The Association Between Psychological Distress and Diabetic Retinopathy Among U.S. Adults After Controlling for Age, Educational Level, and Income, A Retrospective, Quasi-Experimental Study

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Abstract:

➤ *Background:*

Diabetes could lead to diabetic retinopathy, an eye disease that causes damaged blood vessels and the growth of abnormal ones. The quantitative study examined 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.

➤ *Methods:*

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.

➤ *Result:*

There was no association between psychological distress and diabetic retinopathy among U.S. adults when controlling for education level, income, and age. 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.

➤ *Conclusion:*

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.

Keywords: Psychological Distress, Diabetic Retinopathy, Diabetes.

I. 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

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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).

II. 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.

III. 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

(CDC, 2017)

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

(CDC, 2017)

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.

IV. 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).

V. 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.

VI. 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.

VII.   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.

VIII. 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.

DECLARATION

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