FACTORS RELATED TO UNDIAGNOSED DIABETES AND PREDIABETES IN ASIAN AMERICANS:
A CROSS SECTIONAL ANALYSIS OF NHANES 2011-2016

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Factors Related to Undiagnosed Diabetes and Prediabetes in Asian Americans:

A cross-sectional analysis of NHANES 2011-2016

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ABSTRACT

OBJECTIVES: Asian Americans, the fastest growing race in the U.S., are disproportionately affected by diabetes (DM), particularly undiagnosed DM (51% of all diabetes cases) and prediabetes. The goal of this study was to examine differences and identify predictors in social determinants of health factors and health-related factors associated with undiagnosed diabetes, diagnosed diabetes, prediabetes, and no diabetes/prediabetes among Asian Americans.

METHODS: Three cycles of National Health and Nutrition Examination Survey (NHANES) from 2011-2016 were analyzed for exploratory and inferential statistics—using the chi square test of independence, linear regression and multinomial logistic regression models—to assess the associations and predictive factors (i.e., Social Determinants of Health, obesity, HbA1c, and sleep) in those with undiagnosed diabetes, diagnosed diabetes, prediabetes, and no diabetes/prediabetes among Asian Americans (n=1,685).

RESULTS: Diabetes estimates—both undiagnosed and diagnosed—were different when stratifying by nativity (U.S.-born vs. foreign-born). Differences in age (p<.001), marital status (p<.001), education(p<.001), acculturation (p=0.010), poverty (p=0.009), regular healthcare provider (p<.001), overweight/obese body mass index (BMI) (p<.001), and sleep duration (p=0.033) were observed. Education was a significant predictor especially when comparing those who attained college degrees or higher to high school graduates; they are 3.3 times more likely to have no diabetes or prediabetes compared to undiagnosed diabetes (p=0.0031) OR: 3.337, (CI: 1.534 to 7.261). In addition, those who had some college or an Associate's degree when compared to high school graduates were 2.5 times more likely to not have diabetes/prediabetes compared to having undiagnosed diabetes (p=0.0453), OR: 2.497 (CI:1.020 to 6.112).

CONCLUSIONS: This study suggests that BMI is an inadequate predictor of diabetes—either diagnosed or undiagnosed—and prediabetes. Nativity, gender, education, regular healthcare provider and sleep duration are potential factors that need to be considered when developing interventions, preventive strategies, and clinical guidelines for Asian Americans.

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Chapter I
INTRODUCTION

BACKGROUND OF THE PROBLEM

Diabetes Statistics: Prevalence, Incidence, Mortality

By 2035, the escalating diabetes epidemic is estimated to affect 592 million adults worldwide,[7,8] a drastic increase compared to a previous 2010 projection estimate of 439 million (9% of the population).[8] The World Health Organization estimates the current global prevalence of diabetes to affect 422 million (8.5%) of adults worldwide. Diabetes incidence, as reported by "high-income countries," is said to be rising 3% annually.[9] A high prevalence of undiagnosed diabetes is estimated to affect 174.8 million (45.8%) of those with diabetes.[10] Of the 1.5 million deaths caused by diabetes, 43% were premature before 70 years of age;[9] it is projected to become the 7th leading cause of death.[11]

In the U.S., diabetes is responsible for 12% of deaths making it the third leading cause of death following heart disease. Those with the condition have an increased risk of death by 90%[12]. According to national estimates by the Centers for Disease Control (CDC), diabetes affects 30.3 million (9.4% of the U.S. population), of which 7.2 million (23.8%) remain undiagnosed.[4,13, 14] Of the 86 million people who have prediabetes—a condition where sugars are elevated but not at diabetes level—88% do not know they have it.[15] Gestational diabetes is estimated to affect 4.6%-9.2% of women and occur in 1-14% of all pregnancies. Although the diabetes-level glucose normalizes after giving birth, it increases the risk of diabetes onset in women 5-10 years later.[16]

An alarming increase in incidence of both Type-1 and Type-2 diabetes mellitus (T2DM) have been detected in youth.[17] Among youth 12-19 years of age, T2DM was prevalent in 43% of diabetes cases, of which 34% was undiagnosed.[18]

Another inconspicuous population that has seen a growing incidence and prevalence of diabetes is Asians. Asia accounts for 60% of diabetes worldwide[19] with the highest prevalence in China estimated to be 25% of the global population.[20] In the U.S., the diabetes prevalence in Asians residing in the U.S. comprised 8.0% of the U.S. population according to a study conducted

by the CDC. However, an analysis of the National Health and Nutrition Examination (NHANES) estimated a higher prevalence in Asian-Americans (20.6%) compared to white (11.3%).[14,21]

Table 1. Estimated Prevalence of Diagnosed Diabetes, Undiagnosed Diabetes, Prediabetes in the U.S., Asia, and Globally[4,5]

	U.S. Total	White	Black	Hispanic/ Latino	Asian-American	Total Global	Asians Global Est.
Total Diabetes	9.4%	9.3%	17.7%	12.1%	8.0%	8.5%	~10-14%
Undiagnosed Diabetes*	12.2	2.0%	4.4%	4.5%	5.7% (51% of total diabetes)	24-62%**	--
Diagnosed Diabetes*	7.2%	7.3%	12.7%	12.1%	10.3%	--	--
Prediabetes	33.9%	--	--	--	--	--	--

