMIR Formative Research. 4*(6). Barriers to Gestational Diabetes Management and Preferred Interventions for Women With Gestational Diabetes in Singapore: Mixed Methods Study - PMC (nih.gov)

International Diabetes Federation. (2022). Diabetes around the world in 2022. *Diabetes Atlas*. https://www.diabetesatlas.org/en/sections/worldwidetoll-of-diabetes.ht

International Diabetes Federation. (2023). Understanding Diabetes. International Diabetes Federation - Home (idf.org)

Jiwani, N., Gupta, K., and Afreen, N. (2022). A convolutional neural network approach for diabetic retinopathy classification. *IEEE 11th International Conference on Communication Systems and Network Technologies (CSNT)*. 357-361. Doi: 10.1109/CSNT54456.2022.9787577

Kang, Q., & Yang, C. (2020). Oxidative stress and diabetic retinopathy: Molecular mechanisms, pathogenetic role and therapeutic implications. *Redox, 37,* 2213-2317. https://doi.org/10.1016/j.redox.2020.101799

Kautzky-Willer, A., Harreiter, J., Pacini, G. (2016). Sex and gender differences in risk, pathophysiology and complications of type 2 diabetes mellitus. *National Library of Medicine. National Center for Biotechnology Information. 37*(3). 278-316. Doi: 10.1210/er.2015-1137

Kautzy-Willer, A., Harreiter, J., Abrahamian, H., Weitgasser, R., Fasching, P., Hoppichler, F., Lechleitner, M. (2019). Gender-specific aspects of prediabetes and diabetes mellitus-clinical recommendations. *SpringerLink. 131* (1), 221-228. Gender-specific aspects of prediabetes and diabetes mellitus – clinical recommendations (Update 2019) | SpringerLink

Khoo, K., Man, R.E.K., Rees, G., Gupta, P., Lamoureux, E.L., Fenwick, E. K. (2019). The relationship between diabetic retinopathy and psychosocial functioning: a systematic review. *Quality of Life Research, 28*, (2017-2039). https://doi.org/10.1007/s11136-019-02165-1

Kovoor, E., Chauhan, S. K., and Hajrasouliha, A. (2022). Role of inflammatory cells in pathophysiology and management of diabetic retinopathy. *Survey of*

Ophthamology. *67* (6). 1563-1573. https://doi.org/10.1016/j.survophthal.2022.07.008

Kowluru, R. A. (2023). Cross talks between oxidative stress, inflammation and epigenetics in diabetic retinopathy. *Cells*, *12*(2), 300. https://doi.org/10.3390/cells12020300

Lauffenburger, J. C., Lewey, J., Jan, S., Lee, J., Ghazinouri, R., & Choudhry, N. K. (2020). Association of potentially modifiable diabetes care factors with glycemic control in patients with insulin-treated type 2 diabetes. *JAMA Network Open, 3*(1), e1919645– e1919645. https://doi.org/10.1001/jamanetworkopen.2019.19645

Li, Q., Wang, M., Li, X., Shao, Y. (2023). Aging and diabetic retinopathy: Inherently intertwined pathophysiological processes. *Experimental Gerontology 175* (112138), 0531-5565. https://doi.org/10.1016/j.exger.2023.112138

Li, F., Wang, Y., Xu, T., Dong, L., Yan, L., Jiang, M., Zhang, X., Jiang, H., Wu, Z., & Zou, H. (2022). Deep learning-based automated detection for diabetic retinopathy and diabetic macular oedema in retinal fundus photographs. *Eye, 36*, 1433-1441. https://doi.org/10.1038/s41433-021-01552-8

Li, Q., Chang, Y., Zhang, K., Chen, H., Tao, S., and Zhang, Z. (2020). Implication of the gut microbiome composition of type 2 diabetic patients from northern China. *Sci. Rep. 10* (1). Doi: 10.1038/s41598-020-62224-3

Li, X., Jiang, Y., Zhang, J., Li, M., Luo, H., and Yin, S. (2022). Lesion-attention pyramid network for diabetic retinopathy grading. *Artificial Intelligence in Medicine*. 126. https://doi.org/10.1016/j.artmed.2022.102259

Lien, A. S., & Jiang, Y. D. (2017). Integration of diffusion of innovation theory into diabetes care. *Journal of diabetes investigation, 8*(3), 259-260. Doi: 10.1111/jdi.12568

Madhuri, C., & Srilakshmi, B. (2019). Retrospective study on prevalence, risk factors, maternal and fetal outcome in gestational diabetes mellitus. *International Archives of Integrated Medicine*, *6*(11), 94-98. iaim_2019_0611_14.pdf (iaimjournal.com)

Magne, F., Gotteland, M., Gauthier, L., Zazueta, A., Pesoa, S., Navarrete, P., and Balamurugan, R. (2020).The firmicutes/bacteroidetes ratio: A relevant marker of gut dysbiosis in obese patients? *Nutrients, 12*(5), 1474. Doi: 10.3390/nu12051474

Mahs, M., Pithan, J. S., Bergmann, I., Gabrys, L., Graf, J., Holzemann, A., Van Laerhoven, K., Otto-Hagemann, S., Popescu, M. L., Schwermann, L., Wenz, B., Pahmeier, I., Teti, A. (2022). Activity tracker-based intervention to increase physical activity in patients with type 2 diabetes and healthy individuals: study protocol for a randomized controlled trial. *BioMed Central*, *23,* 617. Activity tracker-based intervention to increase physical activity in patients with type 2 diabetes and healthy individuals: study protocol for a randomized controlled trial | Trials | Full Text (biomedcentral.com)

Mamo, Y., Bekele, F., Nigussie, T., & Zewudie, A. (2019). Determinants of poor glycemic control among adult patients with type 2 diabetes mellitus in Jimma University Medical Center, Jimma zone, south west Ethiopia: A case control study. *BMC Endocrine Disorders*, *19*(1), 91. https://doi.org/10.1186/s12902-019-0421-0

McLachlan, K., & Gale, C. R. (2018). The effects of psychological distress and its interaction with socioeconomic position on risk of developing four chronic diseases. *Journal of psychosomatic research, 109,* 79-85. doi: 10.1016/j.jpsychores.2018.04.004

Mikkola, I., Hagnäs, M., Hartsenko, J., Kaila, M., & Winell, K. (2020). A personalized care plan is positively associated with better clinical outcomes in the care of patients with type 2 diabetes: A cross-sectional real-life study. *Canadian Journal of Diabetes, 44*(2), 133– 138. https://doi.org/10.1016/j.jcjd.2019.05.003

Muche, A. A., Olayemi, O. O., & Gete, Y. K. (2020). Effects of gestational diabetes mellitus on risk of adverse maternal outcomes: a prospective cohort study in Northwest Ethiopia. *BMC Pregnancy & Childbirth, 20*(1), 1-13. Effects of gestational diabetes mellitus on risk of adverse maternal outcomes: a prospective cohort study in Northwest Ethiopia | BMC Pregnancy and Childbirth | Full Text (biomedcentral.com)

Muhwava, L. S., Murphy, K., Zarowsky, C., & Levitt, N. (2019). Experiences of lifestyle change among women with gestational diabetes mellitus (GDM): A behavioural diagnosis using the COM-B model in a low-income setting. *Plos One Journal*, *14*(11). https://doi.org/10.1371/journal.pone.0225431

National Institute of Diabetes and Digestive and Kidney Diseases. (n.d.).

Diabetes. Diabetes | NIDDK (nih.gov). Diabetes - NIDDK (nih.gov)

National Institutes of Health. (2019). *Diabetic retinopathy*. National Eye Institute. Diabetic Retinopathy | National Eye Institute (nih.gov)

Parthasharathi, G. U., Kumar, K. V., Premnivas, R., and Jasmine, K. (2022). Diabetic retinopathy detection using machine learning. *Journal of Innovative Image Processing*. *4*(1), 26-33. Doi:10.36548/jiip.2022.1.003

Patel, D., Ananthakrishnan, A., Lin, T., Channa, R., Liu, T.Y.A, Wolf, R.M. (2022). Social determinants of health and impact on screening, prevalence, and management of diabetic retinopathy in adults: A narrative review. *Journal of Clinical Medicine*, *11*(23), 7120. Doi: 10.3390/jcm11237120

Poly, T. N., Islam, M., Walther, B. A., Lin, M., C., & Li, Y.-C. (2023). Artificial intelligence in diabetic retinopathy: Bibliometric analysis. *Computer Methods and Programs in Biomedicine*. *231*, Article 107358. https://doi.org/10.1016/j.cmpb.2023.107358

Porter, D. (2022). What is fluorescein angiography. *American Academy of Ophthalmology*. What Is Fluorescein Angiography? - American Academy of Ophthalmology (aao.org)

Prasad, R., Floyd, J. L., Dupont, M., Harbour, A., Agyeiwaah, Y. A., Bediako, B. A., Chakraborty, D., Kichler, K., Rohella, A., Calzi, S. L., Lammendella, R., Wright, J., Boulton, M. E., Oudit, G. Y., Raizada, M. K., Stevens, B. R., Li, Q., Grant, M. B. (2023). Maintenance of enteral ACE2 prevents diabetic retinopathy in type 1 diabetes. *Circulation Research. 132* (1).

https://doi.org/10.1161/CIRCRESAHA.122.322003

Qiao, L., Zhu, Y., & Zhou, H. (2020). Diabetic retinopathy detection using prognosis of microaneurysm and early diagnosis system for non-proliferative diabetic retinopathy based on deep learning algorithms. *IEEE Access, 8,* 104292-104302. Doi: 10.1109/ACCESS.2020.2993937

Qummar, S., Khan, F. G., Shah, S., Khan, A., Shamshirband, S., Rehman, Z. U., Khan, I. A., and Jadoon, W. (2019). A deep learning ensemble approach for diabetic retinopathy detection. *IEEE, 7,* 150530-150539. Doi: 10.1109/ACCESS.2019.2947484

Regeneron Pharmaceuticals. (2021). About diabetic retinopathy. *Now Eye See*. Now Eye See | Diabetic Retinopathy

Rezazadeh-Gavgani, E., Oladghaffari, M., Bahramian, S., Majidazar, R., & Dolati, S. (2023). MicroRNA-21: A critical underestimated molecule in diabetic retinopathy. *Gene, 859.* https://doi.org/10.1016/j.gene.2023.147212

Romero, L. F. (2016). Diabetes: The current state of affairs from a population management view. *MLO: Medical Laboratory Observer, 48*(8), 12-20. https://ezp.waldenulibrary.org/login?url=https://search.ebscohost.com/login.aspx?

Ruamviboonsuk, P., Tiwari, R., Sayres, R., Nganthavee, V., Hemarat, K., Kongprayoon, A., Raman, R., Levinstein, B., Liu, Y., Schaekermann, M., Lee, R., Virmani, S., Widner, K., Chambers, J., Hersch, F., Peng, L., and Webster, D. (2022). Real-time diabetic retinopathy screening by deep learning in a multisite national screening programme: a prospective interventional cohort study. *The Lancet Digital Health*. *4* (4), e235-e244. https://doi.org/10.1016/S2589-7500(22)00017-6

Saadane, A., Veenstra, A. A., Minns, M. S., Tang, J., Du, Y., Elghazali, F. A., Lessieur, E. M., Pearlman, E., & Kern, T. S. (2023). *Diabetologia*. *66,* 590-602. https://doi.org/10.1007/s00125-022-05860-w

Setia, M. S. (2016). Methodology series module 3: Cross-sectional studies. *Indian Journal of Dermatology, 61*(3), 261-264. https://doi.org/10.4103/0019-5154.182410

Stanford.edu. (n.d.). Patient Health Questionnaire (PHQ-9). *Patient Health Questionnaire (PHQ-9)* (stanford.edu)

Teo, Z. L., Tham, Y. C., Yu, M., Chee, M. L., Rim, T. H., Cheung, N., Bikbov, M. M., Wang, Y. X., Tang, Y., Lu, Y., Wong, I. Y., Ting, D. S. W., Tan, G. S. W., Jonas, J. B, Sabanayagam, Wong, T. Y., Cheng, C. Y. (2020). Global prevalence of diabetic retinopathy and protection of burden through 2045: Systemic review and meta-analysis. *Ophthalmology, 128*(11), 1580-1591. https://doi.org/10.1016/j.ophtha.2021.04.027

Torpy, J. M., Glass, T. J., Glass, R. M. (2007). Retinopathy. *Journal of American Medical Association (JAMA), 298*(8), 944. Doi:10.1001/jama.298.8.944

Tymchenko, B., Marchenko, P., and Spodarets, D. (2020). Deep learning approach to diabetic retinopathy detection. *Cornell University. arXiv*. https://doi.org/10.48550/arXiv.2003.02261

University of North Carolina. (n.d.). Diabetes questionnaire. *Campus Health*. diabetes_questionnaire (unc.edu)

Vitger, T., Langberg, H., Grabowski, D. (2017). Mutual involvement in families with type 2 diabetes through web-based health care solutions: Quantitative survey study of family preferences, challenges, and potentials. *Journal of Medical Internet Research Publication (JMIR)*, *2*(2), 2371-4379. Doi: 10.2196/diabetes.7456

Vujosevic, S, Aldington, S. J., Silva, P., Hernandez, C., Scanlon, P., Peto, T., & Simo, R. (2020). Screening for diabetic retinopathy: new perspectives and challenges. *The Lancet Diabetes & Endocrinology*, *8*(4), 337-347. https://doi.org/10.1016/S2213-8587(19)30411-5

Wang, M., Yang, Y., Liao, Z. (2020). Diabetes and cancer: Epidemiological and biological links. *World Journal of Diabetes*. *11*(6), 227-238. Doi: 10.4239/wjd.v11.i6.227

Winston-Salem State University. (n.d.). Quantitative design. *Key Elements of a Research Proposal*. Key Elements of a Research Proposal - Quantitative Design (wssu.edu)

Zhang, H., Wang, Q., He, S., Wu, K., Ren, M., Dong, H., Di, J., Yu, Z., & Huang, C. (2020). Ambient air pollution and gestational diabetes mellitus: A review of evidence from biological mechanisms to population epidemiology. *Science of The Total Environment. 719*. https://doi.org/10.1016/j.scitotenv.2020.137349

Zheng, D., Li, N., Hou, R., Zhang, X., Wu, L., Sundquist, J., Sundquist, K., & Ji, J. (2023). Glucagon-like peptide-1 receptor agonists and diabetic retinopathy: nationwide cohort and mendelian randomization studies. *BMC Medicine, 21* (40). https://doi.org/10.1186/s12916-023-02753-6

Zhou, A., Y., Taylor, B., E., Barber, K., G., Lee, C., A., Taylor, Z., R., R., Howell, S., J., Taylor, P., R. (2023). Anti-IL17A halts the onset of diabetic retinopathy in type I and II diabetic mice. *International Journal of Molecular Sciences. 24*, 1347. https://doi.org/10.3390/ijms24021347

Determining the Role of Gender in Diabetic Retinopathy After Controlling for Age, Educational Level, and Income

Claret Onukogu

Walden University

Doctoral Study

Outlet for Manuscript

The Pan American Journal of Public Health is ideal for this manuscript's publication because of its peer-reviewed open access journal that covers case studies and research on significant issues in the public health field. The journal's focus on the improvement of health for the American people and on the local and national health systems makes it a suitable outlet to publish data on determining the role of gender in diabetic retinopathy, thereby filling a public health knowledge gap contributing to population health planning and implementation, after controlling for age, educational level, and income.

Abstract

Diabetes could lead to diabetic retinopathy, an eye disease that causes damaged blood vessels and the growth of abnormal ones. The disease could cause vision loss because high blood sugar levels damage retinal blood vessels. The two stages of the disease are nonproliferative and proliferative diabetic retinopathy. In the nonproliferative stage, diabetics develop macular edema from retinal swelling and macular ischemia with a shortage of blood in the macula region of the eye and the vision eventually becomes blurry. The proliferative is the advanced stage of the disease when the retina grows new blood vessels and diabetics may experience detached retina. The quantitative study employed the socioecological model as the theoretical framework to examine the relationship between psychological distress and diabetic retinopathy while considering gender. The aim was to determine the role of psychological distress in diabetic retinopathy after controlling for covariates such as age, educational level, and income. The study examined the association between the independent variables, gender and psychological distress, and the dependent variable, diabetic retinopathy. For the study, a nationally representative dataset, The National Health and Nutrition Examination Survey (NHANES), was used to analyze data. There was no association between psychological distress, gender, and diabetic retinopathy among U.S. adults when controlling for education level, income, and age. The results of the study have implications for positive social change which would fill a public health knowledge gap contributing to population health planning and implementation. Further research on patient education and regular screening for diabetic retinopathy in the United States for diabetic patients is necessary.

Introduction

The exploration of the socioemotional impact of diabetic retinopathy involves the investigation of vision-related quality of life. The use of different quality of life outcome measures is important to focus on (Fenwick et al., 2011). Different studies have highlighted the data on social life subscales, roles, and mental health decline related to diabetic retinopathy, and as they fall under the definition of social and emotional well-being. With the use of the National Eye Institute Visual Function Questionnaire (NEI-VFQ), a popular vision-specific quality of life instrument, studies explore the socioemotional impact of diabetic retinopathy (Fenwick et al., 2011; Forrester et al., 2020; Gadekallu et al., 2020). Particularly in individuals with greater disease severity and vision loss, the four psychosocial domains, dependency, role difficulty, social function, and mental health, tend to be compromised. Most studies on diabetic retinopathy reiterate its impact on security, vision function, and emotional well-being (Fenwick et al., 2011). In terms of its effects on vision impairment, diabetic retinopathy has a significant impact on vision-specific distress. For people with diabetic retinopathy, there is a high level of difficulty linked to frustrations with eyesight, feeling like a burden or nuisance, and worrying about worsening eyesight. Instruments used in measuring socioemotional domains of diabetic-retinopathy-related outcome measures are usually small and might not fully capture the emotional and social impact of the disease. Low vision instruments, like the Impact of Vision Impairment, were created mainly for retired and older individuals and not people with diabetic retinopathy (Atwany et al., 2022; Fenwick et al., 2011; Gomulka & Ruta, 2023; Grzybowski et al., 2020).

Individuals with diabetic retinopathy are usually younger and still in the workforce and the education system trying to cope with several vision-related issues that the current range of items on the low vision instruments fail to capture. There are many debilitating effects associated with diabetic retinopathy-related vision loss. The effects include work prospect deterioration that leads to increased financial strain, increased dependence, and social isolation, and disruptions in relationships, roles, and family functioning. Anxiety, distress, and depressive symptoms are some of the adverse emotional responses linked to diabetic retinopathy (Bora et al., 2021; Fenwick et al., 2011). Fluctuating vision acuity and vision-threatening stages of diabetic retinopathy seem to be critical factors linked with impaired emotional functionality. Many studies on vision impairment linked to diabetic retinopathy are qualitative in nature and most of the quantitative studies highlight peripherally emotional and social issues. Many quantitative studies conducted over a decade ago are often limited by their small sample size and cross-sectional design. Because of the variety of outcome measures used, it is difficult to have meaningful result comparisons. An ideal tool for investigating the impact of diabetic retinopathy on work functioning, social interaction, family life, and the severity and range of emotional reactions to diabetic retinopathy is an item bank for the measurement of diabetic retinopathy socioemotional well-being (Allen, 2017; Fenwick et al., 2011; Hayati et al., 2023; International Diabetes Federation, 2023; Jiwani et al., 2022). The numerous items in the bank and the diversity and flexibility in their use significantly surpass that of existing scales while ensuring high reliability, good targeting, and comprehensive coverage. Rausch model's strict requirements would provide unidimensional and valid measurement. With the condition-specific nature of the bank, researchers would be assured that the items are relevant and suitable to the older and younger age groups.

Evidence obtained through research suggests that diabetic retinopathy has a significant impact on the social and emotional well-being of individuals. Research addressing the topic has substantive limitations and the actual processes underlying the associations are often unknown to researchers. For the determination of the specific predictors and nature of the emotional and social impact of diabetic retinopathy, there is a need for more qualitative research to examine the quality of life issues resulting from diabetic retinopathy and the incorporation of more developed outcome measures. An improvement in the comprehension of the extent and type of emotional and social impact of diabetic retinopathy could assist researchers, rehabilitation workers, and policy planners in developing better intervention strategies for the improvement of quality of life outcomes for individuals with diabetic retinopathy. It would result in reduced healthcare costs for society, disease management, positive implications for patient clinical outcomes, and overall well-being (Ansari et al., 2022; Antonetti et al., 2021; Aziz et al., 2023; Boyd & Gregori, 2020; Farooq et al., 2022; Grzybowski et al., 2020).

The role of gender and sex in the prevalence of diseases such as diabetes is important. Researchers have gathered evidence that the differences in gender and sex are important in the treatment, outcomes, pathophysiology, and epidemiology of many diseases especially as they pertain to noncommunicable diseases (Kautzky-Willer et al., 2016; Kautzy-Willer et al., 2019). Considering such information, it is important for organizations to include the gender and sex components in biomedical research for the improvement of the societal relevance and scientific quality of produced innovation, technology, and knowledge. When it comes to the field of metabolism and endocrinology, an important body of evidence for clinical implications of sexual dimorphism arises from studies stemming from the study of type 2 diabetes mellitus (T2DM). Environmental, lifestyle, background, and genetic background contribute immensely to an increase in the pandemic of Type 2 diabetes mellitus, and its related complications, which poses a challenge for healthcare systems. There is important and unrecognized knowledge related to gender and sex when it comes to the differences in T2DM and it is important for healthcare professionals and individuals interested in endocrinology to increase their awareness of the disease (Cleveland Clinic, 2022; Fenwick et al., 2011: Kang & Yang, 2020; Kowluru, 2023; McLachlan & Gale, 2018).

The differences in sex provide explanations of the biologically linked differences between men and women attributed to differences found in the sex hormones, gene expressions of autosomes that are sex-specific, and differences in sex chromosomes and their effects on the human organ systems. Compared to their male counterparts, because of the reproductive factors during their lifetime, women have more dramatic changes in hormones. Gender differences often stem from sociocultural processes such as differences in the attitudes towards the prevention and treatment of diseases, stress or lifestyles, types of nutrition, exposure to certain influences in the environment, and behaviors of men and women. Researchers would need to be mindful that the gender or sex parameters are not always straightforward binary categories and that masculinity and femininity coincide with other socioeconomic variables. An interplay of social, endocrine, and genetic factors influences gender identity and gender roles (Kang & Yang, 2020; Kautzky-Willer et al., 2016; Kautzy-Willer et al., 2019).

The differences in gender and sex are important in the diagnosis and therapy, presentation, awareness, development, and prevention of lifestyle-related diseases such as Type 2 diabetes and diabetic retinopathy. When studying diabetic complications, such as diabetic retinopathy, it is important to emphasize gender differences and sexual dimorphism as they pertain to nephropathy, cardiomyopathy, and cardiovascular diseases. Gender and sex are complex processes that interact or interrelate in humans. Researchers often describe the primary biological differences in humans using sex and gender for the description of psychosocial influences. A clear judgment between the interaction of societal and biological influences in the clinical outcomes and the development of diabetic retinopathy and T2DM is often difficult to achieve (Centers for Disease Control and Prevention, 2020; Dai et al., 2021; International Diabetes Federation, 2022; Kautzky-Willer et al., 2016; Kautzy-Willer et al., 2019). Psychosocial and biological risk factors impact the trajectories and differences in the prevalence rates of T2DM in adults. Age dependency is obvious in men and women with slight differences in age-specific prevalence. Although similar, the proportion of overweight females is slightly higher than their male counterparts, and based on systematic analysis, females are usually more obese than males. Compared to more males who tend to be overweight at a younger age, more women have the tendency to be obese or overweight after 45 years of age (Kautzky-

Willer et al., 2016; Kautzy-Willer et al., 2019; Lauffenburger et al., 2020; Lien & Jiang, 2017).

