Factors Related to Diabetes Mellitus among Asian-American Adults in the United States Using the 2011 to 2020 National Health and Nutrition Examination Survey

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Academic Abstract

Type 2 diabetes mellitus (T2DM) disproportionality affects under-represented groups, specifically Asian Americans. Asian Americans are less likely to receive proper diabetes mellitus screening compared to other racial and ethnic groups, potentially due to improper screening guidelines by clinicians, and Asian Americans being unaware of their increased risk for diabetes mellitus. There are differences in the etiology of T2DM in Asian Americans compared to White Americans. Due to the increasing rates of T2DM among Asian Americans, new approaches in the screening of T2DM should be tailored based on race and ethnicity. The aging process is frequently associated with decreased muscle mass and increased adipose tissue, which can contribute to insulin resistance and lead to elevated hemoglobin A1c (HbA1c) percentages. Although sex has not been classified as an independent risk factor for T2DM, it is important to consider sex-specific conditions in the context of the disease. Body mass index (BMI) alone is insufficient to properly evaluate adiposity in Asian-American adults due to Asian Americans having a lower BMI with a higher body fat percentage. Waist circumference,

waist-to-height ratio (WHtR), and visceral adiposity index (VAI) may be better for screening Asian Americans for T2DM. Multiple modifiable risk factors, such as sedentary behavior, and dietary intake (specifically dietary magnesium intake) can increase the risk for T2DM. Lack of physical activity can result in insulin resistance and impaired glucose metabolism as a result of muscle disuse and decreased lean body mass. Half of the Asian-American population is not consuming the recommended amounts of magnesium from foods, drinks, and dietary supplements. There is an inverse relationship between increased dietary magnesium intake and the risk of T2DM. In addition, the main language spoken in the household may influence lifestyle and risk of T2DM. The overarching goal of the present study was to establish which independent variables (age, sex, BMI, waist circumference, WHtR, VAI, sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language) were the strongest predictors of HbA1c percentage (a measure of blood glucose control) in Asian-American adults using the National Health and Nutrition Examination Survey (NHANES) data from 2011 to 2020. The present study also evaluated the relationship among multiple predictors of HbA1c percentage, including age, sex, body composition, sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language among Asian-American adults, 18 years of age and older, using the NHANES data from 2011 to 2020.

Factors Related to Diabetes Mellitus among Asian-American Adults in the United States Using the 2011 to 2020 National Health and Nutrition Examination Survey

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General Audience Abstract

Asian Americans have been disproportionately affected by type 2 diabetes mellitus (T2DM). Compared to other racial and ethnic groups, Asian Americans are less likely to receive proper diabetes mellitus screening. This may be due to inadequate screening guidelines and lack of awareness about their increased risk for diabetes mellitus. The cause of T2DM in Asian Americans differs from that in White Americans, which calls for tailored screening approaches based on race and ethnicity. The aging process is frequently associated with decreased muscle mass and increased adipose tissue, which can contribute to insulin resistance and lead to elevated hemoglobin A1c (HbA1c) percentages. Although sex has not been classified as an independent risk factor for T2DM, it is important to consider sex-specific conditions in the context of the disease. Body mass index (BMI) alone is not enough to accurately assess body fat in Asian-American adults, because they tend to have a lower BMI, but higher body fat percentage. Waist circumference, waist-to-height ratio (WHtR), and visceral adiposity index (VAI) might be more suitable for screening Asian Americans for T2DM. Several modifiable risk factors, such as a sedentary lifestyle and dietary intake (specifically, dietary magnesium intake), can increase the risk of T2DM. Lack of physical activity can lead to insulin resistance and impaired glucose metabolism due to muscle disuse and

reduced lean body mass. Half of the Asian-American population does not consume the recommended amounts of magnesium from food, drinks, and dietary supplements. Researchers have shown that increased dietary magnesium intake is linked to a reduced risk of T2DM. In addition, the main language spoken in the household may influence lifestyle and risk of T2DM. The main goal of this study was to identify which factors (age, sex, BMI, waist circumference, WHtR, VAI, sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language) were the strongest predictors of HbA1c percentage (a measure of blood glucose control) in Asian Americans. This was completed using the National Health and Nutrition Examination Survey (NHANES) data from 2011 to 2020. Additionally, the study aimed to establish the relationship among multiple predictors of HbA1c percentage, including age, sex, body composition, sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language among Asian-American adults, 18 years of age and older, using the same NHANES data.

Dedication

This dissertation is dedicated to my Obāsan (Grandmother) Yoko Kato and my son, Kenzo Wade Nichols, the past and the future of our Japanese lineage. Even though you are no longer with us Obāsan, I hope you are proud of everything I have accomplished. I wish you were here to see me finish my PhD, while holding your great grandson. You inspired this work, and I hope that it helps our community. I love you and miss you immensely, Obāsan.

~ Q-Chan

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

ADA	American Diabetes Association
AANHPI	Asian American, Native Hawaiian, and Pacific Islander
BMI	Body mass index
CDC	Centers for Disease Control and Prevention
HbA1c	Glycosylated Hemoglobin / Hemoglobin A1c
kg/m^2	kilograms/meters squared
kcal(s)	kilocalorie(s)
METs	Metabolic equivalents
NHANES	National Health and Nutrition Examination Survey
T2DM	Type 2 diabetes mellitus
U.S.	United States
USPSTF	United States Preventative Services Task Force
VAI	Visceral adiposity index
WHO	World Health Organization
WHtR	Waist-to-height ratio

CHAPTER 1: SPECIFIC AIMS AND HYPOTHESES

1.1 Introduction

As of 2020, diabetes mellitus has affected 37.1 million adults in the United States (U.S.); 28.5 million adults have a diabetes mellitus diagnosis, while 8.5 million are undiagnosed.[1] Of the 37.1 million adults with diabetes mellitus, the Centers for Disease Control and Prevention[2] (CDC) reported that 33 to 35 million adults have type 2 diabetes mellitus (T2DM). Lin et al.[3] projected that the adult diabetes mellitus diagnosis would increase to 39.7 million by 2030, and 60.6 million by 2060. In 2017, the American Diabetes Association[4] (ADA) reported the cost of pre-diabetes, diabetes mellitus, and undiagnosed diabetes mellitus to be $403.9 billion per year. Type 2 diabetes mellitus is a combination of altered glucose metabolism and insulin resistance.[5] The ADA "Standards of Medical Care in Diabetes" state that fasting plasma glucose concentrations, 2-hour plasma glucose concentrations during a 75-gram oral glucose tolerance test, and glycosylated hemoglobin (or hemoglobin A1c [HbA1c]) percentage are each appropriate to screen for pre-diabetes and T2DM.[6]

In addition to the increase in the diagnosis of T2DM, the prevalence of obesity has risen to 41.9% in the United States.[7] Overweight and obesity are important risk factors leading to insulin resistance and the eventual development of T2DM. Due to the rise in obesity rates, the United States Preventative Services Task Force (USPSTF) and

the ADA have lowered the pre-diabetes and T2DM screening from 40 to 35 years of age for asymptomatic, nonpregnant adults who are living with overweight and obesity.[8] Additional risk factors for T2DM include a family history of diabetes mellitus, physical inactivity, increased energy consumption, and race and ethnicity. Among the at-risk ethnicities, Asian Americans, Native Hawaiians, and Pacific Islanders are at an increased risk.[6–8]

Asian Americans are the fastest-growing under-represented ethnic group in the United States.[9] There are 19.9 million Asian Americans, and 4.1 million Asian Americans combined with another ethnicity, living in the United States.[10] The Asian-American population is expected to reach 46 million by 2060.[9] In addition to the population growth, the prevalence of T2DM has increased among Asian Americans. The CDC reported that one in three Asian Americans has undiagnosed diabetes mellitus.[11] Further, Asian Americans are diagnosed with pre-diabetes and T2DM at a lower mean body mass index (BMI) and waist circumference than other racial and ethnic groups.[12,13] The USPSTF states that pre-diabetes and T2DM screening with one risk factor should begin at 35 years of age.[8] However, the USPSTF recognizes that Asian Americans should be screened at earlier ages, yet did not make any Asian ethnic group-specific diabetes mellitus screening recommendations.[8,14] Aggarwal et al.[15] proposed that diabetes mellitus screening for Asian Americans should begin at 23 years of age, which would parallel the 35 years of age screening for non-Hispanic White Americans.

Tung et al.[16] reported that Asian Americans are less likely to receive proper diabetes mellitus screening compared to other ethnic groups, potentially due to improper screening guidelines by clinicians, and Asian Americans being unaware of their increased risk for diabetes mellitus. To delay or prevent pre-diabetes and T2DM, the ADA recommends lifestyle modifications such as weight reduction, routine physical activity, and healthy eating patterns that may improve insulin resistance and glycemic control.[17,18 19]

Age is an important risk factor for the development of T2DM. Hemoglobin A1c percentages have been reported to increase with age, even in the absence of T2DM.[20] This may partly be due to decreases in muscle tissue, which can lead to decreased insulin sensitivity.[21] Furthermore, with age, the body's ability to metabolize glucose decreases due to a reduction in insulin sensitivity and β-cell function, leading to higher blood glucose concentrations, which, in turn, lead to increased HbA1c percentages.[22]

The International Diabetes Federation[23] states that there are 17.7 million more men globally with diabetes mellitus than women, 20 to 79 years of age. Sex differences in HbA1c percentages among Asians have not been extensively studied. However, some research has shown differences in HbA1c percentages between women and men in various populations. Men typically receive a diagnosis at a younger age and with lower body fat mass compared to women.[24] Conversely, women carry a higher burden

of risk factors, particularly obesity, at the time of T2DM diagnosis.[24] Additionally, reproductive factors, such as pregnancy and menopause, exert a substantial influence on the risk of developing T2DM in women.[24] These sex-specific disparities in T2DM underscore the importance of considering sex-related factors when addressing the complexities of the disease.

Anthropometric index measurements such as BMI, waist circumference, waist-to-height ratio (WHtR), and visceral adiposity index (VAI) are measurements that have been useful in identifying individuals at-risk for T2DM, obesity, and cardiometabolic risk.[25,26] Body mass index is not a direct measure of body fat; however, BMI is a screening tool that can indicate adiposity.[27–29] However, using standardized BMI measurements underestimates the risk for pre-diabetes and T2DM in the Asian-American population.[12,15,30–32] Aggarwal et al.[15] used the USPSTF's Asian-specific BMI of 23 kilograms (kg)/meters squared (m^2) to appropriately screen for diabetes mellitus among Asian Americans. The researchers[15] reported that lowering the BMI from 23 kg/m^2 to 20 kg/m^2 resulted in 27.6% of Asian Americans with undiagnosed diabetes mellitus to be diagnosed. Aggarwal et al.[15] determined that, for Asian Americans, lowering the BMI to 20 kg/m^2 or greater would be equal to screening non-Hispanic White adults using a BMI of 25 kg/m^2 or greater.

Although BMI is the most widely used clinical tool to estimate body fat, it has its limitations in estimating body fat composition.[12,15,30–32] Body mass index alone is insufficient to properly evaluate adiposity in Asian-American adults due to Asian Americans having a lower BMI with a higher body fat percentage.

Waist circumference measurements can be an easy and cost-effective measurement tool to serve as a proxy for visceral adiposity and HbA1c percentage in Asian Americans.[33–35] The World Health Organization (WHO) recommends that lowering the waist circumference cut-off points for Asian Americans to values of 80 centimeters (cm) and 85 cm for women and men, respectively, would better identify their metabolic risk.[30]

Like waist circumference, the waist-to-height ratio is a screening tool for cardiometabolic risk related to body fat distribution. The WHtR, calculated by dividing waist circumference by height, has recently gained attention as an anthropometric index for measuring central adiposity.[36] Waist-to-height ratio is a more sensitive universal screening tool than BMI to detect health risks.[27] The WHtR has been shown to be a stronger predictor for T2DM among Asian Americans compared to BMI.[33,34] Asian Americans have higher amounts of visceral adiposity compared to other races and ethnicities with the same BMI.[35,37] The proximity of visceral fat to the vital organs puts Asian Americans at higher risk for insulin resistance and for developing T2DM.[38]

Therefore waist-to-height ratio may succeed in identifying risk for T2DM compared to other anthropometric measures such as BMI or waist circumference.

Waist circumference and WHtR are clinical screening tools used for the indirect evaluation of increased visceral fat.[26] Yet, waist circumference and WHtR do not distinguish between subcutaneous and visceral fat mass.[26] Asian Americans tend to accumulate more visceral fat at a lower BMI and waist circumference. Accumulation of visceral adiposity reduces insulin sensitivity, leading to an increased risk of developing diabetes mellitus.[39] Visceral adiposity index is a mathematical formula that consists of BMI and waist circumference, as well as clinical measurements such as triglyceride and high density lipoprotein cholesterol (HDL-C) concentrations.[26] The visceral adiposity index (VAI) seems to be a better predictor for metabolic disorders associated with insulin resistance than a single anthropometric index.[40–42]

According to the CDC, not meeting the recommended amount of physical activity per week is associated with 117 billion dollars in annual health care costs.[43] In addition, meeting the recommended amounts of physical activity can prevent 1 in 12 cases of T2DM.[43] Exercise leads to adaptations in skeletal muscle, which, in turn, lead to improved skeletal muscle insulin sensitivity.[44]

There is an association between dietary quality and the risk of T2DM.[45,46] Specifically, researchers have reported an inverse relationship between increased

dietary magnesium intake and the risk of T2DM.[46,47] Further, data from the National Health and Nutrition Examination Survey (NHANES) 2011 to 2020 have shown that less than half of the Asian-American population is not consuming the recommended amounts of magnesium from food, drinks, and dietary supplements.[47] Previous researchers have reported mixed results in determining the correlation between dietary magnesium intake and the risk of T2DM in Asian countries.[48,49] The relationship between dietary magnesium intake and the risk of T2DM in Asian Americans is limited and needs further investigation.

The primary language spoken in the household can also affect if individuals are meeting physical activity and dietary guidelines. Typically, if the main language spoken in a household of those who have immigrated to the United States is English, physical activity and dietary guidelines are more likely to be met.

The National Health and Nutrition Examination Survey uses survey weights to create a representative sample for the United States (U.S.) population to produce similar estimates if all of the eligible individuals in the U.S. were surveyed.[50] Excluded in NHANES data are U.S. citizens living overseas, those in custody in institutional settings, and those under supervised care. The NHANES data are collected through in-person interviews and questionnaires, laboratory measures, and physical assessments conducted in mobile examination centers across the U.S. The NHANES did not have an

Asian demographic data until the 2011 to 2012 cycles. Due to this, the Asian population has been oversampled in every NHANES cycle following 2011 to 2012.

The overarching goal of the present study was to establish which independent variables (body mass index [BMI], waist circumference, waist-to-height ratio [WHtR], visceral adiposity index [VAI], sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language) are the strongest predictors of hemoglobin A1c percentage in Asian-American adults using NHANES data from 2011 to 2020. Determining associations between the various predictor variable and hemoglobin A1c percentage will enable the use of tools specifically for determining Asian-Americans risk for type 2 diabetes mellitus. Therefore, the following Specific Aims and Hypotheses were examined:

1.2 Specific Aims

Specific Aim 1:

To determine which predictor variables have the strongest association with hemoglobin A1c percentage measured on a continuum among age, sex, body composition (body mass index [BMI], waist circumference, waist-to-height ratio [WHtR], visceral adiposity index [VAI]), sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language variables in Asian-American adults, 18 years of age and older, using NHANES data from 2011 to 2020.

Hypothesis for Specific Aim 1:

It was hypothesized that higher hemoglobin A1c percentage would be positively associated with increased age, sex (greater prevalence in men than women), increased body composition (higher BMI, waist circumference, WHtR, and VAI), increased sedentary behavior time, low dietary magnesium intake, lower self-reported dietary status, and lower proficiency in speaking English in Asian-American adults, 18 years of age and older, using the NHANES data from 2011 to 2020.

Specific Aim 2:

Using machine learning and decision tree modeling approaches, to estimate relative importance scores for predicting hemoglobin A1c ≥ 6.5% among age, sex, body composition (body mass index [BMI], waist circumference, waist-to-height ratio [WHtR], visceral adiposity index [VAI]), sedentary behavior time, dietary magnesium intake, self-reported dietary status, and language in Asian-American adults, 18 years of age and older, using NHANES data from 2011 to 2020.

Hypothesis for Specific Aim 2:

It was hypothesized that the relative importance scores for predicting hemoglobin A1c ≥ 6.5% using machine learning and decision tree modeling approaches would

demonstrate that age, sex, body composition measures (BMI, waist circumference, WHtR, VAI), sedentary behavior time, dietary magnesium intake, self-reported dietary status, and language would have a significant effect on the prediction of hemoglobin A1c ≥ 6.5% in Asian-American adults, 18 years of age and older, using the NHANES data from 2011 to 2020.

Specific Aim 3:

To build upon the models established in Specific Aims 1 and 2, the best fitting logistic regression model was used for predicting a hemoglobin A1c ≥ 6.5% in Asian-American adults, 18 years of age and older, using NHANES data from 2011 to 2020.

1.3 Significance

The most recent statistic (2018) lists diabetes mellitus as the fifth leading cause of mortality among Asian Americans.[51,52] Researchers continue to push for disaggregation of Asian-American subgroups due to the higher prevalence of diabetes mellitus among those groups that becomes masked by the overall prevalence of diabetes mellitus among the group as a whole. The current reported overall prevalence of diagnosed diabetes mellitus among Asian Americans is 9.2%, yet when separated by subgroups, Asian Indians, Filipino, and Other Asians, the prevalence of diagnosed diabetes mellitus increases to 12.6%, 10.4%, and 9%, respectively, except for the Chinese population (5.6%).[1] Type 2 diabetes mellitus affects many aspects of health care,

including health care costs and quality of life, which is reflected in the estimated number of years lost due to the progression of the disease. The emerging literature is identifying appropriate body composition and age cut-off points for diagnosing diabetes mellitus in Asian Americans. Additionally, environmental diabetes mellitus risk factors, such as sedentary behavior patterns and diet, are being identified among Asian Americans.

Widening the adult age range to 18 years of age and older, versus the USPSTF's and ADA's recommended 35 to 70 years of age, would effectively capture the majority of the population who is at-risk.[33,53] The present research is the first to use NHANES data to compare the proposed lower BMI, and waist circumference to other indirect measures of body composition (waist-to-height ratio, visceral adiposity index). The research is limited to the United States regarding the association between sedentary behavior, and the risk for T2DM in Asian-American adults.[54–57] The present study will add further insight into the sedentary behaviors of Asian Americans. Furthermore, the association of dietary magnesium intake and T2DM among Asian Americans was examined. Understanding the association between dietary magnesium and T2DM in Asian Americans requires further investigation due to the paucity of research. In addition, the main language spoken in the household may influence lifestyle and risk of T2DM. Thus, language spoken in the home was also assessed. The researcher in the present study wanted to address the previously mentioned gaps in the literature by

establishing ethnicity-specific risk factors. The researcher examined how those risk factors influenced the strength and association of each other in predicting the risk for diabetes mellitus in Asian Americans. Finally, the present study adds more evidence to assist in diabetes mellitus prevention among under-represented populations.

1.4 Rationale

1. Why explore the association among hemoglobin A1c percentage, body mass index (BMI), waist circumference, waist-to-height ratio (WHtR), and visceral adiposity index (VAI) in Asian-American adults, 18 years of age and older, using the NHANES data from 2011 to 2020?

Body fat distribution is thought to influence the risk of T2DM, and body fat mass is considered to be the underlying contributor to insulin resistance. Due to Asian Americans having a lower BMI with a higher body fat percentage,[12,32] it may be beneficial to use a combination of indirect measures of body composition. Waist circumference measurements can be used as an easy and cost-effective measurement tool in determining risk for T2DM.[58–60] Although, the USPTF and ADA have not determined a waist circumference measurement recommendation that may lead to undiagnosed diabetes mellitus in Asian Americans, the World Health Organization has determined ethnicity-specific thresholds.[8] Specific to the Asian population, WHtR has been shown to be a sensitive universal screening tool compared to BMI

due to the higher amounts of visceral adiposity compared to other races and ethnicities of the same BMI.[37,61,62] Additionally, waist circumference and WHtR do not distinguish between subcutaneous and visceral fat mass.[26] However, the visceral adiposity index (VAI) may be a better predictor of metabolic disorders associated with insulin resistance than a single anthropometric index. Visceral adiposity index has been validated by magnetic resonance imaging (MRI), computed tomography (CT), and the euglycemic hyperinsulinemic clamp in predicting insulin resistance and visceral adipose tissue amounts.[26,63] Researchers who have studied Asian populations have reported VAI as a stronger predictor of T2DM compared to BMI, waist circumference, and WHtR.[35,39,63]

2. Why explore the association between hemoglobin A1c percentage and sedentary behavior time in Asian-American adults, 18 years of age and older, using the NHANES data from 2011 to 2020?

Only 50% of the United States population are meeting the recommended amount of physical activity, with 19% of women and 26% of men meeting the recommended amount of aerobic and muscle-strengthening activities.[64,65] Increased sedentary time is associated with an increased risk for T2DM.[66,67] Lack of physical activity can result in insulin resistance and impaired glucose metabolism due to muscle disuse and decreased lean body mass.[68] Sheng et al.[69] conducted analyses of

the Asian-American population using NHANES data from 2011 to 2016. The aim of their study was to determine if acculturation modified the relationship between moderate-to-vigorous physical activity (≥ 150 minutes/week) and metabolic syndrome among Asian Americans (n=2,259). The authors[69] reported that 64.4% of Asian Americans did not meet the recommended ≥ 150 minutes/week of physical activity. Further, Asian Americans who did not meet the recommended amount of physical activity had a higher risk of metabolic syndrome. However, Asian Americans who were born in the United States met the physical activity recommendations at a higher percentage compared to Asian Americans who lived in the United States for more than 15 years (48.9% vs. 34.1%, respectively) and less than 15 years (48.9% vs. 32.7%, respectively).[69]

3. Why investigate the relationship between dietary magnesium intake and hemoglobin A1c percentage in Asian-American adults, 18 years of age and older, using the NHANES data from 2011 to 2020?

Magnesium supplementation improves insulin action and glycemic control among individuals with diabetes mellitus.[70] Kirii et al.[48] reported that, after a five-year follow-up in Japanese middle-aged women and men, magnesium intake was inversely associated with the risk of T2DM. In contrast, the intake of magnesium in the diet among Chinese individuals was not significantly associated with diabetes mellitus ($p > 0.05$), but serum magnesium concentrations were strongly inversely associated with

diabetes mellitus (0.92 ± 0.07 mmol/L, $p < 0.001$).[49] In general, however, it has been reported that the risk of T2DM-related disease decreased by 13% per 100 mg/day increase in magnesium intake in Asian populations.[71]

4. Why explore age, sex, body mass index (BMI), waist circumference, waist-to-height ratio (WHtR), visceral adiposity index (VAI), sedentary behavior time, dietary magnesium intake, self-reported dietary status, and language as predictors of hemoglobin A1c percentage in Asian-American adults, 18 years of age and older, using the NHANES data from 2011 to 2020?

Aging is often accompanied by decreased muscle mass and increased adipose tissue, which can contribute to insulin resistance and subsequently higher HbA1c percentages. Although the ADA does not specifically classify sex as an independent risk factor for T2DM, they emphasize the importance of considering sex-specific conditions in relation to the disease. The current literature reports associations among BMI and waist circumference, using ethnicity-specific cut-off values, with waist-to-height ratio, visceral adiposity index, increased sedentary behaviors, and insufficient dietary magnesium intake and overall poor dietary intake with increased risk of T2DM.[32,54,72–75] Furthermore, the main language spoken in the household may affect lifestyle and risk of T2DM. The interaction among the aforementioned variables acting as either confounders or modifiers is unclear. Investigating the strength of each variable would

provide insight into prevention practices, including meeting recommended physical activity recommendations and dietary adequacy specifically for Asian Americans.

1.5 Summary

Asian Americans are under-represented in health-related research literature, and the prevalence of undiagnosed diabetes mellitus continues to rise. There is a need to provide evidence behind relational risk factors for developing T2DM in Asian Americans. The goal of the current study was to determine the association of HbA1c percentage with age, sex, body composition (BMI, waist circumference, WHtR, VAI), sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language in Asian-American adults, 18 years of age and older, using the NHANES data from 2011 to 2020. In addition, to effectively screen Asian Americans for T2DM, and due to BMI not being a reliable proxy for adiposity among Asian Americans, the researcher wanted to establish better indirect measures of body composition to use within a clinical setting.

CHAPTER 2: LITERATURE REVIEW

Before 2000, the United States (U.S.) Census categorized all Asian subgroups, in addition to Native Hawaiians and Pacific Islanders, as "Asian".[76,77] In 2003, the U.S. Census created subgroups of Chinese, Filipino, Indian, Japanese, Korean, Vietnamese, and Other Asian; while also creating the Native Hawaiian or Other Pacific Islander (NHPI) groups. The U.S. Census reported 21 Asian-American subgroups that comprise the total population, yet 97% of the total population is comprised of Chinese, Filipino, Indian, Japanese, Korean, and Vietnamese populations.[10] Further, the Other Asian category that is listed on the U.S. Census is comprised of Bangladeshi, Bhutanese, Burmese, Cambodian, Hmong, Indonesian, Laotian, Malaysian, Mongolian, Nepalese, Okinawan, Pakistani, Sri Lankan, Taiwanese, and Thai populations. Native Hawaiians and Pacific Islanders are not included in this literature review; they have often been categorized as Asian Americans in the research literature.

Data for Asian American, Native Hawaiian and Pacific Islanders' (AANHPI's) communities, including immigrants and refugees, are frequently combined, masking heterogeneity within the group. Doan et al.[78] reported that, between 1992 and 2018, the National Institutes of Health (NIH) budget for clinical research on AANHPI's communities was 0.17% of the total NIH budget, with a 0.06% increase in funding since 2000. Due to mis-representation and under-representation in clinical research and

funding, the data have been limited in discovering the mechanisms underlying obesity and type 2 diabetes mellitus (T2DM) within each AANHPI subgroup.[76,79–81]

The purpose of this study was to determine predictors of hemoglobin A1c (HbA1c) percentage among Asian-American adults, 18 years of age and older, living in the United States using the National Health and Nutrition Examination Survey (NHANES) data from 2011 to 2020. The first section of this chapter presents an overview of the literature relevant to the pathophysiology and prevalence of T2DM among Asian-American adults in the United States. The following sections provide an overview of the predictor variables, including body mass index (BMI), waist circumference, waist-to-height ratio (WHtR), visceral adiposity index (VAI), sedentary behavior time, dietary magnesium intake, self-reported dietary status, and language.

2.1 Type 2 Diabetes Mellitus and Asian Americans

2.1.1 Type 2 Diabetes Mellitus Pathophysiology

Type 2 diabetes mellitus is characterized by elevated blood glucose concentrations caused primarily by cellular resistance to the effects of insulin, and is followed by impairment of beta cells that produce insulin, the hormone that regulates blood glucose concentrations.[5,82] The development of T2DM requires the coexistence of insulin resistance and pancreatic beta cell dysfunction. Typically, T2DM is caused by insulin resistance, initially compensated by increased beta cell responses, and ultimately leading to T2DM through depletion of pancreatic beta cells.[5,82] As the disease

progresses, insulin secretion fails to maintain glucose homeostasis, resulting in hyperglycemia. However, in East Asian populations, the pathogenesis of T2DM is characterized by pre-existing impaired beta cell functioning capacity, resulting in impaired insulin secretion.[83–85] Further, it has been shown that beta cell function is heritable and critically determines glucose intolerance and T2DM in different racial and ethnic groups.[86]

Hur et al.[87] conducted a genome-wide association study on 58,701 Koreans (38,408 women and 20,293 men), 40 to 79 years of age, to determine the effects of genetic variants associated with a higher risk of T2DM. Hur et al.[87] reported that the genetic variants associated with T2DM risk are involved in the development, growth, and secretion of pancreatic cells, and are associated with T2DM of the young genes ($p < 0.001$). Further, they reported that mutations in the KCNQ1 gene were associated with decreased pancreatic beta cell mass and reduced insulin secretion.

The risk of developing T2DM occurs more frequently in certain racial and ethnic subgroups, such as Asian Americans. Furthermore, key factors associated with increased risk for developing diabetes mellitus include family history, genetics, sedentary behavior, acculturation, smoking status, and alcohol intake. All of which can result in the progressive loss of beta cell mass and/or function that manifests clinically as hyperglycemia, and subsequently, T2DM.

2.1.2 Hemoglobin A1c Percentage

The American Diabetes Association's (ADA's) Standards of Medical Care in Diabetes[6] state that type 2 diabetes mellitus can be diagnosed based on a hemoglobin A1c criteria of 5.7% to 6.5% for pre-diabetes, and 6.5% or higher for a T2DM diagnosis. The International Diabetes Federation,[88] and the Japanese and Korean Diabetes Mellitus Guidelines[89,90] also use a HbA1c of 6.5% or higher for a T2DM diagnosis. Conversely, China does not use HbA1c of 6.5% for T2DM diagnosis, due to lack of standardization and routine clinical use.[91] Additionally, a HbA1c of 6.3% has been used to diagnosis T2DM in Chinese adults, yet this is not the standard of practice.[91] The use of HbA1c percentage testing is more convenient than fasting plasma glucose concentrations and the oral glucose tolerance test because fasting is not required for HbA1c percentage testing.

2.2. Age

The "Standards of Medical Care in Diabetes", published by the ADA, acknowledge age as a notable risk factor for T2DM.[92] According to these standards, individuals 35 years of age and above, particularly those with additional risk factors such as overweight or obesity, and specific racial and ethnic backgrounds, should undergo screening for T2DM. This recommendation underscores the importance of early detection and intervention in populations at high-risk to mitigate the burden of T2DM. Previous researchers have documented an increase in HbA1c percentage with

advancing age in the general population, and among Asian or Asian-American populations, specifically.[93] Several mechanisms may explain the observed association between HbA1c percentage and age. As individuals age, the insulin sensitivity of tissues tends to decrease, leading to impaired glucose metabolism and increased HbA1c percentages.[94] Additionally, aging is associated with a decline in pancreatic beta cell function, which contributes to the deterioration of glycemic control.[95] Age-related changes in body composition, such as an increase in visceral fat and a decrease in muscle mass, can also exacerbate insulin resistance and contribute to elevated HbA1c percentages.[96]

Yamada et al.[96] conducted a cross-sectional study to assess the variations in skeletal muscle mass and visceral fat area relative to age in Japanese adults. The researchers also evaluated gender disparities in skeletal muscle deterioration in the upper and lower limbs. In addition, they explored the correlation between skeletal muscle mass and the area of visceral fat. They included healthy women (n=21,660) and men (n=16,379), 40 to 79 years of age. Skeletal muscle mass and visceral fat area were quantified using bioelectrical impedance analysis. Skeletal Muscle Index (SMI) was calculated by taking the muscle mass data and dividing it by the square of height, expressed in kilograms (kg)/meters squared (m^2). The authors[96] reported that both female and male participants showed a decrease in SMI with age; a total decrease of 6.4% for women and 10.8% for men ($p < 0.001$). Particularly, the decrease in arm SMI

was more evident, with a 4.1% decrease for women and a 12.6% decrease for men. In addition, both sexes demonstrated an increase in the visceral fat area: 65.3% in women and 42.9% in men. A negative correlation was found between SMI and the visceral fat area in both sexes ($p < 0.001$). These findings indicate that the loss of skeletal muscle mass starts around 40 years of age, and becomes more prevalent after 50 years of age in Japanese adults.