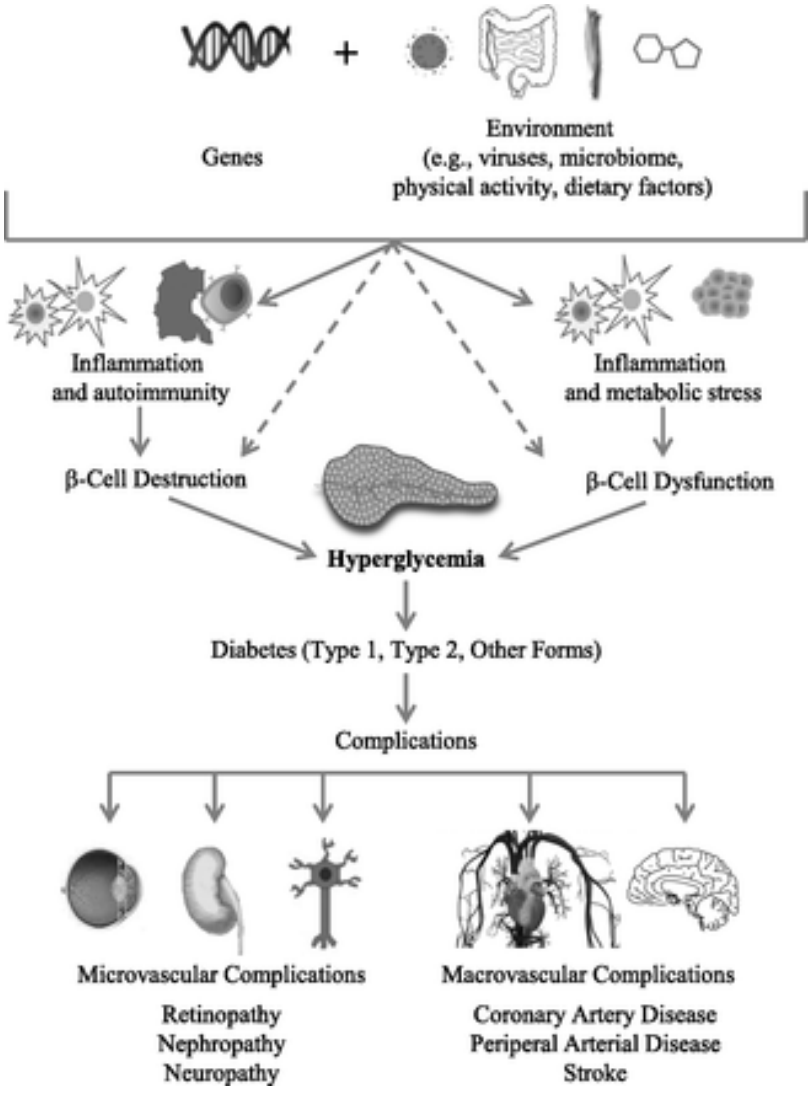
*of total diabetes prevalence
** based on WHO estimate from 7 countries

Pathophysiology of Diabetes

Diabetes is a chronic disease characterized by high glucose (sugars in the blood) due to the failure of effectively regulating levels of glucose. Insulin, which is produced by the pancreas, manages glucose levels in the blood. The onset of diabetes is caused by lack of sufficient insulin production and/or insulin resistance resulting in sugars that cannot be transported to cells needed for energy conversion; the liver continuously produces glucose which remains in the blood at high levels.[22] Several pathophysiological dysfunctions—pancreatic B–cell, pancreatic α-cell, incretin, inflammation, liver, muscle, adipose tissue, kidney, brain, stomach/intestine, and colon—have been identified explaining the mechanism of diabetes onset and its influential factors. Various factors stemming from genetic to environmental have a significant impact on the development of diabetes (Figure 1).[23]

Figure 1. Pathophysiology of Diabetes[1]

American Diabetes Association. Differentiation of Diabetes by Pathophysiology, Natural History, and Prognosis, American Diabetes Association, 2017. Copyright and all rights reserved. Material from this publication has been used with the permission of American Diabetes Association.



Genome-wide association studies (GWAS) have identified multiple mechanisms and traits related to the risk and development of type-2 diabetes. To date, a total of ~140 loci of single nucleotide polymorphisms (SNPs) and ~400 genetic variants have been found to be associated with type-2 diabetes enhanced by inclusion of epigenetic fine-mapping to pinpoint trait loci. [24] [25] Other discoveries include marked differences in the gut microbiota between those with and without type-2 diabetes. Approximately 60,000 genetic markers were found by carefully evaluating the changes in gut bacteria—and its ratios—such as "β-proteus, Bacteroides, Bifidobacteria, Clostridium, Firmicutes, Verrucomicrobium." [26]

There are two types of diabetes: 1) type-1 diabetes mellitus (T1DM), characterized as an autoimmune failure resulting in low or no insulin, is diagnosed during youth and 2) type-2 diabetes mellitus (T2DM) represents ~95% of all diabetes cases and is brought on by insulin resistance leading to issues with glucose metabolism prohibiting the effective use of insulin.