Based on the gender inequality index in multi-country ecological studies and the quantitative assessment through the global gender gap index; in terms of obesity, the differences in sex are larger in countries with more gender inequality. Based on economic and social data, the extent of female obesity tends to be greater in countries with gender inequality. Some researchers found that if the United States population was examined in a cross-sectional representative multiethnic sample, there would be a reverse association between obesity and comprehensive measures of income-based socioeconomic inequality among young white women. In both sexes with a stronger effect on women, the rate of diabetes mortality and obesity are related to income inequality in developed countries (Demmin & Silverstein, 2020). For females, the effect that income inequality has on obesity is independent of the average consumption of calories. In type 2 diabetes, obesity is a major risk factor in both male and female and their prevalence patterns tend to be similar across regions. Globally, more males are diagnosed with diabetes than their female counterparts. Compared to women, men are nearly twice as likely to develop type 2 diabetes (Demmin & Silverstein, 2020; DiaGundluru et al., 2022; Kautzky-Willer et al., 2016; Kautzy-Willer et al., 2019; Lien & Jiang, 2017). With increases in the ages of both sexes, the incidence of diabetes rises reaching its highest rates in elderly women. Independent of age, impaired glucose tolerance (IGT) occurs more in females than in males. Most individuals with T2DM reside in low and middle income countries. However, in high-income countries, prevalence rates of T2DM are higher because of disproportionally affected lower socioeconomic groups. Obvious regional and sex differences in the increase of the prevalence of obesity-related type 2 diabetes have developed in the last 3 decades showing significant differences in social roles and socioeconomic status (SES), culture, gene-environment interactions, migration, ethnicity, and lifestyle (Centers for Disease Control and Prevention, 2020; International Diabetes Federation, 2022; Kautzky-Willer et al., 2016; Kautzy-Willer et al., 2019).

Compared to the men in Belize, the prevalence of T2DM doubled in women based on the results gathered from blood glucose measurements and self-reporting. There can be limitations with global estimates of sex differences because of selection bias, random testing, and sex disparities associated with the accessibility of healthcare in some countries. Across different age ranges and at lower body mass indexes (BMI) with the most significant sex difference being at a younger age, European men are the most likely to get a T2DM diagnosis at an earlier age. In 1940, time trends showed that in Sweden, there was a male predominance. The male to female ratio in the 10-55 age range was 1.4 and it expanded and increased to 2 with time, particularly in the 45-65 age groups (Kautzky-Willer et al., 2016; Kautzy-Willer et al., 2019; Madhuri & Srilakshmi, 2019; Magne et al., 2020). An explanation of the trend would be partly because of a decrease in physical work especially in men and an increase in automation. On the other hand, in most studies, diabetic women are usually more obese than diabetic men. Despite the close curvilinear associations between the risk of diabetes and increasing BMI in both sexes, diabetic women also show stronger associations between the risk of diabetes and an increase in BMI. Sex differences in fat deposition and body composition add to the risk of sex-dimorphic diabetes. Compared to women, for men with more fat-free muscle, BMI overestimates body fat mass for them (De Ritter et al., 2020; International Diabetes Federation, 2022; Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019; Lien & Jiang, 2017; Magne et al., 2020).

In terms of lifestyle, sex differences are consistent when it comes to physical activity, nutrition, and behavior which are associated closely with the risk of type 2 diabetes. Although women tend to be more inactive, they focus their efforts on healthy nutrition by consuming less meat and more vegetables and fruits. Even though high glycemic index diets usually increase abdominal fat, women often consume more sugar, especially sedentary women compared to sedentary men. High glycemic index diets are often related to a higher risk of type 2 diabetes. There is a strong association between environmental factors and body weight. Obesity is associated with the availability of inexpensive meals. The rise in the consumption of fast food and the fast economic development have simultaneously led to an increase in the consumption of sugary beverages. Independent of adiposity, it contributes to the type 2 diabetes mellitus epidemic. In both sexes, gene-environmental interaction indicates interactions showing that higher sugary beverage consumption is linked to an increased obesity predisposition. With the consumption of sugary drinks daily, women are at a greater risk of developing incident coronary heart disease. Compared to men, women are at a higher risk of having incident diabetes, and the risk is heightened for women who consume sugary drinks daily compared to nonconsumers. There are slightly higher proportions of diabetes-related deaths in women compared to men, with an especially lower number of deaths linked to sugary drink consumption. There are regional differences in mortality from the consumption of sugary drinks (Centers for Disease Control and Prevention, 2020; Kovoor et al., 2022; Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019; Mahs et al., 2022; Mamo et al., 2019).

The moderate consumption of alcohol is associated with a lower risk of type 2 diabetes mellitus. With nondrinkers and never drinkers who have low levels of alcohol intake, there is a reduced risk of type 2 diabetes. There is often a significant sex interaction for drinkers with an increased risk of type 2 diabetes. A stratified analysis of sex and ethnicity has shown a reduction of T2DM in the non-Asian population and in women. A likely explanation for such a finding could be that considering the sex dimorphism, men tend to have worse drinking habits and engage in the behavior and in frequent episodic drinking. Another explanation could be that on glucose metabolism, alcohol has sex-dimorphic effects. Moderate alcohol consumption tends to improve insulin sensitivity in women and glycated haemoglobin in both sexes (Kautzky-Willer et al., 2019). When consumed frequently, alcohol intake could result in higher levels of endogenous estradiol. Whether it is acting alone or with Sex Hormone-Binding Globlin (SHBG), estradiol has an effect on the protective association between the risk of diabetes in premenopausal women and alcohol consumption (International Diabetes Federation, 2022; International Diabetes Federation, 2023; Li et al., 2022; Mikkola et al., 2020). An opportunity for further research would be to get clarification on the sex-specific dose-response relationships between alcohol consumption and the risk of type 2 diabetes mellitus and the underlying mechanisms.

Passive and active smoking is linked with high risks of developing type 2 diabetes in women and men. Compared to women, the overall effects tend to be more pronounced in men. However, adjusting confounding factors such as educational level, physical activity, and obesity strengthens the association in women and lessens it in men. It is usually attributable to smoking when the association with type 2 diabetes is causal. There has been a substantial change in smoking behavior between women and men in the past decade. It has increased in young women and could be a possible contributing factor to a higher incidence of smoking-related diabetes in the future for females. The risk of myocardial infarction, a frequent complication in diabetic patients, related to smoking appears higher in women than in men (International Diabetes Federation, 2022; International Diabetes Federation, 2023; Li et al., 2020; Kautzky-Willer et al., 2019). During pregnancy, certain environmental factors have a strong influence on sex-specific fetal development. Conditions such as acute stress situations, hyperglycemia, and under or overnutrition, without directly affecting the genetic coding, influence the phenotype of the progeny through epigenetic effects. The changes in epigenetics involve micro-RNAs, histone modifications, and DNA methylation. There is a possibility that those changes could lead to the inactivation or activation of genes and their products in various ways and possibly lead to the modification of the evolution of future generations in a sex-specific and transgenerational way (Hewage et al., 2020; Kautzky-Willer et al., 2019; Li et al., 2022; Madhuri & Srilakshmi, 2019). Finding studies pertaining to the effects of epigenetics on the risk of diabetes in humans is scarce. Instead, researchers use rodents for such studies. In an epigenetic manner, hyperglycemia or maternal undernutrition can cause intragenerational transmission of glucose tolerance and fat distribution from one generation to another (Kautzky-Willer et al., 2019).

Females and males born during famines or in times when there were low nutritional resources tend to be more susceptible to the risk of diabetes in adulthood particularly in men. Examples would be the effects of the famines that happened in Austria between the two world wars. Compared to the females, male offspring are usually vulnerable in the early postnatal period and in intrauterine life. Researchers are concerned about sexual dimorphisms after perinatal undernutrition. It is common to detect hyperinsulinemia and an increase in postprandial glucose levels in adults with limited food during their pregnancies. In individuals who experienced malnutrition during the Dutch famine, sex-dimorphic alterations of epigenetic profiles were evident. The variations could lead to explanations of sex differences at birth, during fetal development, and later in life. There could be higher BMI and dyslipidemia in women in famine or food limitations (Hewage et al., 2020; Kautzky-Willer et al., 2019; Madhuri & Srilakshmi, 2019). In a population without or with diabetes, there could be high levels of variations between male and female first generation offspring in terms of transgenerational transmission of cardiometabolic traits. Female offsprings of diabetic mothers tend to be more susceptible to metabolic syndrome (MetS) effects, higher body fat content, and glucose levels compared to female offsprings of diabetic fathers, or those whose parents did not have diseases. Female offspring of parents with diabetes might have lower high-density lipoprotein (HDL)-cholesterol. When the mother as opposed to the father has diabetes, both male and female offspring may have higher blood pressure.

Compared to the offspring of parents without a history of diabetes, the offspring of diabetic parents usually have higher risks of increased body fat content, BMI, and increased waist (Kautzky-Willer et al., 2019; Magne et al., 2020; Mahs et al., 2022; Mamo et al., 2019; National Institutes of Health, 2019).

The sex differences conveyed through type 2 diabetes mellitus make it easier to understand why the MetS predictors differ in sex-specific ways. The most obvious predictors in males were body fat and BMI, but in females, they were age, BMI, and diabetic mothers. Parental history of type 2 diabetes and the body weight of the offspring determine the future risks of type 2 diabetes in offspring considering the sexes. In normal-weight individuals, the higher risk of type 2 diabetes mellitus is associated with maternal history of type 2 diabetes. A paternal history of type 2 diabetes is related to a higher risk of type 2 diabetes in overweight individuals. Fetal exposure to parental smoking is linked with adult type 2 diabetes. For defining the risk of type 2 diabetes and gestational diabetes mellitus development after pregnancy, determining fetal sex in pregnancies is important. Compared to a 7% risk of developing GDM when carrying a boy in their second pregnancy, women carrying a boy during their first pregnancy have a 3% to 4% lower risk of GDM (Kautzky-Willer et al., 2019; Muche et al., 2020; Muhwava et al., 2019; Parthasharathi et al., 2022). They tend to maintain normal glucose tolerance (NGT) during the first pregnancy when carrying a girl. When they carry a girl, women with GDM during their first pregnancies had a 6% to 7% higher risk of having type 2 diabetes mellitus over an average follow-up period of 5 years (Kautzky-Willer et al., 2019).

Women carrying a male fetus have higher postprandial glucose levels and a lower β-cell capacity compared with those carrying a female fetus. The underlying mechanism is unclear and could be that the various pathophysiological causes of the sex differences are attributable to the β-cell functionalities in the mothers. It might be associated with the activities of the Y chromosome based on the sex-specific differences in the hormones linked to the placenta. The placenta has several sex-specific alterations, particularly as it relates to epigenetic mechanisms that might have a significant impact on the complications occurring during and after pregnancy. The notion behind women having a higher risk of developing type 2 diabetes mellitus after having a GDM pregnancy while carrying a girl could be because they already had a poor β-cell capacity in comparison to mothers with a male fetus. Carrying a male fetus results in a reduction of the β-cell function during pregnancy, but after delivery, it restitutes back to its normal capacity (Kautzky-Willer et al., 2019; Muhwava et al., 2019; Poly et al., 2023; Porter, 2022; Zhang et al., 2020). Mothers with GDM carrying a female fetus often have a lower capacity of β-cell that leads to an increased risk of type 2 diabetes mellitus and also an earlier onset of the condition over a period of time. Pregnant women carrying a female fetus tend to have less insulin resistance during fasting in the early pregnancy stage and not in the late stage (Kautzky-Willer et al., 2019).

Compared with male newborns, female offspring tend to have higher levels of insulin resistance. Compared to boys, the usual lower birth weight in girls could be attributed to higher insulin resistance in girl fetuses during pregnancy. Female fetuses do not have the same reaction to insulin and its effects as the males. Sex-specific differences already exist at the beginning of life and are possibly responsible for several differences in diseases and health later in life for men and women. Fetal sex impacts maternal glucose metabolism. The continuous interaction between mother and fetus, with the possibilities of negative health impact in the future for both, shows that there is a neglect of health determinants in the field of fetal sex, GDM, and glucose metabolism (Kautzky-Willer et al., 2019; Madhuri & Srilakshmi, 2019; Muhwava et al., 2019). Females have more SAT and its centralized pattern at birth is assessed through skinfold thickness. The accumulation of SAT of neonates, which is sex-specific, is linked to their insulin levels. The association between various SAT locations and cord blood insulin is more obvious in certain areas known as the preferential fat storage for each sex. The associations are usually higher in male neonates. Out of the different storage locations, insulin levels affect the upper abdomen and neck the most. The association is more noticeable with the hip SAT thickness for female neonates. Lipid accumulation and sex-specific body shape could be determined in utero, particularly in locations that are insulin sensitive, and defers based on fetal sex. The differences in SAT might be linked to smaller insulin effects on SAT and higher insulin resistance in female neonates (Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019; Qiao et al., 2020; Winston-Salem State University, n.d.; Zhang et al., 2020).

Birthweights that are over or under normal ranges correlate with metabolic diseases. Sex differences play a role in the risk of developing type 2 diabetes mellitus for individuals born with high birth weight (HBW) or with low birth weight (LBW). The risk of obesity and type 2 diabetes is linked to HBW. In women, HBW and LBW could result in a higher risk of developing type 2 diabetes. Compared to men, women with HBW had a higher risk for type 2 diabetes. Women with LBW had higher risk for type 2 diabetes. In very LBW offspring, an independent risk factor for hyperglycemia is the male sex. In comparison with the women who have similar insulin resistance, men with very low birth weight have reduced β-cell functionality, lower insulin levels, and higher glucose levels (Hewage et al., 2020; Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019; Madhuri & Srilakshmi, 2019).

During pregnancy, hyperglycemia, and under and overnutrition are linked with an increased risk of cardiorenal disease in offspring. During this period, the kidney is usually prone to various mechanistic changes that could result in diminished vasodilative renal vessel function, glomerular hypertrophy, renal dysfunction, and renin-angiotensin system expression changes followed by adult life hypertension, which affects mostly men. Following a prescription of prenatal glucocorticoids, there is usually a higher reactivity of the HPA axis in female offspring between ages 6 and 11 years (Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019; Muche et al., 2020; Muhwava et al., 2019; Qummar et al., 2019). In female offspring, there is a possibility of the presence of a higher sensitivity of the HPA axis during their early period of life. Compared to their male counterparts, a more responsive HPA axis exists more in elderly women. There is a higher HPA axis activity associated with lower birth weights in both sexes. There is an opportunity for further research to gain clarification on the relationship between offspring HPA axis activity, pregnancy-related stress, birth weight, and the impact of programming adult diseases in young women and men (Hewage et al., 2020; Madhuri & Srilakshmi, 2019; Muche et al., 2020; Muhwava et al., 2019).

In humans, exposure to endocrine disruptors could lead to a higher risk of type 2 diabetes mellitus and obesity. In both sexes, the dose-dependent positive relationship could become evident between parameters of glucose metabolism, which is the fasting glucose and insulin resistance, and urinary phthalate metabolites. Although they are not well understood at the moment, pathophysiological mechanisms responsible for disruptive actions are based on surrogate markers. In low and persistent dosages, endocrine disruptors could act as hormones and emulate estrogen properties (Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019; Muhwava et al., 2019; Zhang et al., 2020). They may inactivate or activate cell responses, cellular receptors, and any other targets. They can cause hyperinsulinemia and higher insulin resistance. Constant exposure to small dosages is likely related to the dysfunctionality of the mitochondria resulting from intracellular glutathione depletion. It relates to ectopic fat and inflammation and could possibly lead to type 2 diabetes mellitus. Candidate obesogens encompass a variety of compounds including phthalates and bisphenol A (BPA). Endocrine disruptors spread with lipids in the body and gather in adipocytes and lead to reactive changes in adipokine levels and it occurs in a sex-and disruptor-specific manner (Kautzky-Willer et al., 2019; Muche et al., 2020; Muhwava et al., 2019; Zhang et al., 2020).

There are often significant sex differences in adiponectin and leptin levels in newborns that are linked to BPA exposures in utero. Female offspring often have higher levels of leptin than males. BPA is inversely related to adiponectin in males. When compared to mono-(3-carboxypropyl), high levels of leptin in males are evident in moderate to high exposure. Late in-utero BPA exposure in the mother-child pair is related to an increase in the levels of plasma leptin in boys. Early exposure is associated with higher plasma adiponectin in girls at 9 years of age (Kautzky-Willer et al., 2019; Muche et al., 2020; Mamo et al., 2019). In terms of phthalate and BPA exposure in childhood and utero, there are sex differences in metabolism-related hormones considering exposure time and pubertal status in adolescent offspring. Decreased insulin secretion in boys going through puberty and higher leptin levels in girls is associated with in utero monoethyl phthalate. In boys, phthalate exposure and peripubertal BPA are linked to higher levels of leptin, and a combination of monoisobutyl phthalates and mono-n-butyl-phthalates are associated with C-peptides. Because of different urinary phthalate metabolites, pubertal boys tend to have lower Insulin-like Growth Factor 1 (IGF-1) concentrations. A compound, di-2-ethylhexyl phthalate, is linked to an increase in IGF-1 levels in prepuberty girls (Alperet et al., 2019; American Diabetes Association, 2018; Kautzky-Willer et al., 2019). During fasting, pubertal girls often experience higher glucose levels that are associated with different phthalate metabolites.

There is a sex-specific association between leptin and BPA in boys with various developmental periods and exposure times. The discrepancies occur because of the various populations from rural or urban areas with different BPA exposures. Despite the lack of clarity about the mechanisms of endocrine disruption through chemicals in humans, the reactive oxygen species and the peroxisome proliferator-activated receptors

(PPARs) play vital roles (Kautzky-Willer et al., 2019; Madhuri & Srilakshmi, 2019; Magne et al., 2020). The expression of the PPAR is sex-dependent. In humans, if endocrine disruptors could change the metabolism through the alterations in PPAR expression, there would be a causal explanation for sex-specific differences. Researchers could carry out further studies on the interactions of the environment and genes of humans and animals while taking into consideration the phenotypic transmission and transfer throughout the generations of the offspring. The underlying mechanisms are limited in humans and there is a need for sex-specific investigations into the effects of epigenetics on a limited supply of nutrients, hyperglycemia, environmental factors, and food overload (Kautzky-Willer et al., 2019; Mikkola et al., 2020; Romero et al., 2016).

In terms of genetic predisposition, autosomes exhibit certain patterns of expression in gene regulation that are directly modulated through sex chromosomes or mediated through hormones. Across organs, there are variations in sexually dimorphic gene expressions between the liver and the brain mainly in small effects. Sex differences play roles in the transcriptome of human placental cells and it shows on placental gene expression, there is an influence of fetal sex in a cell-type dependent manner. In female and male offspring, the effects of placental function are different framing sex differences in inflammatory, immunological, and metabolic responses (Hewage et al., 2020; International Diabetes Federation, 2022; Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019). Researchers often investigate genome-wide association metaanalysis, emphasizing the genetic background of the accumulation of body fat and its association with cardiometabolic traits. Sex-specific differences are evident in genetic loci that are responsible for the regulatory functions of insulin and adipose biology. In almost all of the associations of the loci, the effects appear to be stronger in women. The associations are related to lower hip circumferences in men and higher waist circumferences (WCRs) in women.

The genes involved in glycolysis and lipid metabolism are linked with female-specific genes, and hepatic detoxification, secretion, and metabolism are associated with male-specific genes (International Diabetes Federation, 2023; Kautzky-Willer et al., 2019; McLachlan & Gale, 2018). In hepatic genes, there is a wide variety of genes depicting sex dimorphism that in a sex-specific way could influence drug pharmacokinetics. The pathway-based approach is another way of examining the results of genome-wide association because it connects the SNPs considered to be involved in a pathway. The approach is multilevel and could provide additional understanding of the mechanisms of genes and their roles in diseases. In the gene sets linked with type 2 diabetes mellitus in humans, there is heterogeneity between females and males. There are more pathways in females than in males and some of the pathways overlap. In males, the gene transcription factor 7 like 2 (TCFL7L2) influences the significance of the pathways (Kautzky-Willer et al., 2019; McLachlan & Gale, 2018; Mikkola et al., 2020).

Within cells, the amount of X chromosomes influences sex differences in adiposity. The acceleration of weight gain in high-fat diet (HFD), hyperinsulinemia, and incident hepatic steatosis is dependent mainly on the number of X chromosomes. The number of X inactivation and X chromosomes may stimulate GH expression which is instrumental in energy metabolism. On the X chromosome, a locus near the dual specificity phosphatase 9 is directly associated with a higher risk of type 2 diabetes mellitus (Kautzky-Willer et al., 2019; Kautzky-Willer et al., 2019; National Institute of Diabetes and Digestive and Kidney Diseases, n.d.). There are sex differences in genes linked with type 2 diabetes mellitus. Most of the genes responsible for sex differences in the risk of diabetes have the tendency to increase in one sex and not have any effect on another. For some genes, the ability of type 2 diabetes mellitus risk reduction is different between women and men. The differences in glucose, lipid, and leptin metabolism are based on genetic sex differences. In type 2 metabolism, compared to women who have leucine repeat in carnosinase gene, cardiovascular mortality tends to be lower in men (Ansari et al., 2016; Atlanta Diabetes Association, 2020; Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019; Regeneron Pharmaceuticals, 2021).

In humans, there are sex-specific differences in the ANKK1 (rs1800497) polymorphism of dopamine receptor D2 that contributes to an increased risk of type 2 diabetes in women, and such risk would not be found in men. In women, polymorphism is associated with an elevated secretion of first-phase insulin. The key element in the explanation of sexual dimorphism could be the sex differences in the regulatory gene mechanisms which could result in differences in phenotype through interactions in the gene environment. With the use of a genetic risk model, it is possible to achieve a subtle improvement in type 2 diabetes risk prediction even in a high risk sex-specific group like women with gestational diabetes mellitus (GDM) (Centers for Disease Control and Prevention, 2019; Centers for Disease Control and Prevention 2021; Hewage et al., 2020). With metabolic clinical and traditional anthropometric parameters, the prediction of diabetes risk could appear to be minimal. A reason could be the heterogeneity of individuals with type 2 diabetes mellitus coupled with the polygenetic nature of the disease, missing heritability, or neglected biological factors such as ethnicity, age, and sex. Sex has a significant and small impact on the genetic risk model of type 2 diabetes mellitus which becomes invisible in the combined lipid and genetic metabolite risk model. Based mainly on traditional clinical risk factors, diabetes risk genetic markers could moderately improve the predictive accuracy of the occurrence of type 2 diabetes mellitus. Improved sex-specific epigenetic and genetic risk models could assist in the development of future personalized medicine. Genes are often associated with type 2 diabetes mellitus and metabolic functions as they relate to mortality and complications and are linked with sex dimorphism (Centers for Disease Control and Prevention, 2019; Centers for Disease Control and Prevention, 2021; Cleveland Clinic, 2021; Kautzky-Willer et al., 2019; Regeneron Pharmaceuticals, 2021).

In terms of glucose tolerance, IGT is more prevalent in women and IFG is more frequent in men regardless of ethnicity. Type 2 diabetes mellitus and these metabolic conditions are related to bodily glucose handling evaluated with glycemic levels in postprandial conditions and during fasting. The main processes responsible for normal glucose level maintenance are insulin secretion, and insulin sensitivity and resistance. There can be maintenance of NGT if insulin secretion increases could compensate for the reduction of insulin sensitivity with increases in age and BMI. When there is a failure in the insulin secretion and sensitivity balance, people could become prediabetic or IGM and eventually get to type 2 diabetes status (Curry, 2020; De Ritter et al., 2020; Kautzky-

Willer et al., 2016; Kautzky-Willer et al., 2019; Rezazadeh-Gavgani et al., 2023). The same concept applies when evaluating a large population with possible sex differences considering metabolic parameters in various glucose tolerance categories. There are usually glucometabolic sex differences in obese individuals usually with normal glucose tolerance (NGT), but men tend to be less sensitive than women. Women experience more insulin sensitivity than men with the deterioration of glucose tolerance and impaired glucose metabolism (IGM). In both sexes, there could be increased glucose secretion in normal weight healthy individuals. The impairment of insulin secretion and insulin sensitivity in type 2 diabetes mellitus is similar and substantial in both sexes. With increasing BMI, insulin sensitivity decreases in both sexes in all glucose tolerance categories. In men, insulin secretion increases at a faster rate with BMI which compensates for the increases in insulin resistance (De Ritter et al., 2020; Emani et al., 2018; Kautzky-Willer et al., 2019; Magne et al., 2020).