Lee et al.[97] examined the correlation between appendicular skeletal muscle mass and insulin resistance in a group of older individuals residing in a community in Korea. They included 241 women (70.6 ± 7.8 year of age) and 158 men (71.8 ± 7.3 years of age), who were part of the Korean Social Life, Health and Aging Project. It is important to note that these participants had no previous medical history of diabetes mellitus or cardiovascular disease. The researchers utilized bioelectrical impedance analysis to measure appendicular skeletal muscle mass. The authors used the homeostasis model assessment of insulin resistance (HOMA-IR) to assess insulin resistance. Lee et al.[97] reported a significant inverse correlation between appendicular skeletal muscle mass and HOMA-IR, especially among men ($p < 0.001$). The researchers[97] stated that their results reaffirmed the link between age-related muscle loss and insulin resistance, highlighting the importance of maintaining muscle mass in mitigating insulin resistance in the older population.

Huang et al.[98] evaluated the association between age, sex, and HbA1c percentages in Taiwanese adults without prior diagnosis of T2DM. The researchers included 2,563 women and 2,183 men, 30 to 70 years of age. The authors[98] reported that HbA1c percentages increased with age in women. They reported a positive association between HbA1c percentages and age across all age categories in women: 30 to 70 ($p < 0.0001$), 30 to 49 ($p < 0.0001$), and 50 to 70 ($p < 0.0001$) years of age.[98] For men, a positive association between HbA1c percentages and age was reported for the following age groups: 30 to 70 ($p < 0.0001$) and 30 to 49 ($p = 0.0003$) years of age. However, Huang et al.[98] did not observe a significant relationship between HbA1c percentages and age in men, 50 to 70 years of age ($p = 0.3567$). The results are consistent with the fact that age is a significant factor in the likelihood of increased HbA1c percentages.[98]

Inoue et al.[99] conducted a study including 33,959 Japanese people (17,090 women and 16,869 men), 15 to 93 years of age, without a T2DM diagnosis. They aimed to determine how the prevalence of T2DM differs among age and sex, using HbA1c percentage and fasting plasma glucose concentrations. The participants were separated by the following age categories: ≤ 37, 38 to 45, 46 to 53, 54 to 59, 60 to 65, and ≥ 66 years of age. Among the women, a significant increase in HbA1c percentage and age was reported ($p < 0.001$). Among the men, HbA1c percentage and T2DM prevalence were significantly higher than in women ($p < 0.001$).

Aging is often accompanied by decreased muscle mass and increased adipose tissue, which can contribute to insulin resistance and subsequently higher HbA1c percentages.[100] It is important to note that, while the relationship between age and HbA1c percentage has been shown to be significant, it does not imply causation. Other factors, including genetics, lifestyle, and environmental influences, may also contribute to the risk of having an HbA1c percentage ≥ 6.5%.[101] Further research is needed to elucidate the underlying mechanisms driving this relationship, as well as to examine the potential influence of other factors, such as physical activity, dietary intake, and medication adherence, on HbA1c percentages in the aging Asian-American population.

2.3 Sex

Type 2 diabetes exhibits notable sex differences, encompassing variations in risk factors and diagnoses. While the ADA[92] does not explicitly identify sex as a distinct risk factor for T2DM, they do highlight certain considerations related to sex-specific conditions. Specifically, women with polycystic ovarian syndrome (PCOS) are deemed to be at higher risk of developing T2DM compared to women without PCOS. Additionally, women who are pregnant and with risk factors should undergo screening for gestational diabetes mellitus. Indeed, women who are pregnant and with undiagnosed diabetes mellitus should also be screened. These recommendations from the ADA underscore the importance of recognizing age-specific factors that may contribute to the risk and management of diabetes mellitus.

Kautzky-Willer et al. [24] conducted a clinically focused narrative review to enhance the knowledge and awareness of health care professionals and researchers regarding the variations between women and men in terms of the risk, diagnoses, and treatment of T2DM and its associated complications. The researchers[24] reported that men exhibit distinct physiological characteristics and risk factors that contribute to their unique T2DM profile. They commonly display higher prevalence of insulin resistance compared to women, indicating reduced responsiveness of their cells to insulin's regulation of blood glucose concentrations.[24,102] Additionally, men tend to have elevated fasting glucose concentrations, suggesting impaired glucose metabolism.[24,102] Testosterone, a male sex hormone, plays a crucial role in modulating glucose homeostasis.[24,103] It enhances glucose-stimulated insulin secretion, augments the action of glucagon-like peptide-1 (GLP-1), a hormone that stimulates insulin release, and reduces inflammation, thereby promoting the health of beta cells.[24,103]

Kautzky-Willer et al.[24] reported that women, exhibit unique physiological characteristics, risk factors, and clinical features that shape their distinctive profile with respect to diabetes mellitus. They have a higher prevalence of gluteofemoral fat, stored in the hips and thighs, which releases beneficial adipokines and potentially provides protection against T2DM.[24,103] This is evidenced by higher concentrations of adiponectin and leptin in the bloodstream.[24,103] In terms of fat distribution, women generally have

higher levels of intramyocellular fat in their leg muscles, but lower levels of visceral adipose tissue, liver fat, and pancreatic fat compared to men.[24,104]

However, these sex differences diminish as individuals age and develop glucose intolerance.[24,103,105] The transition to menopause brings changes in fat distribution, shifting from a gynoid (hips and thighs) pattern to an android (abdominal) pattern, accompanied by an increase in cardiometabolic risk factors such as insulin resistance, inflammation, and dyslipidemia.[24,103] In addition, psychosocial factors, such as perceived stress, work demands, sedentary time, and shift work, have a more pronounced impact on the development of T2DM in women compared to men.[24,103] Reproductive factors also play a role. Gestational diabetes during pregnancy increases the risk of developing T2DM later in life. Polycystic ovary syndrome is associated with insulin resistance and an elevated risk of T2DM.[24,103]

Present medical recommendations lack explicit guidance regarding sex-specific or gender-sensitive strategies for the prevention and management of diabetes mellitus.[24,104–106] Consequently, there is a need for further research to address this knowledge gap, focusing on investigating sex differences and elucidating the underlying mechanisms. By expanding the available evidence base, future studies can enhance understanding of the unique aspects of diabetes mellitus prevention and

management specific to sex and gender, thus paving the way for more tailored approaches to care.

2.4 Body Composition

2.4.1 Fat Mass and Type 2 Diabetes Mellitus

The rising incidence of T2DM among adults is closely linked to the global obesity epidemic. Obesity is a major risk factor for T2DM, and, as the prevalence of obesity has increased in recent decades, so has the prevalence of T2DM.[107] This is because obesity is associated with insulin resistance, which is the body's inability to properly utilize insulin to regulate blood glucose concentrations. Insulin resistance is closely linked to body fat distribution; individuals who have a higher BMI are more likely to develop insulin resistance and T2DM.[108] Nonetheless, even lean individuals can have varying levels of insulin sensitivity due to differences in body fat distribution.

Excess adipose tissue, particularly visceral fat, can increase the risk of chronic diseases such as T2DM. Adipose tissue is found in various locations in the body, including under the skin (subcutaneous fat) and around the organs (visceral fat). Visceral fat is a type of adipose tissue that is stored in the abdominal cavity around the organs. It is also known as abdominal fat or intra-abdominal fat. Adipose tissue produces several hormones and other substances that can affect various physiological processes in the body.[109] These substances include cytokines, such as tumor necrosis

factor-alpha (TNF-alpha) and interleukin-6 (IL-6), which are markers of inflammation in the body.[110] Adipose tissue also produces free fatty acids, which can interfere with insulin signaling and contribute to insulin resistance. One way in which free fatty acids can interfere with insulin signaling is by inhibiting the action of the enzyme called AMP-activated protein kinase (AMPK).[111] AMP-activated protein kinase is activated by low concentrations of adenosine triphosphate (ATP) and stimulates the uptake of glucose by cells.[111] When free fatty acids are present in high concentrations, they can inhibit AMPK and reduce the uptake of glucose by cells, leading to insulin resistance.[111]

2.4.2 Body Mass Index

Although body mass index (BMI) is the most widely used clinical tool to estimate body fat, it has its limitations in estimating body composition.[28] Body mass index alone is insufficient to assess or manage the cardiometabolic risk associated with increased adiposity in Asian-American adults.[31,58] Researchers have reported that using standardized BMI measurements underestimates the risk for pre-diabetes and T2DM in the Asian-American population.[15,32] Further, in 2004, the World Health Organization[30] determined that the diagnosis of T2DM among Asian populations occurs at a lower BMI, and subsequently established the overweight risk range to be 22 kg/m^2 to 25 kg/m^2, compared to 25 kg/m^2 to 29.9 kg/m^2, used in White individuals. The World Health Organization then set the public health screening

point at 23 kg/m^2 for the Asian population. The American Diabetes Association's Standards of Medical Care revised their BMI reference ranges from 25 kg/m^2 to 23 kg/m^2 for Asian Americans in 2015, stating that the Asian population is at higher risk for pre-diabetes and T2DM at a lower BMI range.[112] The NHANES does not utilize the revised BMI ranges for Asian-American adults.

Hsia et al.[113] reported that lowering BMI cut-off points to 23 kg/m^2 for pre-diabetes and diabetes mellitus screening in Asian Americans increased the prevalence from 50.2% to 74.1%, respectively. The researchers[83] used NHANES data from 2011 to 2012, which is the first survey featuring Asian Americans separately, with their own ethnicity. Although their sample size was relatively small (n=341), Hsia et al.[113] only included individuals, 45 years of age and older in their analyses.

Kuerban[33] analyzed data from two NHANES cycles (2013 to 2014 and 2015 to 2016) to examine sex differences in body measurements and waist-to-height ratio with hemoglobin A1c percentage in Asian Americans. They included 900 Asian Americans (454 women, 446 men), 20 to 65 years of age, using the Asian-specific BMI cut-off of 23 to 25 kg/m^2. The women and men were categorized into three BMI categories. Of the 454 women, 49% had a BMI less than 23 kg/m^2, 17.4% had a BMI in the 23 kg/m^2 to 25 kg/m^2 range, and 33.6% had a BMI of 25 kg/m^2 or higher. Among the 446 men, 25.3% had a BMI of less than 23 kg/m^2, 23.8% had a BMI in the

23 kg/m^2 to 25 kg/m^2 range, and 50.9% had a BMI of 25 kg/m^2 and higher. When they associated HbA1c percentage to BMI, the researchers[33] reported that, among women, HbA1c percentage increased with BMI, but BMI was not as strong of an indicator compared to waist circumference ($r = 0.393$, $p < 0.001$). Among the men, the authors[33] reported that HbA1c percentage was higher with a BMI of less than 23 kg/m^2, compared to those with a BMI of 23 kg/m^2 to 25 kg/m^2. Further, they reported a stronger correlation ($r = 0.337$, $p < 0.001$) with waist-to-height ratio and HbA1c percentage compared to BMI and waist circumference. Kuerban[33] reported that BMI might not be adequate to reflect the health risk of Asian populations, and suggested using waist circumference for women and waist-to-height ratio for men as screening tools for T2DM.

Park and Kim[114] used the 2008 Korea National Health and Nutrition Examination Survey (KNHANES) data to evaluate metabolic risk factors using participants with a healthy BMI and waist circumference. The researchers also assessed whether BMI, waist circumference, or waist-to-height ratio (WHtR) were associated with metabolic syndrome, high fasting blood glucose concentrations, high blood pressure, high triglyceride concentrations and lower high density lipoprotein cholesterol (HDL-C) concentrations.[114] Their analyses included 2,952 Korean women (n=1,828) and men (n=1,124), 42.6±0.4 and 43.8±0.7 years of age, respectively. The mean BMI was 21.8±0.04 kg/m^2 for women and 22.4±0.1 kg/m^2 for

men, with a waist circumference of 74.3±0.2 cm and 79.9±0.2 cm, for women and men, respectively. The researchers used the American Heart Association/National Heart Lung and Blood Institute criteria to define metabolic syndrome as having ≥ 2 of four risk factors. The risk factors for metabolic syndrome are having three of the five risk factors, yet the authors only used the following four : 1) a fasting plasma glucose concentration of ≥ 100.90 mg/dL (5.6 mmol/L) or being previously treated for diabetes mellitus; 2) a serum HDL-C concentration of < 1.29 mmol/L for women and < 1.03 mmol/L for men; 3) a serum triglyceride concentration of ≥ 1.69 mmol/L or use of anti-lipidemic medications; and, 4) a systolic blood pressure of ≥ 130 mmHg and a diastolic blood pressure of ≥ 85 mmHg, or treatment for hypertension. The only criteria they did not use was the abdominal adiposity measurements for women (≥ 35 inches [≥ 88.9 cm]) and men (≥ 40 inches [≥ 101.6 cm]). Compared to BMI and waist circumference, WHtR had a better predictive value for metabolic syndrome in both women and men, shown by higher area under the curve values.[110] Waist-to-height ratio outperformed BMI and waist circumference in predicting metabolic syndrome and high fasting plasma glucose concentrations in Koreans with a BMI under 23 kg/m^2, which is considered the cut-off point for T2DM screening. Although Park and Kim[85] did not include assessing T2DM in their study, metabolic syndrome is linked to developing insulin resistance and eventually T2DM if not managed properly. In addition, depending on the value of fasting plasma

glucose concentrations, it can be an indicator of T2DM.

Using NHANES data from 2011 to 2018, Aggarwal et al.[15] determined if the 2021 U.S. Preventive Services Task Force's (USPSTF) diabetes mellitus screening recommendations were beneficial for races and ethnicities at-risk for diabetes mellitus. Their analyses included 19, 335 participants, 18 to 70 years of age, from five races and ethnicities (Asian Americans, Black Americans, Hispanic Americans, Americans from other ethnic backgrounds, and White Americans). They used a logistic regression model to determine the prevalence of diabetes mellitus among White Americans, 35 years of age, with a BMI of 25 kg/m^2. They used another logistic regression model to separate each ethnicity to determine the appropriate age and BMI (kg/m^2) equivalent to a White American who is 35 years of age, with a BMI of 25 kg/m^2. Aggarwal et al.[15] reported that the equivalent screening to White Americans using age and BMI were: for Asian Americans, 23 years of age with a BMI of 20 kg/m^2; for Hispanic Americans, 25 years of age with a BMI of 18.5 kg/m^2; for Black Americans, 21 years of age with a BMI of 18.5 kg/m^2. These results add to the data indicating the need to have various BMI cut-off points for different races and ethnicities with respect to T2DM.

Liu et al.[115] analyzed NHANES data from 2011 to 2018 to investigate the prevalence of obesity among Asian Americans compared to other racial or ethnic

groups in the United States. They analyzed various measures of obesity and adiposity, including BMI, waist circumference, body fat percentage, and lean body mass, and examined trends in these measures by race or ethnicity among adults in the United States. Their analyses included 21,399 adults, 20 to 59 years of age. Of the participants, 64.8% were of non-Hispanic White ancestry, 14.9% were Hispanic, 11.3% were non-Hispanic Black, and 5.6% were non-Hispanic Asian. Body mass index measurements were obtained for 21,093 of these adults, waist circumference measurements were collected for 20,080 of their population, and body fat percentage was determined for 10,864 adults. To examine linear trends over time, the authors[115] conducted multivariable linear regressions (for BMI, waist circumference, body fat percentage, and lean body mass) or logistic regressions (for obesity and abdominal obesity) using survey cycles as a continuous independent variable in the models. Age, race or ethnicity, and sex were adjusted in the models, except when used as a stratified variable.

In the overall population, the age-adjusted mean BMI increased significantly from 28.7 kg/m^2 (95% confidence interval [CI]: 28.2 to 29.1 kg/m^2) from 2011 to 2012 to 29.8 kg/m^2 (95% CI: 29.2 to 30.4 kg/m^2) from 2017 to 2018 ($p = 0.001$). This increase was reported in the Hispanic, non-Hispanic White, and non-Hispanic Asian groups ($p < 0.05$). The increases in the Hispanic and non-Hispanic White groups were mainly observed in men, while the increase in the non-Hispanic Asian group was

observed in women and men. The age-adjusted mean BMI did not change significantly among people in the non-Hispanic Black group ($p = 0.33$). When using non-Hispanic Asian-specific cut-off points, the age-adjusted prevalence of obesity increased from 20.8% (95% CI: 17.2% to 24.4%) in 2011 to 2012, to 34.2% (95% CI: 29.8% to 38.6%) in 2017 to 2018 among non-Hispanic Asians ($p < 0.001$). The overall age-adjusted prevalence of abdominal obesity increased from 54.5% (95% CI: 51.2% to 57.8%) from 2011 to 2012 to 59.1% (95% CI: 55.6% to 62.7%) from 2017 to 2018 ($p = 0.02$). However, significant increases were only observed in non-Hispanic Asian women ($p = 0.03$) and men ($p = 0.01$), and non-Hispanic White men ($p = 0.02$). Liu et al.[115] reported that non-Hispanic Asians were the only group that had increases in all adiposity measures, demonstrating the need for further investigation.

2.4.3 Waist Circumference

The current gold standard for measurement of visceral adiposity is the computed tomography (CT) scan. However, due to the cost and time requirement needed for testing, it is not an efficient tool for diabetes mellitus screening. Because Asian Americans having a lower BMI with a higher body fat percentage,[12,32] waist circumference measurements can be used as an easy and cost-effective measurement tool.[58–60] The USPSTF recommends using a lower BMI (≥ 23 kg/m^2) for Asian Americans; however, there are no waist circumference measurement recommendations that may

help identify undiagnosed diabetes mellitus.[8] The World Health Organization states that lowering the waist circumference cut-off points to values of 80 centimeters (cm) for women and 85 cm for men, would result in a more accurate assessment for metabolic risk among Asians.[72] The Centers for Disease Control and Prevention (CDC) have specific resource pages regarding Asian Americans and their risk for T2DM.[72] While the CDC provides the Asian-specific BMI of 23 kg/m^2, they still list the waist circumference values of 88.9 cm for women and 101.6 for men, which have shown to be too high for the Asian-American population. Using waist circumference values higher than the World Health Organization's recommendations will potentially mis-diagnose Asian Americans who are at-risk with undiagnosed T2DM.

Kuerban[33] analyzed NHANES data from 2013 to 2016 to examine the associations among sex and BMI, waist circumference, and WHtR with HbA1c percentage in 900 Asian Americans (454 women, 446 men), 20 to 65 years of age. The BMI cut-off of 23 to 25 kg/m^2, and the World Health Organization's waist circumference recommendations of 80 cm and 85 cm for women and men, respectively, were used. Kuerban[33] reported that waist circumference ($r = 0.393$, $p < 0.001$) was associated with a higher HbA1c percentage and higher percentages of overweight and obesity among Asian-American women.

Zhen et al.[60] examined the relationship of waist circumference with HbA1c percentage in 2,339 individuals in China (1,251 women and 951 men), 18 to 84 years of age (mean = 43.5±11.9 years of age). The researchers[60] identified waist circumference cut-off points to determine pre-diabetes and T2DM risk. Zhen et al.[60] determined that, among the Chinese population, a waist circumference of 78 cm and 86 cm were associated with HbA1c percentages of 5.7% and 6.5%, respectively, among women. In men, a waist circumference of 83 cm and 85 cm was associated with HbA1c percentages of 5.7% and 6.5%, respectively. The waist circumference measurements reported by Zhen et al.[60] are similar to the World Health Organization's recommendations of 80 cm and 85 cm for Asian women and men, respectively, for determining risk of T2DM.

2.4.4 Waist-to-Height Ratio

Like waist circumference, waist-to-height ratio (WHtR) is a screening tool for cardiometabolic risk related to body fat distribution. The WHtR, calculated by dividing waist circumference by height, has recently gained attention as an anthropometric index for measuring central adiposity. Regarding the Asian population, WHtR appears to be a more sensitive universal screening tool than BMI to detect health risks, and is as easy to use as BMI.[36] Asian Americans have higher amounts of visceral adiposity compared to other races and ethnicities of the same BMI.[35,37] The proximity of fat to the vital organs puts Asians at higher risk for insulin resistance and developing T2DM.[35,108]

Ashwell et al.[116] conducted meta-analyses to determine if waist-to-height ratio or waist circumference, is more effective than BMI for identifying risk of diabetes mellitus, hypertension, and cardiovascular disease. Thirty-one studies were included from 18 countries (six countries from Asia); 22 of the studies were specific to diabetes mellitus. The authors[116] reported that, in determining diabetes mellitus risk, the WHtR area under the curve scores were significantly greater for women ($p = 0.007$) and men ($p = 0.001$) compared to BMI. The authors[116] stated that WHtR may be a better screening tool for Asian populations compared to waist circumference, although the differences were not significant. The mean area under the curve scores for WHtR were slightly higher than waist circumference (0.75 vs. 0.74 in women, and 0.71 vs. 0.69 in men, for WHtR and waist circumference, respectively). Based on their data, Ashwell et al.[116] proposed that WHtR cut-off values for diabetes mellitus should be 0.53 for women and 0.52 men.

Kuerban[33] analyzed NHANES data from 2013 to 2016 to examine the associations among sex and BMI, waist circumference, and WHtR with HbA1c percentages in 900 Asian Americans (454 women, 446 men), 20 to 65 years of age. The BMI range of 23 to 25 kg/m^2, and the World Health Organization's waist circumference recommendations of 80 cm for women and 85 cm for men were used. Kuerban[28] reported that the WHtR was significantly correlated ($r = 0.337$, $p < 0.001$) with higher HbA1c percentages in Asian men versus BMI and waist circumference. Among the women, waist

circumference had a stronger correlation ($r = 0.393$, $p < 0.001$) with HbA1c percentage compared to BMI and waist-to-height ratio.

Zeng et al.[117] compared BMI, waist circumference, and WHtR to determine which is most appropriate for determining cardiometabolic risk factors in Chinese adults. The researchers included 84,014 women, 43 to 79 years of age, and 137,256 men, 45 to 61 years of age. All body composition, blood pressure measurements, and blood samples were completed at seven health examination centers nationwide in China. The risk factors examined were: diabetes mellitus, dyslipidemia, hypertension, and metabolic syndrome. The authors[117] reported that, for both women and men, WHtR had the biggest area under the curve for all risk factors, followed by waist circumference, and BMI ($p < 0.05$). Zeng et al.[117] defined area under the curve as a "measure of the diagnostic power of a test. An area under the curve of 1.0 indicates a perfect prediction and an area under the curve of 0.5 indicates the absence of predictive power". Further, WHtR and waist circumference had a larger Area Under the Curve of the Receiver Operating Characteristic (AUROC) in relation to diabetes mellitus among women compared to BMI, but there were no significant differences among the measures ($p > 0.05$). Zeng et al.[117] determined that WHtR is a better predictor of diabetes mellitus and dyslipidemia among women and men. Further, they proposed that ideal WHtR cut-off values should be 0.48 and 0.50 for women and men, respectively.

Nicolo et al.[118] compared NHANES data from 2003 to 2004 and 2012 to 2014, to compare if BMI, waist circumference, and WHtR were predictive of a HbA1c of ≥ 6.5%. The researchers[118] included 1,069 individuals (552 women and 517 men), 48.4±5.5 years of age, from the NHANES 2003 to 2004 data, and 905 individuals (471 women and 434 men), 49±5.7 years of age, from the NHANES 2013 to 2014. The researchers included non-Hispanic White, non-Hispanic Black, and Hispanic/Mexican Americans.

Nicolo et al.[118] reported that each body composition measurement was significantly higher ($p < 0.0001$) in the NHANES data from 2003 to 2004, compared to the NHANES data from 2013 to 2014. Body mass index was significantly higher ($p < 0.0001$) in 2003 to 2004 compared to 2013 to 2014. In the NHANES 2003 to 2004 database, 0.7% of adults had a BMI of < 18.5 kg/m^2, while 20.6% of adults had a BMI of < 18.5 kg/m^2 in 2013 to 2014. They reported a BMI between 18.5 to 24.9 kg/m^2 in 23.6% of adults in 2003 to 2004, and in 29.3% of adults in 2013 to 2014. Nicolo et al.[118] reported that, in 2003 to 2004, 36.5% of adults had a BMI between 25 to 29.9 kg/m^2, while in 2013 to 2014, 23.6% of adults had a BMI between 25 to 29.9 kg/m^2. In addition, the researchers[118] reported a BMI of ≥ 30 kg/m^2 in 39.2% of adults in the NHANES 2003 to 2004 database, and a BMI of ≥ 30 kg/m^2 in 26.5% in the NHANES 2013 to 2014 database. Further, 87.7% of adults had a WHtR that was significantly greater than 0.5 ($p < 0.0001$) in 2003 to 2004, compared to 67.2% in 2013 to 2014.

Nicolo et al.[118] reported that, for the 2003 to 2004 NHANES data, BMI and WHtR were both positively associated with a HbA1c of ≥ 6.5% ($p < 0.0001$). Further, in analyses that adjusted for sex, ethnicity, and BMI, waist circumference and WHtR were both positively associated with a HbA1c of ≥ 6.5% in the 2003 to 2004 NHANES database ($p < 0.0001$). The researchers[118] stated that there were no positive correlations among BMI, waist circumference, WHtR and HbA1c ≥ 6.5% in the 2013 to 2014 NHANES database.

2.4.5 Visceral Adiposity Index

Compared to BMI, waist circumference and WHtR[33,38,119] are better proxies for the evaluation of adiposity. The issue with BMI is that it does not take into account the difference between muscle mass and body fat. Yet, while waist circumference and WHtR measure central adiposity, the limitation with both measures is the inability to separate subcutaneous and visceral fat mass.[26] It is crucial to distinguish between subcutaneous and visceral fat mass in relation to T2DM. Increasing amount of visceral fat has been shown to decrease insulin sensitivity, which can increase the risk for developing T2DM.[26] Further, the Asian population may be genetically predisposed to have higher amounts of visceral fat at a lower BMI and waist circumference compared to other races and ethnicities.[120] The visceral adiposity index (VAI) is a mathematical formula that consists of BMI and waist circumference, as well as clinical measurements such as serum triglyceride and HDL-C concentrations.[26] The VAI formula can be used to

assess visceral adiposity function, which correlates with insulin sensitivity. The VAI may be a better predictor of metabolic disorders associated with insulin resistance than a single anthropometric index.[41,63,121] The VAI equations are as follows:

Females: VAI = (waist circumference [cm]/39.58 + (1.89 x body mass index [kg/m^2]) x (triglyceride concentration [mmol/L]/0.81) x (1.52/high density lipoprotein concentration [mmol/L])[26]

Males: VAI = (waist circumference [cm]/39.68 + (1.88 x body mass index [kg/m^2]) x (triglyceride concentration [mmol/L]/1.03) x (1.31/ high density lipoprotein concentration [mmol/L])[26]

Amato et al.[26] proposed using the visceral adiposity index to determine if VAI was better than BMI and waist circumference for predicting T2DM. The VAI was validated using magnetic resonance imaging (MRI) and the euglycemic-hyperinsulinemic clamp, the gold standard for assessing insulin sensitivity. The euglycemic-hyperinsulinemic clamp procedure, created by DeFronzo et al.[122], infuses insulin to increase plasma insulin concentrations to 100 μU/mL, where it is maintained by continually infusing insulin for 120 minutes. Concurrently, a fixed glucose infusion occurs that must be equal to the rate of glucose being metabolized (M value), which is the measure of whole-body insulin sensitivity.[122] The M value is calculated by dividing

infused glucose (milligrams [mg]) by body weight (kilograms [kg]) during the last 40 minutes of the test (mg per kg per minute).[122]

The researchers included 315 women and men from the Alkam Metabolic Syndrome Study database. The participants had a BMI between 20 kg/m^2 and 30 kg/m^2. Twenty-six participants, who were considered metabolically healthy, had MRI performed. The euglycemic-hyperinsulinemic clamp was performed on 74 participants. The authors[26] reported that MRI showed that VAI was significantly correlated with visceral adipose tissue area ($r = 0.437$, $p = 0.025$) and volume ($r = 0.744$, $p < 0.001$). Further, there was a significant inverse correlation ($r = -0.721$, $p < 0.001$) between visceral adiposity index and euglycemic-hyperinsulinemic clamp M values. No correlation was found between waist circumference, BMI and M values.

Jiang et al.[41] conducted a study using NHANES data from 1999 to 2020 to determine if there is a relationship between VAI and insulin resistance among 27,309 participants (14,010 females and 13,299 males), 47.2±18.9 years of age. The homeostasis model assessment of insulin resistance (HOMA-IR) is a formula used to evaluate insulin resistance. The formula uses fasting blood glucose (mmol/L) x fasting insulin (μU/mL)/22.5. The researchers used HOMA-IR index values of ≥ 2.73 and ≤ 2.73 for positive and negative insulin resistance, respectively. Four logistic regression models were created to determine the relationship between insulin resistance and VAI. Of the

four models, model one was unadjusted and model two adjusted for ethnicity, sex, and age. The authors did not state how models three and four were adjusted, only that they were similar. Yet, regardless of the model and adjustments, there was a positive relationship between insulin resistance and VAI ($p < 0.001$). In addition, regardless of ethnicity (Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, and Other races), as VAI scores increased, the probability of insulin resistance also increased ($p < 0.001$). Although the researchers included data from NHANES when oversampling of Asian Americans began in 2011, the researchers did not include the Asian ethnicity due to incorporating previous cycles before the inclusion of the Asian-American population.

Oh et al.[63] evaluated if VAI could replace computed tomography (CT) scanning in predicting insulin resistance. The participants were 180 Korean women, 25±5 years of age, with polycystic ovary syndrome (PCOS). The women completed a 75-gram oral glucose tolerance test and euglycemic-hyperinsulinemic clamp tests using the DeFronzo et al.[122] protocol to assess insulin sensitivity (M value). A multiple logistic regression determined a positive correlation ($r = 0.57$, $p = 0.002$) between VAI and visceral fat area from the CT scan. Furthermore, they reported a negative correlation with their multiple linear regression ($r = -0.55$, $p = 0.0033$) between VAI and the M value. Women with PCOS may typically have abdominal adiposity or T2DM. The Korean women with PCOS had a mean BMI of 23.0±4.3 kg/m^2 and waist circumference 74.8±11 cm,

demonstrating that insulin resistance and increased visceral adiposity occurred at a lower BMI and waist circumference than the typical T2DM screening cut-off points.

Amato et al.[26] did not provide any cut-off values for the VAI they developed that would identify someone at-risk for insulin resistance, metabolic syndrome, or T2DM. In a follow-up study, Amato et al.[123] determined VAI cut-off values for people at-risk for metabolic syndrome. The researchers studied 1,764 Sicilian women (n=1,179) and men (n=585), 47.80±18.28 years of age. The participants were stratified into five age groups: < 30 years of age, ≥ 30 to < 42 years of age, ≥ 42 to < 52 years of age, ≥ 52 to < 66 years of age, and ≥ 66 years of age. The cut-off values for VAI were determine by Receiver Operating Characteristic (ROC) curve analyses that predicted the risk of metabolic syndrome among participants in their respective age group. Amato et al.[123] reported the following VAI scores for predicting metabolic syndrome based on age stratification: 2.52 for < 30 years of age, 2.23 for ≥ 30 to < 42 years of age, 1.92 for ≥ 42 to < 52 years of age, 1.93 for ≥ 52 to < 66 years of age, and 2.00 for ≥ 66 years of age. The authors[123] cautioned that these scores only apply to a Sicilian population.