Although type 2 diabetes is typically diagnosed in adulthood, it is increasingly being diagnosed in children and teens.[15] In an adjusted model by Mayer-Davis et al., Asian youth experienced a higher annual increase (8.5%) in diabetes incidence compared to their African American (6.3%), Hispanic/Latino (3.1%), Caucasian (0.6%) counterparts.[17] According to a study by Dabelea et al., youth who are diagnosed with T2DM fared worse than those diagnosed with T1DM developing comorbid conditions such as kidney, eye and nerve diseases with a greater risk of hypertension and arterial stiffness (i.e., risk factors for heart disease). They projected that 75% of teens with T2DM are expected to develop complications within 7.9 years of diabetes onset by age 21.[27] Although T2DM in youth is a relatively new phenomenon, one primary explanation for the rapid and deleterious progression of T2DM in youth is related to beta-cell failure. Initially, the function of the pancreatic beta-cell adjusts to insulin resistance resulting in high glucose in the blood. Over time and through various mechanisms, the beta-cells become damaged impairing insulin secretion. Risk alleles highly associated with a genetic predisposition to T2DM in youth include: SLC30A8, GCK, G6PC2, MTNR1B. In addition, several key genetic loci on chromosomes—ADCY5, CRY2, GLIS3, PROX1, and SLC2A2. However, there is a dearth of studies focusing on genetic variants in youth with the exception of a study on TCF7L2.[28]

Comorbidities, Complications, and Risk Factors

Comorbid conditions such as hypertension, metabolic syndrome, prediabetes, dyslipidemia increase the burden of diabetes resulting in complications that are microvascular (e.g., kidney disease, renal failure, blindness, nerve damage and amputations) or macrovascular (e.g., heart disease and stroke).[15] Acute conditions such as diabetic ketoacidosis and hyperosmolar coma are brought on by high sugars in the blood and can result in death.

Additionally, depression[29] and conditions such as sleep apnea (directionality unknown)[30], and cancers[29,31], non-fatty liver disease[32] are well documented sequelae.[29,33] If left unmanaged during pregnancy, there is risk of congenital abnormalities, stillbirth, and complications to both mother and child.[9]

Obesity and lack of physical activity particularly in obese individuals were associated with increased risk of diabetes.[34] Additional modifiable risk factors include, smoking, alcohol intake, unhealthy eating, sleep duration. [35] [36]

Economic Burden and Quality of Life

In addition to the deleterious health effects of diabetes, the economic burden of diagnosed diabetes is $827 billion in direct costs annually worldwide[9] and $245 billion dollars in health expenditures of which $176 billion (72%) were in direct costs in the U.S.[13] After including those with prediabetes, gestational diabetes, and undiagnosed diabetes, the total estimate exceeded the original 2012 estimate by 32% to a grand total of $322 billion.[37] Of the total, $244 billion (76%) were costs attributed to those diagnosed compared to $33 billion (10%) for those undiagnosed and $44 billion (14%) with prediabetes. On average, annual costs per case were estimated as follows: diabetes ($10,970), prediabetes ($510), gestational diabetes ($5,800), and undiagnosed diabetes ($4,030). Compared to previous 2007 estimates, specific costs related to undiagnosed diabetes and prediabetes increased by 82% and 74%, respectively. This cost burden is expected to grow more than 5% annually due to increased prevalence even when factoring in inflation. When considering the overall economic burden, it is critical to reflect costs associated with undiagnosed diabetes and prediabetes.[37]

Decreased quality of life (QOL) has been associated with increased diabetes-related health expenditures[38] as well as the presence of comorbid conditions.[39] Although a subjective measurement, it reflects disease burden that cannot be explained by existing biomarkers and assessments. QOL metrics are grouped into measures of Physical Component Summary (PCS) and Mental Component Summary (MCS). Compared to the highest quartiles, the lowest quartiles of PCS and MCS were attributed to higher expenditures of $54.6 billion and $14.3 billion, respectively.[38] Determinants related to QOL include socio-economic status (SES), age, and time with diabetes diagnosis.[39]

Asymptomatic and Undiagnosed Diabetes

A study by Venkataraman et al. found that those with undiagnosed diabetes had a low level of awareness which was related to normal health-related quality of life indicators compared to their diagnosed counterparts; the authors theorized that individuals may forego diabetes screening because no specific symptoms of illness or comorbidities have prompted them to seek care thus reducing the chances of physician intervention and being screened for diabetes.[40] Over time, diabetes conditions can become exacerbated in undiagnosed, asymptomatic individuals leading to severe complications and comorbid conditions.[15,41]

A sudden rise in glucose (HbA1c) within a trajectory has been well documented with the association of diabetes onset, typically within 3 to 4 years. Although there was no relationship between a trend in rising BMI with diabetes progression, diabetes was most prevalent amongst obese adults.[42,43]

The prevalence of undiagnosed diabetes continues to rise, with a significant increase in younger people under the age of 30 and those with normal and high cholesterol (non-high density lipoprotein). Although obesity is the primary risk factor for diabetes, body mass index (BMI) and central adiposity—derived from waist circumference—did not affect the rates of being diagnosed with T2DM nor did low SES and education in Asian populations.[44] [45]

Diabetes Disparities, Awareness, and Risk Perception

Vulnerable populations are disproportionately impacted by racial and ethnic disparities with diabetes being more prevalent and having a higher incidence resulting in overall poorer outcomes. It has been well documented that undiagnosed African Americans/Blacks and Hispanics/Latinos have increased diabetes incidence as well as preventable hospitalizations stemming from glucose levels that are extremely high yet with no diabetes diagnosis. [41] [46,47]