With normoglycemic levels, compared to males, women exhibit more favorable cardiometabolic risk profiles and better insulin sensitivity. It may be because of sex hormones and their receptors, differences in body fat distribution, and their biomarkers, like higher adiponectin. Estrogen usually improves insulin sensitivity with antidiabetic effects linked to Estrogen Receptor Alpha (ERα), stimulates β-cell secretion, and has protective effects from β-cell. In early postmenopausal women, the administration of estradiol leads to increased insulin-mediated glucose disposal, but such benefit is not evident in late postmenopausal women. Sex differences decrease and lead to an exacerbated metabolic profile aggravation in women than in men with age-induced glucose tolerance deterioration; and greater insulin and adiposity resistance causes the mediation (Farooq et al., 2022; Kautzky-Willer et al., 2019; Lauffenburger et al., 2020; Lien & Jiang, 2017; Ruamviboonsuk et al., 2022). The aggravation could be associated with the fact that to develop type 2 diabetes, women have to gain more weight. In various ethnic groups and at lower levels of BMI, men have a greater rate of the onset of type 2 diabetes mellitus than women. It is important to perform a full test, such as an oral glucose test, for insulin measurement to obtain better characterization of single metabolic parameters in healthy individuals, particularly women (Boyd & Gregori, 2020; Cleveland Clinic, 2021; Doheny, 2020). The differences in the secretion of insulin could be attributed to the exerted effect of the incretin hormones while performing oral tests on pancreatic β-cells. Researchers could focus on the investigation of how sex plays a role in the incretin effect. The extent of the effect of glucagon-like peptide-1 (GLP-1) does not depend to a great extent on patient characteristics such as sex and age. In both sexes, the evaluation of GLP-1 involves various degrees of BMI and ranges from normal glucose tolerance to type 2 diabetes mellitus. Compared to those with NGT with a lower concentration of GLP-1, women with type 2 diabetes mellitus or impaired glucose metabolism (IGM), independent of obesity or age, tend to have lower GLP-1 response to an oral challenge. Because of the association between higher GLP-1 response and better secretion of insulin, low incretin levels could be a partial explanation of β-cell function reduction seen in women when they have impaired glucose metabolism and type 2 diabetes mellitus (Doheny, 2020; Emani et al., 2018; International Diabetes Federation, 2023; Kautzky-Willer et al., 2019; Setia, 2016). In oral tests, intestine glucose absorption and gastric emptying influence postprandial glucose metabolism. There is a positive correlation between gastric emptying of meals containing carbohydrates and postprandial glucose levels when studied using diabetic and healthy patients. Gastric emptying is typically slower in women than in men. Because of its contribution to the explanation of why women have higher glucose levels with oral tests, gut glucose absorption has gotten devoted attention. Irrespective of age, in peripheral circulation in lean individuals, meal appearance is usually higher in women than in men. When adjusted for fat-free mass, height, and age, there is no difference in absorbed glucose, but there is prolonged gut glucose absorption in women. It could be because of slower gastric emptying. During the oral test, the factors could be contributing to higher glycemic levels and provide an explanation of the higher prevalence of IGT in women (Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019; Mahs et al., 2022; Mamo et al., 2019; McLachlan & Gale, 2018; Torpy et al., 2007).

The excessive fatty acid release from adipose tissue and impairment in lipid metabolism could lead to circulating lipids overspill and to an accumulation of ectopic nonadipose lipid in the liver hepatocellular lipids (HCL), myocardial lipids (MYCL), muscle intramyocellular lipids (IMCL), and the dangerous consequence of lipotoxicity. Depending on lifestyle and total body fat, sex-dimorphic results are evident in IMCL. In young normal-weight sedentary individuals and in diabetic and obese individuals, compared to males, females tend to have greater IMCL droplets, higher lipid density, and more IMCL in leg muscle. After engaging in endurance exercise training, women often oxidize more fat than glucose (Curry, 2020; De Ritter et al., 2020; Doheny, 2020; Emani et al., 2018). Compared to men, women have double amounts of IMCL; and during prolonged exercise, they experience a net IMCL reduction. Women with previous insulin-treated gestational diabetes mellitus and who are at a high risk of type 2 diabetes, have increased IMCL and decreased insulin sensitivity and adenosine triphosphate (ATP)-synthesis. Because of the various gonadal hormone and environmental aspect effects, and a pronounced insulin resistance, men usually develop fatty liver disease than women. Estradiol treatment could improve HCL levels and insulin resistance (Alperet et al., 2019; Madhuri & Srilakshmi, 2019; Muche et al., 2020; Muhwava et al., 2019; Vitger et al., 2017).

In both sexes, estrogen is protective. It is important to have balanced sex hormones. High estrogen concentrations or low testosterone levels in males could be a result of metabolic abnormalities and fatty liver disease. Considering body fat and insulin resistance, young women with a previous history of gestational diabetes mellitus tend to be at a higher risk of having liver fat than women who had a normal pregnancy. Those women with gestational diabetes often develop diabetes later in life (Ansari et al., 2016; Ansari et al., 2022; Atlanta Diabetes Association, 2020; Zhang et al., 2020). One of the numerous possible pathophysiologic mechanisms implicated in diabetic cardiomyopathy is an increased MYCL. Men have higher pericardial fat and MYCL than healthy women. Heart steatosis can be independently predicted with male sex and glycemia. Myocardial lipid increase deteriorates with glucose tolerance; it is more pronounced in women and reduces cardiac protection in diabetic women. With an increase in myocardial lipids in diabetic women, the heart rate increases, and the volume of stroke decreases. Such interactions are already obvious in nondiabetic insulin-resistant women. Nondiabetic women with previous gestational diabetes mellitus may not have cardiac dysfunction or steatosis, but because of their blood pressure and glycemia, they may have myocardial wall thickness. In the pathogenesis of diabetes, although myocardial lipid may not be an early marker, it is a consequence of chronic hyperglycemia (Kautzky-Willer et al., 2019; National Institute of Diabetes and Digestive and Kidney Diseases, n.d.; Prasad et al., 2023; Romero et al., 2016; Saadane et al., 2023).

Compared to men, women at rest have more storage of free fatty acids. Women have more lipid oxidation, related to carbohydrates, during exercise. Males rely more on protein and glucose metabolism. Contrary to males, in situations of food deprivations, females experience a reduction in energy expenditure followed by loss of stored fat, which explains the reason men experience more harm in times of undernutrition. Through effects on the brain, estrogen can directly reduce food intake. There is a tight interaction of insulin, leptin, ghrelin, and neuropeptide Y (NPY) that play vital roles in the process. Through the enhancement of preadipocyte proliferation, particularly in females, and the regulation of alpha(α)-2 adrenergic receptors that promote the accumulation of SAT, estrogen can directly exert effects on fat tissue, especially in premenopausal women (Kautzky-Willer et al., 2019; Teo et al., 2020; University of North Carolina, n.d.; Vitger et al., 2017). In young women, polymorphisms in the estrogen receptor alpha (ERα) relate to increases in abdominal fat. With increasing body fat, women have less insulin sensitivity reduction with lowered energy expenditure that declines faster with aging than in men. Decreased total energy expenditure is associated with menopause. It is because of estrogen effect loss on the hypothalamus through an orexigenic hormone NPY increase, agouti-related peptides, and a reduction in lean body mass. Fatty tissue is the most important source of estrogens in postmenopausal women. It is where aromatase catalyzes estrone and adrenal androgens convert to 17Beta (β)-estradiol. A higher number of adipocytes contribute to the higher conversion rate in older and obese women. Females may be susceptible to the enlargement of adipocyte. Adipose tissue plasticity may contribute to ectopic fat deposition and obesity-related metabolic abnormalities. In women, the increased rate of metabolically healthy obese phenotype could be because of a contribution of the total of all these effects (Kautzky-Willer et al., 2016; Kautzky-Willer et al., 2019; Vujosevic et al., 2020; Wang et al., 2020; Tymchenko et al., 2020).

Testosterone tends to hinder lipoprotein lipase and the adipose tissue uptake of triglycerides. It is also responsible for the promotion of the increase of fat-free mass and insulin sensitivity in the muscle through mitochondrial capacity increase and the lipolysis increase through Beta (β)-adrenergic receptors. Estrogen deficiency causes increases in male body fat mass and androgen deficiency leads to a decrease in muscle strength and size and lean body mass. Gut microbiota composition is linked to the risk of insulin resistance, diabetes, and energy balance possibly because of fatty acid metabolism changes or through gut-derived hormone release (Kautzky-Willer et al., 2019; Zhang et al., 2020). In males, there are possible sex-specific gut signatures associated with diabetes and obesity with adverse pro-inflammatory gut microbiota components. Future research should focus on reporting results stratified using sex, providing clarifications on whether differences in sex could play an important role in the regulation of microbiome-related metabolic diseases, such as type 2 diabetes, and microbiome-dependent hormones (Kautzky-Willer et al., 2019; Zhang et al., 2020; Zheng et al., 2023; Zhou et al., 2023).

Methods

I tested the relationship between the role of gender and diabetic retinopathy among adults in the United States while controlling for age, educational level, and income, through a retrospective, quasi experimental study and using descriptive data analysis, multivariate logistic regression of secondary data, and bivariate analysis using chi-square test of independence. I set the significance level for the logistic regression and chi-squared analysis at 0.05. I measured the individual level variable, sex, as having two levels which are female and male. The geographic location or places of residence covered in the study were grouped in districts found in various parts of the United States. I measured age at the individual level based on the Medical Subject Headings (MeSH) for adults which are (age 19-44 years), Middle Aged (age 45-64 years), Aged (age 65-79 years), and Aged 80 and above. I used collected data on the population level through reputable agencies. I transformed the data into nominal data in the order of low, medium, and high depending on the tertiles of the range of data. Some variables were measured at the population level within different districts and by years depending on the data collection method. Education was ranked based on the highest level attained and grouped in the categories of no education, primary (1-some high school education), secondary (2-high school graduate), tertiary (3- some college education) levels measured at a population level. The categories of no education were in measurements of low, medium, and high. The categories of less than secondary education were in low, medium, and high categories. Secondary education was in low, medium, and high categories. Tertiary education was in low, medium, and high.

NHANES has the variables for depression and psychological distress measurement. In measuring psychological distress, the Patient Health Questionnaire (PHQ-9) was instrumental in showing how often individuals experience depressive symptoms. The chosen study design was the most practical because of the existence of large datasets of relevant information, the reduction of the study time, and the elimination of one-on-one interactions with patients, and the inclusion of variables at the population and individual levels. Assessment of the data was through the Centers for Disease Control and Prevention website (CDC). I obtained ethical approval from Walden University.

Results

Complex Samples—Logistic Regression

What is the association between gender and diabetic retinopathy after controlling for age, educational level, and income?

The weighted population size is 16639717.14. The valid number of people included in the analysis is 468 and the number represents the weighted population size.

Table 1

Frequency and Percentage of Each of the Variables Within the Model

Variable	Frequency	Percentage/Mean
Diabetic retinopathy	3,439,814	20.7%
Education level		
Some high school	2,650,510	15.9%
High school graduate	5,683,292	34.2%
Some college	8,305,914	49.9%
Age (mean)	--	60.9
Family poverty-income-ratio (mean)	--	2.87
Psychological distress	4,601,017	27.7%

Table 2

Odds Ratio of Each of the Variables Within the Model

Variable	Odds ratio	95% confidence interval	*p*-value
Age (continuous)	0.98	0.96–1.01	0.30
Gender	1.65	0.77–3.55	0.18
Education			0.06
Some high school	1.20	0.39–3.70	0.06
High school graduate	1.00	0.47–2.13	0.06
Some college	Reference	Reference	Reference
Psychological distress	0.95	0.57–1.57	0.82

The result indicates that there is no association (p=0.06) between education level and diabetic retinopathy. The odds ratio of 1.20 (CI 0.39-3.70) denotes strong evidence for the null hypothesis being true and it is not rejected. The odds ratio of 1.0 (CI 0.47-2.13) denotes strong evidence to fail to reject the null hypothesis. There is no association between those who had some high school education, those who are high school graduates, and people with some college education developing diabetic retinopathy. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for education. The result indicates that there is no association between psychological distress and diabetic retinopathy. The odds ratio of 0.95 (CI 0.57-1.57) denotes strong evidence to fail to reject the null hypothesis. There is no association (p=0.82) between psychological distress and diabetic retinopathy among U.S. adults after controlling for age, educational level, and income. The result shows that there is no association between gender and diabetic retinopathy. The odds ratio of 1.65 (CI 0.77-3.55) denotes strong evidence to fail to reject the null hypothesis. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for gender. The result indicates that there is no association (p=0.30) between age and diabetic retinopathy. The odds ratio of 0.98 (CI 0.96-1.01) denotes strong evidence to fail to reject the null hypothesis. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for age.

The result indicates that there is no association (P=0.20) between income and diabetic retinopathy. The odds ratio of 1.19 (CI 0.92-1.60) denotes strong evidence to fail to reject the null hypothesis. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for income.

Discussion

The p value of 0.06 indicates that there is no association between education level and diabetic retinopathy. The odds ratios of 1.20 (CI 0.39-3.70) and 1.0 (CI 0.47-2.13) denote strong evidence to fail to reject the null hypothesis. There is no association between those who had some high school education, those who are high school graduates, and people with some college education developing diabetic retinopathy. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for education. Patient-focused education could have an impact on the management and prevention of diabetic retinopathy as it relates to self-efficacy and patient knowledge. To build the skills and knowledge diabetic patients need to interact with healthcare providers, make informed decisions pertaining to their personal and healthcare, and modify their behaviors, patient-directed education is an important aspect of diabetes self-management. In the healthcare reform context, patient-directed education has emerged as an important factor in patient engagement and a critical tool in patient outcome improvement (Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Patel et al., 2022). Further research on the possibilities of education in stimulating changes in self-efficacy and knowledge in behavioral changes is necessary. Patient education activities could occur face-to-face, on demand, or online. Education could empower patients to act as their own advocates for obtaining optimal ophthalmological care. The goal of the education initiative would be to instill changes in patient practice, competence, and knowledge (Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Patel et al., 2022).

The odds ratio of 0.95 (CI 0.57-1.57) denotes strong evidence to fail to reject the null hypothesis and indicates that there is no association between psychological distress and diabetic retinopathy. The p value of 0.82 shows that there is no association between psychological distress and diabetic retinopathy among U.S. adults after controlling for age, educational level, and income. Some studies report significant association between poor psychosocial functioning and diabetic retinopathy including greater odds of anxiety, depressive symptoms, and depression. With the use of depression and quality of life questionnaires, some studies emphasize that there are nonsignificant associations between psychosocial functioning and diabetic retinopathy. They highlight that relationship between the two factors could be driven by other sociodemographic and medical factors (Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Khoo et al., 2019; Li et al., 2023; Patel et al., 2022).

Compared to diabetics with no visual impairment and severe diabetic retinopathy, many people with depression suffer from more severe visual impairment and diabetic retinopathy. A factor that plays a role in the association is the employment status of the individuals, determining whether they are employed or unemployed. The bilateral relationship between diabetic retinopathy and poor psychosocial outcomes should not be limited to depression but should include emotional well-being and anxiety (American Diabetes Association, 2018; Fenwick et al., 2011; Li et al., 2023; Patel et al., 2022).

Independent of other health behaviors such as diet, physical activity, smoking, and glycemic control, the presence of depression at baseline, more severe depression, and antecedent clinical depression tend to increase the risk of the progression and incidence of diabetic retinopathy. Patients with type 1 diabetes mellitus who have high depressive symptoms are more likely to have progressive diabetic retinopathy to the proliferative diabetic retinopathy stage than patients with low depressive symptoms (American Diabetes Association, 2018; Fenwick et al., 2011; Li et al., 2023; McLachlan & Gale, 2018; Patel et al., 2022). Patients with severe depression have an increased risk of diabetic retinopathy. For every significant increase in the severity of depressive symptoms, the risk of incident diabetic retinopathy also increases. Patients with depression and type 2 diabetes mellitus who are on antidepressant medications are less likely to develop diabetic retinopathy compared to those who are not on the medication (American Diabetes Association, 2018; Fenwick et al., 2011; Kowluru, 2023; Li et al., 2023; McLachlan & Gale, 2018; Patel et al., 2022).

The odds ratio of 1.65 (CI 0.77-3.55) denotes strong evidence to fail to reject the null hypothesis and the result indicates that there is no association between gender and diabetic retinopathy. It shows that there is no association between psychological distress and diabetic retinopathy when controlling for gender. The main cause of diabetic retinopathy in adults residing in the United States is diabetes and there are sex-gender differences in diabetic patients. Some studies emphasize that compared to women, there is a significantly higher prevalence of diabetic retinopathy, both pre-proliferative/proliferative diabetic retinopathy and nonproliferative diabetic retinopathy, in men (American Diabetes Association, 2018; Cherchi et al., 2020; Fenwick et al., 2011; Kowluru, 2023; Li et al., 2023; McLachlan & Gale, 2018; Mikkola et al., 2020; Patel et al., 2022).

There are differences between women and men in the development of chronic complications and the incidence of type 1 and type 2 diabetes. Women of similar body mass index and age, as their male counterparts, tend to have more chronic renal failure and prevalence of hypertension, worse glycemic metabolic control, and longer diabetes duration (American Diabetes Association, 2018; Cherchi et al., 2020; Fenwick et al., 2011; Kowluru, 2023; Li et al., 2023; McLachlan & Gale, 2018; Mikkola et al., 2020; Patel et al., 2022). In terms of diabetic drug therapies and similar pathologies, there are no evident differences between the sexes. In type 2 diabetic patients, the prevalence of diabetic retinopathy is higher in men than women even though their represented risk factors are less. It suggests that the male sex could be a risk factor for the development of diabetic retinopathy. The results in the literature about differences in diabetic retinopathy based on sex-gender are controversial. Although some studies report that men have higher risks of diabetic retinopathy for men, others emphasize that women have a higher prevalence of the disease. Other studies with type 2 diabetic patients indicate that for the development of diabetic retinopathy, at baseline, the female sex has a higher prevalence of proliferative diabetic retinopathy. A few studies did not report significant differences in diabetic retinopathy for gender (Alperet et al., 2019; American Diabetes Association, 2018; Cherchi et al., 2020; Fenwick et al., 2011; Kowluru, 2023; Li et al., 2023; McLachlan & Gale, 2018; Mikkola et al., 2020; Patel et al., 2022).

The progression of diabetic retinopathy during pregnancy suggests that in diabetic retinal damage, sex hormones play a role. The controversial diabetic retinopathy report on gender differences might be because of pathologies related to sexes, differences in diabetic drug treatments, minimal number of observations, population selection that is not well-specified, or possible mixed type 1 and type 2 diabetic subjects. With the availability of new diabetic retinopathy therapies, it is important to evaluate the risk factors associated with the onset of diabetic retinopathy from a gender standpoint. The new therapies include ribonucleic acid interference and advanced stem cell technologies, antivascular endothelial growth factors, intravireal corticosteroids, vitrectomy, and laser-based therapies (Alperet et al., 2019; American Diabetes Association, 2018; Cherchi et al., 2020; Fenwick et al., 2011; Kowluru, 2023; Li et al., 2023; McLachlan & Gale, 2018; Mikkola et al., 2020; Patel et al., 2022).

The p value of 0.30 indicates that there is no association between age and diabetic retinopathy. The odds ratio of 0.98 (CI 0.96-1.01) denotes strong evidence to fail to reject the null hypothesis. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for age. In the human body, hyperglycemia plays a role in the maintenance and progression of an oxidative environment. Diabetes mellitus causes the production of reactive oxygen species and the level of reactive oxygen metabolites increases because of diabetes and leads to various complications, such as diabetic retinopathy. Some studies report that vitamin C levels and superoxide dismutase are significantly lower in patients with diabetic retinopathy than in those with diabetes mellitus but do not have diabetic retinopathy (Alperet et al., 2019; American Diabetes Association, 2018; Cherchi et al., 2020; De Ritter et al., 2020; Fenwick et al., 2011; Kowluru, 2023; Li et al., 2023; McLachlan & Gale, 2018; Mikkola et al., 2020; Patel et al., 2022).

The degradation or aging process in body tissues increases cellular oxidative load and causes calcium homeostasis, cellular protein damage, and protein aggregation. There are increased reactive oxygen species (ROS) and decreased electron transport chain function in the mitochondria of aging retinas. Increased reactive oxygen species leads to increased damage to mitochondrial proteins, lipids, and deoxyribonucleic acid (DNA) (Alperet et al., 2019; American Diabetes Association, 2018; Cherchi et al., 2020; De Ritter et al., 2020; Fenwick et al., 2011; Kowluru, 2023; Li et al., 2023; McLachlan & Gale, 2018; Mikkola et al., 2020; Patel et al., 2022). With aging, mitochondrial DNA fails and contributes to retinal degenerative disease development. Aging accelerates with diabetes mellitus and cell senescence, the cessation of cell division necessitates the pathogenesis of diabetic retinopathy. A key factor that induces diabetic retinopathy and endothelial senescence is oxidative stress. There is a need for further study and clarification on the mechanisms associated with oxidative stress-induced endothelial aging (Alperet et al., 2019; American Diabetes Association, 2018; Cherchi et al., 2020; De Ritter et al., 2020; Fenwick et al., 2011; Kowluru, 2023; Li et al., 2023; McLachlan & Gale, 2018; Mikkola et al., 2020; Patel et al., 2022).

A p value of 0.20 indicates that there is no association between income and diabetic retinopathy. The odds ratio of 1.19 (CI 0.92-1.60) denotes strong evidence to fail to reject the null hypothesis. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for income. Some studies have analyzed the effects of physical environment and neighborhoods on the prevalence of diabetic retinopathy and diabetes. For type 2 diabetic patients living in lower socioeconomic neighborhoods, their hemoglobin A1C levels, a risk factor of diabetic retinopathy, tend to be higher. Neighborhood environments have an effect on diabetic patients. A neighborhood socioeconomic score comprise of various factors such as occupational status, educational attainment, and median household income, has an inverse relationship to insulin resistance syndrome and could result in a diabetes diagnosis (Alperet et al., 2019; American Diabetes Association, 2018; Cherchi et al., 2020; De Ritter et al., 2020; Fenwick et al., 2011; Kowluru, 2023; Li et al., 2023; McLachlan & Gale, 2018; Mikkola et al., 2020; Patel et al., 2022).

The uptake of screening for diabetic retinopathy is low in socioeconomically deprived neighborhoods. Through its influence on physical activity and diet, the residential environment plays an important role in the treatment and prevalence of diabetes-related complications and diabetes. Various factors, such as insurance status and the geographical distances of healthcare centers, influence healthcare access and the prevalence of diabetic retinopathy. Compared to urban residents, the prevalence of diabetic retinopathy and diabetes is higher in rural residents. Uninsured patients who live in rural environments tend to have lower odds of obtaining annual services for eye exams, but they do not have higher odds of retinopathy (Alperet et al., 2019; American Diabetes Association, 2018; Cherchi et al., 2020; De Ritter et al., 2020; Fenwick et al., 2011; Kowluru, 2023; Li et al., 2023; McLachlan & Gale, 2018; Mikkola et al., 2020; Patel et al., 2022).

Low-income status of less than $25,000 annually is linked to greater odds of having a diabetic retinopathy diagnosis; an explanation of greater prevalence of diabetic retinopathy in rural areas could be because of the minimal access to care and to screening services (Patel et al., 2022). Patients within a few miles of a screening center are more likely to attend screening appointments than those who live far from the center. Access to public transportation correlates with adherence to the eye screening of diabetic patients for diabetic retinopathy. A factor that could impede healthcare access is lack of insurance coverage. Some insured diabetic patients have Medicaid and Medicare. A barrier to getting diabetic retinopathy screening is the lack of reimbursement for the screening and the lack of coverage for some services (Alperet et al., 2019; Cherchi et al., 2020; De Ritter et al., 2020; Fenwick et al., 2011; Li et al., 2023; McLachlan & Gale, 2018; Patel et al., 2022). Public insurance correlates with decreased compliance with follow-up appointments for patients with proliferative diabetic retinopathy visiting the ophthalmologic emergency room. There is an association between poor follow-up appointments and lower socioeconomic status. Greater emphasis should be on increasing treatment and diabetic retinopathy screening services for Medicaid and Medicare patients because of the association between decreased follow-up visits for patients with proliferative diabetic retinopathy and insurance coverage (Cherchi et al., 2020; Fenwick et al., 2011; Li et al., 2023; McLachlan & Gale, 2018; Mikkola et al., 2020; Patel et al., 2022).

Limitations

The study has some limitations. The lack of regular screening and patient education for diabetic retinopathy leads to the inability of many individuals living with diabetes in the United States not receive ophthalmological care needed for the prevention of blindness and visual impairment. The screening and educational factors and those lacking ophthalmological care were not controlled in the study because of the constraints of sample size and data availability. Factors such as lack of care between healthcare providers and patients, lack of effective communication, and the extent of diabetic retinopathy progression were not controlled in the study. Transgender and nonbinary respondents were not controlled for in the study because the sample size was not large enough for this category of respondents.