There are no agreed upon general VAI cut-off points for Asian populations to determine their risk of metabolic syndrome or T2DM. Two groups of researchers in China have reported that a VAI score under 1.59 is metabolically healthy, while a VAI score over 1.59 is metabolically unhealthy for women and men older than 18 years of

age.[121,124] The scores are based on the National Cholesterol Education Program Adult Treatment Panel III criteria for diagnosing metabolic syndrome.[125] The VAI cut-off values are lower than what Amato et al.[123] reported, potentially due to the typical lower body weight, BMI, and waist circumference reported in Asian populations compared to other races and ethnicities. The literature is limited on ideal cut-off values and whether VAI is associated with insulin resistance and T2DM specific to the Asian-American population.

2.5 Sedentary Behavior and Physical Inactivity

According to the Centers for Disease Control and Prevention (CDC), not meeting the recommended amount of physical activity per week is associated with 117 billion dollars in annual health care costs.[43] Further, meeting the recommended amounts of physical activity can prevent 1 in 12 cases of T2DM.[43] One of the most well-established mechanisms through which individuals with T2DM improve metabolic health with exercise is through adaptations to skeletal muscle, which, in turn, lead to improved skeletal muscle insulin sensitivity.[44]

The importance of physical activity cannot be understated. The Diabetes Prevention Program Research Group[126] conducted a three-year landmark trial to determine if lifestyle changes could reduce the risk of T2DM in people with high risk. The researchers included 3,234 individuals (2,191 women and 1,043 men), 50.6±10.7 years of age. The study population was ethnically diverse to include people from racial

and ethnic backgrounds that are at higher risk for T2DM compared to their White counterparts. The races and ethnicities included were: Asian/Pacific Islanders (n=142), American Indian (n=171), Hispanic (n=508), African American (n=645), and White Americans (n=1,768). Eligibility was based on having a BMI of 24 kg/m^2 or higher, and a BMI of 22 kg/m^2 or higher for Asian Americans. In addition, to qualify for the study, participants had to have completed a 75-gram oral glucose tolerance test and have a plasma glucose concentration between 140 and 199 mg/deciliter (dL) two-hours post-test. The participants were randomized into a lifestyle modification group (diet and physical activity), a Metformin group (Metformin is an oral anti-hyperglycemic medication in the biguanide class [prevents glucose synthesis in the liver]), or a placebo group. The lifestyle modification group received 24 weeks of one-on-one teaching of a 16-lesson program based on behavioral modifications of incorporating exercise and healthy eating into their life. The lifestyle modification group was instructed to lose 7% of their initial body weight and maintain it by incorporating 150 minutes of moderate intensity physical activity per week, while consuming a low-energy, low-fat diet. According to the Diabetes Prevention Program, the description of lifestyle intervention was as follows: "The kilocalorie (kcal) goals were calculated by estimating the daily kcal needed to maintain the participant's starting weight and subtracting 500 to 1,000 kcals per day (depending on initial body weight) to achieve a one to two pound per week weight loss. The fat goals, given in grams of fat per day, were based on 25% of calories

from fat. Four standard kcal levels were used: 1,200 kcal per day (33 grams of fat) for participants with an initial weight of 120 to 170 pounds, 1,500 kcal per day (42 grams of fat) for participants with a weight of 175 to 215 pounds, 1,800 kcal per day (50 grams of fat) for participants with a weight of 220 to 245 pounds and 2,000 kcal per day (55 grams of fat) for participants weighing >250 pounds".[127]

The Metformin group took 850 mg of Metformin (Glucophage) twice a day, and were also provided with written documents about standard lifestyle recommendations, such as increasing physical activity and consuming a healthy diet. The placebo group was given a placebo, identical looking to Metformin, plus they were provided lifestyle recommendations through written documents.

At the end of 24 weeks, 50% of the lifestyle modification group lost at least 7% of their body weight, and 74% met their physical activity goals. There was a significant difference ($p < 0.001$) between the kilocalorie (kcal) deficit maintained after a year among the groups. The lifestyle modification group maintained an energy deficit of 450±26 kcals, while the Metformin group maintained an energy deficit of 296±23 kcals, and the placebo group maintained an energy deficit of 249±27 kcals. There was a significant difference ($p < 0.001$) in weight loss among the groups: the lifestyle modification group lost 5.6 kg, the Metformin group lost 2.1 kg, and the placebo group lost 0.1 kg. At the end of the three-year study, the lifestyle modification group had a

58% reduction in the incidence of diabetes mellitus compared to the placebo group. Additionally, the Metformin group reduced their incidence of T2DM by 31% compared to the placebo group. Of note, the Asian-American lifestyle group had a 71% reduction in the incidence of diabetes mellitus compared to the placebo group, while the Metformin group had a 38% reduction compared to the placebo group. The Diabetes Prevention Program was the first to demonstrate that T2DM can be delayed or prevented through physical activity and dietary intake modifications.

The American Diabetes Association recommends that adults with T2DM exercise daily or at least every other day, incorporating both aerobic and anaerobic activities. The aim is to meet the current Physical Activity Guidelines for Americans of at least 150 minutes a week of moderately-intense physical activity, or 75 minutes per week of vigorously-intense physical activity, including two days of resistance training per week.[17] Reducing sedentary time and ensuring breaks from prolonged sedentary behavior of greater than 30 minutes with light activity is also recommended for managing T2DM.[17]

2.5.1 Physical Activity and Glucose Uptake

Skeletal muscle is necessary for glucose clearance and is responsible for 80% of postprandial glucose uptake from circulation.[44] Skeletal muscle contraction stimulates the movement of GLUT4 to the plasma membrane to transport glucose into the cell.[128]

The glucose transporters (GLUTs) are a part of a larger group of 14 glucose transporters.[128] There are only three glucose transporters in skeletal muscle that facilitate the uptake of glucose: GLUT1, GLUT4, and GLUT3, which is only found in neonatal muscle.[128] Further, GLUT4 can be found in adipose tissue, where it also facilitates the uptake of glucose. The activation of GLUT4 occurs via insulin and exercise stimulation.[44,128]

In individuals with T2DM, insulin concentrations are normal or high, but tissues such as skeletal muscle become resistant to insulin.[44] The increase in circulating insulin can result in impaired glucose transport into the skeletal muscle.[44] Insulin is a potent stimulator of glucose transport in skeletal muscle.[44] In individuals with T2DM, insulin-stimulated glucose uptake in skeletal muscle is impaired due to physical inactivity, skeletal muscle lipid accumulation, and skeletal muscles' diminished response to insulin signaling.[44,128–130] Further, insulin resistance in skeletal muscle may be due to mitochondrial dysfunction, leading to impaired glucose and fat metabolism in skeletal muscle.[131]

Physical activity is necessary for individuals with T2DM to improve skeletal mitochondrial dysfunction, which is important for maintaining skeletal muscle insulin sensitivity and glucose uptake.[44,131,132] Physical activity may lead to improvements in

beta cell function by improving insulin sensitivity and secretion, which enables individuals with T2DM to improve glucose uptake and tolerance.[133,134]

2.5.2 Physical Activity, Sedentary Behavior, and Type 2 Diabetes Mellitus

The ADA's and American College of Sports Medicine's position stand on physical activity and diabetes mellitus states that, for prevention and delay of T2DM, physical activity (aerobic and/or resistance training) is crucial for maintaining insulin sensitivity and blood glucose control.[135,136] Furthermore, higher amounts of physical inactivity are associated with an increased risk of developing T2DM. For individuals who are at-risk for developing T2DM, physical inactivity is associated with poor glycemic control.

Physical inactivity is defined as engaging in less than 10 minutes per week of moderate- or vigorous- physical activity established by the 2018 Physical Activity Guidelines for Americans.[137] Moderate and vigorous physical activity is defined as engaging in aerobic exercise at an intensity within 40% to 59%, and 60% to 89% of heart rate reserve, respectively.[137] Heart rate reserve is calculated by subtracting resting heart from predicted maximum heart rate (using the Karvonen equation: 220 – age = predicted maximum heart rate). For resistance training, moderate and vigorous intensity is defined as 50% to 69%, and 70% to 85% of a one-repetition maximum strength, respectively.[137]

The Sedentary Behavior Research Network (SBRN) has defined sedentary behavior as any waking behaviors characterized by an energy expenditure ≤ 1.5 metabolic equivalents (METs), while in a sitting, reclining, or lying posture.[138] Screen time and sitting time are the two main indicators used to quantify the time devoted to sedentary behaviors.[138] Physical activity and sedentary behaviors are not the opposite of each other. Individuals are considered active when they reach physical activity recommendations for their age, which does not prevent them from devoting a significant part of their time to sedentary behaviors.[138] The NHANES reports physical inactivity as sedentary behavior; and thus, for the remainder of this section, sedentary behavior will be used in place of physical inactivity.

According to the National Diabetes Statistics Report from the CDC, of the newly diagnosed T2DM cases in adults (18 years of age and older), 34% reported being physically inactive.[139] Although physical activity may be a modifiable risk factor for glycemic control, increasing time spent in sedentary behavior may be a predictor of hemoglobin A1c percentage. Nicolo et al.[140] compared NHANES data from 2003 to 2004 and 2012 to 2014, to determine if sedentary behavior, defined as television and computer time, was predictive of HbA1c of ≥ 6.5%. Their analyses included 1,069 individuals (552 women and 517 men), 48.4±5.5 years of age, from the NHANES 2003 to 2004 data, and 905 individuals (471 women and 434 men), 49±5.7 years of age, from the NHANES 2013 to 2014. The researchers included non-Hispanic White, non-Hispanic

Black, and Hispanic/Mexican Americans. Nicolo et al.[140] report that sedentary behavior of eight or more hours per week was predictive of having a HbA1c of 6.5% or greater only with the NHANES data from 2003 to 2004. While these researchers[140] did not include Asian Americans, examining the relationship between sedentary behavior and HbA1c percentage should be conducted using NHANES data in years when Asian Americans were included.

Zhu et al.[141] examined NHANES data from 2011 to 2016 to evaluate if a correlation existed between acculturation and physical activity levels among Asian Americans. Their analyses included 1,989 Asian-American adults (1,022 women and 967 men), 20 years of age and older. Acculturation was determined by language spoken at home, country of birth, and years lived in the U.S. There were four stratifications to which the participants were categorized: 1) individuals born in the U.S.; 2) individuals who immigrated to the U.S. and have lived in the U.S. for 30 or more years; 3) individuals who immigrated to the U.S. who have lived in the country for 10 to 29 years; and 4) individuals who have lived in the U.S. less than 10 years.

The measurement of physical activity was assessed in two ways. First by evaluating if participants were meeting the 2010 World Health Organization Physical Activity Guidelines. According to the 2010 World Health Organization Physical Activity Guidelines, adults between 18 and 64 years of age should engage in at least 150

minutes of moderate-intensity aerobic activity per week, or 75 minutes of vigorous-intensity aerobic activity per week, or a combination of both. These activities should be performed in intervals of at least 10 minutes. For even more health benefits, adults should aim to perform 300 minutes of moderate-intensity aerobic activity per week, or 150 minutes of vigorous-intensity activity per week, or a combination of both. In addition, adults should partake in muscle-strengthening activities involving major muscle groups at least two days per week.[142]

Another way physical activity was measured was to evaluate if participants were meeting the metabolic equivalents (METs) of tasks in minutes of moderate-to-vigorous physical activity. The participants were either grouped by not meeting the 2010 World Health Organization Physical Activity Guidelines or by having ≥ 600 MET-minutes of moderate-to-vigorous physical activity. The 600 MET-minutes is the equivalent to meeting 150 minutes of moderately intense aerobic physical activity throughout the week, or performing at least 75 minutes of vigorously intense aerobic physical activity per week. Minutes of vigorously intense aerobic physical activity minutes were measured from completing the International Physical Activity Questionnaire (IPAQ) that is used by NHANES. Further, NHANES states that moderate physical activity is ≥ 4 METs and vigorous physical activity is ≥ 8 METs. A metabolic equivalent is the amount of energy to provide the intensity of an activity. For example, 1.5 METs would be equivalent to sitting or lying down. Zhu et al.[141] stated that "MET-minutes/week for an

activity was the product of MET score for each activity and the minutes per week performing the activity. The total moderate and vigorous physical activity MET-minutes/week was the sum of the MET-minutes from the moderate and vigorous physical activities in a week".

There was a significant difference ($p < 0.05$) in physical activity levels between Asians born in and outside of the U.S.: 56.9% of Asians born in the U.S. and 37.6% of Asians born outside of the U.S. met the 2010 World Health Organization Physical Activity Guidelines. Furthermore, 37.01% of Asian Americans who lived in the U.S. for less than 10 years met the 2010 World Health Organization Physical Activity Guidelines. There was also a significant difference ($p < 0.05$) between language spoken at home and meeting the 2010 World Health Organization Physical Activity Guidelines. The Asian participants who only spoke English at home had the highest rates of meeting the 2010 World Health Organization Physical Activity Guidelines, compared to Asians born outside of the U.S. who spoke English and who did not speak English at home (50.53% vs 45.01%, respectively; $p < 0.05$). Additionally, only 31% of Asians born outside of the U.S. who did not speak English at home met the 2010 World Health Organization Physical Activity Guidelines. The authors[141] reported that two factors determined the likelihood that the 2010 World Health Organization Physical Activity Guidelines would be met. First, U.S. born Asians and non-U.S. born Asians with a longer length of stay in the U.S. increased the likelihood of meeting the 2010 World

Health Organization Physical Activity Guidelines. Moreover, Asians who were not born in the U.S. were more likely to meet the 2010 World Health Organization Physical Activity Guidelines if they spoke English at home.

2.6 Magnesium

Magnesium is a mineral that is required for over 300 metabolic reactions in the body.[143,144] The body contains approximately 21 to 28 grams of magnesium; 99% is in the bone, skeletal muscle, and non-muscle soft tissue.[143,145] Approximately 1% of extracellular magnesium is located in the blood. Magnesium is involved in reactions that generate ATP, which is necessary for glycolysis, anaerobic and aerobic energy production, and the metabolism of protein and fats. [143,145] Magnesium aids in the transport of calcium and potassium across cell membranes. Magnesium is required for deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) synthesis, muscle contraction, relaxation, and nerve function.[145,146] Furthermore, magnesium plays an important role in normal heart rhythm, normal blood pressure, and insulin secretion.[145,146] In addition, magnesium provides a structural function for proteins, nucleic acids, and mitochondria.[145,146]

2.6.1 Magnesium Metabolism

Magnesium functions as a coenzyme in the phosphorylation and transfer of ATP. Magnesium is also involved in metabolic pathways, including thermogenesis, tyrosine

kinase activity, and glucose metabolism.[147,148] Most dietary magnesium intake (24% to 76%) is absorbed in the small intestine, primarily in the distal part of the jejunum and the ileum.[143,147] Magnesium is eliminated from the body through sweat (about 15 mg/day) and feces (about 20 to 50 mg/day).[143,147] The kidneys regulate serum magnesium concentration, filtering, reabsorbing, and removing excess magnesium from the body.[143,147] In addition, 95% of the filtered magnesium is reabsorbed in the kidneys, while 3% to 5% is eliminated in the urine.[143,147,149] The efficiency of magnesium absorption is dependent on intracellular magnesium concentrations.

2.6.2 Measuring Magnesium Status

There are several ways to evaluate magnesium status. More common methods of assessing magnesium status include measuring serum magnesium concentrations, ionized magnesium concentrations, and red blood cell concentration concentrations.[144,149] Although the magnesium loading test, which requires a 4- to 24-hour urine sample, is considered the gold standard to assess magnesium status, it is not typically used due to the cost and time constraints.[150–152] Stable isotopes of magnesium can be used; however, they also are expensive and pose time constraints.[149–151] The most common test for assessing magnesium status is by measuring serum magnesium concentrations. Serum magnesium concentration is often used as a surrogate marker of magnesium status; however, it does not reflect total body magnesium[149–151], and typically

lags behind with respect to a magnesium deficiency. Serum magnesium concentration is still considered a good biomarker of magnesium status, but only because it is what is currently used in clinical practice due to reasonable costs and established assessment methods.[149–151] Magnesium concentrations are generally between 1.5 to 2.7 mg/dL (0.62 to 1.11 mmol/L). Serum magnesium concentrations that fall below 1.2 mg/dL are defined as hypomagnesemia.[149–151] Although magnesium deficiency is not common among healthy individuals, symptoms of magnesium deficiency include: dysrhythmias, muscle spasms, osteoporosis, paresthesia (pins and needles), fatigue, weakness, loss of appetite, nausea, and vomiting. Type 2 diabetes mellitus, medications, such as diuretics, consumption of ultra-processed foods, and alcoholism can cause magnesium deficiency.[153,154]

2.6.3 Food Sources of Magnesium in the United States

The Recommended Dietary Allowances (RDA) for magnesium, established by the Institute of Medicine (now called the National Academy of Medicine), are 310 mg/day for women and 400 mg/day for men, 19 to 30 years of age.[155] For individuals, 31 to 51+ years of age, the RDA increases to 320 mg/day for women and 420 mg/day for men.[155] Good sources of dietary magnesium include: avocados, bananas, blackberries, corn, dark chocolate, dairy products (e.g., milk, yogurt), fatty fish (e.g., salmon, mackerel, halibut), green peas, leafy green vegetables, legumes (e.g., black beans,

edamame, lima beans), nuts (e.g., almonds, cashews, peanuts), papayas, potatoes, seeds (e.g., chia seeds, flaxseeds, pumpkin seeds), tofu, whole grains (oats and bran).[156] Additionally, water intake amounts to around 10% of daily magnesium consumption.[145]

Overconsumption of magnesium typically does not lead to any adverse health risks due to the role of the kidneys in removing excess magnesium.[156] However, some side effects of overconsumption of magnesium and/or diseases that may result in higher magnesium retention (e.g., kidney failure) include: hypotension, nausea, vomiting, facial flushing, urinary retention, depression and fatigue.[157] Symptoms of magnesium toxicity include weakened muscles, abnormally slow heart rate, and cardiac arrest.[157]

2.6.4 Magnesium and *Type 2 Diabetes Mellitus*

Magnesium deficiency may occur due to low dietary intake, poor absorption, and increased waste removal from the body.[144,145,147,149] Medications like immunosuppressants, antibiotics, and proton pump inhibitors can lead to magnesium deficiency.[144,145,147,149] Additionally, insufficient magnesium intake has been correlated with several diseases such as metabolic syndrome, cardiovascular disease, T2DM, and hypertension.[144,145,147,149] Magnesium is involved in metabolic insulin action and the regulation of insulin-mediated cellular glucose uptake.[158] Magnesium deficiency may result in a dysfunction of tyrosine kinase, which decreases insulin sensitivity.[158] Decreased magnesium intake can lead to beta cell dysfunction, resulting in

hyperinsulinemia, leading to impaired insulin signaling.[158,159] Inflammation can occur due to deficient magnesium concentrations that impair insulin signaling.[158] Additionally, carbohydrate metabolism is altered, leading to impaired glucose metabolism. Impaired insulin signaling and glucose metabolism can lead to insulin resistance and hyperglycemia, potentially resulting in T2DM.[158] Normal insulin secretion and glucose metabolism may depend upon sustaining normal serum magnesium concentrations.[158]

Fang et al.[160] conducted a dose-response meta-regression analyses of prospective cohort studies to determine a dose-response relationship among dietary magnesium intake and risk of T2DM, cardiovascular disease, and all-cause mortality. Their meta-analyses included 40 prospective cohort studies (n=1,000,000) that included 26,299 cases of T2DM, 7,678 cases of cardiovascular disease, 6,845 cases of coronary heart disease, 701 cases of heart failure, and 14,755 cases of stroke. Fang et al.[160] selected prospective studies published from 1999 through 2016, with a range of follow-ups, from four to 30 years. The studies that met Fang et al.'s[160] criteria represented a number of countries, and included studies conducted in the following countries: 22 from the United States, six from China, five from Japan, two from Sweden, and one each from Australia, Finland, Germany, Spain and the United Kingdom. The researchers[160] reported a significant ($p < 0.001$) non-linear relationship between magnesium intake and T2DM. Further, the dose-response relationship scale was from 100 mg per day to 500 mg per

day. The most important finding they reported was that the risk of T2DM was reduced by 8% to 13% for every 100 mg/day increase in dietary magnesium intake.

Fang et al.[71] conducted a systematic review and meta-regression analyses of cohort studies to determine a dose-response relationship between dietary magnesium intake and risk of T2DM. They included 25 studies from 17 cohorts (n=637,922) with 26,828 T2DM cases across the U.S., Australia, Europe (Finland, Germany, United Kingdom, Spain, Sweden), and Asia (China, Japan, Taiwan). Fang et al.[71] categorized magnesium intake into four groups: < 50 mg/day, 50 to 99 mg/day, 100 to 149 mg/day, and ≥ 150 mg/day.

The researchers[71] reported a significant ($p < 0.010$) linear dose-response relationship between T2DM and incremental dietary magnesium intake. Fang et al.[71] reported that the risk of T2DM was reduced by 4% to 7% for every 50 mg/day increase in dietary magnesium intake, which is equivalent to a reduction of 8% to 14% for every 100 mg/day increase. This effect was more pronounced in the Asian population, where a 100 mg/day increment was associated with a 13% reduction in T2DM risk ($p < 0.022$). These results are consistent with the results of other meta-analyses.[160] The researchers[71] recommended that dietary magnesium intake be increased above the current RDA of 320 mg/day for women and 420 mg/day for men, 30 years of age and older.

Asbaghi et al.[161] conducted a systematic review and meta-analyses to evaluate the effects of oral magnesium supplementation on glycemic control in individuals with

T2DM. The researchers[161] included 18 eligible randomized clinical trials in their final analyses. Based on their criteria, the researchers included a total of 1,097 participants (571 in the magnesium supplemented groups, and 526 in the control groups). The mean age of the participants in these studies ranged from 18 to 75 years of age. Most of the researchers who conducted the randomized controlled trials used a parallel design, except for two studies, in which the researchers used a crossover design.

Asbaghi et al.[161] evaluated the effects of oral magnesium supplementation on glycemic control in individuals with T2DM from 18 randomized controlled trials. The randomized controlled trials were conducted in various countries, including: Australia, Brazil, India, Iran, Italy, Mexico, Netherlands, and Norway. The dose of oral elemental magnesium supplementation given in these studies ranged from 36.49 mg/day to 500 mg/day, and the duration of the interventions ranged from four to 24 weeks. Based on the Cochrane scores, five of the studies were classified as fair- or weak-quality studies, while the rest were considered to be good-quality studies. The researchers used a one-stage robust error meta-regression model to analyze the data.

Asbaghi et al.[161] reported that oral magnesium supplementation at a dose of 500 mg/day reduced HbA1c percentages by 0.73% ($p < 0.004$). However, the effect on fasting blood glucose concentrations was minimal, and the evidence supporting this effect was not significant ($p < 0.092$). After a period of 24 weeks, the researchers noted significant

improvements in both fasting blood glucose concentrtions, which decreased by an average of 15.58 mg/dL ($p < 0.034$), and HbA1c percentages, which decreased by 0.48% ($p < 0.001$). The researchers[161] concluded that oral magnesium supplementation may be beneficial for glycemic control in individuals with T2DM; however, more research is required to establish clinical guidelines.

2.7 Ultra-Processed Foods

Ultra-processed foods are types of foods that undergo multiple levels of industrial processing. These foods have a lower micronutrient density compared to unprocessed or minimally processed foods, which means they may not provide the same amount of important nutrients, such as vitamins and minerals.[162] One specific nutrient that may be lacking in diets high in ultra-processed foods is magnesium.

Pachipala et al.[163] analyzed NHANES data from 2011 to 2018 to examine ultra-processed food consumption among Asian Americans, including analyses of sociodemographic and self-reported health characteristics, as well as the potential influence of acculturation. The researchers included 2,404 Asian-American adults, over 18 years of age, with at least two 24-hour dietary recalls. They conducted supplementary analyses comparing ultra-processed food consumption among different racial and ethnic groups included Asian-American (n=2,404), non-Hispanic White (n=7,761), non-Hispanic Black (n=4,736), Hispanic (n=4,995), and non-Hispanic "other"

(n=784) adults living in the U.S. with valid 24-hour dietary recall data. The 24-hour dietary recall was used to calculate ultra-processed food consumption, which is defined as the percentage of kcals derived from ultra-processed foods. The NOVA (not an acronym) framework was utilized to classify ultra-processed foods.

The NOVA framework is a classification system that categorizes foods based on their level of processing, allowing for comparison between foods of different cultural backgrounds.[163] It categorizes foods into four categories: unprocessed/minimally processed, processed culinary ingredients, processed foods, and ultra-processed foods.[163] Ultra-processed foods are highly processed and often contain many additives and preservatives, such as instant soups, ready-made sauces, granola bars, and pre-sweetened drinks. Pachipala et al.[163] evaluated the percentage of total energy derived from ultra-processed foods by using the NOVA classification system and analyzing data from two 24-hour dietary recalls.

The researchers[163] assessed acculturation using four proxy measures: self-reported place of birth, length of time living in the United States, language spoken at home, and an acculturation index combining the first two measures. Birthplace status was classified as either U.S.-born or foreign-born. Length of time living in the United States was divided into three categories: less than 10 years, 10 to 19 years, and 20 or more years. Language spoken at home was divided into three categories: non-English

only, a combination of English and another language, and English only. The acculturation index was calculated by summing the first two measures and separating the participants into three categories: least acculturated, somewhat acculturated, and most acculturated, respectively. Pachipala et al.[163] included demographic information such as sex, age, and marital status, as well as socioeconomic factors, such as education level and income. Participants were also asked to self-report their general health status and their perception of the healthiness of their diet, with the options of excellent/very good, good, or fair/poor.

Pachipala et al.[163] reported that the mean percentage of energy intake from ultra-processed foods was significantly higher among American-born Asian Americans (51.5% of kcals) compared to those born abroad (37.1% of kcals) ($p < 0.01$). Similarly, those who had lived in the United States for at least 20 years (33.8% of kcals) had significantly higher ultra-processed food consumption than those living in the United States for less than 10 years (35.0% of kcals) ($p < 0.05$). Overall, classification using the acculturation index revealed that the "most acculturated" Asian Americans consumed significantly more ultra-processed foods (48.8% of kcals) than their "least acculturated" counterparts (34.3% of kcals) ($p < 0.05$). Pachipala et al.'s[163] multivariable adjusted models showed a strong association between greater levels of acculturation and ultra-processed food consumption. The percentage of energy intake from ultra-processed foods was 11.7% greater among Asian Americans born in the U.S. compared to those

born abroad, adjusting for age, sex, marital status, educational level, family income-to-poverty ratio, self-reported general health status, and self-reported dietary health. Consumption of ultra-processed foods was also significantly greater among Asian Americans who were not born in the U.S., but who had been living in the United States for more than 20 years (38.2% of kcals), compared to those living in the United States for less than 10 years (35.0% of kcals) ($p < 0.05$). In addition, those who spoke only English at home consumed significantly more ultra-processed foods (47.4% of kcals) than Asian Americans who spoke only a non-English language, and Asian Americans born in the U.S. compared to Asian Americans not born in the U.S. and living in the U.S. for less than 10 years.

In supplemental analyses, the proportion of total kcals derived from ultra-processed foods was 39.3% for Asian Americans, 57.7% for non-Hispanic Whites, 60.1% for non-Hispanic Blacks, and 52.7% for Hispanic Americans. For the group labeled as "non-Hispanic other", the mean consumption of ultra-processed foods was 57.7%. When compared to all other groups, the percentage of kcals derived from ultra-processed foods was significantly lower for Asian Americans ($p < 0.01$).

Santos et al.[164] conducted a cross-sectional study to evaluate magnesium intake and eating patterns in 147 individuals, 19 to 59 years of age, living in Brazil. Dietary intake was evaluated using 24-hour dietary recalls. Santos et al. (2023) reported that magnesium deficiency (measured via plasma magnesium concentrations) increased the

risk of having a high HbA1c percentage by 5.893 (p = 0.041). Participants with T2DM and with a magnesium deficiency had an 8.312 times greater risk of having a high HbA1c percentage. Magnesium deficiency was associated with an unhealthy dietary pattern (e.g., high consumption of red meat, eggs, salty, and fried foods), which further worsened glycemic control in individuals with T2DM. Although Santos et al.[164] conducted this study in Brazil, and not among an Asian population, it further demonstrates that magnesium intake and a diet high in processed or ultra-processed foods, can lead to poor glycemic control, especially among individuals with T2DM.

2.8 Additional Considerations

Although the primary focus of the present study was to determine predictive risk factors for T2DM among Asian Americans, all variables involved with increasing the risk for T2DM could not be included. However, some additional factors that can affect T2DM will be discussed. The Model Minority Myth is one of these factors. In addition, other factors that are discussed and were used as covariates, include: acculturation, socioeconomic status, social determinants of health, health inequities, smoking, and alcohol consumption.

2.8.1 Model Minority Myth

The "Model Minority Myth" is the notion that Asian Americans have overcome racism and have achieved equality and equity similar to White Americans.[165,166] The

"Model Minority Myth" was used to incorrectly demonstrate that Asian Americans had overcome racism through hard work, in an attempt to discredit the Civil Rights Movement in the 1960s, and to drive a wedge between Asian and Black Americans during the Civil Rights protests. The Model Minority Myth inappropriately stated that Asian Americans were not disadvantaged or underprivileged.[167,168] Further, during the 1970s U.S. Census, Asian Americans were shown to be highly educated with a high household income.[167,168] This statistic did not take into account large multi-generational families, living in one household, with working adults earning an income, and having one family member who had been able to obtain a higher education. The Model Minority Myth has led to an aggregation of data and homogenous treatment of all Asian Americans, Native Hawaiians, and Pacific Islanders (AANHPI) subgroups, ignoring the health inequities and social determinants of health that affect subgroups.[80,169] The Model Minority Myth has led to implicit bias, which has resulted in lack of health research funding, and a decrease in addressing health care needs among Asian Americans.[167,168]

The Model Minority Myth can affect Asian Americans' health care and disease management in several ways. First, the stereotype that all Asian Americans are successful and have no problems can create a barrier to seeking health care. Asian Americans may feel pressure to conform to this stereotype and may be less likely to seek help for health issues because they believe they are supposed to be healthy and

successful.[167,168] Additionally, the stereotype ignores the diversity of experiences within the Asian-American community, including the challenges that some Asian Americans may face. As a result, some Asian Americans may not receive the support and resources they need to manage their health and prevent or treat diseases.[167,168] Finally, the Model Minority Myth can affect the way that health care providers treat their Asian-American patients. Health care providers may have unconscious biases based on the stereotype, and may not provide the same level of care and attention to Asian-American patients as they would their other patients. This can result in inadequate treatment and poorer health outcomes for Asian Americans.