According to the 2014 U.S. Census, Asians constitute 20.3 million of the population[48] with a 7% increase from 2012 becoming the fastest growing population.[21] Subpopulations include: Chinese (22%), Indians (19%), Filipinos (19%), Vietnamese (10%), Korean (9%), Japanese (7%), and Other mixed race/ethnicity (14%). The poverty rate for Asians is 12.5% and 10.2% did not have health insurance.[48]

Although fundamental to primary prevention, disparities have been documented in receiving diabetes screenings. Among 49% of individuals with high risk of diabetes, Bullard et al. found that it was minorities and those of lower socioeconomic status (SES) who lacked these detrimental screenings [49]. Findings related to higher SES resulting in an increased likelihood of receiving diabetes screening have been confirmed by Lavielle et al. [50]

Disease risk perception as illustrated by the Health Belief Model in Figure 2, illustrates the interplay of how an individual's risk perception can be affected by psycho social and demographic factors to influence disease prevention efforts.[51] Risk perception is low among asymptomatic populations that are most vulnerable to diabetes.[52] Studies have demonstrated the relationship between disease awareness and behavior modifications for prediabetes and diabetes confirming the Health Belief Model.[53,54] In a study aimed to assess prediabetes awareness, only 11.8% knew they had prediabetes; those individuals aware of their diagnosis were more likely to incorporate lifestyle modifications such as physical activity. [54]

The Health Belief Model

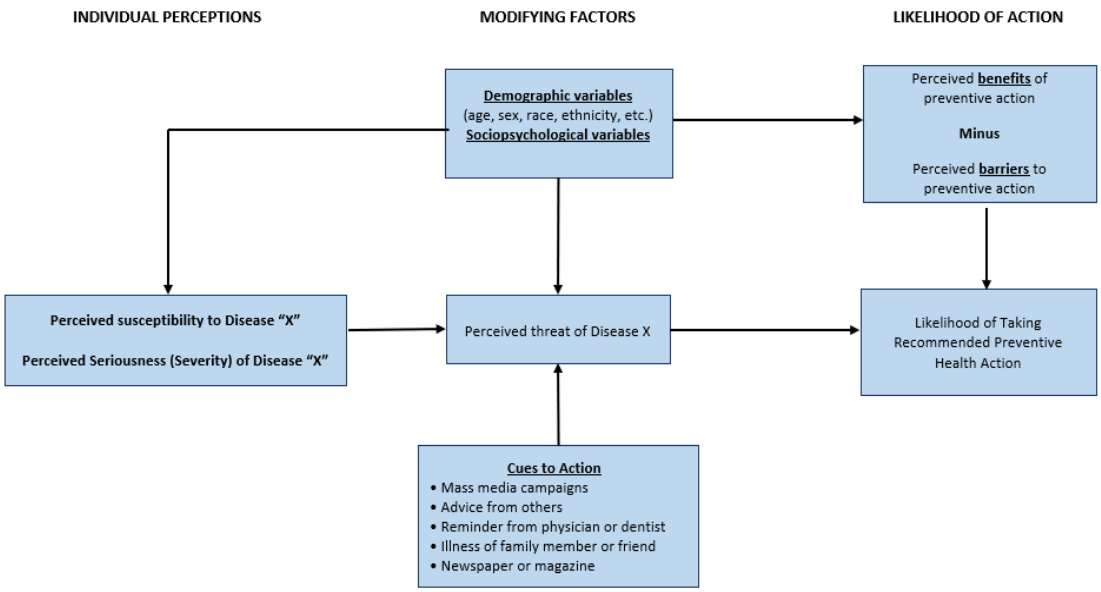


Figure 2. Health Belief Model illustrating the interplay between patient's perceptions and its related factors leading to behavioral changes.[45]

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Public Health—which has traditionally centered on studying epidemiology, disease surveillance, and access to healthcare—has shifted its focus to identifying and addressing social determinants of health. Population health and its outcomes are influenced by various factors (genes and biology, behaviors, medical care access and quality, and social and environmental characteristics) as illustrated in the social determinants of health (SDH) framework. Environmental and social factors are major contributors of health and outcomes compared to just genes and biology (Figure 2).[3]

Social determinants of health (SDH) factors explain the role of key social predictors of diabetes (Figure 3).[5] SDH variables intrinsically associated with diabetes are: income, employment, stress, education, and access to healthy food. One example to illustrate the mechanism of SDH is poverty; it leads to high stress levels, thereby triggering an increase in cortisol levels which then cause high glucose levels. In addition, the impact on diabetes due to poverty can be attenuated by the inability to access healthier foods and other environmental factors.[5]

Population Health: Social Determinants of Health Framework

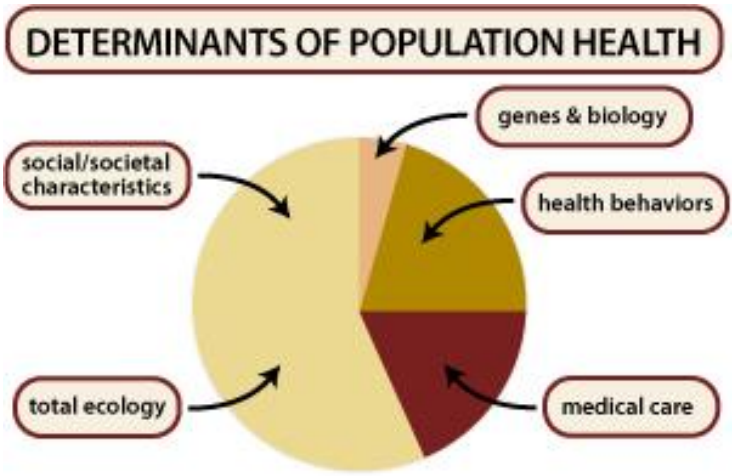


Figure 3. Social Determinants of Health Framework denoting ~25% of population health and outcomes are influenced by health-related behaviors and genes/biology.[3]