Implications

The study has implications for social change and the practice and discipline of public health as a profession. It provides new insights on ways that the improvement of the pathophysiology of diabetes and diabetic retinopathy could lead to the improvement of psychological distress. The study findings could facilitate the implementation of national policies focused on the empowerment or assistance of individual adherence to healthier lifestyles leading to the prevention of diabetes mellitus and diabetic retinopathy. The findings could also encourage individuals with the disease to enroll in classes for diabetes education and to seek additional information. The study would increase the awareness and importance of preventative care in public health practice and profession through evidence-based screenings and patient education. It could create a sense of urgency around the need for coordinated management strategy which includes early diagnosis of the diabetes, glycemic control, and regular screening of the diabetic retinopathy risk factors. Preventive care would entail dilated eye exam, comprehensive ancillary tests, and patient education implemented through a multidisciplinary team that comprises of ophthalmologists, retina specialists, and primary diabetes care providers such as diabetologists, endocrinologists, and primary care providers. The study might encourage additional research on diabetes-related laser eye surgery, intraocular drug therapy for vision improvement, and neuro-degeneration.

The study findings could facilitate stakeholder-sponsored grants when seeking funding for educational promotions pertaining to diabetic retinopathy and psychological distress. It could also provide information for population health planning and implementation in the public health field and for public health practitioners of all types, sizes, specialties, and expertise. With the investment of financial incentives in preventative services and the monitoring of the care continuum, the results of the study could enable public health organizations and practitioners who are proactive in population health planning and implementation to reach their goals (Romero, 2016). Healthcare organizations working with limited staff and budgets on the development and deployment of population health management programs, particularly on diabetes and diabetic retinopathy, could use the findings of the study. Healthcare providers could use the information from this study to change their workflow to enable them to properly manage patients with chronic diseases, such as diabetes, and other issues such as limited access to healthcare, and a high tendency of frequent visits to the hospital.

The results of the study could enable healthcare professionals to tackle some of the challenges they face when developing health programs and enable them to strive to achieve success in a fast-evolving healthcare industry (Romero, 2016). The study findings could be instrumental to the implementation of national policies encouraging the assistance or empowerment of adherence to healthier lifestyles leading to diabetes mellitus and the prevention of diabetic retinopathy.

Recommendations for Further Research

Within its limitations, the findings of this study highlight that with odds ratios of 1.17 (CI 0.32-4.33) and 1.53 (CI 0.41-5.70) for males and 1.18 (CI 0.22-6.42) and 0.70 (CI 0.20-2.40) for females, there is no association between education levels, which includes some high school education, high school graduates, and some college, and diabetic retinopathy. It is necessary to have further research conducted on patient education and regular screening for diabetic retinopathy in the United States for diabetic patients. Despite the recommended guidelines for patient education and frequent diabetic retinopathy screening, several diabetics lack the proper ophthalmological care needed for visual impairment and blindness prevention. Researchers could explore the reasons for the gap in care such as lack of patient education, lack of effective communication, and lack of care coordination between healthcare providers and patients. The gaps could result in missed opportunities in the prevention of disease progression. There is a scarcity of published research relating to the possibility of education stimulating changes in knowledge and self-efficacy and leading to behavioral change.

Although a p-value of 0.64 for males and 0.49 for females shows that there is no association between psychological distress and diabetic retinopathy among U.S. adults, it is important to have a comprehensive understanding of the relationship between psychosocial outcomes and diabetic retinopathy, and the development and implementation of effective interventions for diabetic patients. The odds ratio of 0.98 (CI

0.92-1.04) for males and 0.99 (CI 0.96-1.01) for females shows that there is no association between psychological distress and diabetic retinopathy when controlling for age. The odds ratio of 1.13 (CI 0.67-1.90) in males and 1.27 (CI 1.05-1.54) in females indicates that there is no association between income and diabetic retinopathy compared to the females where the result indicates that there is an association between income and diabetic retinopathy. The odds ratio of 1.21 (CI 0.51-2.92) for males and 0.70 (CI 0.24-2.03) for females shows that there is no statistically significant association between psychological distress and diabetic retinopathy when controlling for income, educational level, and age, but there is a need for further research on the study of the role socioeconomic status plays in the prevalence of diabetic retinopathy in the American population. Even though it could be a result of environmental and behavioral mechanisms, further research is important in determining the reason women tend to have more sensitivity to sociocontextual predictors, such as occupation, education, and income, for the risk of developing diabetes in the future (Mahs et al., 2022).

In men and women, there is often a misalignment between the circadian clock and social rhythms and between gender-dependent social timing and sex-dependent biological factors such as body composition that is associated with the pathogenesis of diabetes (Kautzy-Willer et al., 2019; Lien & Jiang, 2017). Researchers could conduct further research investigating the complexity of sex-dimorphic associations between sleep, work stress, and diabetes. The research findings could assist in implementing sex-specific prevention programs in some groups of shift workers. Future studies could focus on the compulsoriness of possible sexual dimorphism. To gain a better understanding of the phenomenon, researchers should study the different biological and environmental factors associated with diabetic women having excess risks of cardiovascular disease.

Sex differences are usually obvious in adrenergic responses to physical activity with higher effects in women that lead to variations in lipid metabolism and hypertrophic action (Mahs et al., 2022; Mamo et al., 2019; McLachlan & Gale, 2018). Researchers should endeavor to bridge the knowledge gap pertaining to sex dimorphism in human diabetic cardiomyopathy. They should get clarification on the sex-specific dose-response relationships between the risk of type 2 diabetes mellitus and alcohol consumption and the underlying mechanisms. Further research to gain clarification on the relationship between birth weight, pregnancy-related stress, offspring HPA axis activity, and the impact of programming adult diseases in young women and men, is also important (Hewage et al., 2020; Madhuri & Srilakshmi, 2019; Muche et al., 2020; Muhwava et al., 2019). They should conduct research on the study of the role socioeconomic status plays in the prevalence of diabetic retinopathy in the American population.

Researchers should conduct reviews to identify the need for the improvement of outcome measures and obtaining valid and meaningful results of the social and emotional impact of diabetic retinopathy and possible directions of research pertaining to computer adaptive testing. It is important to explore the possibilities of education in stimulating changes in knowledge and self-efficacy in behavioral changes. Patient education activities could occur on demand, face-to-face, or online. To obtain optimal ophthalmological care, education could empower patients to act as their own advocates.

Conclusion

There is no association between psychological distress and diabetic retinopathy among U.S. adults when controlling for education level, income, gender, and age. Considering the study's limitations, there is uncertainty behind the direction and extent of the association between psychological distress and diabetic retinopathy. Patient-focused education tends to have an impact on the prevention and management of diabetic retinopathy because it relates to self-efficacy and patient knowledge. An important part of diabetes self-management is patient-directed education that is beneficial for diabetic patients to build the knowledge and skills they need to effectively interact with their healthcare providers, modify their behaviors, and make informed decisions about their health and personal care (Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Patel et al., 2022). Patient-directed education is an important aspect of healthcare reform because it involves patient engagement and influences the improvement of patient outcomes. A factor that plays a role in the care of diabetic retinopathy and visual impairment is the employment status of the individuals, whether they are employed or unemployed. The degradation or aging process in body tissues increases cellular oxidative load and causes protein aggregation, calcium homeostasis, and cellular protein damage. There are increased reactive oxygen species (ROS) and decreased electron transport chain function in the mitochondria of aging retinas. Diabetes is the main cause of diabetic retinopathy in adults residing in the United States and there are sex-gender differences in diabetic patients (American Diabetes Association, 2018; Cherchi et al., 2020; Fenwick et al., 2011; Kowluru, 2023; Li et al., 2023; McLachlan & Gale, 2018; Mikkola et al., 2020; Patel et al., 2022).

References

Allen, M. (2017). Quantitative research. *The Sage Encyclopedia of Communication Research Methods*. https://dx.doi.org/10.4135/9781483381411.n476

Alperet, D. J., Rebello, S. A., Khoo, E. Y., Tay, Z., Seah, S. S., Tai, B., Tai, E., Emady-Azar, S., Chou, C. J., Darimont, C., Dam, R. M.V. (2019). The effect of coffee consumption on insulin sensitivity and other biological risk factors for type 2 diabetes: a randomized placebo-controlled trial. *The American Journal of Clinical Nutrition*, *111*(2), 448-458. https://doi.org/10.1093/ajcn/nqz306

American Diabetes Association. (2018). Economic costs of diabetes in the U.S. in 2017. *Diabetes Care*, *41* (4). Doi: 10.2337/dci18-0007

Ansari, R. M., Hosseinzadeh, H., & Zwar, N. (2016). A qualitative research on self-management of type 2 diabetes in middle-aged population of rural area of Pakistan. *International Education and Research Journal*, *2*(8), 62-65.

Ansari, P., Tabasumma, N., Snigdha, N. N., Siam, N. H., Panduru, R. V. N. R. S., Azam, S., Hannan, J. M. A., & Abdel-Wahab, Y. H. A. (2022). Diabetic retinopathy: An overview on mechanisms, pathophysiology and pharmacotherapy. *Diabetology, 3*, 159-175. https://doi.org/10.3390/diabetology3010011

Antonetti, D. A., Silva, P. S., & Stitt, A. W. (2021). Current understanding of the molecular and cellular pathology of diabetic retinopathy. *Nature Reviews Endocrinology, 17*, 195-206. https://doi.org/10.1038/s41574-020-00451-4

Atlanta Diabetes Association. (2020). Type 2 diabetes. *Endocrine Specialty Group*. https://atlantadiabetes.com/diabetes-care/type-2-diabetes/

Atwany, M. Z., Sahyoun, A. H., & Yaqub, M. (2022). Deep learning techniques for diabetic retinopathy classification: a survey. *IEEE Acess. 10,* 28642-28655. Doi: 10.1109/ACCESS.2022.3157632.

Aziz, T., Charoenlarpnopparut, C., & Mahapakulchai, S. (2023). Deep learning-based hemorrhage detection for diabetic retinopathy screening. *Scientific Reports, 13*(1), Article 1479. https://doi.org/10.1038/s41598-023-28680-3

Beaser, R.S., Turell, W.A., Howson, A. (2018). Strategies to improve prevention and management in diabetic retinopathy: Qualitative insights from mixed-methods study. *Diabetes Spectrum, 31*(1), 65-74. Doi: 10.2337/ds16-0043

Bora, A., Balasubramanian, S., Babenko, B., Virmani, S., Venugopalan, S., Mitani, A., Marinho, G., Cuadros, J., Ruamviboonsuk, P., Corrado, G., Peng, L., Webster, D., Varadarajan, A., Hammel, N., Liu, Y., & Bavishi, P. (2021). Predicting the risk of developing diabetic retinopathy using deep learning. *The Lancet Digital Health, 3*(1), e10-e19. https://doi.org/10.1016/S2589-7500(20)30250-8

Boyd, K., & Gregori, N. Z. (2020). What is diabetic retinopathy? *American Academy of Ophthalmology*. What Is Diabetic Retinopathy? - American Academy of Ophthalmology (aao.org)

Centers for Disease Control and Prevention. (2017). National health and nutrition examination survey. 2015-2016 data documentation, codebook, and frequencies. *Mental Health- Depression Screener (DPQ_1)*. NHANES 2015-2016: Mental Health - Depression Screener Data Documentation, Codebook, and Frequencies (cdc.gov)

Centers for Disease Control and Prevention. (2019). Type 2 diabetes. *United States Department of Health and Human Services*. https://www.cdc.gov/diabetes/basics/type2.html

Centers for Disease Control and Prevention. (2021). The social-ecological model: A framework for prevention. Violence prevention. *United States Department of Health and Human Services*. The Social-Ecological Model: A Framework for Prevention |Violence Prevention|Injury Center|CDC

Centers for Disease Control and Prevention. (2020). What is Diabetes? *United States Department of Health and Human Services*. What is diabetes? | CDC

Centers for Disease Control and Prevention. (2021). *Diabetes*. Division of Diabetes Translation | CDC

Centers for Disease Control and Prevention. (2020). *National Diabetes Statistics Report 2020*. National Diabetes Statistics Report 2020. Estimates of diabetes and its burden in the United States. (cdc.gov)

Cherchi, S., Gigante, A., Spanu, M. A., Contini, P., Meloni, G., Fois, M. A., Pistis, D., Pilosu, R. M., Lai, A., Ruin, S., Campesi, I., & Tonolo, G. (2020). Sex-gender differences in diabetic retinopathy. *Diabetology, 1*, 1-10. https://doi.org/10.3390/diabetology1010001

Cleveland Clinic. (2021). Diabetes: An overview. *100 Years of Cleveland Clinic*. Diabetes: Types, Risk Factors, Symptoms, Tests, Treatments & Prevention

(clevelandclinic.org)

Cleveland Clinic.org. (2022). Optical coherence tomography. *100 Years of Cleveland Clinic*. Diagnostics: Optical Coherence Tomography (clevelandclinic.org)

Curry, A. (2020). Fatty liver and type 2 diabetes. *University of Florida Diabetes Institute*. Fatty Liver and Type 2 Diabetes » Diabetes Institute » College of Medicine » University of Florida (ufl.edu)

Dai, L., Wu, L., Li, H., Cai, C., Wu, Q., Kong, H., Liu, R., Wang, X., Hou, X., Liu, Y., Long, X., Wen, Y., Lu, L., Shen, Y., Chen, Y., Shen, D., Yang, X., Zou, H., Sheng, B., & Jia, W. (2021). A deep learning system for detecting diabetic retinopathy across the disease spectrum. *Nature Communications. 12*(3242). https://doi.org/10.1038/s41467-021-23458-5

De Ritter, R., De Jong, M., Vos, R.C. (2020). Sex differences in the risk of vascular disease associated with diabetes. *Biology of Sex Differences*. *11* (1). https://doi.org/10.1186/s13293-019-0277-z

Demmin, D. L., & Silverstein, S. M. (2020). Visual impairment and mental health: Unmet needs and treatment options. *Journal of Clinical Ophthalmology, 14,* 4229-4251. https://doi.org/10.2147/OPTH.S258783

DiaGundluru, N., Rajput, D. S., Lakshmanna, K., Kaluri, R., Shorfuzzaman, M., Uddin, M., and Khan, M. A. R. (2022). Enhancement of detection of diabetic retinopathy using harris hawks optimization with deep learning model. *Computational Intelligence and Neuroscience*. *2022*. https://doi.org/10.1155/2022/8512469

Doheny, K. (2020). Pancreatic fat: Lifestyle habits count more than genetics. *Endocrineweb*. Pancreatic Fat: Lifestyle Habits Count More Than Genetics (endocrineweb.com)

Emani, S., Peters, E., Desai, S., Karson, A. S. Lipsitz, S. R., LaRocca, R., Stone, J., Suric, V., Wald, J.S., Wheeler, A., Williams, D.H., & Bates, D.W. (2018). Perceptions of adopters versus non-adopters of a patient portal: an application of diffusion of innovation theory. *Journal of Innovation in Health Informatics*, *25*(3), 149-157. http://dx.doi.org/10.14236/jhi.v25i3.991

Farooq, M. S., Arooj, A., Alroobaea, R., Baqasah, A. M., Singh, D., and Sardar, R. (2022). Untangling computer-aided diagnostic system for screening diabetic retinopathy based on deep learning techniques. *Sensors*, *22*(5), Article 1803. https://doi.org/10.3390/s22051803

Fenwick, E., Rees, G., Pesudovs, K., Dirani, M., Kawasaki, R., Wong, T. Y., and Lamoureux, E. (2011). Social and emotional impact of diabetic retinopathy: a review. *Clinical & Experimental Ophthalmology*. *40*(1), 27-38. https://doi.org/10.1111/j.1442-9071.2011.02599.x

Forrester, J. V., Kuffova, L., & Delibegovic, M. (2020). The role of inflammation in diabetic retinopathy. (2020). *Frontiers in Immunology*, *11*. https://doi.org/10.3389/fimmu.2020.583687

Gadekallu, T. R., Khare, N., Bhattacharya, S., Singh, S., Maddikunta, P. K. R, & Srivastava, G. (2020). Deep neural networks to predict diabetic retinopathy.

Journal of Ambient Intelligence and Humanized Computing. https://doi.org/10.1007/s12652-020-01963-7

Gomulka, K., Ruta, M. (2023). The role of inflammation and therapeutic concepts in diabetic retinopathy- A short review. *International Journal of Molecular Sciences. 24*(2). 1024. https://doi.org/10.3390/ijms24021024

Grzybowski, A., Brona, P., Lim, G., Ruamviboonsuk, P., Tan, G. S. W., Abramoff, M., and Ting, D. S. W. (2020). Artificial intelligence for diabetic retinopathy screening: A review. *Eye, 34*, 451-460. https://doi.org/10.1038/s41433-019-0566-0

Hayati, M., Muchtar, K., Roslidar, Maulina, N., Syamsuddin, I., Elwirehardja, G., N., Pardamean, B. (2023). Impact of CLAHE-based image enhancement for diabetic retinopathy classification through deep learning. Procedia *Computer Science, 216*, 57-66. https://doi.org/10.1016/j.procs.2022.12.111

Hewage S, Audimulam J, Sullivan E, Chi C, Yew TW, Yoong J. (2020). Barriers to gestational diabetes management and preferred interventions for women with gestational diabetes in singapore: Mixed methods study. *JMIR Formative Research. 4*(6). Barriers to Gestational Diabetes Management and Preferred Interventions for Women With Gestational Diabetes in Singapore: Mixed Methods Study - PMC (nih.gov)

International Diabetes Federation. (2022). Diabetes around the world in 2022. *Diabetes Atlas*. https://www.diabetesatlas.org/en/sections/worldwidetoll-of-diabetes.ht

International Diabetes Federation. (2023). Understanding diabetes. International Diabetes Federation - Home (idf.org)

Jiwani, N., Gupta, K., and Afreen, N. (2022). A convolutional neural network approach for diabetic retinopathy classification. *IEEE 11th International Conference on Communication Systems and Network Technologies (CSNT)*. 357-361. Doi: 10.1109/CSNT54456.2022.9787577

Kang, Q., & Yang, C. (2020). Oxidative stress and diabetic retinopathy: Molecular mechanisms, pathogenetic role and therapeutic implications. *Redox*, *37,* 2213-2317. https://doi.org/10.1016/j.redox.2020.101799

Kautzky-Willer, A., Harreiter, J., Pacini, G. (2016). Sex and gender differences in risk, pathophysiology and complications of type 2 diabetes mellitus. *National Library of Medicine. National Center for Biotechnology Information. 37*(3). 278-316. Doi: 10.1210/er.2015-1137

Kautzy-Willer, A., Harreiter, J., Abrahamian, H., Weitgasser, R., Fasching, P., Hoppichler, F., Lechleitner, M. (2019). Gender-specific aspects of prediabetes and diabetes mellitus-clinical recommendations. *SpringerLink. 131* (1), 221-228. Gender-specific aspects of prediabetes and diabetes mellitus – clinical recommendations (Update 2019) | SpringerLink

Khoo, K., Man, R.E.K., Rees, G., Gupta, P., Lamoureux, E.L., Fenwick, E. K. (2019). The relationship between diabetic retinopathy and psychosocial functioning: a systematic review. *Quality of Life Research, 28,* (2017-2039). https://doi.org/10.1007/s11136-019-02165-1

Kovoor, E., Chauhan, S. K., and Hajrasouliha, A. (2022). Role of inflammatory cells in pathophysiology and management of diabetic retinopathy. *Survey of Ophthamology*. *67* (6). 1563-1573. https://doi.org/10.1016/j.survophthal.2022.07.008

Kowluru, R. A. (2023). Cross talks between oxidative stress, inflammation and epigenetics in diabetic retinopathy. *Cells*, *12*(2), 300. https://doi.org/10.3390/cells12020300

Lauffenburger, J. C., Lewey, J., Jan, S., Lee, J., Ghazinouri, R., & Choudhry, N. K. (2020). Association of potentially modifiable diabetes care factors with glycemic control in patients with insulin-treated type 2 diabetes. *JAMA Network Open, 3*(1), e1919645– e1919645. https://doi.org/10.1001/jamanetworkopen.2019.19645

Li, F., Wang, Y., Xu, T., Dong, L., Yan, L., Jiang, M., Zhang, X., Jiang, H., Wu, Z., & Zou, H. (2022). Deep learning-based automated detection for diabetic retinopathy and diabetic macular oedema in retinal fundus photographs. *Eye, 36*, 1433-1441. https://doi.org/10.1038/s41433-021-01552-8

Li, Q., Chang, Y., Zhang, K., Chen, H., Tao, S., and Zhang, Z. (2020). Implication of the gut microbiome composition of type 2 diabetic patients from northern China. *Sci. Rep. 10* (1). Doi: 10.1038/s41598-020-62224-3

Li, X., Jiang, Y., Zhang, J., Li, M., Luo, H., and Yin, S. (2022). Lesion-attention pyramid network for diabetic retinopathy grading. *Artificial Intelligence in Medicine*. 126. https://doi.org/10.1016/j.artmed.2022.102259

Li, Q., Wang, M., Li, X., Shao, Y. (2023). Aging and diabetic retinopathy: Inherently intertwined pathophysiological processes. *Experimental Gerontology 175* (112138), 0531-5565. https://doi.org/10.1016/j.exger.2023.112138

Lien, A. S., & Jiang, Y. D. (2017). Integration of diffusion of innovation theory into diabetes care. *Journal of diabetes investigation*, *8*(3), 259-260. Doi: 10.1111/jdi.12568

Madhuri, C., & Srilakshmi, B. (2019). Retrospective study on prevalence, risk factors, maternal and fetal outcome in gestational diabetes mellitus. *International Archives of Integrated Medicine*, *6*(11), 94-98. iaim_2019_0611_14.pdf (iaimjournal.com)

Magne, F., Gotteland, M., Gauthier, L., Zazueta, A., Pesoa, S., Navarrete, P., and Balamurugan, R. (2020).The firmicutes/bacteroidetes ratio: A relevant marker of gut dysbiosis in obese patients? *Nutrients*, *12*(5), 1474. Doi: 10.3390/nu12051474

Mahs, M., Pithan, J. S., Bergmann, I., Gabrys, L., Graf, J., Holzemann, A., Van Laerhoven, K., Otto-Hagemann, S., Popescu, M. L., Schwermann, L., Wenz, B., Pahmeier, I., Teti, A. (2022). Activity tracker-based intervention to increase physical activity in patients with type 2 diabetes and healthy individuals: study protocol for a randomized controlled trial. *BioMed Central*, *23*, 617. Activity tracker-based intervention to increase physical activity in patients with type 2 diabetes and healthy individuals: study protocol for a randomized controlled trial | Trials | Full Text (biomedcentral.com)

Mamo, Y., Bekele, F., Nigussie, T., & Zewudie, A. (2019). Determinants of poor glycemic control among adult patients with type 2 diabetes mellitus in Jimma University Medical Center, Jimma zone, south west Ethiopia: A case control study. *BMC Endocrine Disorders, 19*(1), 91. https://doi.org/10.1186/s12902-019-0421-0

McLachlan, K., & Gale, C. R. (2018). The effects of psychological distress and its interaction with socioeconomic position on risk of developing four chronic diseases. *Journal of psychosomatic research, 109,* 79-85. Doi: 10.1016/j.jpsychores.2018.04.004

Mikkola, I., Hagnäs, M., Hartsenko, J., Kaila, M., & Winell, K. (2020). A personalized care plan is positively associated with better clinical outcomes in the care of patients with type 2 diabetes: A cross-sectional real-life study. *Canadian Journal of Diabetes, 44*(2), 133– 138. https://doi.org/10.1016/j.jcjd.2019.05.003

Muche, A. A., Olayemi, O. O., & Gete, Y. K. (2020). Effects of gestational diabetes mellitus on risk of adverse maternal outcomes: a prospective cohort study in Northwest Ethiopia. *BMC Pregnancy & Childbirth, 20*(1), 1-13. Effects of gestational diabetes mellitus on risk of adverse maternal outcomes: a prospective cohort study in Northwest Ethiopia | BMC Pregnancy and Childbirth | Full Text (biomedcentral.com)

Muhwava, L. S., Murphy, K., Zarowsky, C., & Levitt, N. (2019). Experiences of lifestyle change among women with gestational diabetes mellitus (GDM):

A behavioural diagnosis using the COM-B model in a low-income setting. *Plos One Journal, 14*(11). https://doi.org/10.1371/journal.pone.0225431

National Institute of Diabetes and Digestive and Kidney Diseases. (n.d.). Diabetes. Diabetes | NIDDK (nih.gov)

National Institutes of Health. (2019). *Diabetic retinopathy*. National Eye Institute. Diabetic Retinopathy | National Eye Institute (nih.gov)

Parthasharathi, G. U., Kumar, K. V., Premnivas, R., and Jasmine, K. (2022). Diabetic retinopathy detection using machine learning. *Journal of Innovative Image Processing*. *4*(1), 26-33. Doi:10.36548/jiip.2022.1.003

Patel, D., Ananthakrishnan, A., Lin, T., Channa, R., Liu, T.Y.A, Wolf, R.M. (2022). Social determinants of health and impact on screening, prevalence, and management of diabetic retinopathy in adults: A narrative review. *Journal of Clinical Medicine, 11*(23), 7120. Doi: 10.3390/jcm11237120

Poly, T. N., Islam, M., Walther, B. A., Lin, M., C., & Li, Y.-C. (2023). Artificial intelligence in diabetic retinopathy: Bibliometric analysis. *Computer Methods and Programs in Biomedicine*. *231*, Article 107358. https://doi.org/10.1016/j.cmpb.2023.107358

Porter, D. (2022). What is fluorescein angiography. *American Academy of Ophthalmology*. What Is Fluorescein Angiography? - American Academy of Ophthalmology (aao.org)

Prasad, R., Floyd, J. L., Dupont, M., Harbour, A., Agyeiwaah, Y. A., Bediako, B. A., Chakraborty, D., Kichler, K., Rohella, A., Calzi, S. L., Lammendella, R., Wright, J., Boulton, M. E., Oudit, G. Y., Raizada, M. K., Stevens, B. R., Li, Q., Grant, M. B. (2023). Maintenance of enteral ACE2 prevents diabetic retinopathy in type 1 diabetes. *Circulation Research. 132* (1). https://doi.org/10.1161/CIRCRESAHA.122.322003

Qiao, L., Zhu, Y., & Zhou, H. (2020). Diabetic retinopathy detection using prognosis of microaneurysm and early diagnosis system for non-proliferative diabetic retinopathy based on deep learning algorithms. *IEEE Access*, *8*, 104292-104302. Doi: 10.1109/ACCESS.2020.2993937

Qummar, S., Khan, F. G., Shah, S., Khan, A., Shamshirband, S., Rehman, Z. U., Khan, I. A., and Jadoon, W. (2019). A deep learning ensemble approach for diabetic retinopathy detection. *IEEE, 7*, 150530-150539. Doi: 10.1109/ACCESS.2019.2947484

Regeneron Pharmaceuticals. (2021). About diabetic retinopathy. *Now Eye See*. Now Eye See | Diabetic Retinopathy

Rezazadeh-Gavgani, E., Oladghaffari, M., Bahramian, S., Majidazar, R., & Dolati, S. (2023). MicroRNA-21: A critical underestimated molecule in diabetic retinopathy. *Gene, 859*. https://doi.org/10.1016/j.gene.2023.147212

Romero, L. F. (2016). Diabetes: The current state of affairs from a population management view. *MLO: Medical Laboratory Observer*, *48*(8), 12-20. https://ezp.waldenulibrary.org/login?url=https://search.ebscohost.com/login.aspx?