2.8.2 Acculturation

Acculturation is the process of assimilating from one's native culture to the dominate one; for example, immigrating from Japan to the United States. The changing food environment, cultural adaptation, socioeconomic status, and health disparities affect Asian Americans similar to other under-represented groups.[170,171] The prevalence of T2DM among Asian Americans is partially accounted for by acculturation to predominant U.S. food choices, and due to being first, second, or third generation Asian Americans.[170] Acculturation to the U.S. has been shown to increase T2DM due to higher consumption of processed foods, combined with a decrease in fruit, vegetable, and fiber consumption, and decreased physical activity.[55,170] Additionally, second and third

generation Asian Americans are more likely to have a Western-focused dietary pattern compared to earlier generations, which may lead to a higher prevalence of T2DM.

Sanjeevi[171] investigated the association between acculturation, physical activity and health care access in Asian-American adults with diabetes mellitus using NHANES data from 2011 to 2018. Sanjeevi[171] also examined the potential role of these factors in mediating the relationship between acculturation and cardiometabolic risk factors in this population. The researcher focused on non-pregnant adults, 20 years of age and older, who self-identified as "non-Hispanic Asian", and had been diagnosed with diabetes mellitus by a medical professional. A total of 336 non-pregnant Asian-American adults with diabetes mellitus and non-missing values for acculturation indicators were included in primary analyses. Out of these, 321 participants underwent clinical measurements, including assessment of HbA1c percentage, total cholesterol concentrations, HDL-C concentrations, and blood pressure at a mobile examination center.

Birthplace and length of residence in the United States, as well as language spoken at home, were used as indicators of acculturation. Sanjeevi[171] classified birthplace and length of residence, and assigned the following scores: (1) U.S.-born (score = 3), (2) foreign-born and living in the U.S. for 20 years or more (score = 2), (3) foreign-born and living in the U.S. for 10 to 19 years (score = 1), and (4) foreign-born

and living in the U.S. for less than 10 years (score = 0). Language spoken at home was divided into three categories, and assigned one of the following scores: (1) only English or more English than non-English (score = 2), (2) English and non-English equally (score = 1), and (3) only non-English or more non-English than English (score = 0). The overall acculturation score, calculated by summing the birthplace/length of residence and language scores, ranged from 0 to 5. Based on previous research and the distribution of overall scores, Sanjeevi[171] created three categories of acculturation: scores of 0 to 1 (least acculturated), 2, and 3 to 5 (most acculturated).

Sanjeevi[171] evaluated glycemic control (indicated by HbA1c percentages), lipid markers (total cholesterol and HDL-C concentrations), and blood pressure. Physical activity and health care access were investigated as mediating variables. Physical activity was self-reported using the Global Physical Activity Questionnaire, which assesses activity across three domains: leisure-time, work-related, and transportation-related.

Sanjeevi[171] reported that approximately 25% of the study participants had low levels of acculturation. The majority of the participants had health insurance and had their HbA1c percentages measured by a physician in the past year. Based on leisure-time physical activity levels, 55.2% of the participants were classified as inactive, 18.6% were insufficiently active, and 26.2% were sufficiently active. For work- and

transportation-related physical activity, 84.8% and 87.3% of the participants were classified as inactive or insufficiently active, respectively. Sanjeevi[171] reported that low levels of acculturation were significantly related to uninsured status ($p < 0.01$), higher leisure-time inactivity ($p < 0.05$), and overall insufficient activity ($p < 0.05$). Additionally, leisure-time activity was significantly related to HbA1c percentages, with inactive individuals having significantly higher HbA1c percentages compared to sufficiently active adults ($p < 0.0007$). Although the aforementioned represents one study, the results demonstrate how acculturation affects lifestyle factors and health (in particular, prevalence and management of diabetes mellitus).

2.8.3 *Socioeconomic Status*

Socioeconomic status (SES), food availability and accessibility affect Asian-Americans subgroups differently. Asian-Americans subgroups with low SES are more likely to have access to low-cost, energy-dense foods that contribute to T2DM.[172,173] Further research is necessary to understand the differences in Asian Americans by disaggregating the subgroups to uncover how cultural adaptations and SES contribute to T2DM.

2.8.4 Social Determinants of Health and Health Inequities

Social determinants of health and health inequities are mechanisms that affect health. Social determinants of health "are conditions in the places where people live,

learn, work, and play that affect a wide range of health risks and outcomes."[174,175] Health inequities are defined as "preventable differences in the burden of disease, injury, violence, or opportunities to achieve optimal health that are experienced by socially disadvantaged populations."[174] Social determinants of health can result in health inequities. Improving factors of social determinants of health can reduce health inequities that increase risk of chronic disease.

Min et al.[176] conducted a systematic review to identify social determinants of health that are related to the prevalence of cardiometabolic diseases (e.g., T2DM) among Asian subgroups. They included 14 studies that met their criteria, and placed them into four topic areas: acculturation (9 studies), SES (6 studies), social context (2 studies), and health literacy (1 study). Min et al.[176] reported that Asian subgroups most represented in research were: Chinese, Filipinos, and South Asians. They reported that acculturation was the most studied area; greater acculturation resulted in a higher incidence of cardiometabolic diseases. In addition, Min et al.[176] reported that social determinants of health affected Asian Americans differently, depending on their subgroup. Their research further emphasizes the need to study chronic disease risk by Asian subgroups, which can lead to better health care and prevention of disease.

2.8.5 Smoking and Alcohol Consumption

Smoking is an established risk factor of T2DM according the Standards of Medical Care for T2DM in the U.S., China, Japan, and Korea.[17,89,91,177] The Centers for Disease Control and Prevention state that cigarette smoking can lead to a 30% to 40% increased risk for developing T2DM.[178] Currently, 11.5% of Asian-American adults smoke and 38% consume alcohol. Alcohol consumption has been shown to have negative effects on the development and progression of T2DM.[179] Excessive alcohol consumption can also lead to chronic pancreatitis, which can contribute to the development of T2DM.[180] This may be due to the toxic effects of alcohol on the pancreas, resulting in inflammation and damage to insulin-producing cells.[180]

2.9 Summary

Growing numbers of Asian-American adults are developing T2DM, and there are inequities among the subgroups of Asian Americans that have been hidden as a result of grouping all Asian Americans together. Additionally, there is a link among age, sex, body composition (BMI, waist circumference, WHtR, VAI), sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language and the risk of T2DM. The complexity of the interaction among age, sex, body composition, sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language must be considered when attempting to identify predictors of T2DM. Unlike the previous studies discussed in this chapter, the present study explored the interaction among age, sex, body composition, sedentary behavior time, dietary

magnesium intake, self-reported healthy diet status, and language, while determining which were the strongest predictors of HbA1c percentage, which may increase the risk of developing T2DM in Asian Americans.

CHAPTER 3: METHODOLOGY

3.1 Institutional Review Board Approval

Approval for this study (IRB #22-268) was obtained from the Virginia Polytechnic Institute and State University (Virginia Tech) Institutional Review Board (IRB). Further review and approval by the Virginia Tech Human Research Protection Program (HRPP) was not required due to the data being available for public use and being de-identified. The Research Determination Letter was received on October 19, 2022 (Appendix A).

3.2 Data Collection

This study included Asian-American adults, 18 years of age and older. Correspondence was sent via email to the National Health and Nutrition Examination Survey (NHANES) to inquire about whether Native Hawaiians and Pacific Islanders were included in the "non-Hispanic Asian" ethnicity, and if not, where could their data be found. Due to small sample sizes, Asian sub-groups were aggregated into one group. The researcher's inquiry was never answered about what happened to the data for the Native Hawaiian and Pacific Islander populations. The NHANES provides the sample sizes for sub-groups within the Asian-American population, which can only be retrieved through a restricted data access clearance from the National Center for Health Statistics (NCHS) Research Data Center in Hyattsville, Maryland.

Data were collected from the National Health and Nutrition Examination Survey (NHANES) from 2011 to 2020. The program started in 1959.[181] The first survey was called the National Health Examination Survey (NHES I), and it was conducted from 1959 to 1962, to focus on individuals with chronic diseases, 18 to 79 years of age.[181] The NHES II occurred from 1963 to 1965, focusing on growth and development of children, 6 to 11 years of age. The NHES III was conducted from 1966 to 1977, focusing on growth and development of adolescents, 12 to 17 years of age.[181] The NHES then became NHANES in 1971, due to the addition of a nutrition section. The first three NHANES occurred from 1971 to 1994. In 1982 to 1984, there was a Hispanic only NHANES to address the needs of the Hispanic population. Beginning in 1999 to the present (2019 to 2020) NHANES cycles, NHANES switched to a two-year survey cycle to address the needs of a growing nation with the various subpopulations.[182]

The NHANES is a cross-sectional survey used to evaluate the nutrition, health, and health behaviors of all eligible individuals living in the United States (U.S.).[182] Excluded are U.S. citizens living overseas, in custody, in institutional settings, and under supervised care. The NHANES is a National Center for Health Statistics (NCHS) program. The NCHS is within the Centers for Disease Control and Prevention (CDC), which use the NHANES data to develop public policy and design health programs.[182] Each year, NHANES surveys 5,000 people across the country who represent the entire U.S. population.[182] The NHANES data are collected through interviews and

questionnaires, laboratory measures, and physical assessments conducted in mobile examination centers across the United States.[182] The NHANES interviews include demographic, socioeconomic, dietary, and health-related questions. The examination component consists of medical, dental, and physiological measurements, as well as laboratory tests.

3.2.1 Inclusion and Exclusion Criteria

The inclusion criteria for the present study were limited to those meeting the following inclusion criteria: non-Hispanic Asian race, 18 years of age and older, with complete data from NHANES 2011 to 2020 on all variables studied (HbA1c percentage, age, sex, body mass index [BMI], waist circumference, waist-to-height ratio [WHtR], visceral adiposity index [VAI], sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language). Adults less than 18 years of age were excluded.

3.2.2 Survey Design and Analytic Guidelines

The National Health and Nutrition Examination Survey utilizes a "multi-year, stratified, clustered four-stage sample with data releases in two-year cycles".[183] The first stage of the sample design selects primary sampling units (PSUs), which are counties divided into 15 groups.[183] The goal of PSU sampling is to provide even distribution of the overall health index, population demographics, and the appropriate ratio of urban

to rural areas.[183] The second stage then divides the PSUs into 20 to 24 groups, with even distribution of under-represented populations. Stage three identifies a sample of 30 households within each group.[183] Stage four is a random sample of household members who are interviewed about information such as age, race and ethnicity, and sex of each household member.

The Asian demographic was not included until the NHANES 2011 to 2012 cycles.[183] The Asian demographic was previously included in non-Hispanic White ethnicity. Due to this, the Asian population has been oversampled in every NHANES cycle following 2011 to 2012. The oversampling provides reliable estimates of Asians with respect to age and sex demographics. However, ethnic subgroup data are not publicly available, and require special permission for on-site analyses at the National Center for Health Statistics Research Data Center in Hyattsville, Maryland.[183]

The National Health and Nutrition Examination Survey provides analytic guidelines to follow when analyzing multiple data cycles.[183–185] According to the NHANES analytic guidelines, two-year sample weights are provided in the public data. The variables are "masked variance pseudo-PSU" and "masked variance pseudo-stratum" found in the demographics data section of each cycle. These sample weights represent the civilian, non-institutionalized population at the midpoint of the combined survey periods.[183–185] As a result of the COVID-19 pandemic, the NHANES stopped their survey in March of 2020 due to the incomplete cycle. The NHANES combined the 2017

to 2018 data with the 2019 to March of 2020 data, creating a 3.2-year cycle.[183–185] To create an appropriate survey weight when combining the cycles, a 9.2-year cycle weight was created. For example, "combining the 2011 to 2016 and 2017 to March 2020 files would result in a data file representing a 9.2-year period, and the survey weights should be adjusted as follows: 2011 to 2016 survey weights should be multiplied by 2/9.2 (the fraction of the 9.2-year period represented by the 2011 to 2016 cycle), and likewise, the 2017 to March 2020 survey weights should be multiplied by 3.2/9.2".[183–185]

However, according to the analytic guidelines, there are steps to follow before combining data cycles. The NHANES analytic guidelines recommend the following: "(1) be aware of sample design changes, (2) verify that data items collected in all combined years are comparable in wording, methods, and inclusions/exclusions, (3) select the proper weight to use for the combined dataset, and (4) examine the inherent assumption of no trend in the estimate over the time period being combined".[183–185] If the names of variables are different between cycles, then the variables need to be re-coded for consistency before merging. The NHANES recommends using respondent sequence numbers (SEQN) to reduce issues in sorting and merging variables.

3.2.3 Variable Selection

Various predictor variables were included in the present study. The predictor variables included were: age, sex, body composition (body mass index [BMI], waist circumference, waist-to-height ratio [WHtR], visceral adiposity index [VAI]), sedentary

behavior time, dietary magnesium intake, self-reported healthy diet status, and language.

3.2.4 Overview of the National Health and Nutrition Examination Survey Data Collection

Data from the National Health and Nutrition Examination Survey are collected in five ways: demographics, dietary intake, physical examination, laboratory testing, and interview questionnaires. The data are collected through what NHANES calls "health interviews" and "health measurements". The health interviews take place in the participants' homes. The measurements are conducted inside of a mobile examination center run by physicians, registered dietitians, medical technicians, and other health care professionals.[182] Personnel performing interviews, questionnaires, laboratory tests, and physical evaluations are guided by specific protocols and processes for data collection. This information is available for public use on the CDC website at: https://www.cdc.gov/nchs/data/nhanes.

3.2.4a Hemoglobin A1c Percentage

Due to extensive missing data for fasting plasma glucose and Asian-Americans. In addition, to the oral glucose tolerance test not being conducted every NHANES cycle, Hemoglobin A1c (HbA1c) percentage was used. Hemoglobin A1c (HbA1c) percentage is a biomarker collected through a venipuncture blood draw that represents an average of glucose concentrations throughout the past three-month period. With

respect to NHANES, a phlebotomist collects blood at a mobile examination center, and the samples are processed, stored, and shipped to the University of Minnesota, Minneapolis, Minnesota, for analyses. Hemoglobin A1c percentage is measured using the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8. According to NHANES, "In this assay, the stable (SA1c) and labile (LA1c) A1c forms can be individually resolved on the chromatogram without manual pretreatment, allowing accurate measurement of the stable form of HbA1c. The analyzer dilutes the whole blood specimen with a hemolysis solution, and then injects a small volume of the treated specimen onto the HPLC (high performance liquid chromatography) analytical column. Separation is achieved by utilizing differences in ionic interactions between the cation exchange group on the column resin surface and the hemoglobin components. The hemoglobin fractions (A1c, A1b, F, LA1c, SA1c, A0 and H-Var) are subsequently removed from the column material by step-wise elution using elution buffers each with a different salt concentration. The separated hemoglobin components pass through the photometer flow cell where the analyzer measures changes in absorbance at 415 nm. The analyzer integrates and reduces the raw data, and then calculates the relative percentages of each hemoglobin fraction".[186] The laboratory procedures information can be found on the NHANES website: https://www.cdc.gov/nchs/nhanes/index.htm.

3.2.4b Measures of Body Composition

Body weight was measured using a digital scale, which displays the weight in kilograms (kg) and pounds. According to the NHANES Anthropometry Procedures Manual, "If participants weighed more than 600 pounds, two portable scales were used, with the participant placing one foot on one scale and the other foot on the other scale. The weight from each scale was combined with the two results to approximate body weight". For a more detailed explanation of body weight assessment, refer to the NHANES Anthropometry Procedures Manual.[187] All of NHANES protocols and procedures are available for public use on the CDC website at: https://www.cdc.gov/nchs/data/nhanes.

According to the NHANES Anthropometry Procedures Manual, "Standing height was measured using a stadiometer with an adjustable headpiece for NHANES. While looking straight ahead, the participants would stand-up straight against the backboard with their heels touching and toes positioned at a 60-degree angle. The participant was asked to take a deep breath, and to stand as tall as possible, while the headpiece was lowered. Participants would hold the position until the measurement was completed. Once the height has been recorded the participant is told to exhale and relax". For a more detailed explanation of height assessment, refer to the NHANES Anthropometry Procedures Manual.[187] All of NHANES protocols and procedures are available for public use on the CDC website at: https://www.cdc.gov/nchs/data/nhanes.

The NHANES calculates body mass index (BMI) using the equation of weight in kilograms divided by height in meters squared. The NHANES classifies BMI based on the standard values: underweight (< 18.5 kg/m^2), healthy body weight (18.5 to 24.9 kg/m^2), overweight (25.0 to 29.9 kg/m^2), Class 1 obesity (30.0 to 34.9 kg/m^2), Class 2 obesity (35.0 to 39.9 kg/m^2), and Class 3 obesity (> 40.0 kg/m^2).[187] The NHANES does not use any ethnicity-specific cut-off points for BMI. For a more detailed explanation of BMI assessment, refer to the NHANES Anthropometry Procedures Manual.[187] All of NHANES protocols and procedures are available for public use on the CDC website at: https://www.cdc.gov/nchs/data/nhanes.

According to the NHANES Anthropometry Procedures Manual, "Each adult participant's waist circumference was measured with a metal tape measure for NHANES. The participant crossed their arms in front of their body, placing the opposite hand on the opposite shoulder. The participant had an "X' drawn above their right and left ilium at the midaxillary line, which extends from the armpit down the side of the torso. The measuring tape was wrapped around the body using the "X" mark as the contact point. The measuring tape was parallel to the floor and did not compress the skin. The zero ends of the tape were below the measurement value. The measurement was read at the end of the participant's exhale. The measurement was recorded to the nearest 0.1 cm". For a more detailed protocol explanation of waist circumference assessment, refer to the NHANES Anthropometry Procedures Manual.[187]

All of NHANES protocols and procedures are available for public use on the CDC website at: https://www.cdc.gov/nchs/data/nhanes.

The NHANES does not have a variable for waist-to-height ratio (WHtR) or visceral adiposity index (VAI). The equation for waist-to-height ratio is waist in centimeters (cm) divided by height in centimeters (cm). There are specific visceral adiposity index equations for women and men. The VAI equations are as follows:

Females: VAI = (waist circumference [cm]/39.58 + (1.89 x body mass index [kg/m^2]) x (triglyceride concentration [mmol/L]/0.81) x (1.52/high density lipoprotein concentration [mmol/L])[26]

Males: VAI = (waist circumference [cm]/39.68 + (1.88 x body mass index [kg/m^2]) x (triglyceride concentration [mmol/L]/1.03) x (1.31/ high density lipoprotein concentration [mmol/L])[26]

3.2.4c Physical Activity Questionnaire (PAQ)

The NHANES assessed physical activity and sedentary behavior with the Global Physical Activity Questionnaire (GPAQ).[188] The GPAQ is administered in the participants' home by NHANES trained interviewers who record the responses with the Computer Assisted Personal Interview system. Participants were asked a number of questions about the time they spent in moderate and vigorous physical activities. Further, the GPAQ asks three questions about sedentary behavior: minutes of sedentary

behavior, hours watching TV or videos, and hours using a computer.[188] The GPAQ screening questionnaire information can be found on the NHANES website at: https://www.cdc.gov/nchs/nhanes/index.htm.

3.2.4d Dietary Magnesium Intake

Dietary magnesium intake data is quantified from calculations of total daily nutrient intakes. Dietary magnesium intake is assessed during the NHANES in-person dietary interviews, completed in a mobile examination center.[189] The NHANES uses the United States Department of Agriculture (USDA) automated multiple-pass method instrument to conduct a comprehensive 24-hour dietary recall interview.[189] During this interview, participants are guided by a trained interviewer who uses automated or computerized prompts to aid in remembering the foods consumed in the previous 24 hours.[189] The information obtained from the recall is coded and connected to a database containing the nutrient compositions of various foods.[189] To ensure accuracy, a follow-up phone interview using the USDA automated multiple-pass method is scheduled within three to 10 days after the initial in-person interview.[189] More information about in-person dietary data collection can be found in the NHANES interviewer's procedures manual.[189] All of the NHANES protocols and procedures are available for public use on the CDC website at: https://www.cdc.gov/nchs/data/nhanes.

3.2.4e Self-Reported Healthy Diet Status

The Diet Behavior and Nutrition Questionnaire (DBQ) is a comprehensive survey designed to collect personal interview data on various aspects of dietary behavior and nutrition.[190] It draws upon questions that have been utilized in previous surveys, including NHANES II, Hispanic HANES (HHANES), NHANES III, and NHANES 1999 to 2014.[190] The DBQ encompasses a broad spectrum of topics, encompassing breastfeeding and childhood feeding practices, milk consumption patterns, participation in community or government meal programs, engagement in school meal programs, individuals' self-assessment of the healthfulness of their diets, frequency of meals prepared away from home or acquired from fast-food establishments, use of convenience foods, awareness of the My Plate program, and utilization of nutrition information available on restaurant menus.[190] "The Diet Behavior and Nutrition Questionnaire measures self-reported healthy diet status by asking participants to rate how healthy they think their overall diet is using the descriptors: 'Excellent', 'Very Good', 'Good', 'Fair', 'Poor', 'Refused to Answer', and 'Don't Know'".[190] Detailed NHANES protocols and procedures can be accessed on the CDC website at: https://www.cdc.gov/nchs/data/nhanes.

3.2.4f Language (Acculturation)

The NHANES survey introduced a question regarding non-Hispanic Asian acculturation in 2011 to 2012, aiming to gather information on the language spoken at home by non-Hispanic Asian participants.[191] The inclusion of this question was

intended to augment the representation of the Asian population in the study.[191] To access more comprehensive and detailed data pertaining to the specific Asian language(s) spoken by participants at home, researchers can utilize the National Center for Health Statistics' Research Data Center (RDC).[191] In the present study, a question specifically designed for the Asian population to account for the influence of acculturation was utilized. This question focused on the language spoken at home and provided options for respondents to indicate their linguistic preferences, including exclusive use of non-English languages, predominant use of non-English languages, equal use of English and non-English languages, predominant use of English, or exclusive use of English. By employing this measure, a more nuanced understanding of the role of acculturation within the context of the present study was obtained. Detailed NHANES protocols and procedures can be accessed on the CDC website at: https://www.cdc.gov/nchs/data/nhanes.

3.3 Missing Data

The NHANES analytic guidelines recommend that if 10% or less of the data for the main outcome variable for a specific component is missing for eligible examinees, it is usually acceptable to continue analyses without further evaluation or adjustment.[183,185] The NHANES code book was used to identify the assigned missing values to distinguish whether the value is missing or the participant “Refused to Answer” or

answered "Don't Know". The "Refused to Answer" and "Don't Know" answers were recoded from the numerical value to an asterisk to prevent skewed analyses.[183,185]

3.4 Statistical Analyses

Data were analyzed using R programming software (R Core Team 2022, R Foundation for Statistical Computing, Vienna, Austria, https://www.R-project.org/). Descriptive data, including means and standard deviations, were evaluated for the following variables: hemoglobin A1c percentage, age, sex, BMI, waist circumference, WHtR, VAI, sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language.

Analyses for Specific Aim 1

Analyses for Specific Aim 1 identified the most effective multivariable general linear model for predicting hemoglobin A1c percentages in Asian-American adults, 18 years of age and older, based on these independent variables: age, sex, body composition (BMI, waist circumference, WHtR, VAI), sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language. First, descriptive statistics were generated to understand the characteristics of the sample and the distribution of the data. Data visualization techniques, such as histograms, scatter plots (as quantile-quantile plots), and bar graphs were used to visually examine the distribution among the variables. A quantile-quantile plot (Q-Q plot) is a graph used to

evaluate if a set of data were derived from a normal or exponential distribution. A Q-Q plot is a scatter plot developed by graphing two sets of data to the other.[192] If each quantile came from similar distributions, the points should basically become a straight line.[192]

Next, bivariate general linear models were constructed to identify the relationship between each independent variable and HbA1c percentage. These models helped to determine which variables had the greatest effect on HbA1c percentages. To estimate the best fitting multivariable general linear model for predicting HbA1c percentage among Asian-American adults, a linear regression model was fitted with HbA1c percentage as the response variable, and age, sex, body composition (BMI, waist circumference, WHtR, VAI), sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language as predictor variables. Multicollinearity was then checked among the predictor variables.

A model selection was performed using the exhaustive, forward and backward search methods, which included interaction terms among age, sex, BMI, waist circumference, WHtR, VAI, sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language. For each search method, the Schwarz Bayesian Information Criterion (BIC) was plotted for the resulting models, and the model with the lowest Schwarz BIC value was identified. The Schwarz BIC serves as a criterion for model selection, simultaneously accounting for model fit and complexity.

A lower Schwarz BIC value is indicative of a preferable model due to its balance between fitting the data well and maintaining parsimony. Upon identifying the optimal model based on the Schwarz BIC, the corresponding coefficients were extracted for further examination and interpretation.

The final linear regression model included age, waist circumference, VAI, self-reported healthy diet status, and the interaction term between sedentary time (minutes) and self-reported healthy diet status as predictor variables. This model was fit to the data and a summary of the model's performance was obtained.

Analyses for Specific Aim 2

Analyses for Specific Aim 2 utilized machine learning and decision tree modeling techniques to estimate the relative importance of age, sex, body composition (BMI, waist circumference, WHtR, VAI), sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language in predicting HbA1c percentages ≥ 6.5% in Asian-American adults, 18 years of age and older. These approaches allowed the researcher to examine the relative contribution of each variable to the prediction of HbA1c percentages, and identify potential moderators and optimal cut-off points for age and BMI. Machine learning techniques involved the use of algorithms that learn from data and improve the accuracy of predictions over time. The researcher used

machine learning algorithms to identify the most important variables and predict HbA1c percentages based on these variables.

Decision tree modeling is a statistical approach that involves creating a tree-like model of decisions and their possible consequences, including the prediction of a target variable. In this study, decision tree modeling was used to examine the relative importance of age, sex, body composition (BMI, waist circumference, WHtR, VAI), sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language in predicting HbA1c percentages. By utilizing these approaches, the researcher was able to identify the most important variables and optimal cut-off points for predicting HbA1c percentages in Asian-American adults, which will inform the development of interventions aimed at improving HbA1c control in this population.

Analyses for Specific Aim 3

Analyses for Specific Aim 3 built on the models developed in Specific Aims 1 and 2 by estimating the best fitting logistic regression model for predicting HbA1c percentages ≥ 6.5% in Asian-American adults, 18 years of age and older. This model was constructed using a series of statistical procedures, which included the generation of descriptive statistics, data visualization, bivariate general linear models, multivariate linear models, and general linear models. The purpose of generating descriptive statistics is to understand the characteristics of the sample and the distribution of the

data. Data visualization techniques, such as histograms, scatter plots (as quantile-quantile plots), bar graphs, were used to visually examine the distribution among the variables.

Bivariate general linear models were used to identify the relationship among each independent variable and HbA1c percentages. These models helped to determine which variables had the greatest effect on HbA1c percentages. The multivariate linear model was used to examine the combined effect of the three independent variables on HbA1c percentages. This allowed the researcher to identify the most effective combination of variables for predicting HbA1c percentages in Asian-American adults. Assumptions of the model were checked and evaluated for moderation and mediation. This allowed the researcher to determine the most accurate and reliable model for predicting HbA1c percentages in Asian-American adults.

CHAPTER 4: MANUSCRIPT 1

Predicting Hemoglobin A1c Percentage from Body Composition, Sedentary Behavior, and Dietary Magnesium Intake in Asian-American Adults, using 2011 to 2020 NHANES Data

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Abstract

Objective: The aim of our study was to determine the association of hemoglobin A1c percentage (HbA1c%) with age, sex, body composition, sedentary time (minutes), dietary magnesium intake, self-reported healthy diet status, and language in Asian-American adults, 18 years of age and older, using the National Health and Nutrition Examination Survey (NHANES) data from 2011 to 2020.

Methods: The optimal linear model was selected through exhaustive, forward, and backward search methods. These methods considered all main effects, and interaction terms among predictors, such as age, sex, body mass index (BMI), waist circumference, waist-to-height ratio (WHtR), visceral adiposity index (VAI), sedentary time, dietary magnesium intake, self-reported healthy diet status, and language. The model selection was performed by minimizing the Schwarz Bayesian Information Criterion (BIC) among competing models.

Results: We reported that several variables were significantly associated with HbA1c%. Specifically, older age ($\beta = 0.01818$, $p < 0.001$), larger waist circumference ($\beta = 0.0166$, $p < 0.001$), higher VAI ($\beta = 0.04005$, $p < 0.001$), and a self-reported healthy diet status rated as "Fair" ($\beta = 0.4942$, $p < 0.001$) were all positively associated with HbA1c%. We also observed a significant interaction effect between sedentary time and self-reported healthy diet ($p < 0.001$). Specifically, there was a significant negative association among sedentary time, a diet rated as "Fair" ($\beta = -0.000709$, $p < 0.001$) and HbA1c%. Overall,

the model explained 21.98% of the variance in HbA1c% (adjusted R-squared = 0.2179, F-statistic = 112.1, $p < 0.001$), suggesting that the predictor variables included in the model account for a significant proportion of the variability in HbA1c%. The residuals of the model had a mean of 0, and a standard deviation of 0.8012, indicating that the model provided a good fit to the data.

Conclusion: We identified significant associations among HbA1c% and age, waist circumference, VAI, and an interaction of sedentary time with self-reported healthy diet status ("Fair") in an Asian-American population. The positive associations of age, waist circumference, and VAI with HbA1c% emphasize the importance of addressing modifiable risk factors, such as central adiposity and dietary habits, to improve blood glucose control and prevent type 2 diabetes mellitus (T2DM) among Asian Americans. Our results also highlight the need for targeted screening and intervention strategies to address the growing burden of T2DM in the Asian-American population.