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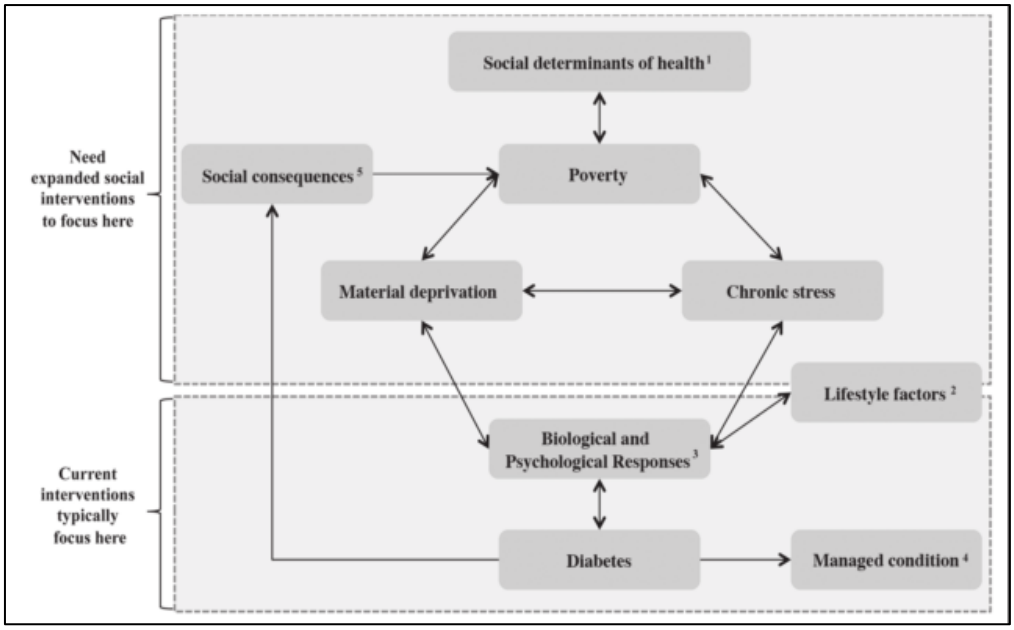


Figure 4. The sociobiologic cycle of diabetes impacted by social determinants of health.[5]

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Due to SDH's notable impact on health and outcomes, the Health and Medicine Division (HMD)—formerly known as the Institute of Medicine (IOM)—proposed guidelines for capturing SDH metrics in EHRs (Appendix A).[6] The Office of Disease Prevention and Health Promotion, utilizes a framework of SDH to set forth robust national objectives to guide efforts promoting health and preventing disease called Healthy People 2020.[55]

Electronic Health Records (EHRs) and Diabetes Surveillance

Electronic Health Records (EHR) utilized in healthcare settings has revolutionized the ability to collect information, report data, manage and coordinate patients. Its adoption was encouraged by the 2009 Health Information Technology for Economic and Clinical Health (HITECH) Act in which ~$19 billion dollars was appropriated as incentive payments to help healthcare providers subsidize their EHR systems. As a result, implementation of EHR is estimated to have reached 75% of hospitals/acute facilities and 78% of U.S. physician practices.[56,57] One caveat was that providers and institutions had to adhere to "meaningful use" guidelines which mandated reporting of key measures.[58] Another mandate within the ACA 2010 includes the collection of data related to race/ ethnicity and language spoken for use in health disparities research.[5]

In addition to enhancing access to charts and supersede paper-based patient charts, EHRs have advanced in technological applications to improve quality of care for patients by increasing adherence to guidelines and prevent medication errors.[59,60] EHR use has been linked with improvements in diabetes care (35.1%) and outcomes (15.2%) compared to practices using paper-based patient charts.[61] Further adding value to EHRs, integration of clinical decision support systems (CDSS) have increased the delivery of HbA1c testing for diabetes prevention.[62] Moreover, patient-level data collected through EHRs have been a key contributor to enhancing research capacity and public health monitoring and surveillance.[63,64]

STATEMENT OF THE PROBLEM

New estimates reveal that 36% of total diabetes cases remain undiagnosed [14] which is considerably higher than the 25% figure reported by the CDC.[15] The prevalence of undiagnosed diabetes was highest in 51%) compared to Caucasian (11.3%), African-American (21.8%), Hispanic/Latino (22.6%).[14] In addition, the Asian population in the U.S. is projected to have the

most rapid growth compared to other racial groups.[21] The impact of the "intergenerational cycle" of diabetes can lead to increased rates of diabetes, its complications, and mortality.[65]

Type 2 diabetes—usually characterized by an adult onset—is now increasing in incidence among youth <20 years of age[17] while accounting for 43% of diabetes cases, 34% of which are undiagnosed.[18] Current guidelines set forth by the American Diabetes Association (ADA) and United States Preventive Services Task Force do not recommend asymptomatic screening for adults under 40 years of age. [35,66] Existing diabetes risk models have varying precision (i.e., comparative validation against another population and "calibration"). Incorporating genetic data did not improve the model which consisted of clinical, social, and demographic variables. Although risk scores claimed to be user-friendly, most were not explicit in terms of specific instructions regarding its use (i.e., when to use and who should use it). Prospective studies incorporating screening scores and interventions were limited demonstrating a need to investigate impact of screening tools and its use among individuals at risk. [67]