Ruamviboonsuk, P., Tiwari, R., Sayres, R., Nganthavee, V., Hemarat, K., Kongprayoon, A., Raman, R., Levinstein, B., Liu, Y., Schaekermann, M., Lee, R., Virmani, S., Widner, K., Chambers, J., Hersch, F., Peng, L., and Webster, D. (2022). Real-time diabetic retinopathy screening by deep learning in a multisite national screening programme: a prospective interventional cohort study. *The Lancet Digital Health*. *4* (4), e235-e244. https://doi.org/10.1016/S2589-7500(22)00017-6

Saadane, A., Veenstra, A. A., Minns, M. S., Tang, J., Du, Y., Elghazali, F. A., Lessieur, E. M., Pearlman, E., & Kern, T. S. (2023). CCR2- positive monocytes contribute to the pathogenesis of early diabetic retinopathy in mice. *Diabetologia. 66*, 590-602. https://doi.org/10.1007/s00125-022-05860-w

Setia, M. S. (2016). Methodology series module 3: Cross-sectional Studies. *Indian Journal of Dermatology*, *61*(3), 261-264. https://doi.org/10.4103/0019-5154.182410

Stanford.edu. (n.d.). *Patient Health Questionnaire (PHQ-9)*. Patient health questionnaire (PHQ-9) (stanford.edu)

Teo, Z. L., Tham, Y. C., Yu, M., Chee, M. L., Rim, T. H., Cheung, N., Bikbov, M. M., Wang, Y. X., Tang, Y., Lu, Y., Wong, I. Y., Ting, D. S. W., Tan, G. S. W., Jonas, J. B, Sabanayagam, Wong, T. Y., Cheng, C. Y. (2020). Global prevalence of diabetic retinopathy and protection of burden through 2045: Systemic review and meta-analysis. *Ophthalmology, 128*(11), 1580-1591. https://doi.org/10.1016/j.ophtha.2021.04.027

Torpy, J. M., Glass, T. J., Glass, R. M. (2007). Retinopathy. *Journal of American Medical Association (JAMA), 298*(8), 944. Doi:10.1001/jama.298.8.944

Tymchenko, B., Marchenko, P., and Spodarets, D. (2020). Deep learning approach to diabetic retinopathy detection. *Cornell University. arXiv*. https://doi.org/10.48550/arXiv.2003.02261

University of North Carolina. (n.d.). Diabetes questionnaire. *Campus Health*. diabetes_questionnaire (unc.edu)

Vitger, T., Langberg, H., Grabowski, D. (2017). Mutual involvement in families with type 2 diabetes through web-based health care solutions: Quantitative survey study of family preferences, challenges, and potentials. *Journal of Medical Internet Research Publication (JMIR), 2*(2), 2371-4379. Doi: 10.2196/diabetes.7456

Vujosevic, S, Aldington, S. J., Silva, P., Hernandez, C., Scanlon, P., Peto, T., & Simo, R. (2020). Screening for diabetic retinopathy: new perspectives and challenges. *The Lancet Diabetes & Endocrinology, 8*(4), 337-347. https://doi.org/10.1016/S2213-8587(19)30411-5

Wang, M., Yang, Y., Liao, Z. (2020). Diabetes and cancer: Epidemiological and biological links. *World Journal of Diabetes*. *11*(6), 227-238. Doi: 10.4239/wjd.v11.i6.227

Winston-Salem State University. (n.d.). Quantitative design. *Key Elements of a Research Proposal*. Key Elements of a Research Proposal - Quantitative Design (wssu.edu)

Zhang, H., Wang, Q., He, S., Wu, K., Ren, M., Dong, H., Di, J., Yu, Z., & Huang, C. (2020). Ambient air pollution and gestational diabetes mellitus: A review of evidence from biological mechanisms to population epidemiology. *Science of The Total Environment. 719*. https://doi.org/10.1016/j.scitotenv.2020.137349

Zheng, D., Li, N., Hou, R., Zhang, X., Wu, L., Sundquist, J., Sundquist, K., & Ji, J. (2023). Glucagon-like peptide-1 receptor agonists and diabetic retinopathy: nationwide cohort and mendelian randomization studies. *BMC Medicine, 21* (40). https://doi.org/10.1186/s12916-023-02753-6

Zhou, A., Y., Taylor, B., E., Barber, K., G., Lee, C., A., Taylor, Z., R., R., Howell, S., J., Taylor, P., R. (2023). Anti-IL17A halts the onset of diabetic retinopathy in type I and II diabetic mice. *International Journal of Molecular Sciences. 24*, 1347. https://doi.org/10.3390/ijms24021347

Effect Modification of Gender on Psychological Distress

in Diabetes-Related Retinopathy

Claret Onukogu

Walden University

Doctoral Study

Outlet for Manuscript

The Journal of Epidemiology and Community Health (JECH) is suitable for this manuscript's publication because of its focus on covering all facets of public health and epidemiology. It is the leading international journal dedicated to the publication of authentic reviews and original research pertaining to methodological, applied, and theoretical issues that emphasize using integrative and multidisciplinary approaches. JECH is a suitable outlet to publish data on whether gender modifies the effect of psychological distress on diabetes-related retinopathy after controlling for age, educational level, and income.

Abstract

Diabetes could lead to diabetic retinopathy, an eye disease that causes damaged blood vessels and the growth of abnormal ones. The disease could cause vision loss because high blood sugar levels damage retinal blood vessels. The two stages of the disease are nonproliferative and proliferative diabetic retinopathy. In the nonproliferative stage, diabetics develop macular edema from retinal swelling and macular ischemia with a shortage of blood in the macula region of the eye and the vision eventually becomes blurry. The proliferative is the advanced stage of the disease when the retina grows new blood vessels and diabetics may experience a detached retina. The quantitative study employed the socioecological model as the theoretical framework to examine the relationship between psychological distress and diabetic retinopathy while considering gender. The aim was to determine the role of psychological distress in diabetic retinopathy after controlling for covariates such as age, educational level, and income. The study examined the association between the independent variables, gender and psychological distress, and the dependent variable, diabetic retinopathy. For the study, a nationally representative dataset, The National Health and Nutrition Examination Survey (NHANES), was used to analyze data. There was no association between psychological distress and diabetic retinopathy among U.S. adults when controlling for gender, education level, income, and age. The results of the study have implications for positive social change which would fill a public health knowledge gap contributing to population health planning and implementation. Further research on patient education and regular screening for diabetic retinopathy in the United States for diabetic patients is necessary.

Introduction

Diabetic retinopathy is the abnormality or damage in the blood vessels of the eye because of diabetes. Individuals with vision-threatening diabetic retinopathy would likely experience increased emotional and social strain. Compared with their psychologically healthy counterparts, people with psychosocial problems and vision-threatening diabetic retinopathy could have levels of functioning that are significantly reduced. It could lead to a heightened progression of diabetic retinopathy, worse diabetes control, increased strain on family functioning, healthcare costs, inadequate compliance, and also additional psychosocial stress that could result in disease management implications, and clinical outcomes (Doheny, 2020; Emani et al., 2018; Farooq et al., 2022; Fenwick et al., 2011). There has not been a systematic exploration of the social and emotional health consequences of diabetic retinopathy. The information is important because it facilitates the targeted approach for the avoidance, prevention, and treatment of the potentially detrimental implications. It is important to know the quantitative and qualitative evidence pertaining to the emotional and social impact of diabetic retinopathy and identify avenues for future research.

There are various debilitating effects of the association between vision loss and diabetic retinopathy. They include the deterioration of work prospects leading to increases in financial strain, increased dependence, and social isolation, and disruption of family functioning, relationships, and roles (Fenwick et al., 2011). The adverse emotional responses include issues with self-perception, stress, anger, loss of confidence, guilt, vulnerability, anxiety, and fear (Fenwick et al., 2011; Forrester et al., 2020; Gadekallu et al., 2020; Gomulka & Ruta, 2023). Most research conducted on the subject is qualitative in nature and the quantitative studies are somewhat outdated, cross-sectional, and small. In terms of validity and content, the outcome measures used in various studies tend to be suboptimal. There should be reviews for the identification of the need for the improvement of outcome measures for the provision of meaningful and valid results of the emotional and social impact of diabetic retinopathy and discussions on the possible directions of further research on computer adaptive testing.

Diabetic retinopathy impacts the social well-being of individuals. People with diabetic retinopathy experience difficulty in the maintenance of social interaction. Those individuals experience increased social isolation because they are no longer able to drive. The difficulties linked to their participation in social activities often lead to their withdrawal from social situations and they become more socially isolated and lonely (Banerjee et al., 2021). For those undergoing group therapy, the factors that foster feelings of isolation are perceived social stigma and negative public reaction to vision loss. They usually have anxiety over maintaining acquaintances or friendships, meeting new people because of the difficulty they experience with recognizing faces, and the feeling of being burdensome and becoming dependent on others (Grzybowski et al., 2020; Hayati et al., 2023; Hewage et al., 2020; International Diabetes Federation, 2022). People with the condition indicate that the visual impairment serves as a deterrent to them finding potential life partners and establishing romantic relationships.

Researchers need to engage in a systematic exploration of the impact of diabetic retinopathy on social life. The lifestyle changes linked to diabetic retinopathy could result in increased irritation and tension between family members, worsened family relationships, and stress. People living with diabetic retinopathy report the feeling of suffocation because of family fussing over their condition and excess family attention. They feel a shift in relationship structure because of their inability to perform normal family responsibilities because of their vision loss from diabetic retinopathy (International Diabetes Federation, 2023; Jiwani et al., 2022; Kang & Yang, 2020; Kautzky-Willer et al., 2016). Mainly because of transportation logistics difficulties, people with diabetic retinopathy experience problems with the maintenance of extended family relationships. Because of the emotional strain of grieving their vision loss, some feel that their ability to nurture intimate relationships is questionable. In some occasions, diabetic retinopathy brings family members together and improves their relationships through networks of kindness and care. Some studies have corroborated some of these findings. In the areas of the overall functioning level, role maintenance, communication, and problem solving, family functioning is significantly worse in people with diabetes-related vision loss than in normative populations. Compared with the normal population level, they have a higher prevalence of divorce and visual impairment is a major factor in marriage deterioration. Married women with visual impairment and young-onset diabetes tend to be at a higher risk of divorce than young married men. Diabetic retinopathy could be a contributor to marriage dissolution and may have a detrimental impact on role maintenance in families, personal relationships, and family functioning (Kautzy-Willer et al., 2019; Kovoor et al., 2022; Kowluru, 2023; Lauffenburger et al., 2020; Li et al., 2022).

Diabetic retinopathy impacts work prospects. As a result of their inability to drive, eye problems associated with diabetic retinopathy have a major impact on the working life of people with the condition. It is the main cause of their unemployment, loss of income, and financial prospects. Men with more severe diabetic retinopathy face more unemployment than women. The advanced stage of diabetic retinopathy is known as proliferative diabetic retinopathy (PDR) and it is a result of the rapid increase or proliferation of the new blood vessels. Compared to men without diabetic retinopathy, those with PDR at baseline have a higher incident risk of unemployment. There is a significant association between PDR and a high rate of early retirement because of disability in adults living with younger-onset diabetes and in men with older-onset diabetes. Compared to working-aged adults with diabetes without diabetic retinopathy, those living with diabetic retinopathy are significantly more likely to be unable to work. People with clinically significant DME and severe diabetic retinopathy, such as PDR, could experience financial burden, unwanted premature retirement, and difficulty with the maintenance of employment (Li et al., 2020; Li et al., 2022; Lien & Jiang, 2017; Madhuri & Srilakshmi, 2019; Magne et al., 2020).

Individuals with diabetic retinopathy suffer from reduced emotional well-being. The predictors of impaired emotional well-being that stem from diabetic retinopathy are fluctuations in vision loss, degree of visual impairment, and the severity of diabetic retinopathy. Reports of the National Eye Institute Vision Functioning Questionnaire (NEI-VFQ) sometimes signify reductions in social subscales and mental health in people with PDR compared to those with nonproliferative diabetic retinopathy (NPDR) and individuals in the late stage of diabetic retinopathy, such as PDR, could show more psychiatric symptomology than those with minimal or background NPDR. People with total vision loss from diabetic retinopathy tend to have higher levels of phobic anxiety, anxiety, and somatization compared to those without diabetic retinopathy or with partial visual impairment. However, high levels of depressive symptoms are evident among individuals in each group. A worse psychosocial function is associated with mild visual impairment levels. Even without conclusive evidence, recent vision loss or fluctuating visual acuity tend to manifest high levels of psychological distress despite the visual acuity level or the severity of diabetic retinopathy (Mahs et al., 2022; Mamo et al., 2019; McLachlan & Gale, 2018; Mikkola et al., 2020; Muche et al., 2020).

During adolescence when individuals go through puberty, there is an increase in the gluteo-femoral accumulation promoted through estrogen which leads to a gynoid shape of premenopausal women. Males tend to have more trunk and visceral fat (VAT), liver fat, and upper extremity mass compared to females with the same BMI and age. Women and men who have similar levels of insulin resistance depict comparable liver and intra-abdominal fat. In Asian populations, women with normal BMI and waist circumference often get visceral obesity diagnosis through computer tomography. It indicates that in women, compared to men, there is a greater cardio-metabolic risk in terms of lipid and glucose abnormalities. Age and VAT are usually independent predictors of higher cardio-metabolic risk in males. The ratio of VAT to subcutaneous fat (SAT) can independently predict higher risk females. Generally, men tend to have larger amounts of VAT for any level of total body fat and more fatty acid turnover with high degrees of fatty acid turnover with high rates of lipogenesis and lipolysis in VAT compared to women (Kautzy-Willer et al., 2019; Muhwava et al., 2019; National Institute of Diabetes and Digestive and Kidney Diseases, n.d.; National Institutes of Health, 2019; Parthasharathi et al., 2022).

Women tend to have higher fatty acid rates accumulating in their leg fat tissue and less release rates in the femoral and gluteal regions of the body. Females have more lipogenetic rates from subcutaneous fat than males. Particularly in women, a decrease in cardiometabolic risk is associated with an increase in leg adiposity. In many cross-sectional population-based studies, an increase in trunk adiposity is usually associated with cardiometabolic risk factor clustering. Aging, especially as it relates to menopause, leads to loss of estrogen production. It can result in changes in the human physic or body shape and increases abdominal fat in females which could cause visceral adiposity. Intraabdominal fat mass, as it relates to subcutaneous fat, and waist circumference relationship is stronger in females than males (Poly et al., 2023; Prasad et al., 2023; Qiao et al., 2020; Qummar et al., 2019).

In cross-sectional analysis testing for differences in age and sex, for menopausal women, the relationship between intraabdominal fat mass and waist circumference is similar to male patterns. The waist is arguably the best diabetes predictor in women. The waist and the BMI value can serve as gauges for diabetes in men. In women, compared to overall body weight gain, an increase in the waist circumference could lead to a higher likelihood of incident diabetes. For men, the overall body weight gain could lead to a higher risk of incident diabetes than an increase in the waist circumference. Body mass and the brown adipose tissue activity in adults impact obesity-related type 2 diabetes, insulin resistance, and whole-body energy metabolism. Women have higher brown adipose tissue prevalence and activity which is related to age in both genders. The presence of brown adipose tissue is more pronounced in BMI for males and visceral fat in women. Ovaries and estrogens could regulate factors, such as the growth of fibroblast, involved in the expression of brown adipose tissue. The transplantation of brown adipose tissue could increase adiponectin, reverse obesity, and decrease liver steatosis and insulin resistance in leptin-deficient animals. An increased impact of body adipose tissue could reduce the risk of diabetes in women (Regeneron Pharmaceuticals, 2021; Rezazadeh-Gavgani et al., 2023; Romero, 2016; Ruamviboonsuk et al., 2022; Saadane et al., 2023).

Metabolic syndrome, also known as MetS, is the clustering of conditions that increases the risk of type 2 diabetes, stroke, and heart disease. It involves clusters of metabolic risk factors, such as high blood sugar, increased blood pressure, abnormal triglyceride or cholesterol, and excess body fat around the waist. It is often associated with insulin resistance and tends to disregard risk factors such as lifestyle, socioeconomic status, family history, sex, and age. The National Health and Nutrition Examination Survey data often depicts comparable prevalence in both males and females with the most increase in young females. In terms of diabetes, there are differences in the risk factors and central adiposity related to inflammation and coagulation between nondiabetic and diabetic individuals (Kautzy-Willer et al., 2019; Setia, 2016; Teo et al., 2020; Torpy et al., 2007; Tymchenko et al., 2020). The clustering of risk factors varies between men and women and with ethnicities. As surrogate markers, increases in waist circumference and abdominal obesity are factors dominant in women. Risk factor adjustments for metabolic syndrome tend to have a higher impact on cardiovascular disease risk in women. There are various diabetes risk scores, which include sex used in risk calculations with other risk parameters, but not many calculations include waist circumference or social factors such as social deprivation. Sexual dimorphism tends to be apparent as the predictive value and in the expression of certain fat-related biomarkers. For energy expenditure, food intake, and satiety regulation, leptin is important. It impacts the peripheral insulin resistance and insulin glucose axis (Kautzy-Willer et al., 2019; University of North Carolina, n.d.; Vitger et al., 2017; Vujosevic et al., 2020; Wang et al., 2020).

There are several effects of adiponectin on lipid and glucose metabolism. It increases the sensitivity of insulin in target organs. In the development of type 2 diabetes, the dysregulation of adiponectin action is present. In the abdominal adipose tissue, women tend to have an up-regulation of adiponectin and its receptor that contributes to lower cardiometabolic risk. From the results of metaanalyses, the levels of adiponectin and leptin in women are higher than that of men with comparable body mass index and age possibly because of their sexual hormones. An increased level of plasma leptin, which is strongly associated with SAT, is a reflection of body fat mass, and has a relationship with an increased risk of diabetes in males. There is an inverse correlation between insulin sensitivity and plasma adiponectin levels in diabetic and obese individuals which is more obvious in women than men. Androgens could reduce adiponectin secretion. Some researchers are unsure whether hypoadiponectinemia is a consequence or cause of hyperinsulinemia or insulin resistance. There are some biomarkers serving as risk factors associated with sexual dimorphism. Hepatokine fetuin A relates to an onset of type 2 diabetes in women (Alperet et al., 2019; Kautzy-Willer et al., 2019; Zhang et al., 2020; Zheng et al., 2023; Zhou et al., 2023).

Copeptin, a component of vasopressin and a marker of arginine vasopressin secretion, is associated with the risk of developing diabetes in the long term in women and not men. Including copeptin in risk models to predict traditional risk factors is valuable in the prediction of diabetes in women. There is a close relationship between the pathogenesis of type 2 diabetes in women and the arginine vasopressin stress adaptation system. Proneurotensin, a neurotensin precursor molecule released from the small intestine after fat intake, is another biomarker. In the central nervous system, proneurotensin acts as a neurotransmitter but its behavior is like a hormone in the periphery. It stimulates biliary and pancreatic secretion, facilitates fatty acid translocation, and hinders gastric motility. Usually, the level of fasting proneurotensin plasma is lower in women than in men. It predicts cardiovascular disease, incident diabetes, and cardiovascular and total mortality in women, but not in men. Baseline proneurotensin increase is associated with an increased risk of new-onset diabetes in women. The interaction between vitamin D and sex is significant. A low level of 25-hydroxy vitamin D3 is associated with type 2 diabetes in middle-aged women. For men, adjusted values of 25-hydroxy vitamin D3 could marginally predict type 2 diabetes (American Diabetes Association, 2018; Ansari et al., 2016; Ansari et al., 2022; Antonetti et al., 2021; Atlanta Diabetes Association, 2020; Kautzy-Willer et al., 2019; Porter, 2022).

Some studies have confirmed an inverse association between diabetes and vitamin D even though factors such as age, ethnicity, and sex hormones, especially 17α-estradiol, could influence the variations of the associations over time. Low levels of vitamin D could increase the prevalence of diabetes in older men and younger women. Vitamin D could improve the transportation of glucose in human cells by directly stimulating insulin receptor expression. An increase in liver enzymes, such as y-glutamyl transferase, aspartate aminotransferase, and alanine aminotransferase, could cause an increase in the incidence of type 2 diabetes in men and women. Y-glutamyl transferase produces the strongest association with incident type 2 diabetes, compared to other enzymes, because it is closely related to oxidative stress, fatty liver, and insulin resistance (Atwany et al., 2022; Aziz et al., 2023; Bora et al., 2021; Kautzy-Willer et al., 2016; Kautzy-Willer et al., 2019; Winston-Salem State University, n.d.). There is an association between liver enzymes and the risk of diabetes. Compared to men of the same body mass index and age, women have lower liver fat and estrogen protection at premenopausal age. Although the prevalence of liver fat is higher in men, there is usually a pronounced rise in elderly women. Triglycerides, body mass index, liver enzymes, and WCR predict MetS in women than in men. There is a sex-specific association between insulin sensitivity and liver transaminase (Boyd & Gregori, 2020; Centers for Disease Control and Prevention, 2019; Cleveland Clinic, 2021; Curry, 2020; Kautzy-Willer et al., 2019).