Keywords: Asian Americans, Dietary Intake, Hemoglobin A1c, Magnesium, NHANES

Introduction

Asian Americans are the fastest-growing under-represented ethnic group in the United States (U.S.).[1] There are 19.9 million Asian Americans, and 4.1 million Asian Americans combined with another race or ethnicity, living in the United States.[2] The Asian-American population is expected to reach 46 million by 2060.[1] In addition to the population growth, the prevalence of type 2 diabetes mellitus (T2DM) has increased among Asian Americans. Diabetes mellitus is a chronic metabolic disorder characterized by high blood glucose concentrations due to inadequate insulin production or impaired insulin action. While several factors contribute to the development of diabetes mellitus, including genetics, environmental influences, and lifestyle behaviors, such as physical inactivity and poor dietary choices, have been shown to play an important role in the development and progression of this disease.[3] The Centers for Disease Control and Prevention (CDC) reported that one in three Asian Americans has undiagnosed diabetes mellitus.[4]

The prevalence of T2DM has been increasing worldwide, and it is now one of the most common chronic diseases among Asian-American adults, affecting approximately 8.5% of the adult population in this demographic group in the United States.[4,5] Diabetes mellitus is the fifth leading cause of mortality among Asian Americans, with recent statistics from 2018 highlighting this health concern.[6,7] Disaggregation of Asian-American subgroups reveals a higher prevalence of diabetes mellitus among specific

groups. When separated by subgroups, Asian Indians, Filipinos, and other Asian Americans, the prevalence of diagnosed diabetes mellitus rises to 12.6%, 10.4%, and 9.9%, respectively.[8] Given the complications and health risks associated with T2DM, it is essential to identify modifiable risk factors that can inform targeted interventions to prevent or delay the onset and progression of this disease.[9] One such risk factor is glycosylated hemoglobin (or hemoglobin A1c [HbA1c]) percentage, which reflects the average blood glucose concentrations over the past two to three months.[10]

Age is an important risk factor for the development of T2DM. Hemoglobin A1c percentages have been reported to increase with age, even in the absence of T2DM.[11] This may partly be due to decreases in muscle tissue, which can lead to decreased insulin sensitivity.[12] Furthermore, with age, the body's ability to metabolize glucose decreases due to a reduction in insulin sensitivity and beta cell function, leading to higher blood glucose concentrations, which, in turn, leads to increased HbA1c percentages.[13]

Sex differences in HbA1c percentages among Asians have not been extensively studied. However, some research has shown differences in HbA1c percentages between women and men in various populations. Men typically receive a diagnosis at a younger age and with lower body fat mass compared to women.[14] Conversely, women carry a higher burden of risk factors, particularly obesity, at the time of T2DM diagnosis.[14]

Additionally, reproductive factors, such as pregnancy and menopause, exert a substantial influence on the risk of developing T2DM in women.[14]

Anthropometric index measurements such as BMI, waist circumference, waist-to-height ratio (WHtR), and visceral adiposity index (VAI) are measurements that have been useful in identifying individuals at-risk for T2DM, obesity, and cardiometabolic risk.[15,16] Body mass index (BMI) is not a direct measure of body fat; however, BMI is a screening tool that can indicate adiposity.[17–19] Nonetheless, using standardized BMI measurements underestimates the risk for pre-diabetes and T2DM in the Asian-American population.[20–24] Insulin resistance, characterized by higher BMI, waist circumference, and total body fat mass, is also positively linked to the development of T2DM. [15,16] However, Asian Americans are diagnosed with pre-diabetes and T2DM at a lower mean BMI and waist circumference than other racial and ethnic groups.[20,25] Although BMI is the most widely used clinical tool to estimate body fat, it has its limitations in estimating body fat composition.[20–24]

Body mass index alone is insufficient to properly evaluate adiposity in Asian-American adults due to Asian Americans having a lower BMI with a higher body fat percentage. Waist circumference measurements can be an easy and cost-effective measurement tool to serve as a proxy for visceral adiposity and HbA1c percentage in Asian Americans.[26–28] The World Health Organization (WHO) recommends that

lowering the waist circumference cut-off points for Asian Americans to 80 centimeters (cm) for women and 85 cm for men would better identify their metabolic risk.[22]

Like waist circumference, the WHtR is a screening tool for cardiometabolic risk related to body fat distribution. The WHtR, calculated by dividing waist circumference by height, has recently gained attention as an anthropometric index for measuring central adiposity.[29] Waist-to-height ratio is a more sensitive universal screening tool than BMI to detect health risks.[27] The WHtR has been shown to be a stronger predictor for T2DM among Asian Americans compared to BMI.[26,27] Asian Americans have higher amounts of visceral adiposity compared to other races and ethnicities with the same BMI.[28,30] The proximity of visceral fat to the vital organs puts Asian Americans at higher risk for insulin resistance and for developing T2DM.[31] Therefore, WHtR may succeed in identifying risk for T2DM compared to other anthropometric measures such as BMI or waist circumference.

Waist circumference and WHtR are clinical screening tools used for the indirect evaluation of increased visceral fat.[16] Yet, waist circumference and WHtR do not distinguish between subcutaneous and visceral fat mass.[16] Asian Americans tend to accumulate more visceral fat at a lower BMI and waist circumference. Accumulation of visceral adiposity reduces insulin sensitivity, leading to an increased risk of developing diabetes mellitus.[32] The VAI seems to be a better predictor for metabolic disorders

associated with insulin resistance than a single anthropometric index.[33–35] Visceral adiposity index is a mathematical formula that consists of BMI and waist circumference, as well as clinical measurements, such as triglyceride and high density lipoprotein cholesterol (HDL-C) concentrations.[16]

Increased sedentary time is associated with an increased risk for T2DM.[36,37] Lack of physical activity can result in insulin resistance and impaired glucose metabolism due to muscle disuse and decreased lean body mass.[38] Sheng et al.[39] conducted analyses of the Asian-American population using the National Health and Nutrition Examination Survey (NHANES) data from 2011 to 2016. The authors[39] reported that 64.4% of Asian Americans did not meet the recommended ≥ 150 minutes/week of physical activity. Further, Asian Americans who did not meet the recommended amount of physical activity had a higher risk of metabolic syndrome.[39]

There is an association between dietary quality and the risk of T2DM.[40,41] Specifically, researchers have reported an inverse relationship between increased dietary magnesium intake and the risk of T2DM.[41,42] Further, data from the 2013 to 2020 NHANES have shown that less than half of the Asian-American population is consuming the recommended amounts of magnesium from food, drinks, and dietary supplements.[42] Previous researchers have reported mixed results in determining the correlation between dietary magnesium intake and the risk of T2DM in Asian

countries.[43,44] The relationship between dietary magnesium intake and the risk of T2DM in Asian Americans is uncertain and needs further investigation.

Self-reported healthy diet status from the NHANES provides valuable insights into the dietary intake of the U.S. population, which can inform the planning and evaluation of nutrition programs and policies.[45] This information allows for the assessment of nutrient intake and the differentiation of diet quality. However, it is crucial to acknowledge that self-reported dietary data may be susceptible to limitations, such as under-reporting or inaccuracies due to recall bias or social desirability bias.

Furthermore, there are significant differences in the consumption of ultra-processed foods between American-born Asian Americans and those born abroad.[46] American-born Asian Americans generally consume a higher proportion of their energy intake from ultra-processed foods compared to those who were born abroad.[46] Similarly, Asian Americans who lived in the U.S. for at least 20 years had a higher consumption of ultra-processed foods compared to those living in the U.S. for less than 10 years.[46] It is important to consider these dietary patterns and their potential implications when investigating the relationship between self-reported healthy diet status, HbA1c percentages, and the risk of T2DM in Asian-American adults.

The primary language spoken in the household can also affect if individuals are meeting physical activity and dietary guidelines.[47] Typically, if the main language

spoken in a household of those who have immigrated to the United States is English, physical activity and dietary guidelines are more likely to be met.

Tung et al.[48] reported that Asian Americans are less likely to receive proper diabetes mellitus screening compared to other racial and ethnic groups, potentially due to improper screening guidelines by clinicians, and Asian Americans being unaware of their increased risk for diabetes mellitus. To delay or prevent pre-diabetes and T2DM, the American Diabetes Association (ADA) recommends lifestyle modifications such as weight reduction, routine physical activity, and healthy eating patterns that may improve insulin resistance and glycemic control.[49,50]

The aim of our study was to deliver new insights into the association among HbA1c percentage and modifiable predictors, while identifying the best subset of available predictors for a multivariable general linear model for predicting HbA1c percentage measured on a continuum among age, sex, body composition (BMI, waist circumference, WHtR, VAI), sedentary behavior, dietary magnesium intake, self-reported healthy diet status, and language in Asian-American adults, 18 years of age and older, using NHANES data from 2011 to 2020. The goal of our study was to address the risk factors associated with elevated HbA1c percentages and the development of T2DM in Asian-American adults. Despite the increasing prevalence of T2DM in this population, there is limited research on the specific predictors contributing to elevated

HbA1c percentages. By examining a wide range of variables related to body composition, sedentary behavior, dietary factors, and language, our analyses will provide valuable insights into the potential risk factors associated with elevated HbA1c percentages and T2DM in Asian-American adults, which can inform targeted interventions to address this important emerging public health issue.

Methods

Study Design and Participants

The National Health and Nutrition Examination Survey is a cross-sectional survey used to evaluate the nutrition, health, and health behaviors of all eligible individuals living in the U.S.[51] The NHANES uses survey weights to create a representative sample for the U.S. population to produce similar estimates if all the eligible individuals in the U.S. were surveyed.[52] Excluded in NHANES data are U.S. citizens living overseas, those in custody in institutional settings, and those under supervised care. The NHANES data are collected through in-person interviews and questionnaires, laboratory measures, and physical assessments conducted in mobile examination centers across the U.S. The NHANES did not have Asian demographic data until the 2011 to 2012 cycles. Due to this, the Asian-American population has been oversampled in every NHANES cycle following 2011 to 2012.

Approval for this study (IRB #22-268) was obtained from the Virginia Polytechnic Institute and State University (Virginia Tech) Institutional Review Board (IRB). Further review and approval by the Virginia Tech Human Research Protection Program (HRPP) was not required due to the data being available for public use and being de-identified. The Research Determination Letter was received on October 19, 2022. [51]The inclusion criteria for our study were as follows: non-Hispanic Asian race, 18 years of age older, using data from the 2011 to 2020 NHANES.

Measurements

The variables included in our analyses were: age, sex, HbA1c percentage, BMI, waist circumference, WHtR, VAI, sedentary time (minutes), dietary magnesium intake, self-reported healthy diet status, and language. According to the NHANES Anthropometry Procedures Manual[53], body weight was measured using a digital scale, which displayed the weight in kilograms and pounds. Further, BMI was calculated using the equation of weight in kilograms divided by height in meters squared. Waist circumference was measured with a metal tape measure. For a more detailed protocol of body weight, BMI, and waist circumference assessment, refer to the NHANES Anthropometry Procedures Manual.[53] The NHANES does not have a variable for waist-to-height ratio or visceral adiposity index. The equation for the WHtR was calculated as waist in centimeters (cm) divided by height in centimeters (cm). To calculate the VAI, the following equations were used:

Females: VAI = (waist circumference [cm]/39.58) + (1.89 x body mass index [kg/m^2]) x (triglyceride concentration [mmol/L]/0.81) x (1.52/high density lipoprotein concentration [mmol/L]).[16]

Males: VAI = (waist circumference [cm]/39.68) + (1.88 x body mass index [kg/m^2]) x (triglyceride concentration [mmol/L]/1.03) x (1.31/ high density lipoprotein concentration [mmol/L]).[16]

The NHANES assessed physical activity and sedentary behavior with the Global Physical Activity Questionnaire (GPAQ).[54] The GPAQ asks three questions about sedentary behavior: minutes of sedentary behavior, hours watching TV or videos, and hours using a computer.[54]

Dietary magnesium intake data were quantified from calculations of total daily nutrient intakes. Dietary magnesium intake was assessed during the NHANES in-person dietary interviews, completed in a mobile examination center.[55] The Diet Behavior and Nutrition Questionnaire measures self-reported healthy diet status by asking participants to rate how healthy they think their overall diet is. They use the following descriptors: “Excellent”, “Very Good”, “Good”, “Fair”, “Poor”, “Refused to Answer”, and “Don’t Know”.[45] Subsequently, to account for the influence of acculturation, we utilized a question regarding the language spoken at home as a proxy measure. This question, specifically designed for the Asian population, inquired about

the individual's linguistic preferences, encompassing the following options: exclusive use of non-English languages, predominant use of non-English languages, equal use of English and non-English languages, predominant use of English, or exclusive use of English. This measure enabled a more nuanced understanding of the role of acculturation within the context of our study. All NHANES protocols and procedures are available for public use on the CDC website at: https://www.cdc.gov/nchs/data/nhanes.

Statistical Analyses

To estimate the best fitting multivariable general linear model for predicting HbA1c percentage among Asian-American adults, we initially fit a linear regression model with HbA1c percentage as the response variable, and age, sex, BMI, waist circumference, WHtR, VAI, sedentary time (minutes), dietary magnesium intake, self-reported healthy diet status, and language as predictor variables. We then checked for multicollinearity among the predictor variables.

We performed model selection using the exhaustive, forward and backward search methods, which included interaction terms among age, sex, BMI, waist circumference, WHtR, VAI, sedentary time (minutes), dietary magnesium intake, self-reported healthy diet status, and language. For each search method, we plotted the Schwarz Bayesian Information Criterion (BIC)[56] for the resulting models, and identified the model with the lowest Schwarz BIC value. The Schwarz BIC serves as a criterion for

model selection, simultaneously accounting for model fit and complexity. A lower Schwarz BIC value is indicative of a preferable model due to its balance between fitting the data well and maintaining parsimony. Upon identifying the optimal model based on the Schwarz BIC, the corresponding coefficients can be extracted for further examination and interpretation.

All statistical analyses were conducted using R software version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria). To examine the association between HbA1c percentage and diverse predictor variables, multiple linear regression analyses were conducted. The preliminary linear regression model incorporated the subsequent predictor variables: age, sex, BMI, waist circumference, WHtR, VAI, sedentary time (minutes), dietary magnesium intake, self-reported healthy diet status, and language. We adjusted for acculturation, using language as the acculturation indicator. Interaction terms were then introduced to assess potential effect modification among the variables. Model assumptions, including linearity, independence, homoscedasticity, and normality of residuals were checked using residual plots and formal statistical tests. The significance level was set *a priori* at $p < 0.05$.

Results

Descriptive Statistics

Our study included 5,184 Asian-American adults, 18 years of age or older, who participated in the 2011 to 2020 NHANES. Table 5.1 outlines the descriptive characteristics of our population.

Age

A significant positive relationship was identified between age (49.64 ± 16.95 years of age) and HbA1c percentage (5.79 ± 0.91%) ($\beta = 0.01818$, SE = 0.0006771, $p < 0.001$) (Table 5.2). This indicates that, with every one-year increase in age, there is an associated increase of 0.018 units in HbA1c percentage, holding all other predictor variables constant. The robust statistical significance ($p < 0.001$) suggests that age is an essential determinant of HbA1c percentage among Asian-Americans adults.

Sex

The objective of the subset selection process is to select the predictors that best explain the variance in the response variable, thus achieving optimal predictive performance. Despite rigorous examination, sex was not identified as a significant contributor in the final linear model configuration. As a result, sex was not included in the chosen predictor subset, suggesting its limited explanatory power in the context of this specific dataset.

Body Mass Index

Despite rigorous examination, BMI was not identified as a significant contributor in the final linear model configuration. As a result, BMI was not included in the chosen

predictor subset, suggesting its limited explanatory power in the context of this specific dataset.

Waist Circumference

A significant positive relationship was observed between waist circumference (88.87 ± 11.49 cm) and HbA1c percentage (5.79 ± 0.91%) ($\beta = 0.01660$, SE = 0.001049, $p < 0.001$) (Table 5.2). This finding implies that, with every one-centimeter increase in waist circumference, HbA1c percentage increased by 0.01660%, when keeping all other predictor variables constant. The statistical significance ($p < 0.001$) suggests that waist circumference is an important factor influencing HbA1c percentage, with larger waist circumferences being associated with higher HbA1c percentages among Asian-American adults.

The variance inflation factors (VIF) for waist circumference and VAI in this model were: 1.15 and 1.12, respectively. These values suggest that there was low multicollinearity between these predictors and the other variables in the model. In general, a VIF above 5 or 10 is often used as a threshold to indicate problematic multicollinearity, therefore, these variables do not appear to be causing multicollinearity issues in our model.

Waist-to-Height Ratio

Despite rigorous examination, WHtR was not identified as a significant contributor in the final linear model configuration. As a result, WHtR was not included

in the chosen predictor subset, suggesting its limited explanatory power in the context of this specific dataset.

The variance inflation factors (VIF) for waist circumference and WHtR in this model were: 11.27 and 12.67, respectively. These values suggest that there was strong multicollinearity between these predictor variables in the model. Variables with VIF values above 10 are highly correlated and exhibit significant multicollinearity issues. Because WHtR was not a significant predictor variable in our model, this multicollinearity did not affect our outcomes.

Visceral Adiposity Index

The Visceral Adiposity Index (VAI) (1.73 ± 1.86) exhibited a significant positive association with HbA1c percentage (5.79 ± 0.91%) ($\beta = 0.040$, SE = 0.006, $p < 0.001$) (Table 5.2). This result indicates that higher VAI values correspond to higher HbA1c percentages, all else being equal. The statistical significance ($p < 0.001$) underscores the relevance of VAI as a predictor of HbA1c percentage among Asian-American adults.

Sedentary Time

The relationship between sedentary time (415.32 ± 537.99 minutes) and HbA1c percentage (5.79 ± 0.91%) was not significant ($\beta = -0.00006$, SE = 0.00003, $p = 0.1087$) (Table 5.2). This finding suggests that the effect of sedentary time on HbA1c percentage is not discernable when controlling for all other predictor variables.

Dietary Magnesium Intake

Despite rigorous examination, dietary magnesium intake was not identified as a significant contributor in the final linear model configuration. As a result, dietary magnesium intake was not included in the chosen predictor subset, suggesting its limited explanatory power in the context of this specific dataset.

Self-Reported Healthy Diet Status

The association between self-reported healthy diet status and HbA1c percentage (5.79 ± 0.91%) was significant for specific categories compared to the reference category. HbA1c percentage was significantly higher for individuals who reported a "Fair" diet ($\beta = 0.494$, $SE = 0.080$, $p < 0.001$), and exhibited marginal significance for those who reported a "Good" diet ($\beta = 0.070$, $SE = 0.041$, $p = 0.0916$). Conversely, no significant differences in HbA1c percentage were found for individuals who reported that their diet status was “Excellent”, "Very Good", “Poor”, or “Refused to Answer” (Table 5.2). Our results highlight the influence of diet quality on HbA1c percentage, with "Fair" diets being associated with higher HbA1c percentages among Asian-American adults.

Sedentary Time and Self-Reported Healthy Diet Status Interaction

The interaction between sedentary time and self-reported healthy diet status was significant for the "Fair" diet category ($\beta = -0.0007$, $SE = 0.0001$, $p < 0.001$), but not significant for the “Excellent”, “Very Good, “Good”, "Poor”, or “Refused to Answer” diet categories (Table 5.2). Our results indicate that the effect of sedentary time on HbA1c percentage varies depending on the quality of an individual's diet.

Language

Despite rigorous examination, language was not identified as a significant contributor in the final linear model configuration. As a result, language was not included in the chosen predictor subset, suggesting its limited explanatory power in the context of this specific dataset.

Multivariate Model

The final linear regression model included age, waist circumference, VAI, self-reported healthy diet status, and the interaction term between sedentary time (minutes) and self-reported healthy diet status as predictor variables. We fit this model to the data and obtained a summary of the model's performance (Table 5.3).

Model Fit and Model Significance

The final linear regression model demonstrated an adequate fit to the data (Table 5.3). The residual standard error was 0.8012, indicating a typical deviation of 0.8012% in HbA1c percentage among the observed values and those predicted by the model. The model had 5,170 degrees of freedom, reflecting the large sample size in our analyses. The model's explanatory power, measured by the Multiple R-squared value, was 0.2198, suggesting that approximately 21.98% of the variability in HbA1c percentage could be explained by the predictor variables included in the model. The adjusted R-squared value, which considers the number of predictors in the model, was slightly lower at 0.2179. The F-statistic was 112.1, with 13 and 5,170 degrees of freedom for the

numerator and denominator, respectively. This test statistic indicated a significant overall relationship among the predictor variables and HbA1c percentage ($p < 0.001$). Therefore, the null hypothesis that all predictor variables have no effect on HbA1c percentage was rejected, providing evidence for the association among the predictors and the outcome variables in the population.

In summary, the results of linear regression analyses suggest that age, waist circumference, and VAI are significantly associated with HbA1c percentage in the Asian-American population who participated in the 2011 to 2020 NHANES. We also found a significant interaction between sedentary time and self-reported healthy diet status for the "Fair" diet category. These findings highlight the significance of accounting for various factors such as age, waist circumference, VAI, sedentary behavior, and self-reported healthy diet status, when assessing HbA1c percentages in Asian-American adults.

The fitted linear regression model ($F(8, 5175) = 177$, $p < 0.001$) accounted for 21.98% of the variance in HbA1c percentages (5.79 ± 0.91%) (adjusted R-squared = 0.213). Age (49.64 ± 16.95 years of age, $\beta = 0.018$, SE = 0.0007, $p < 0.001$), waist circumference (88.87 ± 11.49 cm, $\beta = 0.016$, SE = 0.0011, $p < 0.001$), VAI (1.73 ± 1.86, $\beta = 0.037$, SE = 0.006, $p < 0.001$), self-reported healthy diet status rated as “Fair” ($\beta = 0.4942$, $p < 0.001$), and the interaction between sedentary time and self-reported healthy diet

status for the "Fair" diet category (β = -0.0007, SE = 0.0001, $p < 0.001$), were all positively and significantly associated with HbA1c percentages in Asian-American adults.

Discussion

We aimed to investigate the associations among HbA1c percentage with age, sex, measures of body composition (BMI, waist circumference, WHtR, VAI), sedentary time (minutes), dietary magnesium intake, self-reported healthy diet status, and language in an Asian-American population using NHANES data from 2011 to 2020. The new and important findings of this study are the significant relationships among HbA1c percentages with age, waist circumference, VAI, certain categories of self-reported healthy diet status, and an interaction between sedentary time and the "Fair" category of self-reported healthy diet status, which are consistent with previous research conducted among Asian-American populations and other racial and ethnic groups.[34,40,57–59]

Age

We reported a significant positive relationship between HbA1c percentage and age in Asian-American adults. Our finding is consistent with previous research that has documented an increase in HbA1c percentage with advancing age in the general population and among Asian or Asian-American populations, specifically.[60] Several mechanisms may explain the observed association between HbA1c percentage and age. As individuals age, the insulin sensitivity of tissues tends to decrease, leading to

impaired glucose metabolism and increased HbA1c percentages.[61] Additionally, aging is associated with a decline in pancreatic beta cell function, which contributes to the deterioration of glycemic control.[62] Age-related changes in body composition, such as an increase in visceral fat and a decrease in muscle mass, can also exacerbate insulin resistance and contribute to elevated HbA1c percentages.[63] Yamada et al.[63] conducted a cross-sectional study to assess the variations in skeletal muscle mass and visceral fat area relative to age in Japanese adults. The researchers also evaluated sex differences in skeletal muscle deterioration in the upper and lower limbs. In addition, they explored the correlation between skeletal muscle mass and the visceral fat area. They included healthy women (n = 21,660) and men (n = 16,379), 40 to 79 years of age. Skeletal muscle mass and visceral fat area were quantified using bioelectrical impedance analysis. Skeletal Muscle Index (SMI) was calculated by taking the muscle mass data and dividing it by the square of height, expressed in kg/m^2. The authors[63] reported that both female and male participants showed a decrease in SMI with age; a total decrease of 6.4% for women and 10.8% for men ($p < 0.001$). Particularly, the decrease in arm SMI was more evident, with a 4.1% decrease for women and a 12.6% decrease for men. In addition, both sexes demonstrated an increase in the visceral fat area: 65.3% in women and 42.9% in men. A negative correlation was found between SMI and the visceral fat area in both sexes ($p < 0.001$). These findings indicate that the loss of skeletal muscle

mass starts around 40 years of age, and becomes more prevalent after 50 years of age in Japanese adults.

Lee et al.[64] examined the correlation between appendicular skeletal muscle mass and insulin resistance in a group of older individuals residing in a community in Korea. They included 241 women (70.6 ± 7.8 year of age) and 158 men (71.8 ± 7.3 years of age) who were part of the Korean Social Life, Health and Aging Project. It is important to note that these participants had no previous medical history of diabetes mellitus or cardiovascular disease. The researchers utilized bioelectrical impedance analysis to measure appendicular skeletal muscle mass. The authors[64] used the homeostasis model assessment of insulin resistance (HOMA-IR) to assess insulin resistance. Lee et al.[64] reported a significant inverse correlation between appendicular skeletal muscle mass and HOMA-IR, especially among men ($p < 0.001$). The researchers[64] stated that their results reaffirmed the link between age-related muscle loss and insulin resistance, highlighting the importance of maintaining muscle mass in mitigating insulin resistance in the older population.[58]

Waist Circumference

We reported a significant positive relationship between HbA1c percentage and waist circumference among Asian-American adults. Others have reported that larger waist circumferences are associated with higher HbA1c percentages in various populations, including Asian Americans.[65] Sakurai et al.[65] conducted an eight-year

observational study involving 3,992 Japanese individuals (1,459 women and 2,533 men), 35 to 55 years of age, who were generally lean. They evaluated the correlation between anthropometric measurements (specifically BMI and waist circumference) and the likelihood of developing T2DM in the future. The researchers reported a J-shaped relationship between waist circumference and subsequent risk for T2DM, which supports the idea that larger waist circumferences are associated with higher HbA1c percentages. Sakurai et al.[65] reported that the waist circumference measurements at-risk for T2DM were between 74.0 to 80.0 cm for women and 82.5 to 86.0 cm for men. While no significant sex differences were observed in waist circumference, our findings align with the waist circumference guidelines proposed by the Japan Medical Association (85 cm for women and 90 cm for men)[66], and the International Diabetes Federation (80 cm for women and 90 cm for men).[67] These measurements substantiate the appropriateness of the recommended waist circumference thresholds in assessing abdominal obesity and its implications for health in Asian Americans.[67]The relationship between HbA1c percentage and waist circumference can be attributed to the role of abdominal obesity in insulin resistance, which is a major contributor to the development of T2DM. The strong association between HbA1c percentage and waist circumference is particularly relevant for Asian Americans, because they tend to have a higher prevalence of central obesity compared to other racial and ethnic groups[30,68] Moreover, Asian Americans have been reported to develop T2DM at lower waist circumference measurements than other

racial and ethnic groups, emphasizing the importance of monitoring waist circumference as a risk factor for T2DM in this population.[69]

Visceral Adiposity Index

We reported a significant positive association between HbA1c percentage and VAI. This finding implies that higher VAI values correspond to higher HbA1c percentages, with other predictor variables held constant. The statistical significance highlights the importance of VAI as a predictor of HbA1c percentages. We reported VAI scores averaging 1.73 ± 1.86, which are higher than those reported by two research groups in China. These groups have defined metabolic health by VAI scores, stating that a score below 1.59 indicates metabolic health. Conversely, a score above 1.59 signifies metabolic unhealthiness for both women and men, 18 years of age and older .[70,71] Our results are consistent with others who have identified VAI as an effective marker for insulin resistance and cardiometabolic risk in various populations, including Asian Americans.[70,71]

Du et al.[70] reported that VAI could predict T2DM risk in a Chinese population, emphasizing its potential as a useful tool in assessing the risk of T2DM in Asian populations. Oh et al.[72] evaluated if VAI could replace computed tomography (CT) scanning in predicting insulin resistance. The participants were 180 Korean women, 25±5 years of age, with polycystic ovary syndrome (PCOS). The women completed a 75-gram oral glucose tolerance test and euglycemic hyper-insulinemic clamps using the

DeFronzo et al.[73] protocol to assess insulin sensitivity (M value). Using multiple logistic regression, Oh et al.[72] determined a positive correlation ($r = 0.57$, $p = 0.002$) between VAI and visceral fat area from the CT scan. Further, Oh et al.[72] reported a negative correlation ($r = -0.55$, $p = 0.0033$) between VAI and the M value. Women with PCOS may typically have abdominal adiposity or T2DM. The Korean women with PCOS had a mean BMI of 23.0±4.3 kg/m^2 and waist circumference of 74.8±11 cm, demonstrating that insulin resistance and increased visceral adiposity occurred at a lower BMI and waist circumference than the T2DM screening cut-off points. This further supports our finding that VAI plays a significant role in predicting HbA1c percentages among Asian Americans.

Sedentary Time

We reported that the relationship between HbA1c percentage and sedentary time was not significant, suggesting that the effect of sedentary time on HbA1c percentage is not discernable when controlling for all other predictor variables. Our finding contrasts with others who have reported a significant association between sedentary behavior and increased risk of T2DM in various populations, including Asian Americans.[74,75] Nguyen et al.[74] reported that the prevalence of T2DM is increasing among Asian Americans, and that sedentary behavior is a risk factor for the development of T2DM in this population.

According to the National Diabetes Statistics Report from the CDC, of the newly diagnosed T2DM cases in adults (18 years of age and older), 34% reported being physically inactive.[76] Although physical activity may be a modifiable risk factor for glycemic control, increasing time spent in sedentary behavior may be a predictor of HbA1c percentage. Nicolo et al.[77] compared NHANES data from 2003 to 2004 and 2012 to 2014, to determine if sedentary behavior, defined as television and computer time, was predictive of HbA1c of ≥ 6.5%. Their analyses included 1,069 individuals (552 women and 517 men), 48.4 ± 5.5 years of age, from NHANES 2003 to 2004, and 905 individuals (471 women and 434 men), 49 ± 5.7 years of age, from NHANES 2013 to 2014. The researchers included non-Hispanic White, non-Hispanic Black, and Hispanic/Mexican Americans. Nicolo et al.[77] report that sedentary behavior of eight or more hours per week was predictive of having an HbA1c of ≥ 6.5% only with the NHANES data from 2003 to 2004. Nicolo et al.[77] did not specifically address the association between sedentary behavior and T2DM in Asian Americans; however, they did report that sedentary behavior time is a predictor of HbA1c percentage among adults using data from NHANES. Their findings further support the importance of reducing sedentary behavior to prevent the development of T2DM.

Altenburg et al.[78] investigated the prospective relationship between sedentary time and cardiometabolic health in 622 adults, 30 to 50 years of age, who were at an increased risk for cardiometabolic risk. Their study was two years in duration, which

included four follow-up measurements. Indicators of cardiometabolic risk encompassed markers of excess body weight (such as overall body weight, waist circumference measurements, and the waist-to-hip ratio), blood pressure, HbA1c percentage, and plasma fasting glucose, insulin, total cholesterol, HDL-C, low density lipoprotein cholesterol (LDL-C), and triglyceride concentrations. Altenburg et al.[78] reported that sedentary time was positively associated with HbA1c percentage in adults at increased cardiometabolic risk. However, the effect of sedentary time on HbA1c percentage may be obscured by other factors, such as body composition and diet quality. Their results align with our results, suggesting that the influence of sedentary time on HbA1c percentage may be affected by other factors, such as body composition and diet quality.

It is also possible that the lack of a significant association between sedentary time and HbA1c percentage in our study could be attributed to measurement error, because self-reported sedentary time may be subject to recall bias and social desirability bias. Future studies employing objective measures of sedentary behavior could help to better elucidate the relationship between sedentary time and HbA1c percentage in Asian Americans.

Self-Reported Healthy Diet

We found a significant association between HbA1c percentage and self-reported healthy diet status for specific categories when compared to the reference category.

HbA1c percentage was significantly higher for individuals who reported a "Fair" diet, and exhibited marginal significance for those who reported a "Good" diet. Jacobs et al.[79] investigated the association between diet quality and the risk of T2DM in a multiethnic cohort, including Asian Americans. The researchers investigated the associations between different dietary indices: Healthy Eating Index-2010 (HEI-2010), Alternate Healthy Eating Index-2010 (AHEI-2010), Mediterranean Diet Score (aMED), and Dietary Approaches to Stop Hypertension (DASH) and the risk of T2DM. Jacobs et al.[79] also explored potential underlying pathways between diet quality and metabolic parameters involved in T2DM etiology. They reported that diet quality was inversely related to the incidence of T2DM. The researchers used data from the Multiethnic Cohort study, which included 215,418 women and men, 45 to 75 years of age. The researchers reported that individuals with the highest scores, indicating better diet quality, had a 15% to 25% lower risk of developing type T2DM compared to those with the lowest scores, representing poorer diet quality ($p < 0.001$).