Awareness of prediabetes and diabetes is associated with increased uptake of behaviors, namely physical activity and healthy eating.[44] According to a study by Gopalan et al., prediabetes awareness was significantly lower (12%) than national estimates.[54] Furthermore, individuals with undiagnosed diabetes are often labeled as "low risk".[44] Although obesity is a major risk factor to diabetes and prediabetes, BMI is insufficient as an objective measurement of risk particularly in Asians. There is dearth of studies comparing social determinants of health and psycho-social factors in undiagnosed to diagnosed diabetes while assessing for ethnic differences amongst Asians.

Identifying high risk populations, such as those undiagnosed and asymptomatic, through diabetes screening are the first steps to primary prevention. However, disparities have been observed in the receipt of diabetes screenings resulting in under-diagnosis of diabetes. Receipt of preventative screenings has a potential to directly impact an individual's perceived disease risk thereby increasing the likelihood of behavior modification towards prevention.[53]

At the frontlines of patient care, primary care providers are critical to diabetes prevention efforts including opportunistic screening and early intervention.[68] However, available diabetes risk

screening tools are underutilized due to their low validity.[67,69] In addition, these screening tools have not been validated for the Asian population and subgroups residing in the U.S.

RESEARCH HYPOTHESES

Specific aims and objectives of this research is to: 1) assess the prevalence of undiagnosed diabetes and prediabetes among Asian-Americans and by nativity; 2) identify risk factors (i.e., social determinants of health, overweight/obese body-mass index, sleep duration, and depression) and differences in those risk factors related to undiagnosed diabetes and prediabetes compared to diagnosed diabetes in Asians; 3) identify the best model for risk factors associated with undiagnosed diabetes and prediabetes compared to diagnosed diabetes in Asians;

Hypotheses proposed in this research study include:

1) Are specific sociodemographic (i.e., gender or age) or social determinant of health (SDH) factors (i.e., nativity, education, income, insurance status, routine medical provider (proxy for access to healthcare),language spoken (proxy for acculturation), marital status (proxy for social support) associated with undiagnosed diabetes and prediabetes compared to those with diagnosed diabetes or without diabetes/prediabetes amongst Asian Americans?

2) Is nativity status (i.e., foreign born vs. U.S. born) associated with undiagnosed diabetes or prediabetes?

3) Is unhealthy sleep duration (<7 hours or >9 hours) or overweight/obese body mass index (BMI) associated with undiagnosed diabetes or prediabetes compared to those with diagnosed diabetes or without diabetes/prediabetes amongst Asian Americans?

4) Is unhealthy sleep duration (<7 hours or >9 hours) or overweight/obese body mass index (BMI) predictors of undiagnosed diabetes or prediabetes compared to those with diagnosed diabetes or without diabetes/prediabetes amongst Asian Americans?

5) Are there differences in BMI means, sleep duration, or HbA1c means with undiagnosed diabetes or prediabetes compared to those with diagnosed diabetes or without diabetes/prediabetes amongst Asian Americans?

6) Is depression associated with undiagnosed vs. diagnosed diabetes/prediabetes compared to those with diagnosed diabetes or without diabetes/prediabetes amongst Asian Americans?

Research conducted to answer these questions has the potential to modify existing algorithms and models, thereby increasing the validity to identify asymptomatic, high-risk patients that have undiagnosed diabetes and prediabetes. In turn, this would provide strategic prevention and promotion efforts in a timely manner to vulnerable populations. It also has tremendous implications on population management in public health, development of policy, guidelines, provider and patient education, and reimbursement.

NEED FOR THE STUDY

Undiagnosed diabetes in asymptomatic populations can be exacerbated resulting in diabetes-related complications, comorbidities, and poor outcomes. Those with diagnosed diabetes are estimated to have healthcare expenses that 2.3 times greater than those without diabetes.[70] In addition to indirect health expenditures—associated with productivity loss, absenteeism, disability[70]—quality of life is reduced and physical health impacted.[39] However, earlier diagnosis is documented to reduce overall economic burden by ameliorating health, outcomes and quality of life.[15,71]

Early detection and intervention of asymptomatic populations are critical to prevent, improve outcomes, and reduce complications of diabetes.[35,72] With the rapidly increasing population growth of Asians in the U.S., diabetes prevention and control efforts will need to be individualized to address factors related to the overwhelmingly high rates of undiagnosed diabetes in Asian Americans.[21] Although obesity is a primary risk factor associated with diabetes, it lacks precision in identifying asymptomatic cases by using body mass index (BMI) measures that do not accurately predict risk amongst Asians.[73,74,75,2]

Evidence of racial and ethnic disparities exist relating to the control and management of glucose, blood pressure, and lipids/cholesterol. However, the role of social determinants of health in addition to racial and ethnic factors need to be examined to address the underlying causes of diabetes while tailoring interventions appropriately. Specifically, environmental factors (i.e., healthy food availability and food insecurity) and psycho-social factors (i.e., depression, stress, social support, self-efficacy) are linked to improved quality of life, diabetes management and outcomes.[76]