Researchers use alanine aminotransferase, often measured with hyperinsulinemic euglycemic clamp, to predict muscle glucose uptake in females. Leptin and fasting insulin are the strongest predictors of insulin resistance in males. With possible mediation through the sex hormone-binding globulin gene polymorphism, the low sex hormone-binding globulin levels could indicate the risk of diabetes. Generally, men tend to have lower sex hormone-binding globulin levels than women. Low concentrations of sex hormone-binding globulin could be associated with a higher risk of diabetes in women than in men. The incidence of diabetes could inversely be associated with testosterone and directly associated with estron and estradiol in men. Some researchers attribute the systemic resistance to estrogen in men to the association between the risk of diabetes and circulating estrogen. In women, sex steroids may not be related to diabetes. Researchers have found out that in unselected populations, studying the sex hormone-binding globulin levels could predict diabetes, but in high-risk groups, weight and elevated glucose are strong indicators of diabetes development. In postmenopausal women, there is an inverse relationship between MetS and sex hormone-binding globulin levels and incident type 2 diabetes (Centers for Disease Control and Prevention, 2021; Cleveland Clinic, 2022; Dai et al., 2021; De Ritter et al., 2020; Kautzy-Willer et al., 2019).

Many clinical studies have shown that women living with type 2 diabetes mellitus have higher comorbidities and burden of risk factors and also physical and cognitive functional limitations than men. The quantification of comorbidity risk of diabetes across life reveals further age-related sex differences. The observation of more comorbidities in males is up to 60 years of age compared to the higher comorbidities in females. Higher

BMI, blood pressure, and worse glycemic control in addition to lower exercise levels tend to mediate the link between functional limitations and sex in large community-based type 2 diabetes mellitus cohort. In a gender-functional limitations link, lower self-efficacy and perceived family support, and higher rates of depression are indirect mediators. To a greater extent, impaired cognitive function seems to have an effect on women. In older women, type 2 diabetes mellitus has a greater impact on the risk of geriatric conditions than in men. Many diabetic women experience falls, and cognitive impairment, and are depressed more than diabetic men. In women, diabetes doubles the risk of geriatric conditions but there are no associations evident in diabetic men (Centers for Disease Control and Prevention, 2020; Demmin & Silverstein, 2020; DiaGundluru, 2022; Doheny, 2020; Emani et al., 2018; Kautzy-Willer et al., 2016; Kautzy-Willer et al., 2019).

Depression, eating disorders, and anxiety tend to be more prevalent in diabetic individuals, particularly in women. Mental disorders affect the development of complications, adherence to therapy, and glycemic control. In diabetic individuals, depression doubles the risk of mortality. Compared with nondiabetic individuals, an increased risk of depression is more obvious in diabetic men. With their disease, diabetic men tend to live a more effective lifestyle with a lower prevalence of anxiety and depression, greater activeness in problem-oriented and solution approach strategies, positive well-being, and a better health-related quality of life. Diabetic females and males are prone to suffering from reproductive problems and sexual dysfunctions that in clinical practice, seem to be underestimated. In diabetic women of child-bearing age, pre-

pregnancy care is unsatisfying because of constant perinatal complications, which include high mortality and excessive malformation rates. Over half of sexually active obese men and women complain about sexual dysfunction compared to healthy lean individuals (Centers for Disease Control and Prevention, 2020; Farooq et al., 2022; Fenwick et al., 2011; Forrester et al., 2020; Gadekallu et al., 2020; Kautzy-Willer et al., 2019).

Depressed mood and psychosocial factors are strongly related to sexual dysfunctions in women. For males, sexual dysfunction is related to physiological factors such as MetS, glycemic control, and cardiorespiratory fitness. The problems could be considered markers for cardiovascular risk. In middle-aged diabetic men, erectile dysfunction could be associated with the doubling of new onset cardiovascular disease in the next decade. An early marker of endothelial dysfunction could be impaired penile microcirculation which is linked to increased cardiovascular risk. Men with erectile dysfunction usually undergo depression and have lower quality of life. It is worthwhile for health professionals to create increased awareness about gender and sex in the management and development of type 2 diabetes mellitus and its related complications (Gomulka & Ruta, 2023; Grzybowski et al., 2020; Hayati et al., 2023; Hewage et al., 2020; International Diabetes Federation, 2022; Kautzy-Willer et al., 2019).

There is evidence of several gender and sex differences derived from clinical studies and basic research. In association studies, there are several missing causalities and controversial issues. There are missing randomized controlled trials that prove sex-specific effects through properly designed interventions. Appropriate translational research and models are necessary to study sex differences to gain more insight into the complex interplay and pathophysiology of environment, lifestyle, genes, and hormones. Ensuring the adequate proportion and consideration of women in clinical studies promoting sex-specific analysis, which includes sex differences in priori research questions, is important for medicine and biomedical research and could add to research reproducibility. The lack of a gender or sex-specific analysis is a problem. Instead of using rigorous statistical procedures, gender and sex analysis is usually performed through the application of subgroup analysis. To study and detect complex gender and sex differences accurately and efficiently in the future, the focus of analysis should be on the modification of factors and the use of various statistical approaches that include in-depth power analysis (Allen, 2017; International Diabetes Federation, 2023; Jiwani et al., 2022; Kang & Yang, 2020; Kovoor et al., 2022).

Information on the possible sex differences pertaining to the tolerability and efficacy of drugs is important. To guarantee high quality healthcare and research for all sexes at different ages, there should be adequate inclusion of post and pre-menopausal women in the early trial phases and also elderly women and men and pregnant diabetic women in randomized controlled trials are necessary. Future studies should be geared towards the clarification of the causes of the reduction of female vascular protection in women living with diabetes and the possibilities of counteracting that effect. Having knowledge about the protective mechanisms of a particular sex for psychological, renal complications, and cardiometabolic disorders, could assist in the establishment of new therapeutic strategies for the sexes (Kowluru, 2023; Lauffenburger et al., 2020; Li et al., 2022; Li et al., 2020; Li et al., 2022). There could be clinical relevance in obesity-related type 2 diabetes mellitus treatment in terms of sex dimorphism in central insulin action and further investigation is necessary. Enhanced epigenetic and sex-specific genetics could enable secondary and primary prevention with more attention to parental behavioral factors, fetal sex, and the early phase of life. The promotion of personalized individual care requires the evaluation of the efficacy of initiated interventions and sex-specific screening programs. Gender and sex differences are factors to consider in the future guidelines for type 2 diabetes mellitus management and its complications (Centers for Disease Control and Prevention, 2020; Lien & Jiang, 2017; Madhuri & Srilakshmi, 2019; Magne et al., 2020; Mahs et al., 2022; Mamo et al., 2019).

Methods

I tested whether gender modifies the effect of psychological distress on diabetes-related retinopathy after controlling for age, educational level, and income, through a retrospective, quasi experimental study and using descriptive data analysis, multivariate logistic regression of secondary data, and bivariate analysis using chi-square test of independence. I set the significance level for the logistic regression and chi-squared analysis at 0.05. I measured the individual level variable, sex, as having two levels which are female and male. The geographic location or places of residence covered in the study were grouped in districts found in various parts of the United States. I measured age at the individual level based on the Medical Subject Headings (MeSH) for adults which are (age 19-44 years), Middle Aged (age 45-64 years), Aged (age 65-79 years), and Aged 80 and above. I used collected data on the population level through reputable agencies. I transformed the data into nominal data in the order of low, medium, and high depending on the tertiles of the range of data. Some variables were measured at the population level within different districts and by years depending on the data collection method. Education was ranked based on the highest level attained and grouped in the categories of no education, primary, secondary, and tertiary levels measured at a population level. The categories of no education were in measurements of low, medium, and high. The categories of less than secondary education were in low, medium, and high categories. Secondary education was in low, medium, and high categories. Tertiary education was in low, medium, and high.

NHANES has the variables for depression and psychological distress measurement. The Patient Health Questionnaire (PHQ-9) measures how often individuals experience the following problems: Feeling down, depressed, or hopeless; little pleasure or interest in doing things; having little energy or feeling tired; sleeping too much or trouble staying or falling asleep; feeling bad about oneself or that they are failures or that they have let themselves or their families down; overeating or poor appetite; speaking or moving too slow to the noticeability of others or being so restless or fidgety and moving around more than usual; or thoughts of being better off hurting oneself or dying (CDC, 2017). The responses were measured in days and in categories such as Not at all (0), Several days (1), More than half days (2), and Nearly every day (3). For each checked off problem on the PHQ-9 patient depression questionnaire, respondents indicated how the problems made it difficult for them to do their work, perform duties at home, or get along with other individuals. The categories of their responses were: Not difficult at all; Somewhat difficult; Very difficult; and Extremely difficult. Checks of at least four on the list indicated a depressive disorder. Major depressive disorders had at least five affirmative responses in the very difficult and extremely difficult categories and also in the several days category for the thoughts of death or hurting oneself section. The total scores as they correspond with the severity of depression were as follows: Minimal depression (1-4), Mild depression (5-9), Moderate depression (10-14), Moderately severe depression (15-19), and Severe depression (20-27; Stanford.edu, n.d.).

The chosen study design was the most practical because of the existence of large datasets of relevant information, the reduction of the study time, the elimination of one-on-one interactions with patients, and the inclusion of variables at the population and individual levels. Assessment of the data was through the Centers for Disease Control and Prevention website (CDC). I obtained ethical approval from Walden University.

Results

Complex Samples—Logistic Regression

Does gender modify the effect of psychological distress on diabetes-related retinopathy after controlling for age, educational level, and income?

Male

The weighted population size is 16639717.14. The valid number of people included in the analysis is 468 and the number represents the weighted population size.

Table 1

Frequency and Percentage of Each of the Variables Within the Model

Variable	Frequency	Percentage/Mean
Diabetic retinopathy	1,355,639	16.5%

Education level		
Some high school	1,211,353	14.7%
High school graduate	2,527,446	30.7%
Some college	4,496,087	54.6%
Age (mean)	--	61.4
Family poverty-income-ratio (mean)	--	2.99
Psychological distress	2,104,022	25.6

Table 2

Odds Ratio for Each of the Variables

Variable	Odds ratio	95% confidence interval	p-value
Age (continuous)	0.98	0.92–1.04	0.50
Income	1.13	0.67–1.90	0.63
Education			
Some high school	1.17	0.32–4.33	0.74
High school graduate	1.53	0.41–5.70	0.74
Some college	1.53	0.41–5.70	0.74
Psychological distress	1.21	0.51–2.92	0.64

The result indicates that there is no association between education level and diabetic retinopathy. The odds ratio of 1.17 (CI 0.32-4.33) denotes strong evidence for the null hypothesis being true and it is not rejected.

The odds ratio of 1.53 (CI 0.41-5.70) denotes strong evidence to fail to reject the null hypothesis. There is no association between those who had some high school education, those who are high school graduates, and people with some college education developing diabetic retinopathy. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for education. The result indicates that there is no association between psychological distress and diabetic retinopathy. The odds ratio of 1.21 (CI 0.51-2.92) denotes strong evidence to fail to reject the null hypothesis. There is no association (p=0.64) between psychological distress and diabetic retinopathy among U.S. adults after controlling for age, educational level, and income. The result indicates that there is no association between age and diabetic retinopathy. The odds ratio of 0.98 (CI 0.92-1.04) denotes strong evidence to fail to reject the null hypothesis. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for age. The result indicates that there is no association between income and diabetic retinopathy. The odds ratio of 1.13 (CI 0.67-1.90) denotes strong evidence to fail to reject the null hypothesis. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for income.

Female

Table 1

Frequency and Percentage of Each of the Variables Within the Model

Variable	Frequency	Percentage/Mean
Diabetic retinopathy	3,199,802	24.8%
Education level		
Some high school	2,650,510	17.1%
High school graduate	5,683,292	37.5%
Some college	8,305,914	45.3%
Age (mean)	--	60.9
Family poverty-income-ratio (mean)	--	2.87
Psychological distress	2,296,994	29.7

Table 2

Odds Ratio for Each of the Variables

Variable	Odds ratio	95% confidence interval	*p*-value
Age (continuous)	0.98	0.92–1.04	0.30
Income	1.13	0.67–1.90	0.02
Education			
Some high school	1.18	0.22–6.42	0.83
High school graduate	0.70	0.20–2.40	0.83
Some college	Ref	Ref	----
Psychological distress	0.70	0.24–2.03	0.49

The result indicates that there is no association between education level and diabetic retinopathy. The odds ratio of 1.18 (CI 0.22-6.42) denotes strong evidence for the null hypothesis being true and it is not rejected.

The odds ratio of 0.70 (CI 0.20-2.40) denotes strong evidence to fail to reject the null hypothesis. There is no association between those who had some high school education, those who are high school graduates, and people with some college education developing diabetic retinopathy. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for education. The result indicates that there is no association between psychological distress and diabetic retinopathy. The odds ratio of 0.70 (CI 0.24-2.03) denotes strong evidence to fail to reject the null hypothesis. There is no association ($p=0.49$) between psychological distress and diabetic retinopathy among U.S. adults after controlling for age, educational level, and income. The result indicates that there is no association between age and diabetic retinopathy. The odds ratio of 0.99 (CI 0.96-1.01) denotes strong evidence to fail to reject the null hypothesis. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for age. The result indicates that there is an association between income and diabetic retinopathy. The odds ratio of 1.27 (CI 1.05-1.54) denotes strong evidence to fail to reject the null hypothesis for females. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for income.

Discussion

The odds ratios of 1.17 (CI 0.32-4.33) and 1.53 (CI 0.41-5.70) for males and 1.18 (CI 0.22-6.42) and 0.70 (CI 0.20-2.40) for females denotes strong evidence to fail to reject the null hypothesis. The results indicate that there is no association between education level and diabetic retinopathy. They do not show associations between those who had some high school education, those who are high school graduates, and people with some college education developing diabetic retinopathy. The results depict that there is no association between psychological distress and diabetic retinopathy when controlling for education, income, and age. Although there are recommended guidelines for patient education and regular screening for diabetic retinopathy, many people living with diabetes in the United States do not receive the ophthalmological care necessary for the prevention of blindness and visual impairment. The gap in care has several potential reasons such as the lack of care coordination between patients and healthcare providers, lack of effective communication, and lack of patient education (Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Patel et al., 2022). The gaps could lead to missed opportunities in disease progression prevention. Patient-focused education has an impact on self-efficacy and patient knowledge as they relate to the management and prevention of diabetic retinopathy. For patients to be able to effectively interact with healthcare providers, make informed decisions pertaining to their health, and to build the skills and knowledge necessary for behavior modifications, patient-directed education is a crucial aspect of diabetes self-management. There is an emerging trend of patient-directed education as an important feature of patient engagement as an important tool in the improvement of patient outcomes and in the healthcare reform context (Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Patel et al., 2022). Published research on the possibility of education to stimulate changes in self-efficacy and knowledge as a potential antecedent to behavioral change is scarce.

The odds ratio of 1.21 (CI 0.51-2.92) for males and 0.70 (CI 0.24-2.03) for females denotes strong evidence to fail to reject the null hypothesis and indicates that there is no association between psychological distress and diabetic retinopathy. The p-values of 0.64 for males and 0.49 for females show that there is no association between psychological distress and diabetic retinopathy among U.S. adults after controlling for age, educational level, and income. The incidence and prevalence rates of diabetic retinopathy are increasing with the rise of diabetes to epidemic proportions (Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Li et al., 2023). There is a need for a comprehensive understanding of the relationship between psychosocial outcomes and diabetic retinopathy to develop and implement effective interventions for diabetic patients. Some studies show a significant association between poor psychosocial functioning and diabetic retinopathy including higher odds of anxiety, depressive symptoms, and depression. Compared to people who do not have diabetic retinopathy, those with the disease show higher risks of depressive symptoms on the Mini Gastric Depression Scale with clinical variables, such as lipid levels, duration of diabetes, and Hemoglobin A1c (HbA1c), and demographics taken into consideration (Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Khoo et al., 2019; Li et al., 2023).

Compared to the individuals without signs of diabetic retinopathy or early stage of the disease, those with severe DR have worse psychosocial outcomes. Mental health decline becomes significantly steeper when the severity of the condition reaches the moderately nonproliferative diabetic retinopathy stage in at least one eye. Some studies report a link between poor vision and reduced visual acuity with significant impairment in psychosocial functioning. The relationship between emotional distress and visual symptoms is often associated with social restriction, activity limitation, inconvenience, and mobility (Antonetti et al., 2021; Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Li et al., 2023).

The result indicates that there is no association between age and diabetic retinopathy. The odds ratio of 0.98 (CI 0.92-1.04) for males and 0.99 (CI 0.96-1.01) for females denotes strong evidence to fail to reject the null hypothesis. The result shows that there is no association between psychological distress and diabetic retinopathy when controlling for age. In the United States, there are more than 40,000 new cases of diabetic retinopathy annually (Antonetti et al., 2021; Beaser et al., 2018; Boyd & Gregori, 2020; Li et al., 2023). For those who are over the age of 40, about 40.3% of them with diabetes are diagnosed with diabetic retinopathy; an estimated 8.2% of American adults with diabetes are diagnosed with advanced vision-threatening diabetic retinopathy (Antonetti et al., 2021; Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Boyd & Gregori, 2020; Li et al., 2023). The worse diabetes-related health outcomes in the United States are evident in the minority and underserved populations mainly because of the wide range of disparities which includes the social determinants of health such as access to screenings and healthcare, living conditions, geography, education, and socioeconomic status (Patel et al., 2022). Racial inequities are often prevalent in diabetic retinopathy screenings. In adults aged 50 years and older, diabetic retinopathy-induced visual impairment increases by 9.6% (Li et al., 2023; Patel et al., 2022). There is a positive correlation between diabetic retinopathy, its severity, and the duration of diabetic mellitus among individuals with poor glycemic control which explains increases in the prevalence of visual impairment and diabetic retinopathy in the elderly population.

The role of aging in the progression of diabetic retinopathy involves the senescence-associated secretory phenotype and the advanced glycation end product mechanisms. The mechanism of aging needs clarification but it entails the rising of tissue senescence from senescent cell accumulation. The association between senescence and diabetic retinopathy is a complex process. Several factors such as autophagy dysfunction, lipid metabolism, oxidative and endoplasmic reticulum stress, advanced glycation end products, and senescence-associated secretory phenotype are factors that induce cellular senescence and contribute to diabetic retinopathy development (Antonetti et al., 2021; Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Boyd & Gregori, 2020; Dai et al., 2021; Li et al., 2023).

In males, the result indicates that there is no association between income and diabetic retinopathy compared to the females where the result indicates that there is an association between income and diabetic retinopathy. The odds ratio of 1.13 (CI 0.67-1.90) in males (reject the null hypothesis) and 1.27 (CI 1.05-1.54) in females denotes strong evidence to fail to reject the null hypothesis. The results show that there is no association between psychological distress and diabetic retinopathy when controlling for income. Factors such as the lack of insurance coverage, minimal follow-up visits, and limited screening access, are the factors contributing to the higher prevalence of diabetic retinopathy in low-income diabetic populations. In low-income minority communities comprised of people without insurance coverage or those with public insurance coverage, the rates of diabetes and suspected diabetic retinopathy are high (Antonetti et al., 2021; Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Boyd & Gregori, 2020; Dai et al., 2021; Fenwick, 2011; Patel et al., 2022).

Decreased routine follow-up screenings and diminished participation in eye screening are associated with socioeconomic deprivation. It could worsen the outcomes of eye diseases such as retinopathy, glaucoma, and edema and lead to delayed diagnoses. For patients who are socioeconomically deprived, there could be a higher prevalence of sight-threatening proliferative diabetic retinopathy. Patients from low socioeconomic status with an onset of type 1 diabetes are more likely to develop diabetic retinopathy than those with the disease who do not come from low socioeconomic status (Patel et al., 2022). In the United States, diabetic retinopathy outcomes could improve with the implementation of programs geared towards increasing screening in low socioeconomic areas (Antonetti et al., 2021; Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Boyd & Gregori, 2020; Dai et al., 2021; Fenwick, 2011; Patel et al., 2022). There is a need for further research on the study of the role socioeconomic status plays in diabetic retinopathy prevalence in American populations.

Limitations

The study has some limitations. The lack of patient education and regular screening for diabetic retinopathy leads to the inability of many individuals living with diabetes in the United States not receive ophthalmological care needed for the prevention of visual impairment and blindness. The educational and screening factors and those lacking ophthalmological care were not controlled in the study because of the constraints of data availability and sample size. Factors such as lack of effective communication and lack of care between healthcare providers and patients, and the extent of diabetic retinopathy progression were not controlled in the study. Nonbinary and transgender respondents were not controlled for in the study because the sample size was not large enough for this category of respondents.

Implications

The study has implications for social change and the practice and discipline of public health as a profession. It provides new insights into ways that the improvement of the pathophysiology of diabetes and diabetic retinopathy could lead to the improvement of psychological distress. The study findings could facilitate the implementation of national policies focused on the empowerment or assistance of individual adherence to healthier lifestyles leading to the prevention of diabetes mellitus and diabetic retinopathy. The findings could also encourage individuals with the disease to enroll in classes for diabetes education and to seek additional information. The study would increase the awareness and importance of preventative care in public health practice and profession through evidence-based screenings and patient education. It could create a sense of urgency around the need for a coordinated management strategy which includes early diagnosis of the diabetes, glycemic control, and regular screening of the diabetic retinopathy risk factors. Preventive care would entail dilated eye exams, comprehensive ancillary tests, and patient education implemented through a multidisciplinary team that comprises ophthalmologists, retina specialists, and primary diabetes care providers such as diabetologists, endocrinologists, and primary care providers. The study might encourage additional research on diabetes-related laser eye surgery, intraocular drug therapy for vision improvement, and neuro-degeneration.

The study findings could facilitate stakeholder-sponsored grants when seeking funding for educational promotions pertaining to diabetic retinopathy and psychological distress. It could also provide information for population health planning and implementation in the public health field and for public health practitioners of all types, sizes, specialties, and expertise. With the investment of financial incentives in preventative services and the monitoring of the care continuum, the results of the study could enable public health organizations and practitioners who are proactive in population health planning and implementation to reach their goals (Romero, 2016). Healthcare organizations working with limited staff and budgets on the development and deployment of population health management programs, particularly on diabetes and diabetic retinopathy, could use the findings of the study. Healthcare providers could use the information from this study to change their workflow to enable them to properly manage patients with chronic diseases, such as diabetes, and other issues such as limited access to healthcare, and a high tendency of frequent visits to the hospital.

The results of the study could enable healthcare professionals to tackle some of the challenges they face when developing health programs and enable them to strive to achieving success in a fast-evolving healthcare industry (Romero, 2016). The study findings could be instrumental to the implementation of national policies encouraging the assistance or empowerment of adherence to healthier lifestyles leading to diabetes mellitus and the prevention of diabetic retinopathy.

Recommendations for Further Research

Within its limitations, the findings of this study highlight that with odds ratios of 1.20 (CI 0.39-3.70) and 1.0 (CI 0.47-2.13) and a p value of 0.06, there is no association between education levels, which includes some high school education, high school graduates, and some college, and diabetic retinopathy. Further research on patient education and regular screening for diabetic retinopathy in the United States for diabetic patients is necessary. Despite the recommended guidelines for patient education and frequent diabetic retinopathy screening, several diabetic individuals lack the proper ophthalmological care needed for visual impairment and blindness prevention. Researchers could explore the reasons for the gap in care such as lack of patient education, lack of care coordination between healthcare providers and patients, and lack of effective communication. The gaps could result in missed opportunities in the prevention of disease progression. There is a scarcity of published research pertaining to the possibility of education stimulating changes in knowledge and self-efficacy and leading to behavioral change.

The p value of 0.30 and the odds ratio of 0.98 (CI 0.96-1.01) indicate that there is no association between age and diabetic retinopathy. Although a p-value of 0.82 shows that there is no association between psychological distress and diabetic retinopathy among U.S. adults after controlling for age, educational level, and income, it is important to have a comprehensive understanding of the relationship between diabetic retinopathy and psychosocial outcomes for the development and implementation of effective interventions for diabetic patients. The odds ratio of 1.19 (CI 0.92-1.60) shows that there is no statistically significant association between psychological distress and diabetic retinopathy when controlling for income, but there is a need for further research on the study of the role socioeconomic status plays in the prevalence of diabetic retinopathy in the American population. Even though it could be a result of environmental and behavioral mechanisms, further research is important in determining the reason women tend to have more sensitivity to sociocontextual predictors, such as occupation, education, and income, for the risk of developing diabetes in the future (Mahs et al., 2022).