Sullivan et al.[80] evaluated the relative accuracy of NHANES self-rated diet quality in comparison to a validated measure of diet quality, specifically the Healthy Eating Index-2015 (HEI-2015). Additionally, they investigated the associations between self-rated diet quality and cardiometabolic risk factors. The authors used NHANES data from 2011 to 2018, which included 39,156 adults, 20 years of age and older. The participants in this study identified their race and/or ethnicity as non-Hispanic White

(n=6,629), non-Hispanic Black (n=3,913), non-Hispanic Asian (n=1,868), Hispanic (including Mexican American and Other Hispanic origin; n=3,880), and Other (including individuals with multiracial backgrounds; n=623).[80]Key factors related to cardiometabolic disease risk were assessed, including BMI, waist circumference, seated blood pressure (systolic and diastolic), HbA1c percentage, and fasting plasma glucose, fasting serum insulin, fasting serum total cholesterol, fasting serum HDL-C, fasting serum LDL-C, and fasting serum triglyceride concentrations.[80]

The researchers[80] reported that the majority of U.S. adults (41.2%) self-rated their diet quality as "good". Approximately, 31.6% reported having an "excellent" or "very good" diet, while the remaining 27.2% rated their diets as "fair" or "poor". Additionally, adults with higher self-rated diet quality reported lower rates of smoking and engaged in greater levels of recreational physical activity compared to those with lower self-rated diet quality. There was a positive association between self-rated diet quality and mean total HEI-2015 scores ($p < 0.001$). Individuals who rated their diets as "excellent" had, on average, 8.9 points higher total HEI-2015 scores compared to those who rated their diets as "poor". The researchers also reported that HEI-2015 component scores increased with self-rated diet quality ($p < 0.01$). The association between self-rated diet quality and total HEI-2015 scores varied across different racial and ethnic groups. Among Asian-American adults, there was a significant gradation in total HEI-2015 scores based on self-rated diet quality, with a notable 15.9-point difference

between the "excellent" and "poor" self-rated categories ($p < 0.001$). After accounting for demographic and lifestyle factors, higher self-rated diet quality was linked to lower HbA1c percentage ($p < 0.001$) and waist circumference ($p < 0.001$). These inverse associations held true across all races and ethnicities.[80]

Lv et al.[81] evaluated the association between adherence to a healthy lifestyle and the risk of T2DM in Chinese adults. They used data from the China Kadoorie Biobank study, which included 482,591 adults, 30 to 79 years of age. They reported that adherence to a healthy lifestyle (consuming a healthy diet, participating in regular exercise, and not smoking), was associated with a lower risk of T2DM. Lv et al.[81] reported that participants who adhered to a healthy lifestyle had a 35% lower risk of T2DM compared to those who did not adhere to a healthy lifestyle ($p < 0.001$).

Sedentary Time and Self-Reported Healthy Diet Status Interaction

We found a significant interaction between sedentary time and self-reported healthy diet status for the "Fair" diet category ($p < 0.001$), suggesting that the effect of sedentary time on HbA1c percentage may vary depending on diet quality. Our results add to the existing literature on the combined effects of sedentary behavior and dietary quality on T2DM risk among various populations, including Asian Americans.[82]

The significance of physical activity and diet in preventing T2DM has been well-established.[9,83] The Diabetes Prevention Program (DPP) Research Group evaluated if lifestyle changes could reduce T2DM risk in individuals at high-risk.[9] In this three-year

landmark trial, the researchers included 3,234 ethnically diverse participants, 50.6 ± 10.7 years of age. Eligibility criteria included a BMI of 24 kg/m^2 or higher (22 kg/m^2 for Asian Americans), and a plasma glucose concentration between 140 to 199 mg/dL, two hours after a 75-gram oral glucose tolerance test. Participants were randomized into a lifestyle group (physical activity and diet), a Metformin group, or a placebo group. The lifestyle group received a 24-week one-on-one teaching program focused on exercise and healthy eating. They were instructed to lose 7% of their initial body weight, engage in 150 minutes of moderate-intensity physical activity per week, and consume a low-energy, low-fat diet. At the end of 24 weeks, 50% of the lifestyle group lost at least 7% of their body weight, and 74% met their physical activity goals. After one year, the lifestyle group maintained a significantly higher energy deficit (450 ± 26 kilocalories [kcals]) compared to the Metformin (296 ± 23 kcals) and placebo groups (249 ± 27 kcals). At the end of the three-year study, the lifestyle modification group had a 58% reduction in the incidence of T2DM compared to the placebo group. Additionally, the Metformin group reduced their incidence of T2DM by 31% compared to the placebo group. Notably, the Asian-American lifestyle group demonstrated a 71% reduction in T2DM incidence. The DPP provided strong evidence that T2DM can be delayed or prevented through physical activity and dietary modifications.[70]

Hemmingsen et al.[84] conducted a systematic review and meta-analyses where they evaluated the effect of physical activity, diet or a combination of physical activity

and diet in preventing or delaying T2DM and its associated complications in individuals at increased risk of developing the disease. The authors[84] reported on data from 49 randomized controlled trials involving over 12,000 people. They reported that lifestyle interventions that included both physical activity and diet were more effective than either intervention alone in reducing the risk of developing T2DM. They also reported that lifestyle interventions were associated with improvements in glycemic control, blood pressure, and lipid concentrations. Hemmingsen et al.[84] concluded that lifestyle interventions that include both physical activity and diet should be recommended for people at increased risk of developing T2DM.

Strengths

Our study had several strengths. First, we leveraged data from a substantial sample of Asian Americans, collated through the NHANES, a survey offering a national snapshot of health behaviors and conditions among the U.S. populace. In addition, we conducted an assessment specifically targeting the Asian-American population, a population often under-represented in research studies.

The data featured in our study are founded on objective measurements conducted by skilled personnel. Notably, we are the first to investigate HbA1c percentage with predictors such as age, sex, body composition (BMI, waist circumference, WtHR, and VAI), sedentary time, dietary magnesium intake, self-reported healthy diet status, and language among Asian Americans, utilizing the

complete NHANES dataset. In our analyses, we employed rigorous statistical methodologies, including control for multicollinearity among body composition variables.

Limitations

Although we made significant contributions to scientific knowledge regarding the associations among HbA1c percentage and age, waist circumference, VAI, sedentary time, and self-reported healthy diet status among Asian Americans, several limitations must be acknowledged. We relied on cross-sectional data, which restricts the ability to establish causality between HbA1c percentage and our selected predictor variables. Future research should consider using longitudinal data to provide a stronger basis for determining the temporal relationships among HbA1c percentages and age, sex, body composition, sedentary time, dietary status, and language.

Sedentary time and healthy diet status relied on self-reported data, which may be susceptible to recall bias and social desirability bias. The accuracy of these measures could be enhanced by incorporating objective measures. We focused only on Asian Americans, and therefore, the generalizability of our findings to other racial and ethnic groups remains unknown. Future research should investigate these associations in other populations to determine the generalizability of the results. Finally, we did not consider other potential confounding variables such as medication use, physical activity levels, and comorbidities, which may have influenced the associations between HbA1c

percentage and our selected predictor variables. Future research should control for these variables to enhance the validity of the findings.

Despite these limitations, our study offers valuable insights into the determinants of HbA1c percentages among Asian Americans. These findings may inform the development of targeted interventions aimed at preventing and managing diabetes mellitus in this population. Further research that incorporates these variables would provide a more comprehensive understanding of the determinants of HbA1c percentages in Asian-American populations.

Conclusion

The new and important findings of this study are that, when HbA1c percentage is on a continuum, there are significant associations between HbA1c percentage and age, waist circumference, VAI, certain categories of self-reported healthy diet status, and an interaction between sedentary time and self-reported healthy diet status in an Asian-American population. The positive associations of age, waist circumference, and VAI with HbA1c percentages emphasize the importance of addressing modifiable risk factors, such as central adiposity and dietary habits, to improve blood glucose control and prevent T2DM among Asian Americans. The results from our study also highlight the need for targeted screening and intervention strategies to address the growing burden of T2DM in the Asian-American population. To bridge these gaps, researchers should continue to examine the influence of these independent variables on identifying

the risk for T2DM among Asian Americans. Additionally, incorporating the pre-diabetes HbA1c threshold of 5.7% into predictive modeling may yield more useful insights for the development of targeted interventions and preventive strategies among Asian Americans.

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Table 5.1. Descriptive Characteristics of Asian-Americans Adults (n=5,184)

Age (years) (Mean ± SD)	49.64 ± 16.95
Sex n (%)	
Women	3,002 (57.9%)
Men	2,182 (42.1%)
HbA1c (%) (Mean ± SD)	5.79 ± 0.91
BMI (kg/m^2) (Mean ± SD)	25.07 ± 4.40
Waist Circumference (cm) (Mean ± SD)	88.87 ± 11.49
WHtR (Mean ± SD)	0.55 ± 0.07
VAI (Mean ± SD)	1.73 ± 1.86
Sedentary Time (minutes) (Mean ± SD)	415.32 ± 537.99
Dietary Magnesium Intake (mg) (Mean ± SD)	659.39 ± 284.72
Self-Reported Healthy Diet Status n (%)	
Excellent	686 (13.2)
Very Good	1,691 ± 32.6
Good	2,099 ± 40.5
Fair	618 ± 11.9
Poor	87 ± (1.7)
Refused to Answer	3.0 ± (0.1)
NHANES Cycle Year n (%)	
2011 to 2012	923 (17.8)
2013 to 2014	1,158 (22.3)
2015 to 2016	1,152 (22.2)
2017 to 2020	1,951 (37.6)

SD: Standard Deviation; HbA1c %: hemoglobin A1c percentage; BMI: body mass index; kg: kilograms; m^2: meters squared; cm: centimeters; WHtR: waist-to-height ratio; VAI: visceral adiposity index; mg: milligrams; NHANES: National Health and Nutrition Examination Survey

Table 5.2. Hemoglobin A1c Percentage and Predictor Variables (n=5,184)

HbA1c (%) (Mean ± SD)	5.79 ± 0.91
Age (years) (Mean ± SD)	49.64 ± 16.95†
Waist Circumference (cm) (Mean ± SD)	88.87 ± 11.49‡
VAI (Mean ± SD)	1.73 ± 1.86§
Sedentary Time (minutes) (Mean ± SD)	415.32 ± 537.99#
Self-Reported Healthy Diet Status n (%)	
Excellent	686 (13.2)
Very Good	1,691 ± 32.6
Good	2,099 ± 40.5
Fair	618 ± 11.9‖
Poor	87 ± (1.7)
Refused to Answer	3.0 ± (0.1)

HbA1c %: hemoglobin A1c percentage; SD: Standard Deviation; cm: centimeters; VAI: visceral adiposity index

†A significant positive relationship between HbA1c percentage (5.79 ± 0.91%) and age (49.64 ± 16.95 years of age) in Asian-American adults ($p < 0.001$)

‡A significant positive relationship between HbA1c percentage (5.79 ± 0.91%) and waist circumference (88.87 ± 11.49 cm) in Asian-American adults ($p < 0.001$)

§A significant positive relationship between HbA1c percentage (5.79 ± 0.91%) and VAI (1.73 ± 1.86) in Asian-American adults ($p < 0.001$)

#A significant interaction between sedentary time and self-reported healthy diet status for the "Fair" diet category (415.32 ± 537.99) in Asian-American adults ($p < 0.001$)

‖A significant positive relationship between HbA1c percentage (5.79 ± 0.91%) and Asian-American adults who reported a "Fair" diet ($p < 0.001$)

Table 5.3: Linear Regression Analyses Predicting Hemoglobin A1c Percentage

Predictor	B	Standard Error	t-value	p-value
Intercept	3.31	0.09	35.14	< 0.001
Age (years)	0.01	0.00	26.84	< 0.001
Waist Circumference (cm)	0.01	0.00	15.82	< 0.001
Visceral Adiposity Index	0.04	0.00	6.30	< 0.001
Sedentary Time (minutes)	0.00	0.00	-1.60	0.109
Self-Reported Healthy Diet Status (Excellent)	0.10	0.64	0.16	0.867
Self-Reported Healthy Diet Status (Very Good)	-0.01	0.04	-0.25	0.799
Self-Reported Healthy Diet Status (Good)	0.07	0.04	-1.65	0.091
Self-Reported Healthy Diet Status (Fair)	0.49	0.80	6.17	< 0.001
Self-Reported Healthy Diet Status (Poor)	-0.26	0.19	-1.36	0.171
Self-Reported Healthy Diet Status (Refused to Answer)	-0.89	0.54	-1.65	0.098
Sedentary Time (minutes): Self-Reported Healthy Diet Status (Excellent)	0.00	0.00	0.43	0.661
Sedentary Time (minutes): Self-Reported Healthy Diet Status (Very Good)	0.00	0.00	1.19	0.232
Sedentary Time (minutes): Self-Reported Healthy Diet Status (Good)	0.00	0.00	-0.90	0.367
Sedentary Time (minutes): Self-Reported Healthy Diet Status (Fair)	0.00	0.00	-4.40	< 0.001
Sedentary Time (minutes): Self-Reported Healthy Diet Status (Poor)	0.00	0.00	0.60	0.548
Sedentary Time (minutes): Self-Reported Healthy Diet Status (Refused to Answer)	NA	NA	NA	NA

Model summary: Residual standard error: 0.8012 on 5,170 degrees of freedom; Multiple R-squared: 0.2198; Adjusted R-squared: 0.2179; F-statistic: 112.1 on 13 and 5,170 degrees of freedom; p-value: < 0.001
B: unstandardized regression coefficients; cm: centimeters; NA: Not applicable

CHAPTER 5: MANUSCRIPT 2

Predicting Hemoglobin A1c ≥ 6.5% in Asian-American Adults: Evaluating the Role of Body Composition, Sedentary Behavior, and Dietary Magnesium Intake Using Machine Learning, Decision Tree Modeling, and Logistic Regression Approaches with NHANES 2011 to 2020 Data

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Abstract

Objective: The aim of our study was to utilize machine learning techniques and decision tree modeling to estimate the best fitting logistic regression model to determine the association of hemoglobin A1c (HbA1c) percentage (HbA1c %) ≥ 6.5% among age, sex, body mass index (BMI), waist circumference, waist-to-height ratio (WHtR), visceral adiposity index (VAI), sedentary time, dietary magnesium intake, self-reported healthy diet status, and language in Asian-American adults, 18 years of age and older, using the National Health and Nutrition Examination Survey (NHANES) data from 2011 to 2020.

Methods: To select the optimal model through exhaustive, forward, and backward search methods, we included 5,184 Asian-American adults, 18 years of age or older, who participated in the 2011 to 2020 NHANES. These methods considered interaction terms among variables such as age, sex, BMI, waist circumference, WHtR, VAI, sedentary time, dietary magnesium intake, self-reported healthy diet status, and language. A stepwise model selection was employed, with both forward and backward selection, using Akaike Information Criterion (AIC) and Schwarz Bayesian Information Criterion (BIC) criteria. This model was then fitted to the data, and its performance was summarized.

Results: We found statistically significant associations among several variables and HbA1c % ≥ 6.5%. An increase in age ($b = 0.04944$, $p < 0.001$), waist circumference ($b = 0.07961$, $p < 0.001$), and VAI ($b = 0.11222$, $p < 0.001$) were all positively associated with

HbA1c % ≥ 6.5%. In contrast, we found an inverse relationship between BMI (b = -0.06561, p = 0.0014) and HbA1c % ≥ 6.5%.

Conclusion: Overall, our findings suggest that age, waist circumference, and VAI are important predictors among Asian Americans. The significant positive associations observed among age, waist circumference, and VAI with HbA1c % ≥ 6.5% underscore the significance of addressing modifiable risk factors, such as central adiposity, to enhance blood glucose control and prevent the onset of type 2 diabetes mellitus (T2DM) in Asian Americans. These findings emphasize the importance of targeted screening and intervention strategies to tackle the increasing prevalence of T2DM within the Asian-American population. Future research should aim to further clarify the mechanisms behind the negative relationship between BMI and HbA1c %.

Keywords: Asian Americans, Hemoglobin A1c percentage, NHANES, Waist Circumference, Visceral Adiposity Index

Introduction

The prevalence of type 2 diabetes mellitus (T2DM) has increased among Asian Americans, affecting approximately 8.5% of the adult population in this demographic group in the United States (U.S.).[1,2] Type 2 diabetes mellitus is a chronic metabolic disorder characterized by high blood glucose concentrations due to inadequate insulin production or impaired insulin action. The Centers for Disease Control and Prevention[3] (CDC) reported that one in three Asian Americans has undiagnosed T2DM. Type 2 diabetes mellitus is the fifth leading cause of mortality among Asian Americans, with recent statistics from 2018 highlighting this health concern.[4,5] Analyses of distinct Asian-American subcategories disclose an elevated occurrence of diabetes mellitus within certain groups. The aggregate prevalence rate of 9.2% for the entire Asian-American population obscures the higher prevalence of T2DM among Asian subgroups.[6] Type 2 diabetes mellitus has a multifactorial etiology comprising genetic predisposition and environmental factors. Notwithstanding, modifiable lifestyle behaviors, like insufficient physical activity and unhealthy dietary habits, have been found to significantly affect the pathogenesis and progression of T2DM. Given the complications and health risks associated with T2DM, it is essential to identify modifiable risk factors that can inform targeted interventions to prevent or delay the onset and progression of this disease.[6,7] One such risk factor is glycosylated hemoglobin (or hemoglobin A1c [HbA1c])

percentage, which reflects the average blood glucose concentrations over the past two to three months.[6]

Age plays a significant role in the onset of T2DM. Even without the presence of T2DM, Hemoglobin A1c (HbA1c) percentages have been observed to increase with advancing age.[8] One contributing factor to this phenomenon may be a result of sarcopenia[9], which tends to exacerbate the decline in insulin sensitivity.[10] Moreover, as individuals age, the body's capacity to process glucose diminishes due to a decrease in insulin sensitivity and beta cell function. This results in elevated blood glucose concentrations, subsequently leading to increased HbA1c percentages.

Sex differences in HbA1c percentages among Asians have not been extensively studied. However, some research has shown differences in HbA1c percentages between women and men in various populations. Men typically receive a diagnosis at a younger age and with lower body fat mass compared to women.[11] Conversely, women carry a higher burden of risk factors, particularly obesity, at the time of T2DM diagnosis.[11] Additionally, reproductive factors, such as pregnancy and menopause, exert a substantial influence on the risk of developing T2DM in women.[11]

While body mass index (BMI) does not provide a direct assessment of the amount of body fat, it can serve as a preliminary gauge for adiposity.[12–14] Nonetheless, an elevated BMI, waist circumference, and overall adiposity are linked to insulin resistance, which is a contributing factor to the development of T2DM. However, the

utilization of standardized BMI assessments may result in an inadequate evaluation of pre-diabetes and T2DM susceptibility among individuals with Asian-American heritage.[15–19] Asian Americans exhibit lower mean BMI and waist circumference at the time of pre-diabetes and T2DM diagnosis compared to other racial and ethnic groups.[15,20] The American Medical Association (AMA) recently changed their policy with respect to BMI.[21] The AMA recommends that, due to the limitations of BMI, it should be used in conjunction with waist circumference and visceral fat.

Despite being a commonly employed clinical instrument for approximating body fat, BMI exhibits shortcomings in its ability to evaluate adipose tissue composition.[15–19] The utilization of BMI as a sole measure to assess adiposity in any population is inadequate, but in Asian-American adults, in particular, given that this group exhibits a greater percentage of body fat despite having lower BMI values.

Other anthropometric indices, such as waist circumference, waist-to-height ratio (WHtR), and visceral adiposity index (VAI), have been shown to be valuable measurements for detecting a susceptibility towards T2DM, obesity, and cardiometabolic risk.[22,23] Therefore, the inclusion of additional anthropometric indices in addition to BMI, such as waist circumference, WHtR and VAI, can provide a more comprehensive evaluation of adiposity, and assist in early diagnosis of T2DM in Asian-American adults.

Waist circumference measurements can serve as a cost-effective and uncomplicated means of gauging visceral adiposity and HbA1c percentage in the Asian-American population.[24–26] Nonetheless, there needs to be a change in what waist circumference measures are used to be meaningful in the Asian-American population. According to the World Health Organization (WHO), revising the waist circumference cut-off thresholds for Asian Americans to 80 cm for women and 85 cm for men, would enhance the detection of their metabolic risk.[17]

Like waist circumference, the WHtR is a screening tool for cardiometabolic risk related to body fat distribution. The WHtR, calculated by dividing waist circumference (centimeters [cm]) by height (cm), has recently gained attention as an anthropometric index for measuring central adiposity.[27] Waist-to-height ratio is a more sensitive universal screening tool than BMI to detect health risks.[27] The WHtR is a stronger predictor for T2DM among Asian Americans compared to BMI.[24,25] Asian Americans have higher amounts of visceral adiposity compared to other races and ethnicities with the same BMI.[26,28] The proximity of visceral fat to the vital organs puts Asian Americans at higher risk for insulin resistance and developing T2DM.[29] Therefore WHtR may succeed in identifying risk for T2DM compared to other anthropometric measures, such as BMI or waist circumference.

Waist circumference and WHtR are clinical screening tools used for the indirect evaluation of increased visceral fat.[23] Yet, waist circumference and WHtR do not

distinguish between subcutaneous and visceral fat mass.[23] Asian Americans tend to accumulate more visceral fat at a lower BMI and waist circumference. Accumulation of visceral adiposity reduces insulin sensitivity, leading to an increased risk of developing T2DM.[30] The visceral adiposity index (VAI) seems to be a better predictor for metabolic disorders associated with insulin resistance than a single anthropometric index.[31–33] Visceral adiposity index is a mathematical formula that consists of BMI and waist circumference, as well as clinical measurements such as triglyceride and high-density lipoprotein cholesterol (HDL-C) concentrations.[23]

Increased sedentary time is associated with an increased risk for T2DM.[34,35] Lack of physical activity can result in insulin resistance and impaired glucose tolerance due to muscle disuse and decreased lean body mass.[36] Sheng et al.[37] conducted analyses of the Asian-American population using the National Health and Nutrition Examination Survey (NHANES) data from 2011 to 2016. The authors[37] reported that 64.4% of Asian Americans did not meet the recommended ≥ 150 minutes/week of physical activity. Further, Asian Americans who did not meet the recommended amount of physical activity had a higher risk of metabolic syndrome.

Researchers have reported an inverse relationship between increased dietary magnesium intake and the risk of T2DM.[38,39] Further, data from the 2013 to 2020 NHANES have shown that less than half of the Asian-American population is consuming the recommended amounts of magnesium from food, drinks, and dietary

supplements.[39] Previous researchers have reported mixed results in determining the correlation between dietary magnesium intake and the risk of T2DM in Asian countries.[40,41] The relationship between dietary magnesium intake and the risk of T2DM in Asian Americans is limited and needs further investigation.

In addition to magnesium intake, there is an association between dietary quality and the risk of T2DM.[38,42] Self-reported healthy diet status from the NHANES provides valuable insights into the dietary intake of the U.S. population.[43] This information allows for the assessment of nutrient intake and the differentiation of diet quality. However, self-reported dietary data may be susceptible to limitations, such as under-reporting or inaccuracies due to recall bias or social desirability bias.

The language predominantly spoken within a household significantly influences the degree to which individuals adhere to physical activity and dietary guidelines.[44] Specifically, within immigrant households in the United States, when English is the primary language of communication, there is a heightened probability of adhering with recommended physical activity and dietary practices.

In addition to the aforementioned variables, Tung et al.[45] reported that Asian Americans are less likely to receive proper diabetes mellitus screening compared to other racial and ethnic groups, potentially due to improper screening guidelines by clinicians, and Asian Americans being unaware of their increased risk for diabetes mellitus. To delay or prevent pre-diabetes and T2DM, the American Diabetes

Association (ADA) recommends lifestyle modifications such as weight reduction, routine physical activity, and healthy eating patterns that may improve insulin resistance and glycemic control.[46,47]

Therefore, the purpose of our study was to utilize machine learning techniques and decision tree modeling to estimate the best fitting logistic regression model to predict HbA1c percentage ≥ 6.5% among age, sex, BMI, waist circumference, WHtR, VAI, sedentary time, dietary magnesium intake, self-reported healthy diet status, and language in Asian-American adults, 18 years of age and older, using the 2011 to 2020 NHANES data.

Methods

We employed a two-pronged approach to estimate and predict the hemoglobin A1c percentage ≥ 6.5% among Asian-American adults, 18 years of age and older, using NHANES data from 2011 to 2020. First, we utilized machine learning techniques and decision tree modeling to estimate the relative importance scores of age, sex, body composition (BMI, waist circumference, WtHR, and VAI), sedentary time, dietary magnesium intake, self-reported healthy diet status, and language. Subsequently, we applied a logistic regression model to predict the HbA1c percentage based on these factors.

Study Design and Participants

The National Health and Nutrition Examination Survey uses survey weights to create a representative sample for the U.S. population to produce similar estimates if all of the eligible individuals in the U.S. were surveyed.[48] Excluded in NHANES data are U.S. citizens living overseas, those in custody in institutional settings, and those under supervised care. NHANES data are collected through in-person interviews and questionnaires, laboratory measures, and physical assessments conducted in mobile examination centers across the U.S. NHANES did not have an Asian-American demographic data until the 2011 to 2012 cycles. Due to this, the Asian-American population has been oversampled in every NHANES cycle following 2011 to 2012.

Approval for this study (IRB #22-268) was obtained from the Virginia Polytechnic Institute and State University (Virginia Tech) Institutional Review Board (IRB). Further review and approval by the Virginia Tech Human Research Protection Program (HRPP) was not required due to the data being available for public use and de-identified. Data will be collected from the NHANES 2011 to 2020.

The National Health and Nutrition Examination Survey is a cross-sectional survey used to evaluate the nutrition, health, and health behaviors of all eligible individuals living in the U.S.[49] The inclusion criteria for the study were limited to those meeting the following: non-Hispanic Asian race, 18 years of age and older, with complete data from NHANES 2011 to 2020 on all variables studied (HbA1c percentage, age sex, BMI, waist circumference, waist-to-height ratio, visceral adiposity index,

sedentary time, dietary magnesium intake, self-reported healthy diet status, and language).

Measurements

The NHANES determines BMI by dividing weight in kilograms by the square of height in meters.[50] Body weight is measured using a digital scale, which shows the weight in both kilograms and pounds. The NHANES does not provide variables for waist-to-height ratio or visceral adiposity index. The waist-to-height ratio formula involves dividing waist circumference (cm) by height (cm). Separate equations are used for calculating the visceral adiposity index (VAI) for women and men:

Females: VAI = (waist circumference [cm]/39.58 + (1.89 x BMI [kg/m2])) x (triglyceride concentration [mmol/L]/0.81) x (1.52/high-density lipoprotein cholesterol concentration [mmol/L]).[23]

Males: VAI = (waist circumference [cm]/39.68 + (1.88 x BMI [kg/m2])) x (triglyceride concentration [mmol/L]/1.03) x (1.31/high-density lipoprotein cholesterol concentration [mmol/L]).[23]

The NHANES evaluates physical activity and sedentary behavior using the Global Physical Activity Questionnaire (GPAQ). The GPAQ inquiries about sedentary behavior through three questions related to minutes of sedentary behavior, hours spent watching television (TV) or videos, and hours spent on a computer. All NHANES

protocols and procedures can be accessed on the CDC website at: https://www.cdc.gov/nchs/data/nhanes.

Dietary magnesium intake data are derived from the calculations of total daily nutrient intakes. The NHANES assesses dietary magnesium intake during in-person dietary interviews conducted in a mobile examination center.

The Diet Behavior and Nutrition Questionnaire measures self-reported healthy diet status by asking participants to rate how healthy they think their overall diet is. They use the following descriptors: “Excellent”, “Very Good”, “Good”, “Fair”, “Poor”, “Refused to Answer”, and “Don’t Know”.[43]

To account for the influence of acculturation, we utilized a question regarding the language spoken at home as a proxy measure. This question was designed for the Asian population, asked about the individual's linguistic preferences, with the following options: exclusive use of non-English languages, predominant use of non-English languages, equal use of English and non-English languages, predominant use of English, or exclusive use of English. This measure allowed us to evaluate the effects of acculturation within the context of our study. All NHANES protocols and procedures are available for public use on the CDC website at: https://www.cdc.gov/nchs/data/nhanes.

Statistical Analyses

All statistical analyses were conducted using R software version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria). The descriptive characteristics of Asian Americans was reported as mean ± standard deviation. To examine the association between HbA1c percentage and diverse predictor variables, multiple linear regression analyses were conducted. The preliminary linear regression model incorporated the subsequent predictor variables: age, sex, BMI waist circumference, WHtR, VAI, sedentary time (in minutes), and dietary magnesium intake. Adjustments were: self-reported healthy diet status, and language serving as a proxy for acculturation. Additionally, interaction terms were then introduced to assess potential effect modification between variables. Model assumptions, including linearity, independence, homoscedasticity, and normality of residuals, were checked using residual plots and formal statistical tests. The significance level was set *a priori* at $p < 0.05$.

Random Forest Model

For our analyses, the dataset was partitioned into a 70% training set and a 30% testing set. A random forest model, utilizing the ranger[51], was constructed with high HbA1c percentage (≥ 6.5%) as the response variable, and age, sex, BMI, waist circumference, WHtR, VAI, sedentary time, dietary magnesium intake, self-reported healthy diet status, and language as the predictor variables. The variable importance was determined using impurity as the measure. A confusion matrix was generated,

comparing predicted high HbA1c percentage with actual high HbA1c percentage in the test dataset, to evaluate the random forest model's performance. Accuracy, sensitivity, specificity, and additional performance metrics were calculated.

Logistic Regression Supervised Learning

A logistic regression model was fitted with the same predictor variables as in the random forest model using the General Linear Model (GLM) function with the caret package[52]. The model summary provided estimated coefficients and their statistical significance. The logistic regression model's performance was evaluated by generating a confusion matrix comparing the predicted high HbA1c percentage with the actual high HbA1c percentage in the test dataset.

The optimal classification threshold was determined using the Receiver Operating Characteristic (ROC) curve and Youden index to enhance the logistic regression model's performance. The Area Under the Curve (AUC) was computed as a performance measure, and a confusion matrix was generated using the optimal threshold. The model's performance was assessed by calculating accuracy, sensitivity, specificity, and additional performance metrics.

The objective was to identify the optimal set of predictor variables and potential interactions for predicting high HbA1c percentages (≥ 6.5%) among the following predictor variables: age, sex, BMI, waist circumference, WHtR, VAI, sedentary time, dietary magnesium intake, self-reported healthy diet status, and language. An initial

logistic regression model, encompassing all main effects and two-way interactions of predictor variables, was fitted. A stepwise model selection was employed, with both forward and backward selection, using the Akaike Information Criterion (AIC) and the Schwarz Bayesian Information Criterion (BIC). Both the AIC and the Schwarz BIC are information criteria that balance model complexity and goodness-of-fit. Lower AIC and Schwarz BIC values signify a better-fitting model, with Schwarz BIC generally emphasizing parsimony. The best model was chosen based on the lowest Schwarz BIC value. Comparing AIC and Schwarz BIC values allowed us to evaluate whether the optimal model struck a balance between data fit and model complexity. This comparison facilitated assessing the selected model's adequacy in predicting high HbA1c percentages (≥ 6.5%) among Asian-American adults using the given predictor variables and interaction terms.