Research is currently needed to examine the relationship between social determinants of health factors (i.e., social determinants of health: food insecurity, education, access to healthcare, work status, social support in addition to sleep and mental health) to undiagnosed diabetes in Asians compared to those diagnosed or with no diabetes as well as compared to other racial groups. For example, a study by Chu et al., indicated a relationship between lack of social support with uncontrolled hypertension.[77] There is a lack of evidence examining the relationship of SDH to diabetes prevention, care coordination, healthcare quality, and outcomes.[76]

In order to achieve health equity, it is imperative to understand diabetes disparities and to assess potential differences in risk factors across ethnic subgroups and modify existing algorithms appropriately.[73,78] An example of modifying risk factor parameters is the reduction of the overweight BMI cutoff from $\geq$25 to $\geq$23 for Asian Americans; this modification increased the sensitivity of the ADA diabetes risk screening tool by 23.9% (from 50.2% to 74.1%).[73] Furthermore, diabetes risk screening and detection models and algorithms are primarily studied in Asian populations within Asia rather than Asians residing in the U.S.[79-82] There are ramifications to studying the Asian population and undiagnosed diabetes without factoring in the impact of immigration and acculturation variables.

In addition, inconspicuous groups such as those who are not obese or of younger age will need to be studied. Presently, obesity and >45 years of age are highlighted as key risk factors of diabetes. [83, 84] Findings from this proposed research will contribute to building an evidence base for improved detection of individuals with undiagnosed diabetes and towards diabetes prevention.

Healthcare providers increasingly utilize electronic health records (EHR) and Clinical Decision Support Systems integrated within. Its effectiveness in behavior change, decreased incidence of disease and morbidity, and cost reduction has been documented in a systematic review of 9 randomized controlled trials (RCT) of CDSS [85] Additional meta-analyses have documented key features of CDSS (i.e., alerts and reminders) to be linked to clinicians' adherence to guidelines and increased receipt of preventive screenings.[86] Providers need to be equipped with an understanding of mechanisms related to influences of SDH, incorporating SDH data into decision making, and document SDH for epidemiologic inquiries through public health surveillance.[76]

Public and population health agencies rely on prevention efforts of primary care providers alongside informatics systems that collect data for the purposes of surveillance towards disease prevention and control. Information is then used for epidemiologic inquiries and translated to effective population-level control and management through appropriate interventions. However, without factoring in SDH and establishing them as routinely collected metrics in EHR, the information garnered in support of public health initiatives will fall behind in addressing potential factors closely related to undiagnosed diabetes.

In addition, only when a patient is aware of the disease and their risk, will it prompt changes in behaviors in support of prevention. Furthermore, awareness raises health literacy, in turn, promoting increased self-efficacy and the ability to have improved communication between patients and their health providers.[53 77]

By studying the underlying factors related to undiagnosed diabetes in Asian-Americans, it has the potential for improved diabetes detection and early intervention to reduce progression to diabetes. Newly identified risk factors can promote awareness in patients, providers, and the public health community at large to appropriate individualized resources, revise existing screening guidelines, customize EHR/CDSS interfaces, create data repositories. Diabetes prevention in this vulnerable, asymptomatic population has implications on intergenerational impact and increasing disease burden.[87,88]

Chapter II

REVIEW OF RELATED LITERATURE

Diabetes Risk Factors and Comorbidities in Asians

Among Asians with diabetes, key factors associated with increased risk for developing diabetes include family history, genetics/epigenetics, increasing age, overweight/obese BMI, adiposity (waist circumference), decreased muscle mass, environmental changes brought on by urban/western lifestyle, lack of physical activity and healthy eating, smoking status, and alcohol intake. In addition, psycho-social variables included the inability to access healthcare and lack of health insurance, disrupted sleep, stress, and cultural stigma.[89]

According to a meta-analysis, 78% of cardiovascular deaths in 5 Asian populations were related to diabetes, hypercholesteremia, and hypertension.[90] Hypertensive patients with diabetes or prediabetes level glucose and hypertension represented 56% of the rural population in China. Of those with diabetes, 50% recently received their diagnosis denoting an increase in incidence in rural populations. The risk factors that were strongly associated included: older age, BMI (overweight or obese), high cholesterol, blood pressure, high triglycerides and low HDL. Interestingly, low income was associated with a decreased risk of diabetes in hypertensive patients in addition to other factors such as smoking and a high dietary summary score.[91]

Sleep disturbances, lack of sleep, and too much sleep are associated with metabolic syndrome[36] and insulin resistance[92] irrespective of obesity.

In a study by Zhang et al., the prevalence of depression among patients with type-2 diabetes mellitus (T2DM) was 18.3% in Hong Kong. The PHQ-9 instrument, which is used in the U.S., was used as the primary depression screener. This study highlighted the need for depression screening related to issues of glucose metabolism and control, currently underdiagnosed.[93]

Undiagnosed Diabetes in Asians and Social Determinants of Health

People of Pacific origin residing in New Zealand had the highest prevalence (6.4%) of undiagnosed diabetes compared with European descent (1.5%) and Maori (2.2%).[94]