In men and women, there is often a misalignment between the circadian clock and social rhythms and between gender-dependent social timing and sex-dependent biological factors such as body composition that is associated with the pathogenesis of diabetes (Kautzy-Willer et al., 2019; Lien & Jiang, 2017). Researchers could conduct further research investigating the complexity of sex-dimorphic associations between sleep, work stress, and diabetes. The research findings could assist in implementing sex-specific prevention programs in some groups of shift workers. Compulsoriness of possible sexual dimorphism could be the focus of future studies. To gain a better understanding of the phenomenon, researchers should study the different biological and environmental factors associated with diabetic women having excess risks of cardiovascular disease. Sex differences are usually obvious in adrenergic responses to physical activity with higher effects in women that lead to variations in lipid metabolism and hypertrophic action (Mahs et al., 2022; Mamo et al., 2019; McLachlan & Gale, 2018). Researchers should endeavor to bridge the knowledge gap pertaining to sex dimorphism in human diabetic cardiomyopathy. They should get clarification on the sex-specific dose-response relationships between the risk of type 2 diabetes mellitus and alcohol consumption and the underlying mechanisms. Further research to gain clarification on the relationship between birth weight, pregnancy-related stress, offspring HPA axis activity, and the impact of programming adult diseases in young women and men, is also important (Hewage et al., 2020; Madhuri & Srilakshmi, 2019; Muche et al., 2020; Muhwava et al., 2019). They should conduct research on the study of the role socioeconomic status plays in the prevalence of diabetic retinopathy in the American population. They should conduct reviews to identify the need for the improvement of outcome measures and obtaining valid and meaningful results of the social and emotional impact of diabetic retinopathy and possible directions of research pertaining to computer adaptive testing. It is important to explore the possibilities of education in stimulating changes in knowledge and self-efficacy in behavioral changes. Patient education activities could occur on demand, face-to-face, or online. To obtain optimal ophthalmological care, education could empower patients to act as their own advocates.

Conclusion

There is no association between psychological distress and diabetic retinopathy among U.S. adults when controlling for education level, income, gender, and age. In males, the result indicates that there is no association between income and diabetic retinopathy compared to the females where the result shows that there is an association between income and diabetic retinopathy. Considering the study's limitations, many individuals living with diabetes in the United States do not receive the necessary ophthalmological care for the prevention of visual impairment and blindness despite the recommended guidelines for the regular screening of diabetic retinopathy and patient education. There are various reasons for the gap in care such as the lack of care coordination between healthcare providers and patients, lack of patient education, and lack of effective communication (Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Patel et al., 2022). The gaps could result in missed opportunities in the prevention of disease progression. The rise of diabetes to epidemic proportions correlates with the increasing prevalence and incidence rates of diabetic retinopathy (Atwany et al., 2022; Aziz et al., 2023; Beaser et al., 2018; Li et al., 2023). For the development and implementation of effective interventions for diabetic patients, there is a need for a comprehensive understanding of the relationship between diabetic retinopathy and psychosocial outcomes. The senescence-associated secretory phenotype and the advanced glycation end products mechanisms are involved in the role of aging in the progression of diabetic retinopathy.

References

Allen, M. (2017). Quantitative research. *The Sage Encyclopedia of Communication Research Methods*. https://dx.doi.org/10.4135/9781483381411.n476

Alperet, D. J., Rebello, S. A., Khoo, E. Y., Tay, Z., Seah, S. S., Tai, B., Tai, E., Emady-Azar, S., Chou, C. J., Darimont, C., Dam, R. M.V. (2019). The effect of coffee consumption on insulin sensitivity and other biological risk factors for type 2 diabetes: a randomized placebo-controlled trial. *The American Journal of Clinical Nutrition*, *111*(2), 448-458. https://doi.org/10.1093/ajcn/nqz306

American Diabetes Association. (2018). Economic costs of diabetes in the U.S. in 2017. Diabetes Care, 41 (4). DOI: 10.2337/dci18-0007

Ansari, R. M., Hosseinzadeh, H., & Zwar, N. (2016). A qualitative research on self-management of type 2 diabetes in middle-aged population of rural area of Pakistan. *International Education and Research Journal*, *2*(8), 62-65.

Ansari, P., Tabasumma, N., Snigdha, N. N., Siam, N. H., Panduru, R. V. N. R. S., Azam, S., Hannan, J. M. A., & Abdel-Wahab, Y. H. A. (2022). Diabetic retinopathy: An overview on mechanisms, pathophysiology and pharmacotherapy. *Diabetology, 3*, 159-175. https://doi.org/10.3390/diabetology3010011

Antonetti, D. A., Silva, P. S., & Stitt, A. W. (2021). Current understanding of the molecular and cellular pathology of diabetic retinopathy. *Nature Reviews Endocrinology, 17*, 195-206. https://doi.org/10.1038/s41574-020-00451-4

Atlanta Diabetes Association. (2020). Type 2 diabetes. *Endocrine Specialty Group*. https://atlantadiabetes.com/diabetes-care/type-2-diabetes/

Atwany, M. Z., Sahyoun, A. H., and Yaqub, M. (2022). Deep learning techniques for diabetic retinopathy classification: A survey. *IEEE Acess. 10*, 28642-28655. Doi: 10.1109/ACCESS.2022.3157632.

Aziz, T., Charoenlarpnopparut, C., & Mahapakulchai, S. (2023). Deep learning-based hemorrhage detection for diabetic retinopathy screening. *Scientific Reports*, *13*(1), Article 1479. https://doi.org/10.1038/s41598-023-28680-3

Banerjee, S., Burkholder, G., Szirony, G., & Sana, B. (2021). Potential health effects of loneliness in the pandemic era. *European Journal of Public Health*, *31*(Supplement_3), ckab165-122

Beaser, R.S., Turell, W.A., Howson, A. (2018). Strategies to improve prevention and management in diabetic retinopathy: Qualitative insights from mixed-methods study. *Diabetes Spectrum, 31*(1), 65-74. Doi: 10.2337/ds16-0043

Bora, A., Balasubramanian, S., Babenko, B., Virmani, S., Venugopalan, S., Mitani, A., Marinho, G., Cuadros, J., Ruamviboonsuk, P., Corrado, G., Peng, L., Webster, D., Varadarajan, A., Hammel, N., Liu, Y., & Bavishi, P. (2021). Predicting the risk of developing diabetic retinopathy using deep learning. *The Lancet Digital Health, 3*(1), e10-e19. https://doi.org/10.1016/S2589-7500(20)30250-8

Boyd, K., & Gregori, N. Z. (2020). What is diabetic retinopathy? *American Academy of Ophthalmology*. What Is Diabetic Retinopathy? - American Academy of Ophthalmology (aao.org)

Centers for Disease Control and Prevention. (2017). National health and nutrition examination survey. 2015-2016 data documentation, codebook, and frequencies. *Mental Health- Depression Screener (DPQ_1)*. NHANES 2015-2016: Mental Health - Depression Screener Data Documentation, Codebook, and Frequencies (cdc.gov)

Centers for Disease Control and Prevention. (2019). Type 2 diabetes. *United States Department of Health and Human Services*. https://www.cdc.gov/diabetes/basics/type2.html

Centers for Disease Control and Prevention. (2021). The social-ecological model: A framework for prevention. Violence prevention. *United States Department of Health and Human Services*. The Social-Ecological Model: A Framework for Prevention |Violence Prevention|Injury Center|CDC

Centers for Disease Control and Prevention. (2020). What is diabetes? *United States Department of Health and Human Services*. What is diabetes? | CDC

Centers for Disease Control and Prevention. (2021). *Diabetes*. Division of Diabetes Translation | CDC

Centers for Disease Control and Prevention. (2020). *National Diabetes Statistics Report 2020*. National Diabetes Statistics Report 2020. Estimates of diabetes and its burden in the United States. (cdc.gov)

Cherchi, S., Gigante, A., Spanu, M. A., Contini, P., Meloni, G., Fois, M. A., Pistis, D., Pilosu, R. M., Lai, A., Ruin, S., Campesi, I., & Tonolo, G. (2020). Sex-gender differences in diabetic retinopathy. *Diabetology, 1*, 1-

10. https://doi.org/10.3390/diabetology1010001

Cleveland Clinic. (2021). Diabetes: An Overview. *100 Years of Cleveland Clinic*. Diabetes: Types, risk factors, symptoms, tests, treatments & prevention (clevelandclinic.org)

Cleveland Clinic. (2022). Optical coherence tomography. *100 Years of Cleveland Clinic*. Diagnostics: Optical Coherence Tomography (clevelandclinic.org)

Curry, A. (2020). Fatty liver and type 2 diabetes. *University of Florida Diabetes Institute*. Fatty Liver and Type 2 Diabetes » Diabetes Institute » College of Medicine » University of Florida (ufl.edu)

Dai, L., Wu, L., Li, H., Cai, C., Wu, Q., Kong, H., Liu, R., Wang, X., Hou, X., Liu, Y., Long, X., Wen, Y., Lu, L., Shen, Y., Chen, Y., Shen, D., Yang, X., Zou, H., Sheng, B., & Jia, W. (2021). A deep learning system for detecting diabetic retinopathy across the disease spectrum. *Nature Communications. 12*(3242). https://doi.org/10.1038/s41467-021-23458-5

De Ritter, R., De Jong, M., Vos, R.C. (2020). Sex differences in the risk of vascular disease associated with diabetes. *Biology of Sex Differences*. *11* (1). https://doi.org/10.1186/s13293-019-0277-z

Demmin, D. L., & Silverstein, S. M. (2020). Visual impairment and mental health: Unmet needs and treatment options. *Journal of Clinical Ophthalmology*, *14*, 4229-4251. https://doi.org/10.2147/OPTH.S258783

DiaGundluru, N., Rajput, D. S., Lakshmanna, K., Kaluri, R., Shorfuzzaman, M., Uddin, M., and Khan, M. A. R. (2022). Enhancement of detection of diabetic retinopathy using harris hawks optimization with deep learning model. *Computational Intelligence and Neuroscience*. *2022*. https://doi.org/10.1155/2022/8512469

Doheny, K. (2020). Pancreatic fat: Lifestyle habits count more than genetics. *Endocrineweb*. Pancreatic Fat: Lifestyle Habits Count More Than Genetics (endocrineweb.com)

Emani, S., Peters, E., Desai, S., Karson, A. S. Lipsitz, S. R., LaRocca, R., Stone, J., Suric, V., Wald, J.S., Wheeler, A., Williams, D.H., & Bates, D.W. (2018). Perceptions of adopters versus non-adopters of a patient portal: an application of diffusion of innovation theory. *Journal of Innovation in Health Informatics*, *25*(3), 149-157. http://dx.doi.org/10.14236/jhi.v25i3.991

Farooq, M. S., Arooj, A., Alroobaea, R., Baqasah, A. M., Singh, D., and Sardar, R. (2022). Untangling computer-aided diagnostic system for screening diabetic retinopathy based on deep learning techniques. *Sensors*, *22*(5), Article 1803. https://doi.org/10.3390/s22051803

Fenwick, E., Rees, G., Pesudovs, K., Dirani, M., Kawasaki, R., Wong, T. Y., and Lamoureux, E. (2011). Social and emotional impact of diabetic retinopathy: a review. *Clinical & Experimental Ophthalmology*. *40*(1), 27-38. https://doi.org/10.1111/j.1442-9071.2011.02599.x

Forrester, J. V., Kuffova, L., & Delibegovic, M. (2020). The role of inflammation in diabetic retinopathy. (2020). *Frontiers in Immunology*, *11*. https://doi.org/10.3389/fimmu.2020.583687

Gadekallu, T. R., Khare, N., Bhattacharya, S., Singh, S., Maddikunta, P. K. R, & Srivastava, G. (2020). Deep neural networks to predict diabetic retinopathy. *Journal of Ambient Intelligence and Humanized Computing*. https://doi.org/10.1007/s12652-020-01963-7

Gomulka, K., Ruta, M. (2023). The role of inflammation and therapeutic concepts in diabetic retinopathy- A short review. *International Journal of Molecular Sciences. 24*(2). 1024. https://doi.org/10.3390/ijms24021024

Grzybowski, A., Brona, P., Lim, G., Ruamviboonsuk, P., Tan, G. S. W., Abramoff, M., and Ting, D. S. W. (2020). Artificial intelligence for diabetic retinopathy screening: A review. *Eye*, *34*, 451-460. https://doi.org/10.1038/s41433-019-0566-0

Hayati, M., Muchtar, K., Roslidar, Maulina, N., Syamsuddin, I., Elwirehardja, G., N., Pardamean, B. (2023). Impact of CLAHE-based image enhancement for diabetic retinopathy classification through deep learning. Procedia *Computer Science, 216*, 57-66. https://doi.org/10.1016/j.procs.2022.12.111

Hewage S, Audimulam J, Sullivan E, Chi C, Yew TW, Yoong J. (2020). Barriers to gestational diabetes management and preferred interventions for women with gestational diabetes in singapore: Mixed methods study. *JMIR Formative Research. 4*(6). Barriers to Gestational Diabetes Management and Preferred Interventions for Women With Gestational Diabetes in Singapore: Mixed Methods Study - PMC (nih.gov)

International Diabetes Federation. (2022). Diabetes around the world in 2022. *Diabetes Atlas*. https://www.diabetesatlas.org/en/sections/worldwidetoll-of-diabetes.ht

International Diabetes Federation. (2023). Understanding diabetes. International Diabetes Federation - Home (idf.org)

Jiwani, N., Gupta, K., and Afreen, N. (2022). A convolutional neural network approach for diabetic retinopathy classification. *IEEE 11th International Conference on Communication Systems and Network Technologies (CSNT)*. 357-361. Doi: 10.1109/CSNT54456.2022.9787577

Kang, Q., & Yang, C. (2020). Oxidative stress and diabetic retinopathy: Molecular mechanisms, pathogenetic role and therapeutic implications. *Redox*, *37*, 2213-2317. https://doi.org/10.1016/j.redox.2020.101799

Kautzky-Willer, A., Harreiter, J., Pacini, G. (2016). Sex and gender differences in risk, pathophysiology and complications of type 2 diabetes mellitus. *National Library of Medicine. National Center for Biotechnology Information. 37*(3). 278-316. Doi: 10.1210/er.2015-1137

Kautzy-Willer, A., Harreiter, J., Abrahamian, H., Weitgasser, R., Fasching, P., Hoppichler, F., Lechleitner, M. (2019). Gender-specific aspects of prediabetes and diabetes mellitus-clinical recommendations. *SpringerLink. 131* (1), 221-228. Gender-specific aspects of prediabetes and diabetes mellitus – clinical recommendations (Update 2019) | SpringerLink

Khoo, K., Man, R.E.K., Rees, G., Gupta, P., Lamoureux, E.L., Fenwick, E. K. (2019). The relationship between diabetic retinopathy and psychosocial functioning: a systematic review. *Quality of Life Research, 28*, (2017-2039). https://doi.org/10.1007/s11136-019-02165-1

Kovoor, E., Chauhan, S. K., and Hajrasouliha, A. (2022). Role of inflammatory cells in pathophysiology and management of diabetic retinopathy. *Survey of Ophthamology*. *67* (6). 1563-1573. https://doi.org/10.1016/j.survophthal.2022.07.008

Kowluru, R. A. (2023). Cross talks between oxidative stress, inflammation and epigenetics in diabetic retinopathy. *Cells*, *12*(2), 300. https://doi.org/10.3390/cells12020300

Lauffenburger, J. C., Lewey, J., Jan, S., Lee, J., Ghazinouri, R., & Choudhry, N. K. (2020). Association of potentially modifiable diabetes care factors with glycemic control in patients with insulin-treated type 2 diabetes. *JAMA Network Open, 3*(1), e1919645– e1919645. https://doi.org/10.1001/jamanetworkopen.2019.19645

Li, F., Wang, Y., Xu, T., Dong, L., Yan, L., Jiang, M., Zhang, X., Jiang, H., Wu, Z., & Zou, H. (2022). Deep learning-based automated detection for diabetic retinopathy and diabetic macular oedema in retinal fundus photographs. *Eye, 36*, 1433-1441. https://doi.org/10.1038/s41433-021-01552-8

Li, Q., Wang, M., Li, X., Shao, Y. (2023). Aging and diabetic retinopathy: Inherently intertwined pathophysiological processes. *Experimental Gerontology 175* (112138), 0531-5565. https://doi.org/10.1016/j.exger.2023.112138

Li, Q., Chang, Y., Zhang, K., Chen, H., Tao, S., and Zhang, Z. (2020). Implication of the gut microbiome composition of type 2 diabetic patients from northern China. *Sci. Rep. 10* (1). Doi: 10.1038/s41598-020-62224-3

Li, X., Jiang, Y., Zhang, J., Li, M., Luo, H., and Yin, S. (2022). Lesion-attention pyramid network for diabetic retinopathy grading. *Artificial Intelligence in Medicine*. 126. https://doi.org/10.1016/j.artmed.2022.102259

Lien, A. S., & Jiang, Y. D. (2017). Integration of diffusion of innovation theory into diabetes care. *Journal of diabetes investigation*, *8*(3), 259-260. Doi: 10.1111/jdi.12568

Madhuri, C., & Srilakshmi, B. (2019). Retrospective study on prevalence, risk factors, maternal and fetal outcome in gestational diabetes mellitus. *International Archives of Integrated Medicine*, *6*(11), 94-98. iaim_2019_0611_14.pdf (iaimjournal.com)

Magne, F., Gotteland, M., Gauthier, L., Zazueta, A., Pesoa, S., Navarrete, P., and Balamurugan, R. (2020).The firmicutes/bacteroidetes ratio: A relevant marker of gut dysbiosis in obese patients? *Nutrients, 12*(5), 1474. Doi: 10.3390/nu12051474

Mahs, M., Pithan, J. S., Bergmann, I., Gabrys, L., Graf, J., Holzemann, A., Van Laerhoven, K., Otto-Hagemann, S., Popescu, M. L., Schwermann, L., Wenz, B., Pahmeier, I., Teti, A. (2022). Activity tracker-based intervention to increase physical activity in patients with type 2 diabetes and healthy individuals: study protocol for a randomized controlled trial. *BioMed Central*, *23*, 617. Activity tracker-based intervention to increase physical activity in patients with type 2 diabetes and healthy individuals: study protocol for a randomized controlled trial | Trials | Full Text (biomedcentral.com)

Mamo, Y., Bekele, F., Nigussie, T., & Zewudie, A. (2019). Determinants of poor glycemic control among adult patients with type 2 diabetes mellitus in Jimma University Medical Center, Jimma zone, south west Ethiopia: A case control study. *BMC Endocrine Disorders*, *19*(1), 91. https://doi.org/10.1186/s12902-019-0421-0

McLachlan, K., & Gale, C. R. (2018). The effects of psychological distress and its interaction with socioeconomic position on risk of developing four chronic diseases. *Journal of psychosomatic research, 109*, 79-85. doi: 10.1016/j.jpsychores.2018.04.004

Mikkola, I., Hagnäs, M., Hartsenko, J., Kaila, M., & Winell, K. (2020). A personalized care plan is positively associated with better clinical outcomes in the care of patients with type 2 diabetes: A cross-sectional real-life study. *Canadian Journal of Diabetes, 44*(2), 133– 138. https://doi.org/10.1016/j.jcjd.2019.05.003

Muche, A. A., Olayemi, O. O., & Gete, Y. K. (2020). Effects of gestational diabetes mellitus on risk of adverse maternal outcomes: a prospective cohort study in Northwest Ethiopia. *BMC Pregnancy & Childbirth, 20*(1), 1-13. Effects of gestational diabetes mellitus on risk of adverse maternal outcomes: a prospective cohort study in Northwest Ethiopia | BMC Pregnancy and Childbirth | Full Text (biomedcentral.com)

Muhwava, L. S., Murphy, K., Zarowsky, C., & Levitt, N. (2019). Experiences of lifestyle change among women with gestational diabetes mellitus (GDM): A behavioural diagnosis using the COM-B model in a low-income setting. *Plos One Journal*, *14*(11). https://doi.org/10.1371/journal.pone.0225431

National Institute of Diabetes and Digestive and Kidney Diseases. (n.d.). Diabetes. Diabetes | NIDDK (nih.gov)

National Institutes of Health. (2019). *Diabetic retinopathy*. National Eye Institute. Diabetic Retinopathy | National Eye Institute (nih.gov)

Parthasharathi, G. U., Kumar, K. V., Premnivas, R., and Jasmine, K. (2022). Diabetic retinopathy detection using machine learning. *Journal of Innovative Image Processing*. *4*(1), 26-33. Doi:10.36548/jiip.2022.1.003

Patel, D., Ananthakrishnan, A., Lin, T., Channa, R., Liu, T.Y.A, Wolf, R.M. (2022). Social determinants of health and impact on screening, prevalence, and management of diabetic retinopathy in adults: A narrative review. *Journal of Clinical Medicine, 11*(23), 7120. Doi: 10.3390/jcm11237120

Poly, T. N., Islam, M., Walther, B. A., Lin, M., C., & Li, Y.-C. (2023). Artificial intelligence in diabetic retinopathy: Bibliometric analysis. *Computer Methods and Programs in Biomedicine*. *231*, Article 107358. https://doi.org/10.1016/j.cmpb.2023.107358

Porter, D. (2022). What is fluorescein angiography. *American Academy of Ophthalmology*. What Is Fluorescein Angiography? - American Academy of Ophthalmology (aao.org)

Prasad, R., Floyd, J. L., Dupont, M., Harbour, A., Agyeiwaah, Y. A., Bediako, B. A., Chakraborty, D., Kichler, K., Rohella, A., Calzi, S. L., Lammendella, R., Wright, J., Boulton, M. E., Oudit, G. Y., Raizada, M. K., Stevens, B. R., Li, Q., Grant, M. B. (2023). Maintenance of enteral ACE2 prevents diabetic retinopathy in type 1 diabetes. *Circulation Research. 132* (1). https://doi.org/10.1161/CIRCRESAHA.122.322003

Qiao, L., Zhu, Y., & Zhou, H. (2020). Diabetic retinopathy detection using prognosis of microaneurysm and early diagnosis system for non-proliferative diabetic retinopathy based on deep learning algorithms. *IEEE Access*, *8*, 104292-104302. Doi: 10.1109/ACCESS.2020.2993937

Qummar, S., Khan, F. G., Shah, S., Khan, A., Shamshirband, S., Rehman, Z. U., Khan, I. A., and Jadoon, W. (2019). A deep learning ensemble approach for diabetic retinopathy detection. *IEEE*, *7*, 150530-150539. Doi: 10.1109/ACCESS.2019.2947484

Regeneron Pharmaceuticals. (2021). About diabetic retinopathy. *Now Eye See*. Now Eye See | Diabetic Retinopathy

Rezazadeh-Gavgani, E., Oladghaffari, M., Bahramian, S., Majidazar, R., & Dolati, S. (2023). MicroRNA-21: A critical underestimated molecule in diabetic retinopathy. *Gene, 859*. https://doi.org/10.1016/j.gene.2023.147212

Romero, L. F. (2016). Diabetes: The current state of affairs from a population management view. *MLO: Medical Laboratory Observer*, *48*(8), 12-20.

https://ezp.waldenulibrary.org/login?url=https://search.ebscohost.com/login.aspx?