Fitting the Logistic Regression Model

The glmnet[53,54] package was used for automated model selection. The function explored all possible combinations of predictors such as; age, sex, BMI, waist circumference, WHtR, VAI, sedentary time, and language, as well as significant interaction terms among all variables. The best model's coefficients were obtained, and the model's goodness-of-fit was evaluated by the Schwarz[55] Bayesian Information Criterion (BIC) values of the initial regression subset model. The best model based on the Schwarz BIC included age, BMI, waist circumference, and VAI.

All statistical analyses were conducted using R software version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria). Model assumptions, including linearity, independence, homoscedasticity, and normality of residuals were checked using residual plots and formal statistical tests. The significance level was set *a priori* at $p < 0.05$.

Results

Descriptive Statistics

Our study included 5,184 Asian-American adults, 18 years of age or older, who participated in the 2011 to 2020 NHANES. Table 6.1 outlines the descriptive characteristics of our population.

Random Forest Model Performance

A Random Forest model was developed and applied to a dataset partitioned into a 70% training set and a 30% testing set. The model's predictive accuracy was gauged through a confusion matrix and associated classification metrics. The confusion matrix accounted for 1,346 true negatives and 123 true positives, with 4 false negatives and 105 false positives. The model demonstrated an overall accuracy of 93.77% (95% confidence interval [CI]: 92.45% to 94.92%), signifying a robust capacity to distinguish between individuals with high and normal HbA1c percentages. A p-value < 0.001 was used for the model's accuracy, exceeding the no information rate of 86.95%, indicating the

model's superiority over chance predictions, established with a high degree of statistical significance.

The model presented a Kappa statistic of 0.6675, denoting a moderate to good concordance between the model's predictions and the actual HbA1c percentages. The p-value for McNemar's test was $p < 0.001$, implying a significant disparity in the counts of false positives and false negatives produced by the model. In evaluating the model's ability to correctly classify each instance, we observed a sensitivity rate of 99.48%, indicating a robust capacity to identify “No” instances. However, the specificity rate was lower at 55.67%, suggesting moderate effectiveness in correctly pinpointing “Yes” cases. The Positive Predictive Value and Negative Predictive Value of the model were 93.73% and 94.17%, respectively, portraying high precision in classifying both positive and negative cases. The model discerned “No” instances with a rate of 86.95%, whereas the detection prevalence, which denotes the proportion of instances predicted as positive, was 92.29%. The model's balanced accuracy, an amalgam of sensitivity and specificity, was computed as 77.57%.

To summarize, the model demonstrated considerable accuracy, sensitivity, and predictive values, but its moderate specificity suggests potential for enhancement, particularly in correctly identifying “Yes” instances. Subsequent iterations of the model should strive to fortify its specificity without undermining other performance indicators. In conclusion, the Random Forest model showcased solid predictive

accuracy for high HbA1c percentages among Asian-American adults using selected predictor variables. However, there is room for enhancement in terms of specificity and balanced accuracy. The significant disparity between false positives and false negatives also warrants further examination and model refinement.

Interpretation of Variable Importance

The variable importance scores suggest the following order of importance among the predictor variables for predicting high HbA1c percentages: age, waist circumference, and VAI appeared to be the most influential variables for predicting high HbA1c percentages, with importance scores of 129.84, 123.85, and 129.14, respectively. Conversely, sex had the lowest importance score (14.06), indicating that it may have the least influence on predicting high HbA1c percentages among the predictor variables. Overall, these results indicate that the random forest model identified several important predictor variables for high HbA1c percentages among Asian-American adults, with age, waist circumference, and VAI being the most influential factors.

Logistic Regression Supervised Learning

A logistic regression model was developed to investigate the relationships between the response variable, HbA1c percentage (High: ≥ 6.5%, Normal: < 6.5%), and a set of predictor variables: age, sex, BMI, waist circumference, WHtR, VAI, sedentary time (minutes), dietary magnesium intake, self-reported healthy diet status, and

language as a proxy for acculturation. The dataset was divided into a training set (70% of the data) and a testing set (30% of the data) using stratified random sampling to ensure balanced representation of the response variable in both sets. The logistic regression model was fitted to the training data, and its performance was evaluated using the testing data.

The confusion matrix and associated performance metrics were calculated as follows: The model yielded an overall accuracy of 87.71% (95% CI: 85.97% to 89.30%), representing the proportion of correctly classified cases. The No Information Rate (NIR) was 87.71%, indicating that 87.71% of the individuals in the dataset have HbA1c percentages < 6.5%. The p-value associated with the accuracy surpassing the NIR was calculated as 0.519, suggesting that the model's performance did not exhibit a statistically significant improvement over random chance.

The Kappa statistic, measuring the agreement between the observed and predicted classifications, was 0.159. The McNemar's Test p-value, which assesses the symmetry of the confusion matrix, was found to be $p < 0.0001$. The model's sensitivity, or the proportion of true positive cases among individuals with HbA1c percentages ≥ 6.5%, was 98.24%. The specificity, or the proportion of true negative cases among individuals with HbA1c percentages < 6.5%, was 12.57%. The positive predictive value (PPV), or the proportion of true positive cases among those predicted as positive, was 88.91%. The negative predictive value (NPV), or the proportion of true negative cases

among those predicted as negative, was 50%. The prevalence of HbA1c percentages ≥ 6.5% in the population was 87.71%. The detection rate, or the proportion of true positive cases in the population, was 86.16%. The detection prevalence, or the proportion of cases predicted as positive in the population, was 96.91%. The balanced accuracy, which is the average of sensitivity and specificity, was 55.40%.

Lowering the Threshold

The logistic regression dataset had its default threshold lowered to 0.3, which likely reduced the accuracy, but improved the specificity and balanced accuracy. Balanced accuracy in a confusion matrix is the average of sensitivity and specificity, which are metrics used to evaluate the performance of a binary classification model. Balanced accuracy is particularly useful when dealing with imbalanced datasets, where one class significantly outnumbers the other.

The confusion matrix and associated performance metrics were calculated as follows: The model yielded an overall accuracy of 84.88% (95% CI: 83% to 86%), representing the proportion of correctly classified cases. The No Information Rate (NIR) was 87.71%, indicating that 87.71% of the individuals in the dataset have HbA1c percentages < 6.5%. The p-value associated with the accuracy surpassing the NIR was calculated as 0.999, suggesting that the model's performance did not exhibit a statistically significant improvement over random chance.

The Kappa statistic, which measures the agreement between the observed and predicted classifications, was 0.242. The McNemar's Test p-value, which assesses the symmetry of the confusion matrix, was $p < 0.036$. The model's sensitivity, or the proportion of true positive cases among individuals with HbA1c percentages ≥ 6.5%, was 90.40%. The specificity, or the proportion of true negative cases among individuals with HbA1c percentages < 6.5%, was 29.84%. The positive predictive value (PPV), or the proportion of true positive cases among those predicted as positive, was 90.40%. The negative predictive value (NPV), or the proportion of true negative cases among those predicted as negative, was 36.08%. The prevalence of HbA1c percentages ≥ 6.5% in the population was 87.71%. The detection rate, or the proportion of true positive cases in the population, was 81.21%. The detection prevalence, or the proportion of cases predicted as positive in the population, was 89.83%. The balanced accuracy, which is the average of sensitivity and specificity, was 61.22%.

Receiver Operating Characteristic (ROC)

We conducted Receiver Operating Characteristic (ROC) analyses to evaluate the predictive prowess of our logistic regression model. This involved computing the area under the curve (AUC), an integral metric encapsulating the model's overall predictive performance. We also pinpointed the optimal Youden Index point, a point on the ROC curve that optimizes sensitivity and specificity, thus boosting the effectiveness of the model or diagnostic test.

The Youden Index, also known as Youden's J statistic, is a valuable tool in binary classification scenarios, helping identify the best cut-off point for a classifier or diagnostic test. When visualizing the ROC curve, a graphic representation of a classifier's performance against a spectrum of threshold values, the Youden Index is calculated as the maximum value of (sensitivity + specificity - 1) for every feasible threshold. This optimal Youden Index point is where the maximum value is achieved on the ROC curve, encapsulating the most beneficial equilibrium between sensitivity and specificity.

Selecting the optimal Youden Index point as the cut-off threshold can help achieve a balance between the true positive rate (sensitivity) and true negative rate (specificity), essential for making accurate predictions and minimizing misclassifications. The AUC for the logistic regression model is shown in Figure 6.1, indicating the model's overall predictive ability. The optimal Youden Index point was identified, and the corresponding threshold value was obtained using the optimal Youden Index point "cut-off". Utilizing this threshold, a new confusion matrix was generated to evaluate the model's performance.

The model exhibited an accuracy of 65.64%, denoting that it correctly predicted the status of a participant with a confidence interval of 63.22% to 68%. The No Information Rate (NIR) was 87.71%, indicating that 87.71% of the individuals in the dataset have HbA1c percentages < 6.5%. The p-value associated with the accuracy

surpassing the NIR was calculated as 1, suggesting that the model's performance did not exhibit a statistically significant improvement over random chance.

The Kappa statistic was 0.2255, illustrating a moderate level of agreement between the predicted and observed classifications, beyond what could be expected by mere chance. Furthermore, McNemar's Test indicated a statistically significant ($p < 0.001$) asymmetry in the model's misclassifications. In terms of the model's capacity to correctly classify cases, it displayed a sensitivity of 63.17% (the proportion of individuals with HbA1c percentage ≥ 6.5% accurately identified), and a specificity of 83.25% (the proportion of individuals with HbA1c percentage < 6.5% correctly classified). The positive predictive value was calculated to be 96.42%, suggesting a high accuracy in predicting those with HbA1c percentages ≥ 6.5%. Conversely, the model's negative predictive value was 24.05%. The prevalence of the condition (HbA1c percentage ≥ 6.5%) in the population was calculated as 87.71%. The model's detection rate, which signifies the percentage of actual positives correctly identified from the entire population, was 96.42%. Furthermore, the model correctly identified true negatives in 57.46% of the overall population, a measure known as the detection prevalence. The model's balanced accuracy, a metric that averages the model's ability to correctly identify both positive (sensitivity) and negative (specificity) cases, was found to be 73.21%. This suggests a reasonable level of effectiveness in equally distinguishing between positive and negative instances.

Logistic Regression Supervised Learning

We examined the relationships between HbA1c percentage ≥ 6.5% and various predictor variables: age, sex, BMI, waist circumference, WHtR, VAI, sedentary time, dietary magnesium intake, self-reported healthy diet status, and language in an Asian-American population. We found statistically significant relationships among HbA1c percentage and sex, BMI, waist circumference, and VAI (Table 6.2). A generalized linear model (GLM) with a binomial distribution was employed for analyses. The results of the GLM, including coefficients, standard errors, and p-values, are presented in Table 6.3.

The coefficients from the GLM analyses indicated the following relationships between the predictor variables and having HbA1c percentage ≥ 6.5%. Age: a positive coefficient ($b = 0.04944$, $p < 0.001$) suggests that, as age increases, the likelihood of HbA1c percentage being ≥ 6.5% also increases. Body mass index: a negative coefficient ($b = -0.06561$, $p = 0.0014$) indicates that, as BMI increases, the probability of HbA1c percentage being ≥ 6.5% decreases. Waist circumference: a positive coefficient ($b = 0.07961$, $p < 0.001$) implies that, as waist circumference increases, the probability of an HbA1c percentage ≥ 6.5% also increases. Visceral adiposity index: a positive coefficient ($b = 0.11222$, $p < 0.001$) implies that, as VAI increases, the probability of HbA1c percentage being ≥ 6.5% also increases.

The statistical significance of the coefficients suggests that each predictor variable has a meaningful impact on the likelihood of HbA1c percentage being ≥ 6.5% in the Asian- American population. These findings support the existing literature on the importance of age, BMI, waist circumference, and VAI in predicting HbA1c percentages, and provide a foundation for further investigation into the interplay between these factors in the Asian-American population.

Discussion

We investigated the relationship among age, sex, BMI, waist circumference, WHtR, VAI, sedentary time, dietary magnesium intake, self-reported healthy diet status, and language with the likelihood of having HbA1c percentage ≥ 6.5% as a high-risk health outcome in Asian-American adults using NHANES data from 2011 to 2020. The generalized linear model (GLM) with a binomial distribution was employed to analyze the data. The new and important findings of this study are that there exists a significant positive relationship between age, waist circumference, and VAI and the likelihood of having an HbA1c percentage of ≥ 6.5%. Conversely, a significant negative relationship was observed between BMI and the likelihood of an HbA1c percentage being ≥ 6.5%.

Age

We found a significant positive relationship between age and the likelihood of HbA1c percentage being ≥ 6.5%. A significant positive coefficient indicated that, with an

increase in age, the likelihood of an HbA1c percentage being ≥ 6.5% also increases. This finding aligns with the existing literature on the association between age and increased risk for high HbA1c percentages, which are indicative of diabetes mellitus or pre-diabetes. Becerra and Becerra[56] reported that Asian Americans have disparities in age at diabetes mellitus diagnosis, with some subgroups being at a heightened risk for T2DM. The positive relationship suggests that older individuals within the Asian-American population are at a higher risk for having a HbA1c percentage ≥ 6.5% compared to their younger counterparts.

The significant association between age and the likelihood of high HbA1c percentages can be attributed to several factors. As people age, their insulin sensitivity may decline, leading to impaired glucose metabolism and a higher likelihood of elevated HbA1c percentages.[57] Huang et al.[57] evaluated the association between age, sex, and HbA1c percentages in Taiwanese adults without prior diagnosis of T2DM. The researchers included 2,563 women and 2,183 men, 30 to 70 years of age. The authors[57] reported that HbA1c percentages increased with age in women. They also reported a positive association between HbA1c percentages and age across all age categories: 30 to 70 ($p < 0.0001$), 30 to 49 ($p < 0.0001$), and 50 to 70 ($p < 0.0001$) years of age.[57] For men, a positive association between HbA1c percentages and age was reported for the following age groups: 30 to 70 ($p < 0.0001$) and 30 to 49 ($p = 0.0003$) years of age. However, Huang et al.[57] did not observe a significant relationship between HbA1c percentages and age in

men 50 to 70 years of age ($p = 0.3567$). Their results are consistent with the fact that age is a significant factor in the likelihood of high HbA1c percentages[57].

Inoue et al.[58] conducted a study including 33,959 Japanese people (17,090 women and 16,869 men), 15 to 93 years of age, without a T2DM diagnosis. They evaluated how the prevalence of T2DM differs among age and sex, using HbA1c percentage and fasting plasma glucose concentrations. The participants were separated by the following age categories: ≤ 37, 38 to 45, 46 to 53, 54 to 59, 60 to 65, and ≥ 66 years of age. Among the women, a significant increase in HbA1c percentage and age was reported ($p < 0.001$). Among the men, HbA1c percentage and T2DM prevalence were significantly higher than women ($p < 0.001$) in all age groups, except those in the ≥ 66 years of age group.

Aging is often accompanied by a decrease in muscle mass and an increase in adipose tissue, which can contribute to insulin resistance and subsequently higher HbA1c percentages.[59] It is important to note that, while we found a significant relationship between age and HbA1c percentage, it does not imply causation. Other factors, including genetics, lifestyle, and environmental influences, may also contribute to the risk of having an HbA1c percentage ≥ 6.5%.[60] Further research is needed to elucidate the underlying mechanisms driving this relationship, as well as to examine the potential influence of other factors, such as physical activity, diet, and medication adherence on HbA1c percentages in the aging Asian-American population.

Body Mass Index

We found a significant negative association between BMI and the likelihood of HbA1c percentage being ≥ 6.5%. A negative coefficient indicates that, as BMI increases, the probability of HbA1c percentage being ≥ 6.5% decreases. This observation may appear counterintuitive, because the existing literature has consistently shown a positive association and increased risk between a higher BMI and an increased risk of T2DM.[61,62] However, our finding of a negative association between BMI and the likelihood of high HbA1c percentages may be explained by several factors specific to the Asian-American population. Asian populations have been shown to develop T2DM at a lower BMI threshold compared to other populations.[19,63] Researchers have reported that using standardized BMI measurements underestimates the risk for pre-diabetes and T2DM in the Asian-American population.[16,19] Asian individuals may exhibit higher risks of insulin resistance and T2DM at lower BMI categories than their non-Asian counterparts. Consequently, the observed inverse relationship between BMI and HbA1c percentage in our study could potentially be attributed to the propensity for Asian Americans to develop T2DM at comparatively lower BMI categories. For example, Kuberan[64] analyzed NHANES data from 2013 to 2016 to examine the associations among sex, BMI, waist circumference, and WHtR with HbA1c percentages in 900 Asian Americans (454 women, 446 men), 20 to 65 years of age. They used a BMI range of 23 to 25 kg/m^2. When associating HbA1c percentage with BMI, the researchers[64] reported

that, among women, HbA1c percentage increased with BMI; however, among men, the HbA1c percentage was higher with a BMI of less than 23 kg/m^2, compared to those with a BMI of 23 kg/m^2 to 25 kg/m^2.

Lee et al.[65] conducted the Korean Metabolic Risk Factor (KOMERIT) study, which included 12,815,006 participants (5,522,942 women and 7,292,064 men), 44.40 ± 14.2 years of age. Their study population included individuals with previously diagnosed type 1 and type 2 diabetes mellitus (n = 359,645), and those newly diagnosed with either condition (n = 546,232). Additionally, the participants were stratified by age and sex. Lee et al.[65] evaluated the link between BMI and mortality, and established the most beneficial BMI for lifespan relative to diabetes mellitus status. The authors[65] use the BMI reference ranges for Asian populations. Lee et al.[65] reported a higher rate of diabetes mellitus prevalence and newly diagnosed diabetes mellitus among individuals 18 to 44 years of age, with a BMI between 19 kg/m^2 and 20 kg/m^2.[57] A potential explanation could be due to a reduction in muscle tissue and a rise in body fat. These changes can potentially lead to increased insulin resistance, resulting in elevated HbA1c percentages.

Waist Circumference

We found a significant positive association between waist circumference and the likelihood of HbA1c percentage being ≥ 6.5%. A positive coefficient indicates that, as waist circumference increases, the probability of HbA1c percentage being ≥ 6.5% also

increases. This observation aligns with existing literature on the relationship between waist circumference, a widely used proxy for abdominal obesity, and the risk of T2DM. Kuerban[24] analyzed NHANES data from 2013 to 2016 to examine the associations among sex, BMI, waist circumference, WHtR with HbA1c percentage in 900 Asian Americans (454 women, 446 men), 20 to 65 years of age. The BMI cut-off of 23 to 25 kg/m^2 was used, as well as the WHO waist circumference recommendations of 80 cm and 85 cm for women and men, respectively. Kuerban[24] reported that waist circumference ($r = 0.393$, $p < 0.001$) was associated with a higher HbA1c percentage and higher percentages of overweight and obesity among Asian-American women. An increase in waist circumference is indicative of a higher amount of visceral adipose tissue, which has been associated with insulin resistance and the development of T2DM. The significant positive relationship between waist circumference and the likelihood of high HbA1c percentages suggests that individuals with larger waist circumferences within the Asian-American population are at a higher risk for having an HbA1c percentage ≥ 6.5%, compared to those with smaller waist circumferences.

Zhen et al.[66] examined the correlation between HbA1c percentage and waist circumference in a Chinese population. They included 1,251 women and 951 men, 18 to 84 years of age, with a mean waist circumference of 82.10 ± 10.20 cm. Zhen et al.[66] used the Asian-specific waist circumference measurements of ≥ 80 cm for women and ≥ 90 cm for men.[67] The authors[66] reported that, the participants with an HbA1c percentage ≥

6.5%, had a significantly larger waist circumference than participants with a HbA1c percentage < 6.5% (89.90 ± 9.0 cm vs. 81.70 ± 9.9 cm, respectively, $p < 0.001$). Zhen and colleagues[66] reported a significant linear correlation between waist circumference and HbA1c percentage, which underscores the crucial role of waist circumference measurements in assessing central adiposity and the risk of type T2DM. This observation also highlights the necessity of employing sex-specific cut-off values for women and men, respectively, to enhance the accuracy of risk evaluation for T2DM.

Nicolo et al.[68] compared NHANES data from 2003 to 2004 and 2012 to 2014, to evaluate if BMI, waist circumference, and WHtR were predictive of HbA1c percentage ≥ 6.5%. The researchers included 1,069 individuals (552 women and 517 men), 48.4 ± 5.5 years of age, from the NHANES 2003 to 2004 data, and 905 individuals (471 women and 434 men), 49 ± 5.7 years of age, from the NHANES 2013 to 2014. Nicolo et al.[68] included non-Hispanic white, non-Hispanic black, and Hispanic/Mexican Americans. Standard BMI measurements were used, and waist circumference measurements of < 80 cm (optimal) and ≥ 80 cm (at-risk), and a WHtR of < 0.50 (optimal) and ≥ 0.50 (at-risk), for all women and men. While there were no Asian Americans in their study, the waist circumference measurements were lower than the WHO waist circumference recommendations of 80 cm for women and 85 cm for men.[69]

Nicolo et al.[68] reported that, each body composition measurement was significantly higher ($p < 0.0001$) in the NHANES data from 2003 to 2004, compared to

the data from 2013 to 2014. Further, 91.7% of adults had a waist circumference that was significantly greater than 80 cm ($p < 0.0001$) in 2003 to 2004, compared to 63.5% in 2013 to 2014. The authors[68] stated that using waist circumference may potentially identify more adults susceptible to T2DM than the use of body mass index (BMI) alone. There may be instances where adults having increased central or abdominal adiposity may not be recognized due to their BMI being within healthy limits.

The significant association between waist circumference and the likelihood of high HbA1c percentages can be attributed to several factors. Visceral adipose tissue is known to produce various adipokines and cytokines that can contribute to insulin resistance and inflammation, which, in turn, may lead to elevated HbA1c percentages.[70] Moreover, increased waist circumference may also be indicative of visceral fat deposition in organs such as the liver and pancreas, which can further impair glucose metabolism and contribute to higher HbA1c percentages.[71]

Visceral Adiposity Index (VAI)

We found a significant positive association between VAI and the likelihood of HbA1c percentage being ≥ 6.5%. A positive coefficient indicates that, as VAI increases, the probability of an HbA1c percentage being ≥ 6.5% also increases. This observation aligns with existing literature on the relationship between visceral adiposity and the risk of T2DM. Our findings showed an average VAI score of 2.48 ± 2.15, which is higher compared to the scores reported by two different research teams in China.[72,73] The

authors[72,73] have used VAI scores to indicate metabolic health, suggesting that a score below 1.59 signifies good metabolic health. In contrast, a score above 1.59 is indicative of metabolic unhealthiness in women and men, 18 years of age and older. Our findings align with others who have recognized VAI as a useful indicator for insulin resistance and the risk of cardiometabolic diseases in Asian Americans. Du et al.[72] highlighted that VAI could be a potential predictor for T2DM risk in Chinese individuals, further underlining its utility in assessing T2DM risk in Asian populations.

Yu et al.[74] analyzed data from the China Health and Retirement Longitudinal study to determine the association between the risk for developing T2DM and VAI between rural and urban populations. They included 7,245 participants (3,858 women and 3,387 men), 45 years of age and older, with a mean VAI of 2.02 ± 2.37. To differentiate between high and low risk groups, Yu et al.[74] utilized receiver operating characteristic analyses, setting the VAI cut-offs at 1.63 for women and 1.06 for men. Yu et al.[74] reported a significant positive association between the high VAI group and risk for T2DM regardless of an urban or rural setting ($p < 0.05$). The researchers[74] concluded that VAI scores are useful to determine the associated risk with developing T2DM among a Chinese population.

Nusrianto et al.[75] conducted a systematic review to investigate if VAI can serve as a predictor for T2DM in an Asian population. They included seven studies with 29,966 participants. The researchers[75] stated that there was not a fixed VAI cut-off point across

all the studies included. Each study had unique VAI cut-off points, possibly due to variations in body composition among different populations. Their results suggest that it may be beneficial for each population to create their own VAI formula, preferably derived from local data specific to each population. Further, Nusrianto et al.[75] reported that VAI had a better predictive or similar value compared to waist circumference, indicating that VAI may be another valuable predictor of T2DM in Asian populations.

Visceral adipose tissue has been implicated in the development of insulin resistance and T2DM due to its production of various adipokines and cytokines that can contribute to inflammation and impaired glucose metabolism.[70,71] Identifying markers such as VAI can help identify individuals who may benefit from targeted interventions to prevent or delay the onset and progression of T2DM and related metabolic disorders, especially Asian populations, where VAI has been shown to be more predictive. Our finding that there was a positive association between VAI and the likelihood of elevated HbA1c percentages suggests that increased visceral adiposity correlates with a heightened risk of having a HbA1c percentage ≥ 6.5% in the Asian-American population.

Strengths

Our research is notable for several reasons. We capitalized on a robust dataset drawn from the NHANES, which evaluates the nutrition, health, and health behaviors of all eligible individuals living in the U.S.[49] . We focused specifically on Asian

Americans, and under-represented population in the scientific literature, Our investigation marks the inaugural examination of the relationships between HbA1c percentage and a range of predictor variables (age, sex, BMI, waist circumference, WHtR, VAI, sedentary time, dietary magnesium intake, self-reported healthy diet status, and language) within the Asian American community, using the comprehensive NHANES database. We adhered to rigorous statistical techniques, which incorporated measures to account for potential multicollinearity among body composition variables. This diligence in methodology ensured the reliability and validity of our findings.

Limitations

Our study has several limitations that warrant careful consideration when interpreting the outcomes. The cross-sectional nature of our study prohibits the drawing of causal inferences between the examined variables and the likelihood of HbA1c percentage being ≥ 6.5%. Longitudinal research is imperative to elucidate the temporal associations among age, BMI, waist circumference, VAI, and HbA1c percentages in the Asian and Asian-American populations. The reliance on self-reported data may engender biases, such as recall and social desirability biases, potentially compromising the accuracy and dependability of the findings. Subsequent research should use objective measurements, including clinical or laboratory evaluations, to corroborate self-reported data.

The study population, comprised solely of Asian-American individuals, may circumscribe the applicability of the findings to other racial and ethnic groups. Additional research is necessary to examine the connections among age, BMI, waist circumference, VAI, and HbA1c percentages across diverse populations. Our study did not consider potential confounding factors, including physical activity, smoking status, alcohol consumption, and medication adherence, which could affect HbA1c percentages. Accounting for these factors in future investigations may yield a more holistic understanding of the relationships between the studied variables and HbA1c percentages.

Conclusion

The new and important findings of this study are the significant relationships among age, BMI, waist circumference, and VAI with the likelihood of having a HbA1c percentage ≥ 6.5% in an Asian-American population. These findings reaffirm the significance of age, BMI, waist circumference, and VAI as important risk factors for elevated HbA1c percentages in the Asian-American population. They also raise interesting questions about the unique metabolic profile of Asian Americans and the potential implications for diabetes mellitus risk assessment and management strategies. Future research should aim to further clarify the mechanisms behind the observed relationships, particularly the negative relationship between BMI and HbA1c percentage. Additionally, researchers should consider other potentially influential

factors such as physical activity, diet, medication adherence, and genetic predisposition to fully understand the risk profile for T2DM in the Asian-American population. Ultimately, the goal is to develop effective, targeted interventions to mitigate T2DM risk among Asian Americans.