Ruamviboonsuk, P., Tiwari, R., Sayres, R., Nganthavee, V., Hemarat, K., Kongprayoon, A., Raman, R., Levinstein, B., Liu, Y., Schaekermann, M., Lee, R., Virmani, S., Widner, K., Chambers, J., Hersch, F., Peng, L., and Webster, D. (2022). Real-time diabetic retinopathy screening by deep learning in a multisite national screening programme: a prospective interventional cohort study. *The Lancet Digital Health*. *4* (4), e235-e244. https://doi.org/10.1016/S2589-7500(22)00017-6

Saadane, A., Veenstra, A. A., Minns, M. S., Tang, J., Du, Y., Elghazali, F. A., Lessieur, E. M., Pearlman, E., & Kern, T. S. (2023). *Diabetologia. 66*, 590-602. https://doi.org/10.1007/s00125-022-05860-w

Setia, M. S. (2016). Methodology series module 3: Cross-sectional Studies. *Indian Journal of Dermatology*, *61*(3), 261-264. https://doi.org/10.4103/0019-5154.182410

Stanford.edu. (n.d.). *Patient health questionnaire (PHQ-9)*. Patient Health Questionnaire (PHQ-9) (stanford.edu)

Teo, Z. L., Tham, Y. C., Yu, M., Chee, M. L., Rim, T. H., Cheung, N., Bikbov, M. M., Wang, Y. X., Tang, Y., Lu, Y., Wong, I. Y., Ting, D. S. W., Tan, G. S. W., Jonas, J. B, Sabanayagam, Wong, T. Y., Cheng, C. Y. (2020). Global prevalence of diabetic retinopathy and protection of burden through 2045: Systemic review and meta-analysis. *Ophthalmology, 128*(11), 1580-1591. https://doi.org/10.1016/j.ophtha.2021.04.027

Torpy, J. M., Glass, T. J., Glass, R. M. (2007). Retinopathy. *Journal of American Medical Association (JAMA), 298*(8), 944. Doi:10.1001/jama.298.8.944

Tymchenko, B., Marchenko, P., and Spodarets, D. (2020). Deep learning approach to diabetic retinopathy detection. *Cornell University. arXiv*. https://doi.org/10.48550/arXiv.2003.02261

University of North Carolina. (n.d.). Diabetes Questionnaire. *Campus Health*. diabetes_questionnaire (unc.edu)

Vitger, T., Langberg, H., Grabowski, D. (2017). Mutual involvement in families with type 2 diabetes through web-based health care solutions: Quantitative survey study of family preferences, challenges, and potentials. *Journal of Medical Internet Research Publication (JMIR), 2*(2), 2371-4379. Doi: 10.2196/diabetes.7456

Vujosevic, S, Aldington, S. J., Silva, P., Hernandez, C., Scanlon, P., Peto, T., & Simo, R. (2020). Screening for diabetic retinopathy: new perspectives and challenges. *The Lancet Diabetes & Endocrinology, 8*(4), 337-347. https://doi.org/10.1016/S2213-8587(19)30411-5

Wang, M., Yang, Y., Liao, Z. (2020). Diabetes and cancer: Epidemiological and biological links. *World Journal of Diabetes*. *11*(6), 227-238. Doi: 10.4239/wjd.v11.i6.227

Winston-Salem State University. (n.d.). Quantitative design. *Key Elements of a Research Proposal*. Key Elements of a Research Proposal - Quantitative Design (wssu.edu)

Zhang, H., Wang, Q., He, S., Wu, K., Ren, M., Dong, H., Di, J., Yu, Z., & Huang, C. (2020). Ambient air pollution and gestational diabetes mellitus: A review of evidence from biological mechanisms to population epidemiology. *Science of The Total Environment. 719*. https://doi.org/10.1016/j.scitotenv.2020.137349

Zheng, D., Li, N., Hou, R., Zhang, X., Wu, L., Sundquist, J., Sundquist, K., & Ji, J. (2023). Glucagon-like peptide-1 receptor agonists and diabetic retinopathy: nationwide cohort and mendelian randomization studies. *BMC Medicine, 21* (40). https://doi.org/10.1186/s12916-023-02753-6

Zhou, A., Y., Taylor, B., E., Barber, K., G., Lee, C., A., Taylor, Z., R., R., Howell, S., J., Taylor, P., R. (2023). Anti-IL17A halts the onset of diabetic retinopathy in type I and II diabetic mice. *International Journal of Molecular Sciences. 24*, 1347. https://doi.org/10.3390/ijms24021347

Part 3: Summary

The findings in the three studies highlighted and confirmed the social problem of the burden of the association between psychological distress, gender, and diabetic retinopathy among U.S. adults after controlling for age, educational level, and income. The first study examined the association between psychological distress and diabetic retinopathy among U.S. adults after controlling for age, educational level, and income. The second study determined the role of gender in diabetic retinopathy after controlling for age, educational level, and income. The third study analyzed the effect of modification of gender on psychological distress in diabetes-related retinopathy. Considering its dedication to publicizing original work pertaining to program evaluations, research methods, and research in the public health field, the *American Journal of Public Health* (AJPH) is ideal for this manuscript's publication. Its mission of advancing public health education, research, practice, and policy makes it a suitable outlet to publish data on the association between psychological distress, gender, and diabetic retinopathy among U.S. adults after controlling for age, educational level, and income.

Diabetic retinopathy is a common microvascular complication associated with diabetes that can cause blindness. The risk factors of diabetic retinopathy are the longer duration of diabetes, hyperglycaemia, dyslipidaemia, and hypertension (Ansari et al., 2022; Antonetti et al., 2021). Individuals could develop diabetic retinopathy after years of suffering from gestational, type 1, or type 2 diabetes. The disease diagnosis is based on the presence and severity of objective clinical signs that include the appearance of tortuous, superfluous, and new blood vessels; venous beading or intraretinal microvascular abnormalities; cotton wool spots; microaneurysms; and intraretinal hemorrhages (Aziz et al., 2023; Boyd & Gregori, 2020; Farooq et al., 2022; Grzybowski et al., 2020). The different stages of diabetic retinopathy are proliferative diabetic retinopathy (PDR), severe nonproliferative diabetic retinopathy, moderate nonproliferative diabetic retinopathy, and mild nonproliferative diabetic retinopathy (NPDR). In moderate and mild nonproliferative stages of diabetic retinopathy, visual acuity, and visual functioning are often not affected, but as the disease progresses to PDR or NPDR, visual impairment, leading to difficulty with mobility, daily tasks, and driving, can occur (Kang & Yang, 2020; Li et al., 2022; National Institutes of Health, 2019; Poly et al., 2023).

The study examined the relationship between psychological distress, gender, and diabetic retinopathy among adults in the United States, while controlling for age, educational level, and income, through a retrospective, quasi-experimental study using descriptive data analysis, multivariate logistic regression of secondary data, and bivariate analysis using chi-square test of independence and included the statistical information at the end of each section. The significance level for the complex samples logistic regression and chi-squared analysis was set at 0.05. The measurement for the individual level variable, sex, was set for females and males. The places of residence or geographic location covered in the study were grouped in districts found in different parts of the United States. The measurement for age was at the individual level based on the Medical Subject Headings (MeSH) for adults, which are (age 19–44 years), Middle Aged (age 45–64 years), Aged (age 65–79 years), and Aged 80 and above. Already collected data on the population level from reputable agencies was instrumental in the study. Depending on the tertiles of the range of data, it was transformed into nominal data in the order of low, medium, and high. According to the data collection method, some variables were measured at the population level within different districts and by years. Education was ranked based on the highest level attained and grouped in the categories of no education, primary (1—some high school education), secondary (2—high school graduate), and tertiary (3—some college education) levels measured at a population level. The categories of no education were in measurements of low, medium, and high. The categories of less than secondary education were in low, medium, and high categories. Secondary education was in low, medium, and high categories. Tertiary education was in low, medium, and high categories.

The variables for depression and psychological distress measurement were obtained from NHANES. The Patient Health Questionnaire (PHQ-9) measures how often individuals experience the following problems: feeling down, depressed, or hopeless; taking little pleasure or interest in doing things; having little energy or feeling tired; sleeping too much or trouble staying or falling asleep; feeling bad about oneself or that one is a failure or has let oneself or one's family down; overeating or poor appetite; speaking or moving too slow to the noticeability of others, or being so restless or fidgety and moving around more than usual; or thoughts of being better off hurting oneself or dying (CDC, 2017). The responses are measured in days and in categories such as *not at all* (0), *several days* (1), *more than half days* (2), and *nearly every day* (3). For each checked-off problem on the PHQ-9 patient depression questionnaire, respondents indicate how the problems made it difficult for them to do their work, perform duties at home, or get along with other individuals. The categories of their responses are as follows: *not difficult at all*, *somewhat difficult*, *very difficult*, and *extremely difficult*. Checks of at least four on the list indicate a depressive disorder. Major depressive disorders have at least five affirmative responses in the *very difficult* and *extremely difficult* categories and also in the *several days* category for the thoughts of death or hurting oneself section. The total scores as they correspond with the severity of depression are as follows: minimal depression (1–4), mild depression (5–9), moderate depression (10–14), moderately severe depression (15–19), and severe depression (20–27; Stanford.edu, n.d.).

Considering the reduction of the study time, existence of large datasets of relevant information, the elimination of one-on-one interactions with patients and the inclusion of variables at the population and individual levels, the chosen study design was the most practical. Assessment of the data was done through the CDC website. Walden University granted ethical approval for the study.

A *p*-value of 0.87 showed that there is no association between psychological distress and diabetic retinopathy among U.S. adults after controlling for age, educational level, and income. The odds ratio of 0.96 (CI 0.60–1.56) denoted strong evidence to fail to reject the null hypothesis. The result showed that although the literature on the topic indicated a link between psychosocial functioning and diabetic macular edema (DME) or diabetic retinopathy, the direction and extent of the association is uncertain. Overall, there is no association between psychological distress, gender, and diabetic retinopathy among U.S. adults when controlling for education level, income, and age.

The study has implications for social change and the practice and discipline of public health as a profession. It provides new insights into ways that the improvement of the pathophysiology of diabetes and diabetic retinopathy could lead to the improvement of psychological distress. The findings could encourage diabetics to enroll in classes for diabetes education and to seek additional information pertaining to the management of the disease. The study has some limitations. The lack of patient education and regular screening for diabetic retinopathy leads to many individuals living with diabetes in the United States not receiving the ophthalmological care needed for the prevention of visual impairment and blindness. Further research on patient education and regular screening for diabetic retinopathy in the United States for diabetic patients is necessary. Researchers could explore the reasons for the gap in care such as lack of patient education, lack of care coordination between healthcare providers and patients, and lack of effective communication.

Consolidated References

Ansari, P., Tabasumma, N., Snigdha, N. N., Siam, N. H., Panduru, R. V. N. R. S., Azam, S., Hannan, J. M. A., & Abdel-Wahab, Y. H. A. (2022). Diabetic retinopathy: An overview on mechanisms, pathophysiology and pharmacotherapy. *Diabetology, 3*, 159-175. https://doi.org/10.3390/diabetology3010011

Antonetti, D. A., Silva, P. S., & Stitt, A. W. (2021). Current understanding of the molecular and cellular pathology of diabetic retinopathy. *Nature Reviews Endocrinology, 17*, 195-206. https://doi.org/10.1038/s41574-020-00451-4

Aziz, T., Charoenlarpnopparut, C., & Mahapakulchai, S. (2023). Deep learning-based hemorrhage detection for diabetic retinopathy screening. *Scientific Reports, 13*(1), Article 1479. https://doi.org/10.1038/s41598-023-28680-3

Boyd, K., & Gregori, N. Z. (2020). *What is diabetic retinopathy?* American Academy of Ophthalmology. Diabetic Retinopathy: Causes, Symptoms, Treatment - American Academy of Ophthalmology (aao.org)

Centers for Disease Control and Prevention. (2017). *National Health and Nutrition Examination Survey (NHANES). 2015-2016 data documentation, codebook, and frequencies*. *Mental Health—Depression Screener (DPQ_1)*. 2015-2016 Questionnaire Data - Continuous NHANES (cdc.gov)

Farooq, M. S., Arooj, A., Alroobaea, R., Baqasah, A. M., Singh, D., & Sardar, R. (2022). Untangling computer-aided diagnostic system for screening diabetic retinopathy based on deep learning techniques. *Sensors*, *22*(5), Article 1803. https://doi.org/10.3390/s22051803

Grzybowski, A., Brona, P., Lim, G., Ruamviboonsuk, P., Tan, G. S. W., Abramoff, M., & Ting, D. S. W. (2020). Artificial intelligence for diabetic retinopathy screening: A review. *Eye, 34*, 451-460. https://doi.org/10.1038/s41433-019-0566-0

Kang, Q., & Yang, C. (2020). Oxidative stress and diabetic retinopathy: Molecular mechanisms, pathogenetic role and therapeutic implications. *Redox*, *37*, 2213-2317. https://doi.org/10.1016/j.redox.2020.101799

Li, F., Wang, Y., Xu, T., Dong, L., Yan, L., Jiang, M., Zhang, X., Jiang, H., Wu, Z., & Zou, H. (2022). Deep learning-based automated detection for diabetic retinopathy and diabetic macular oedema in retinal fundus photographs. *Eye, 36*, 1433-1441. https://doi.org/10.1038/s41433-021-01552-8

National Institutes of Health. (2019). *Diabetic retinopathy*. National Eye Institute. Diabetic Retinopathy | National Eye Institute (nih.gov)

Poly, T. N., Islam, M., Walther, B. A., Lin, M., C., & Li, Y.-C. (2023). Artificial intelligence in diabetic retinopathy: Bibliometric analysis. *Computer Methods and Programs in Biomedicine*. *231*, Article 107358. https://doi.org/10.1016/j.cmpb.2023.107358

Appendix: Additional Tables

Manuscript 1

Categorical Variable Information

		Weighted Count	Weighted Percent
Modified Diabetic Retinopathy[a]	.00	13199902.294	79.3%
	1.00[b]	3439814.841	20.7%
Psychological Distress	.00	12038700.003	72.3%
	1.00	4601017.133	27.7%
Modified Education Level	1.00	2650510.830	15.9%
	2.00	5683292.258	34.2%
	3.00	8305914.048	49.9%
Population Size		16639717.136	100.0%

a. Dependent Variable

b. Reference Category

Pseudo R Squares

Cox and Snell	.019
Nagelkerke	.030
McFadden	.019

Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), Psychological_Distress, RIDAGEYR, INDFMPIR, Education

Covariate Information

	Mean
Age in years at screening	60.89
Ratio of family income to poverty	2.8679

Tests of Model Effects

Source	df1	df2	Wald F	Sig.
(Corrected Model)	5.000	11.000	2.204	.128
(Intercept)	1.000	15.000	5.465	.034
Psychological_Distress	1.000	15.000	.027	.871
RIDAGEYR	1.000	15.000	1.165	.298
INDFMPIR	1.000	15.000	2.048	.173
Education	2.000	14.000	.049	.952

Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), Psychological_Distress, RIDAGEYR, INDFMPIR, Education

Odds Ratios 1[a]

		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval	
				Lower	Upper
Psychological Distress	.00 vs. 1.00	.00	.963	.595	1.560

Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), Psychological_Distress, RIDAGEYR, INDFMPIR, Education

a. Factors and covariates used in the computation are fixed at the following values: Psychological Distress=1.00; Modified Education Level=3.00; Age in years at screening=60.89; Ratio of family income to poverty=2.8679

Odds Ratios 2[a]

		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval	
				Lower	Upper
Modified Education Level	1.00 vs. 3.00	.00	1.179	.370	3.753
	2.00 vs. 3.00	.00	.964	.443	2.097

Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), Psychological_Distress, RIDAGEYR, INDFMPIR, Education

a. Factors and covariates used in the computation are fixed at the following values: Psychological Distress=1.00; Modified Education Level=3.00; Age in years at screening=60.89; Ratio of family income to poverty=2.8679

Odds Ratios 3[a]

	Units of Change	Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval	
				Lower	Upper
Age in years at screening	1.000	.00	.985	.956	1.015

Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), Psychological_Distress, RIDAGEYR, INDFMPIR, Education

a. Factors and covariates used in the computation are fixed at the following values: Psychological Distress=1.00; Modified Education Level=3.00; Age in years at screening=60.89; Ratio of family income to poverty=2.8679

Odds Ratios 4[a]

Units of Change		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval Lower	Upper
Ratio of family income to poverty	1.000	.00	1.202	.914	1.582

Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), Psychological_Distress, RIDAGEYR, INDFMPIR, Education

a. Factors and covariates used in the computation are fixed at the following values: Psychological Distress=1.00; Modified Education Level=3.00; Age in years at screening=60.89; Ratio of family income to poverty=2.8679

Manuscript 2

Categorical Variable Information

		Weighted Count	Weighted Percent
Modified Diabetic Retinopathy[a]	.00	13199902.294	79.3%
	1.00[b]	3439814.841	20.7%
Modified Education Level	1.00	2650510.830	15.9%
	2.00	5683292.258	34.2%
	3.00	8305914.048	49.9%
Psychological Distress	.00	12038700.003	72.3%
	1.00	4601017.133	27.7%
Gender	1	8234887.954	49.5%
	2	8404829.181	50.5%
Population Size		16639717.136	100.0%

a. Dependent Variable

b. Reference Category

Pseudo R Squares

Cox and Snell	.029
Nagelkerke	.045
McFadden	.029

Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress, RIAGENDR

Covariate Information

	Mean
Age in years at screening	60.89
Ratio of family income to poverty	2.8679

Tests of Model Effects

Source	df1	df2	Wald F	Sig.
(Corrected Model)	6.000	10.000	2.049	.151
(Intercept)	1.000	15.000	5.791	.029
RIDAGEYR	1.000	15.000	1.371	.260
INDFMPIR	1.000	15.000	2.055	.172
Education	2.000	14.000	.056	.945
Psychological_Distress	1.000	15.000	.056	.816
RIAGENDR	1.000	15.000	1.964	.181

Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress, RIAGENDR

Odds Ratios 1[a]

		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval	
				Lower	Upper
Modified Education Level	1.00 vs. 3.00	.00	1.201	.389	3.704
	2.00 vs. 3.00	.00	.998	.468	2.129

Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress, RIAGENDR

a. Factors and covariates used in the computation are fixed at the following values: Modified Education Level=3.00; Psychological Distress=1.00; Gender=2; Age in years at screening=60.89; Ratio of family income to poverty=2.8679

Odds Ratios 2[a]

		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval	
				Lower	Upper
Psychological Distress	.00 vs. 1.00	.00	.945	.570	1.568

Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress, RIAGENDR

a. Factors and covariates used in the computation are fixed at the following values: Modified Education Level=3.00; Psychological Distress=1.00; Gender=2; Age in years at screening=60.89; Ratio of family income to poverty=2.8679

Odds Ratios 3[a]

			Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval	
					Lower	Upper
Gender	1 vs. 2		.00	1.653	.770	3.553

Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress, RIAGENDR

a. Factors and covariates used in the computation are fixed at the following values: Modified Education Level=3.00; Psychological Distress=1.00; Gender=2; Age in years at screening=60.89; Ratio of family income to poverty=2.8679

Odds Ratios 4[a]

Units of Change		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval	
				Lower	Upper
Age in years at screening	1.000	.00	.984	.956	1.013

Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress, RIAGENDR

a. Factors and covariates used in the computation are fixed at the following values: Modified Education Level=3.00; Psychological Distress=1.00; Gender=2; Age in years at screening=60.89; Ratio of family income to poverty=2.8679

Odds Ratios 5[a]

Units of Change		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval	
				Lower	Upper
Ratio of family income to poverty	1.000	.00	1.193	.918	1.552

Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress, RIAGENDR

a. Factors and covariates used in the computation are fixed at the following values: Modified Education Level=3.00; Psychological Distress=1.00; Gender=2; Age in years at screening=60.89; Ratio of family income to poverty=2.8679

Manuscript 3

Male

Categorical Variable Information

		Weighted Count	Weighted Percent
Modified Diabetic Retinopathy[a]	.00	6879249.157	83.5%
	1.00[b]	1355638.797	16.5%
Modified Education Level	1.00	1211353.944	14.7%
	2.00	2527446.928	30.7%
	3.00	4496087.083	54.6%
Psychological Distress	.00	6130865.430	74.4%
	1.00	2104022.524	25.6%
Subpopulation Size		8234887.954	100.0%

Subpopulation: Gender = 1

a. Dependent Variable

b. Reference Category

Covariate Information

	Mean
Age in years at screening	61.42
Ratio of family income to poverty	2.9949

Subpopulation: Gender = 1

Pseudo R Squares

Cox and Snell	.018
Nagelkerke	.030
McFadden	.020

Subpopulation: Gender = 1
Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress

Tests of Model Effects

Source	df1	df2	Wald F	Sig.
(Corrected Model)	5.000	11.000	.608	.696
(Intercept)	1.000	15.000	1.878	.191
RIDAGEYR	1.000	15.000	.459	.508
INDFMPIR	1.000	15.000	.239	.632
Education	2.000	14.000	.305	.742
Psychological_Distress	1.000	15.000	.223	.644

Subpopulation: Gender = 1
Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress

Odds Ratios 1[a]

		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval	
				Lower	Upper
Modified Education Level	1.00 vs. 3.00	.00	1.170	.316	4.333
	2.00 vs. 3.00	.00	1.527	.410	5.689

Subpopulation: Gender = 1
Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress

a. Factors and covariates used in the computation are fixed at the following values: Modified Education Level=3.00; Psychological Distress=1.00; Age in years at screening=61.42; Ratio of family income to poverty=2.9949

Odds Ratios 2[a]

		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval	
				Lower	Upper
Psychological Distress	.00 vs. 1.00	.00	1.214	.505	2.920

Subpopulation: Gender = 1
Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress

a. Factors and covariates used in the computation are fixed at the following values: Modified Education Level=3.00; Psychological Distress=1.00; Age in years at screening=61.42; Ratio of family income to poverty=2.9949

Odds Ratios 3[a]

Units of Change		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval Lower	95% Confidence Interval Upper
Age in years at screening	1.000	.00	.981	.923	1.042

Subpopulation: Gender = 1
Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress

a. Factors and covariates used in the computation are fixed at the following values: Modified Education Level=3.00; Psychological Distress=1.00; Age in years at screening=61.42; Ratio of family income to poverty=2.9949

Odds Ratios 4[a]

Units of Change		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval Lower	95% Confidence Interval Upper
Ratio of family income to poverty	1.000	.00	1.127	.668	1.902

Subpopulation: Gender = 1
Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress

a. Factors and covariates used in the computation are fixed at the following values: Modified Education Level=3.00; Psychological Distress=1.00; Age in years at screening=61.42; Ratio of family income to poverty=2.9949

Female

Sample Design Information

		N
Unweighted Cases	Valid	468
	Invalid	8786
	Total	9254
Population Size		16639717.136
Subpopulation Size[a]		8404829.181
Stage 1	Strata	15
	Units	30
Sampling Design Degrees of Freedom		15

a. Subpopulation: Gender = 2

Categorical Variable Information

		Weighted Count	Weighted Percent
Modified Diabetic Retinopathy[a]	.00	6320653.137	75.2%
	1.00[b]	2084176.044	24.8%
Modified Education Level	1.00	1439156.886	17.1%
	2.00	3155845.330	37.5%
	3.00	3809826.965	45.3%
Psychological Distress	.00	5907834.572	70.3%
	1.00	2496994.609	29.7%
Subpopulation Size		8404829.181	100.0%

Subpopulation: Gender = 2

a. Dependent Variable

b. Reference Category

Covariate Information

	Mean
Age in years at screening	60.38
Ratio of family income to poverty	2.7435

Subpopulation: Gender = 2

Pseudo R Squares

Cox and Snell	.036
Nagelkerke	.054
McFadden	.033

Subpopulation: Gender = 2
Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress

Tests of Model Effects

Source	df1	df2	Wald F	Sig.
(Corrected Model)	5.000	11.000	4.752	.015
(Intercept)	1.000	15.000	3.015	.103
RIDAGEYR	1.000	15.000	1.158	.299
INDFMPIR	1.000	15.000	7.005	.018
Education	2.000	14.000	.184	.834
Psychological_Distress	1.000	15.000	.514	.485

Subpopulation: Gender = 2
Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress

Odds Ratios 1[a]

		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval	
				Lower	Upper
Modified Education Level	1.00 vs. 3.00	.00	1.182	.218	6.416
	2.00 vs. 3.00	.00	.700	.204	2.404

Subpopulation: Gender = 2
Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress

a. Factors and covariates used in the computation are fixed at the following values: Modified Education Level=3.00; Psychological Distress=1.00; Age in years at screening=60.38; Ratio of family income to poverty=2.7435

Odds Ratios 2[a]

		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval	
				Lower	Upper
Psychological Distress	.00 vs. 1.00	.00	.698	.240	2.031

Subpopulation: Gender = 2
Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress

a. Factors and covariates used in the computation are fixed at the following values: Modified Education Level=3.00; Psychological Distress=1.00; Age in years at screening=60.38; Ratio of family income to poverty=2.7435

Odds Ratios 3[a]

Units of Change		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval Lower	Upper
Age in years at screening	1.000	.00	.986	.960	1.014

Subpopulation: Gender = 2
Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress

a. Factors and covariates used in the computation are fixed at the following values: Modified Education Level=3.00; Psychological Distress=1.00; Age in years at screening=60.38; Ratio of family income to poverty=2.7435

Odds Ratios 4[a]

Units of Change		Modified Diabetic Retinopathy	Odds Ratio	95% Confidence Interval Lower	Upper
Ratio of family income to poverty	1.000	.00	1.272	1.048	1.543

Subpopulation: Gender = 2
Dependent Variable: Modified Diabetic Retinopathy (reference category = 1.00)
Model: (Intercept), RIDAGEYR, INDFMPIR, Education, Psychological_Distress

a. Factors and covariates used in the computation are fixed at the following values: Modified Education Level=3.00; Psychological Distress=1.00; Age in years at screening=60.38; Ratio of family income to poverty=2.7435