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Table 6.1. Descriptive Characteristics of Asian-American Adults (n=5,184)

Predictor Variables	Hemoglobin A1c Percentage ≥ 6.5%	Hemoglobin A1c Percentage < 6.5%
Age (years) (Mean ± SD)	61.29 ± 12.41*	48.00 ± 16.86
Sex (n)		
Women	321	2,681
Men	318	1,864
HbA1c (%) (Mean ± SD)	7.66 ± 1.19	5.52 ± 0.41
BMI (kg/m^2) (Mean ± SD)	27.09 ± 4.48**	24.79 ± 4.31
Waist Circumference (cm) (Mean ± SD)	96.57 ± 11.10†	87.78 ± 11.13
WHtR (Mean ± SD)	0.60 ± 0.07	0.54 ± 0.07
VAI (Mean ± SD)	2.48 ± 2.15††	1.62 ± 1.79
Sedentary Time (minutes) (Mean ± SD)	376.95 ± 569.48	420.71 ± 533.26
Total Dietary Magnesium (mg) (Mean ± SD)	639.13 ± 259.95	662.24 ± 287.95
Self-Reported Healthy Diet Status (n) (%)		
Excellent	60 (9.4)	626 (13.8)
Very Good	184 (28.8)	1507 (33.2)
Good	294 (46)	1805 (39.7)
Fair	96 (15)	522 (11.5)
Poor	5 (0.8)	82 (1.8)
Refused	0 (0.0)	3 (0.1)
NHANES Cycle Year (n) (%)		
2011 to 2012	95 (14.9)	828 (18.2)
2013 to 2014	125 (19.6)	1033 (22.7)
2015 to 2016	145 (22.7)	1007 (22.2)
2017 to 2020	274 (42.9)	1677 (36.9)

SD: Standard deviation; HbA1c %: hemoglobin A1c percentage; BMI: body mass index; kg: kilograms; m^2: meters squared; cm: centimeters; WHtR: waist-to-height ratio; VAI: visceral adiposity index; mg; milligrams; NHANES: National Health and Nutrition Examination Survey

*We found a significant positive relationship between age (61.29 ± 12.41 years of age) and the likelihood of HbA1c percentage (7.66 ± 1.19%) being ≥ 6.5% ($p < 0.0001$)
**We found a significant negative association between BMI (27.09 ± 4.48 kg/m^2) and the likelihood of HbA1c percentage (7.66 ± 1.19%) being ≥ 6.5% ($p = 0.0014$)
†We found a significant positive association between waist circumference (96.57 ± 11.10 cm) and the likelihood of HbA1c percentage (7.66 ± 1.19%) being ≥ 6.5% $p < 0.0001$)
††We found a significant positive association between the VAI (2.48 ± 2.15) and the likelihood of HbA1c percentage (7.66 ± 1.19%) being ≥ 6.5% $p < 0.0001$)

Table 6.2. Logistic Regression Analyses Predicting HbA1c Percentage ≥ 6.5%

Predictor	Coefficients	Standard Error	z-value	p-value
Intercept	-10.55	0.452	-23.34	< 0.0001
Age (years)	0.049	0.003	15.13	< 0.0001
BMI (kg/m^2)	-0.065	0.020	-3.19	0.0014
Waist Circumference (cm)	0.079	0.008	9.49	< 0.0001
VAI	0.112	0.019	5.68	< 0.0001

Model summary: Null deviance: 3871.2 on 5,183 degrees of freedom; Residual deviance: 3,213 on 5,179 degrees of freedom; Akaike Information Criterion (AIC): 3,223; Number of Fisher Scoring iterations: 6

BMI: body mass index; kg: kilograms; m^2: meters squared; cm: centimeters; VAI: visceral adiposity index

Table 6.3. Hemoglobin A1c Percentage ≥ 6.5% and Predictor Variables

HbA1c (%)	7.66 ± 1.19*
Age (years)	61.29 ± 12.4**
BMI (kg/m^2)	27.09 ± 4.48***
Waist Circumference (cm)	96.57 ± 11.10†
VAI	2.48 ± 2.15††

HbA1c %: hemoglobin A1c percentage; BMI: body mass index; kg: kilograms; m^2: meters squared; cm: centimeters; VAI: visceral adiposity index

*We found a significant positive relationship between age (61.29 ± 12.41 years of age) and the likelihood of HbA1c percentage (7.66 ± 1.19%) being ≥ 6.5% ($p < 0.0001$)

**We found a significant negative association between BMI (27.09 ± 4.48 kg/m^2) and the likelihood of HbA1c percentage (7.66 ± 1.19%) being ≥ 6.5% ($p = 0.0014$)

†We found a significant positive association between waist circumference (96.57 ± 11.10 cm) and the likelihood of HbA1c percentage (7.66 ± 1.19%) being ≥ 6.5% ($p < 0.0001$)

††We found a significant positive association between the VAI (2.48 ± 2.15) and the likelihood of HbA1c percentage (7.66 ± 1.19%) being ≥ 6.5% ($p < 0.0001$)

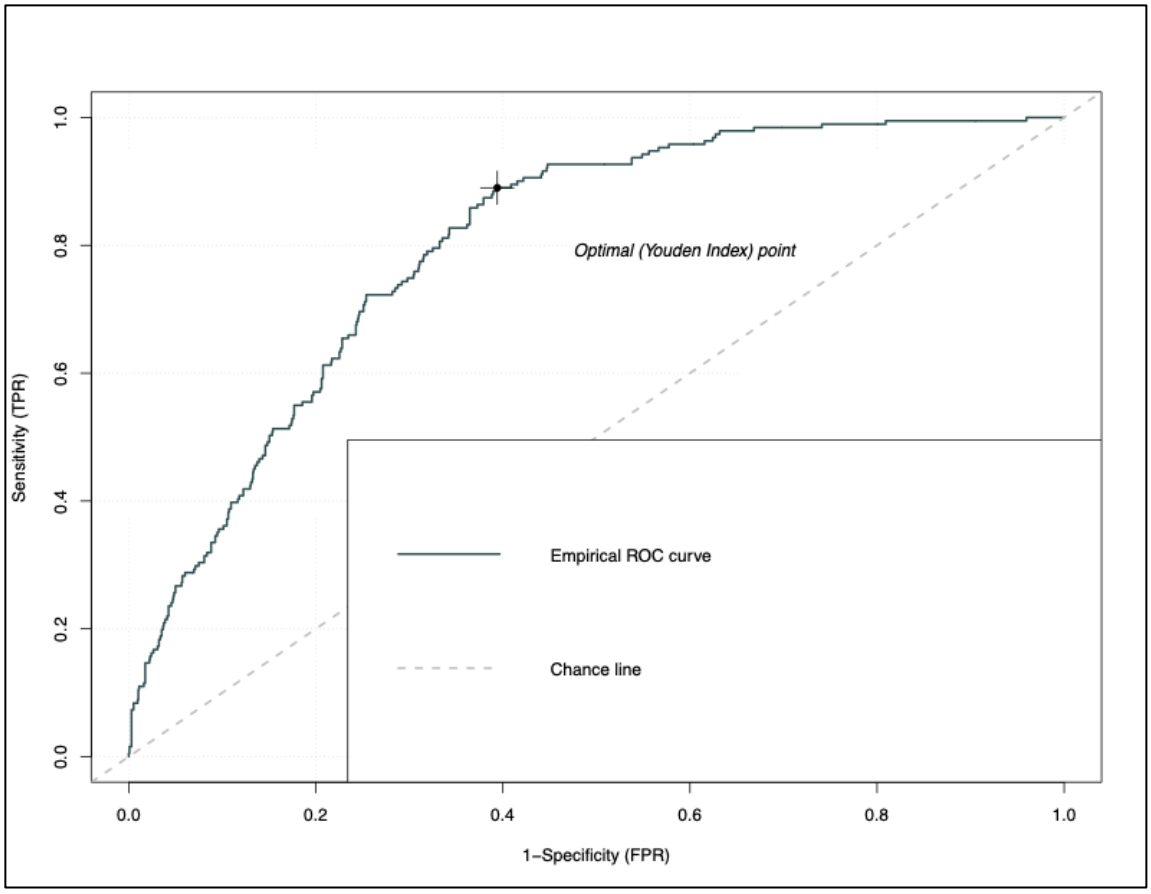


Figure 6.1. The Receiver Operating Characteristic (ROC) curve for our diagnostic test. Each point on the curve represents a different threshold for distinguishing between positive and negative cases. The optimal threshold, indicated by the point farthest from the diagonal line was chosen based on the Youden Index. This point represents the best balance between sensitivity and specificity, maximizing the test's ability to correctly identify both positive and negative cases.

CHAPTER 6: CONCLUSIONS AND FUTURE DIRECTIONS

The main purpose of this study was to determine which independent variables (age, sex, body mass index [BMI], waist circumference, waist-to-height ratio [WHtR], visceral adiposity index [VAI], sedentary behavior time, dietary magnesium intake, self-reported healthy diet status, and language) were the strongest predictors of hemoglobin A1c (HbA1c) percentage in Asian-American adults, 18 years of age and older, using the National Health and Nutrition Examination Survey (NHANES) data from 2011 to 2020.

The study included 5,184 Asian-American adults, 18 years of age or older, who participated in the 2011 to 2020 NHANES. Appendix B outlines the descriptive characteristics of the population. Data visualization techniques, such as histograms (Appendix C), scatter plots (as quantile-quantile plots) (Appendix D), and bar graphs (Appendix E) were used to visually examine the distribution among the variables. Random forest and decision tree modeling was used to examine the relative importance of the independent variables in predicting HbA1c percentages (Appendix F).

The new and important findings of this study are that, when HbA1c percentage is on a continuum, there are significant associations among HbA1c percentage and age, waist circumference, VAI, and certain categories of self-reported healthy diet status, and an interaction between sedentary time (minutes) and self-reported healthy diet status in an Asian-American population (Appendix G). The positive associations of age, waist circumference, and VAI with HbA1c percentages emphasize the importance of

addressing modifiable risk factors, such as central adiposity and dietary habits, in efforts to improve blood glucose control and prevent type 2 diabetes mellitus (T2DM) among Asian Americans. The results from this study also highlight the need for targeted screening and intervention strategies to address the growing burden of T2DM in the Asian-American population.

In addition, when HbA1c percentage was a dichotomous variable (≥ 6.5%), there were significant associations among age, BMI, waist circumference, VAI, and HbA1c percentage (Appendix H). However, due to the cross-sectional nature of this study, these results do not necessarily imply causation. Other determinants, including genetics, lifestyle, and environmental factors, could contribute to the risk of possessing a HbA1c ≥ 6.5%. Further investigation is required to explore the underlying mechanisms governing these associations and to examine the potential influence of additional factors, such as body fat distribution, physical activity, and dietary habits on HbA1c percentages in the Asian and Asian-American population.

Future research is required to delineate the mechanisms by which ultra-processed foods may influence metabolic health, including HbA1c concentrations. Research focusing on the Asian and Asian-American populations would also provide insights into cultural dietary practices and their influence on health outcomes. Investigation into dietary patterns, rather than individual nutrients or foods, may offer a more holistic view of diet and its relationship with health.

Nonetheless, because magnesium intake and magnesium status have been related to glucose metabolism, future research should also focus on identifying particular dietary patterns that may be associated with optimal magnesium status and lower HbA1c concentrations. This may include the study of traditional dietary practices in different Asian populations, and how these patterns correlate with health markers. Understanding these patterns will provide a foundation for dietary guidelines and interventions. Using Sukumar et al.'s [193] Food Frequency Questionnaire to assess dietary magnesium intakes could be a good first step to more specifically target magnesium intake. Comprehending these significant associations can facilitate the development of targeted interventions and preventive strategies aimed at mitigating the risk of pre-diabetes and diabetes mellitus within the Asian-American demographic. Potential measures may encompass age-specific screening and monitoring, specific lifestyle interventions centering on weight management (particularly abdominal and visceral fat reduction), culturally tailored educational programs, and the establishment of specific BMI, waist circumference, and VAI thresholds for screening and monitoring, taking into account distinct metabolic characteristics and risks.

To bridge these gaps, researchers should continue to examine the influence of these independent variables on identifying the risk for T2DM among Asian Americans. Additionally, incorporating the pre-diabetes HbA1c threshold of 5.7% into the

predictive modeling may yield more useful insights for the development of targeted interventions and preventive strategies among Asian Americans.

APPENDIX A: LETTER OF DETERMINATION

Division of Scholarly Integrity and Research Compliance
Institutional Review Board
North End Center, Suite 4120 (MC 0497)
300 Turner Street NW
Blacksburg, Virginia 24061
540/231-3732
irb@vt.edu
http://www.research.vt.edu/sirc/hrpp

MEMORANDUM

DATE: October 19, 2022

TO: Stella Lucia Volpe, Quentin Zacharias Nichols

FROM: Virginia Tech Institutional Review Board (FWA00000572)

PROTOCOL TITLE: Factors Related to Diabetes Among Asian-American Adults in the United States Using the National Health and Nutrition Examination Survey data from 2011 to 2018.

IRB NUMBER: **22-268**

Based on the submitted project description and items listed in the Special Instructions section found on Page 2, the Virginia Tech Human Research Protection Program (HRPP) has determined that the proposed activity is not research involving human subjects as defined by HHS and FDA regulations.

Further review and approval by the Virginia Tech Human Research Protection Program (HRPP) is not required because this is not human research. This determination applies only to the activities described in the submitted project description and does not apply should any changes be made. If changes are made you must immediately submit an Amendment to the HRPP for a new determination. Your amendment must include a description of the changes and you must upload all revised documents. At that time, the HRPP will review the submission activities to confirm the original "Not Human Subjects Research" decision or to advise if a new application must be made.

If there are additional undisclosed components that you feel merit a change in this initial determination, please contact our office for a consultation.

Please be aware that receiving a "Not Human Subjects Research" Determination is not the same as IRB review and approval of the activity. You are NOT to use IRB consent forms or templates for these activities. If you have any questions, please contact the Virginia Tech HRPP office at 540-231-3732 or irb@vt.edu.

PROTOCOL INFORMATION:

Determined As:	**Not Human Subjects Research**
Protocol Determination Date:	**October 19, 2022**

ASSOCIATED FUNDING:

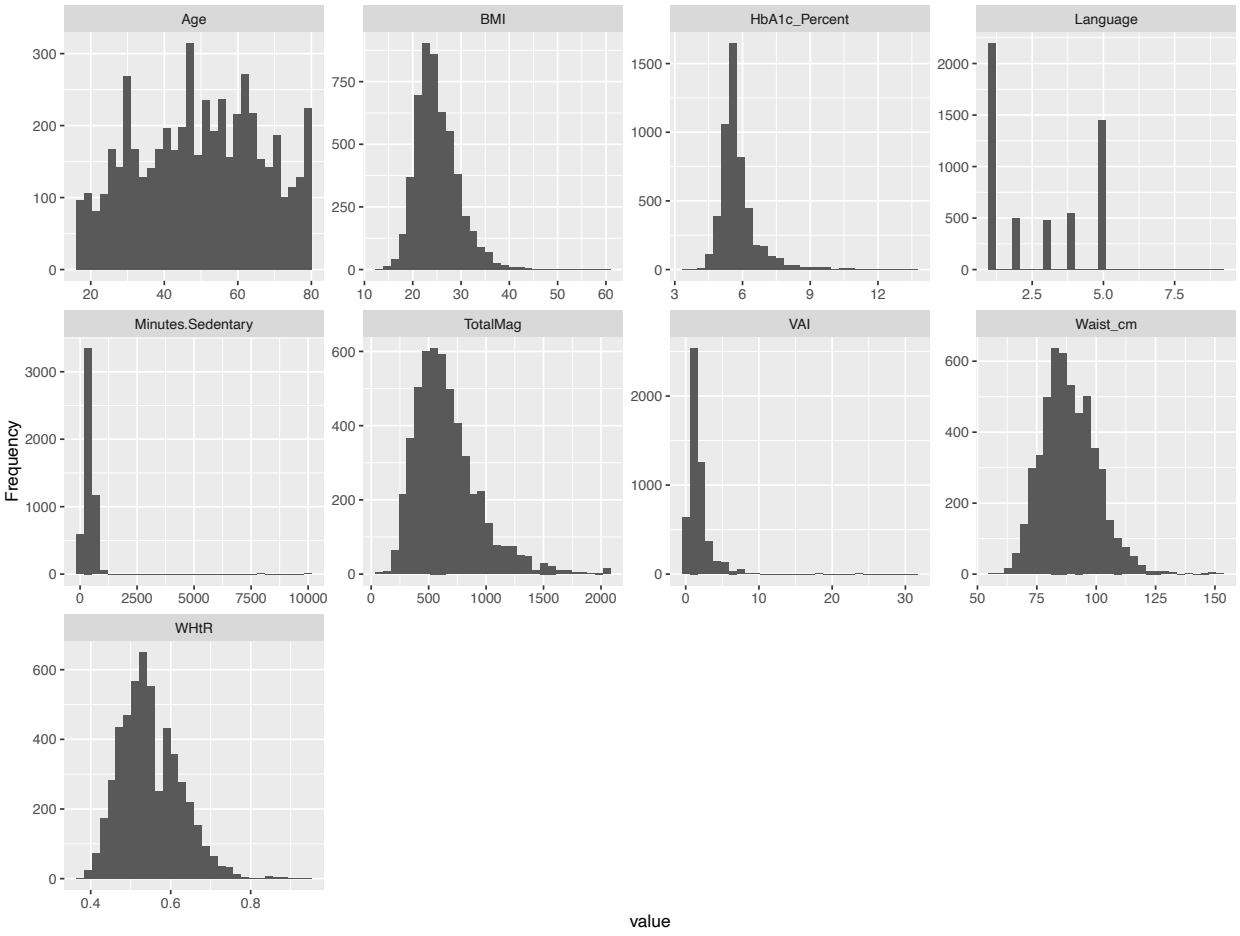
The table on the following page indicates whether grant proposals are related to this protocol, and which of the listed proposals, if any, have been compared to this protocol, if required.

APPENDIX B: DESCRIPTIVE CHARACTERISTICS OF ASIAN-AMERICAN ADULTS (n=5,184)

Age (years) (Mean ± SD)	49.64 ± 16.95
Sex n (%)	
Women	3,002 (57.9%)
Men	2,182 (42.1%)
HbA1c (%) (Mean ± SD)	5.79 ± 0.91
BMI (kg/m2) (Mean ± SD)	25.07 ± 4.40
Waist Circumference (cm) (Mean ± SD)	88.87 ± 11.49
WHtR (Mean ± SD)	0.55 ± 0.07
VAI (Mean ± SD)	1.73 ± 1.86
Sedentary Time (minutes) (Mean ± SD)	415.32 ± 537.99
Dietary Magnesium Intake (mg) (Mean ± SD)	659.39 ± 284.72
Self-Reported Healthy Diet Status n (%)	
Excellent	686 (13.2)
Very Good	1,691 ± 32.6
Good	2,099 ± 40.5
Fair	618 ± 11.9
Poor	87 ± (1.7)
Refused to Answer	3 ± (0.1)
NHANES Cycle Year n (%)	
2011 to 2012	923 (17.8)
2013 to 2014	1,158 (22.3)
2015 to 2016	1,152 (22.2)
2017 to 2020	1,951 (37.6)

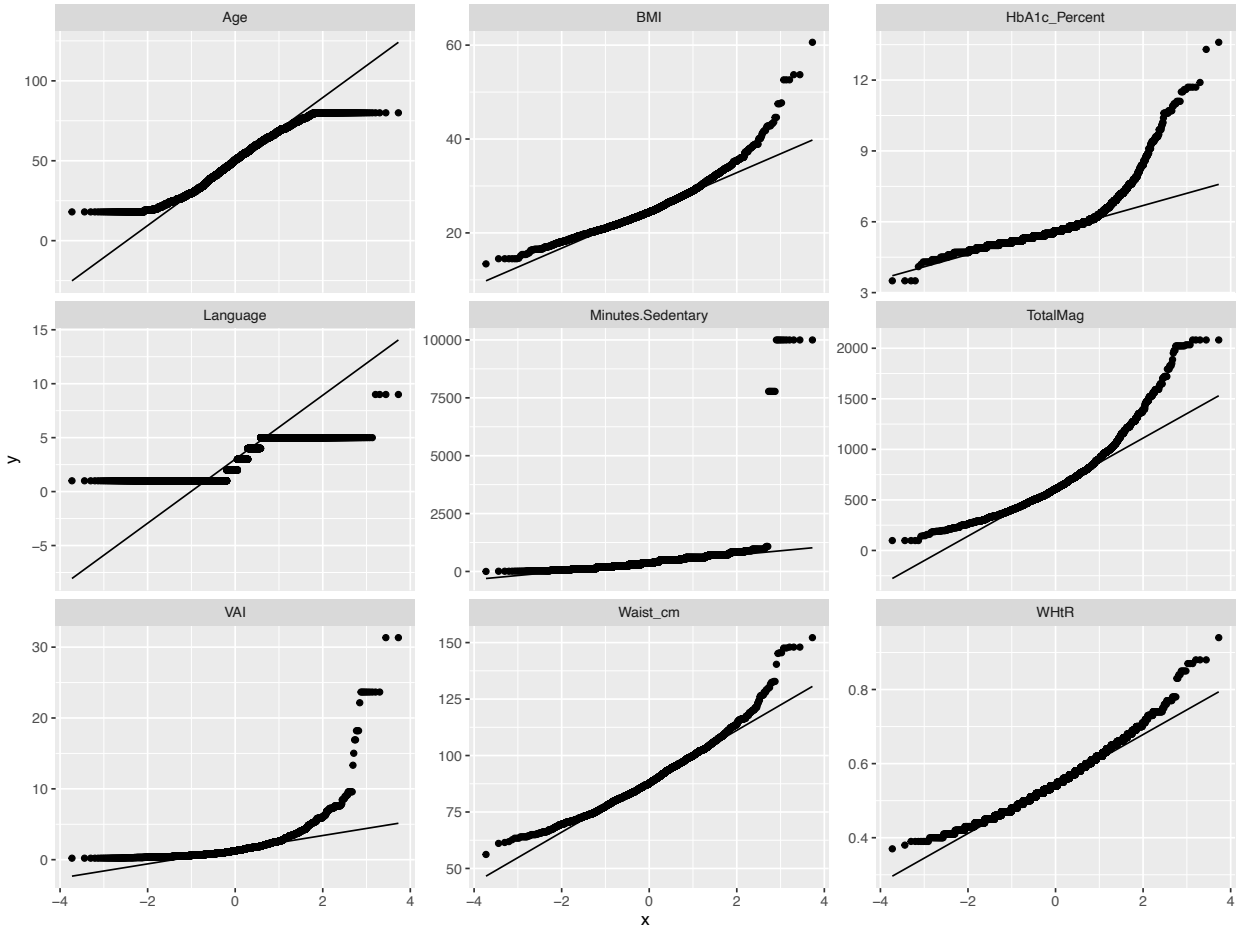
SD: Standard Deviation; HbA1c %: hemoglobin A1c percentage; BMI: body mass index; kg: kilograms; m2: meters squared; cm: centimeters; WHtR: waist-to-height ratio; VAI: visceral adiposity index; mg: milligrams; NHANES: National Health and Nutrition Examination Survey

APPENDIX C: HISTOGRAMS FOR HbA1c PERCENTAGE AND PREDICTOR VARIABLES



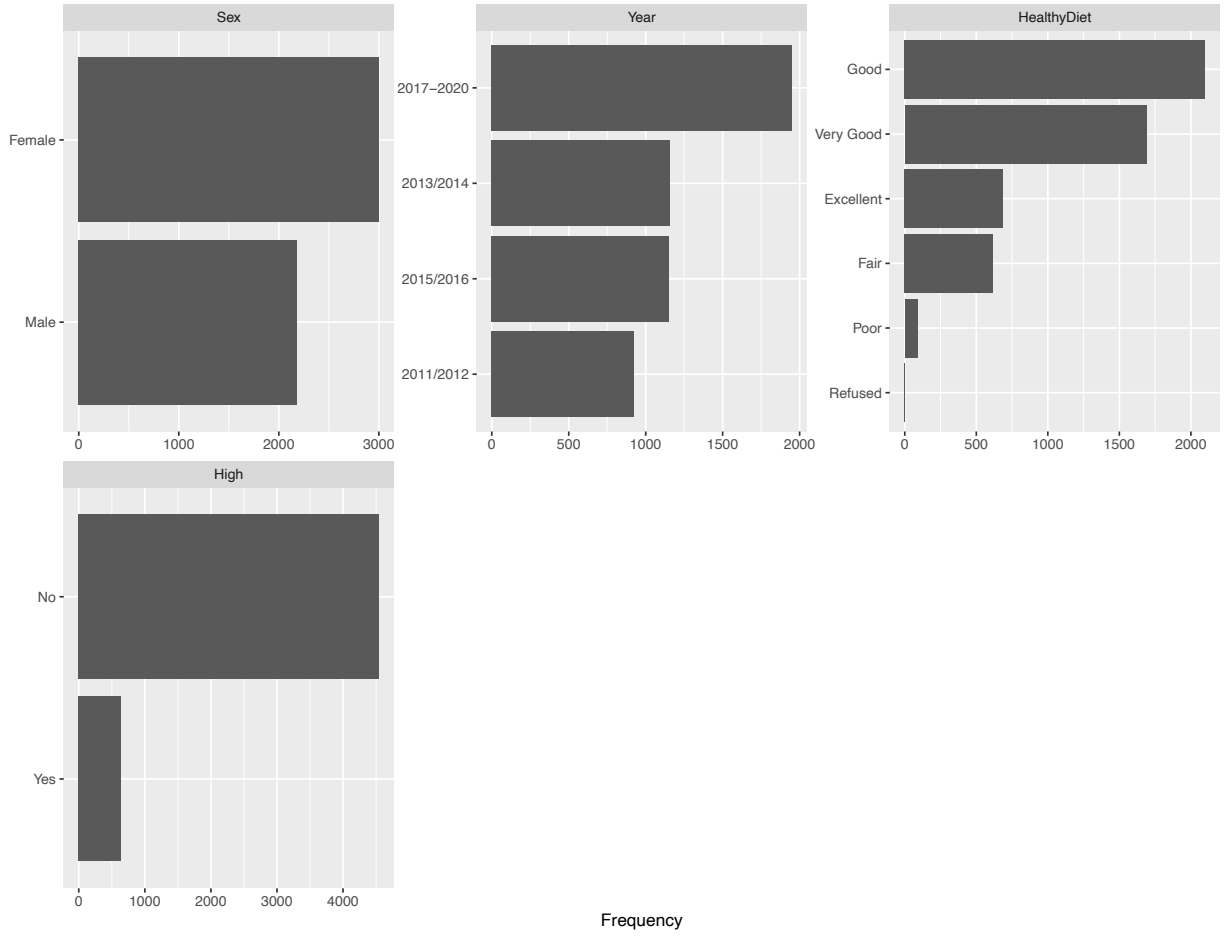
Definitions for Histograms: BMI: body mass index (kg/m2); HbA1c_Percent: Hemoglobin A1c Percentage; Minutes.Sedentary: Sedentary time in minutes; TotalMag: Dietary magnesium intake (mg); VAI: Visceral adiposity index; Waist_cm: Waist circumference (cm); WHtR: Waist-to-height ratio

APPENDIX D: QUANTILE-QUANTILE PLOTS FOR HbA1c PERCENTAGE AND PREDICTOR VARIABLES



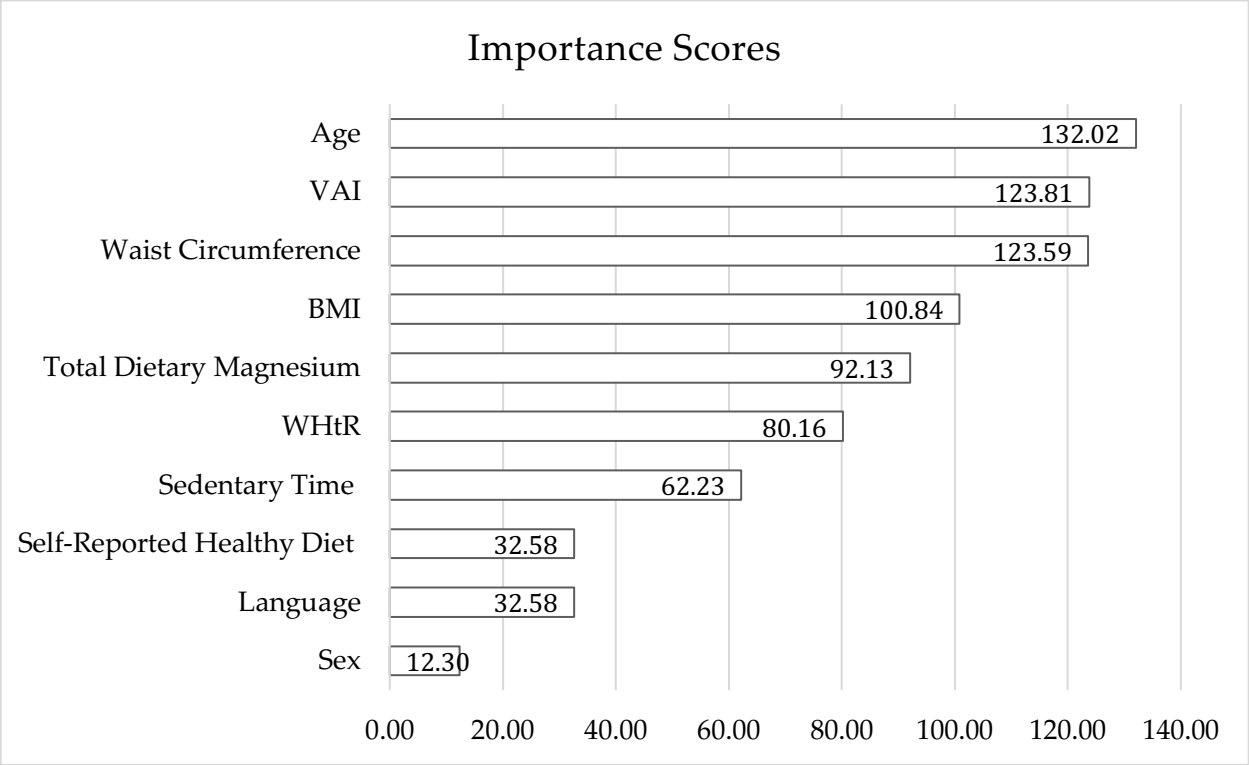
Definitions for Quantile-Quantile (Q-Q) Plots: BMI: body mass index (kg/m^2); HbA1c_Percent: Hemoglobin A1c Percentage; Minutes.Sedentary: Sedentary time in minutes; TotalMag: Dietary magnesium intake (mg); VAI: Visceral adiposity index; Waist_cm: Waist circumference (cm); WHtR: Waist-to-height ratio

APPENDIX E: BAR GRAPHS FOR CATEGORICAL PREDICTOR VARIABLES



Definitions for Bar Graphs: Healthy Diet: Self-reported healthy diet status
"High" is a dichotomous variable indicating: "Yes" for people with an HbA1c ≥ 6.5%, and "No" for people with an HbA1c < 6.5%

APPENDIX F: RANDOM FOREST IMPORTANCE SCORES FOR HbA1c PERCENTAGE AND PREDICTOR VARIABLES



Random forest importance scores indicate the relative importance of predictor variables in a random forest model. Higher importance scores suggest that the predictor variable has a stronger impact on the model's predictions.

Definitions for Random Forest Importance Scores: VAI: Visceral adiposity index; BMI: body mass index (kg/m^2); Total Dietary Magnesium: Total dietary magnesium intake (mg); WHtR: Waist-to-height ratio; Sedentary Time: Sedentary time in minutes; Self-Reported Healthy Diet: Self-reported healthy diet status

APPENDIX G: LINEAR REGRESSION ANALYSES PREDICTING HEMOGLOBIN A1c PERCENTAGE

Predictor	B	Standard Error	t-value	p-value
Intercept	3.31	0.09	35.14	< 0.001
Age (years)	0.01	0.00	26.84	< 0.001
Waist Circumference (cm)	0.01	0.00	15.82	< 0.001
Visceral Adiposity Index	0.04	0.00	6.30	< 0.001
Sedentary Time (minutes)	0.00	0.00	-1.60	0.109
Self-Reported Healthy Diet Status (Excellent)	0.10	0.64	0.16	0.867
Self-Reported Healthy Diet Status (Very Good)	-0.01	0.04	-0.25	0.799
Self-Reported Healthy Diet Status (Good)	0.07	0.04	-1.65	0.091
Self-Reported Healthy Diet Status (Fair)	0.49	0.80	6.17	< 0.001
Self-Reported Healthy Diet Status (Poor)	-0.26	0.19	-1.36	0.171
Self-Reported Healthy Diet Status (Refused to Answer)	-0.89	0.54	-1.65	0.098
Sedentary Time (minutes): Self-Reported Healthy Diet Status (Excellent)	0.00	0.00	0.43	0.661
Sedentary Time (minutes): Self-Reported Healthy Diet Status (Very Good)	0.00	0.00	1.19	0.232
Sedentary Time (minutes): Self-Reported Healthy Diet Status (Good)	0.00	0.00	-0.90	0.367
Sedentary Time (minutes): Self-Reported Healthy Diet Status (Fair)	0.00	0.00	-4.40	< 0.001

Sedentary Time (minutes): Self-Reported Healthy Diet Status (Poor)	0.00	0.00	0.60	0.548
Sedentary Time (minutes): Self-Reported Healthy Diet Status (Refused to Answer)	NA	NA	NA	NA

Model summary: Residual standard error: 0.8012 on 5,170 degrees of freedom; Multiple R-squared: 0.2198; Adjusted R-squared: 0.2179; F-statistic: 112.1 on 13 and 5,170 degrees of freedom; p-value: < 0.001

B: unstandardized regression coefficients; cm: centimeters; NA: Not applicable

APPENDIX H: LOGISTIC REGRESSION ANALYSES PREDICTING HEMOGLOBIN A1c PERCENTAGE ≥ 6.5%

Logistic Regression Analyses Predicting Hemoglobin A1c Percentage ≥ 6.5%

Predictor	Coefficients	Standard Error	z-value	p-value
Intercept	-10.55	0.452	-23.34	< 0.0001
Age (years)	0.049	0.003	15.13	< 0.0001
Body Mass Index (kg/m^2)	-0.065	0.020	-3.19	0.0014
Waist Circumference (cm)	0.079	0.008	9.49	< 0.0001
Visceral Adiposity Index	0.112	0.019	5.68	< 0.0001

Model summary: Null deviance: 3871.2 on 5,183 degrees of freedom; Residual deviance: 3,213 on 5,179 degrees of freedom; Akaike Information Criterion (AIC): 3,223; Number of Fisher Scoring iterations: 6

kg: kilograms; m^2: meters squared; cm: centimeters

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