In South Asian men, differences in fasting glucose levels were observed at 3% higher compared to their European counterparts. Low “Cardiorespiratory fitness” a contributor to insulin resistance measure known as V˙O2max was highly associated to high fasting glucose compared to high adiposity (29%), minimal physical activity (29%); the effects of the three variables explained 63% of the differences in glucose between South Asian and European men.[95] In another South Asian study by Hanif et al., participants were screened using a survey and the oral glucose tolerance test (OGTT); they had high rates of undiagnosed diabetes (20%), glucose dysregulation (48.7%), and impaired glucose tolerance (28.7%). Strongest predictors of diabetes and impaired glucose tolerance were family history and hypertension or heart disease.[82] When comparing diabetes risk factors among South Asians, Chinese, and Indians, Indians had greater risk of mortality. Furthermore, undiagnosed diabetes with impaired fasting glucose or impaired glucose tolerance were significantly associated with this increased risk.[80]

Increased albuminuria is typically associated with renal failure in diabetics.[96] Undiagnosed T2DM patients can be characterized by the presence of microalbuminuria. In a study by Kanakamani et al.,25.5% of patients with T2DM had microalbuminuria. Although median length of diabetes diagnosis was 5 years, those patients diagnosed <1 year had levels of microalbuminuria (24.7%) and macroproteinuria (6.2%) indicating the presence of diabetes that went undiagnosed. The study population was younger mean of 52 years of age and had relatively low BMI mean of 26. Interestingly, waist circumference had an inverse association with macroproteinuria but a positive association with microalbuminuria. Risk factors included HbA1c, calcium channel blocker (CCB) medication use, and retinopathy. [97]

Ethnic differences also exist in different dwelling environments between suburban and rural areas. In Cambodia, 67% of diabetes was undiagnosed prior to the national survey. In addition, differences in prevalence of hypertension and obesity were observed.[98] In the U.S., the Diabetes Prevention Program (DPP) research group found that amongst racial groups diagnosed with pre-diabetes, BMI was not a predictive factor in Asian Americans as compared to other race/ethnic groups. However, age and fasting glucose measurement was among the predictors of identifying those at high risk.[99]

Currently, there is no consensus as to whether BMI is an appropriate predictor of diabetes risk.[100] In a study by Bancks et al., undiagnosed T2DM-level HbA1c was found to increase mortality risk specifically in Chinese participants in Singapore studied who had a mean age of 62 with no comorbidities (i.e., CVD, family history of cancer). Baseline data of participants showed an association of diabetes level HbA1c ($\geq$6.5%) and factors of BMI, hypertension (self report), and age; however, education was inversely associated with HbA1c.[100] In a study of Koreans, diabetes prevalence was higher in those with undiagnosed and uncontrolled hypertension (HTN) irrespective of gender; however high BMI was associated in men with uncontrolled HTN. Women who had higher education were 5 times more likely to have controlled hypertension than those of low educational attainment.[77]

Differences in visceral body fat composition in relation to BMI has been documented highlighting differences in the body phenotypes of Whites and South Asians (Figure 4).[2]

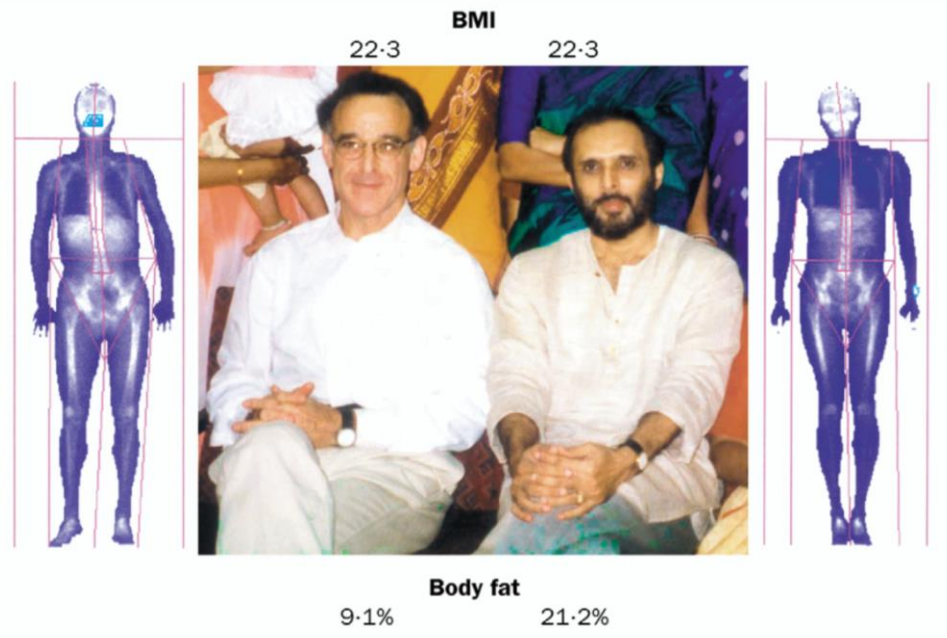


Figure 5. The "Y-Y paradox" explaining the differences in visceral body fat visualized by a x-ray image.[2]

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With regards to obese BMI as a risk factor for diabetes onset, a study by Chiu et al., found an interesting trend in the BMI trajectory of Asians. Prior to > 6 years of diabetes onset, study subjects exhibited a steady increase in weight immediately followed by a sharp decrease in BMI measures. For those with a BMI≥ 24 and males, a more rapid increase in weight was observed in their trajectories. This denotes the need for a focus on BMI trajectories to identify risk patterns to screen asymptomatic patients for diabetes. [101]

Diabetes Screening Guidelines: ADA and USPTF

The United States Preventive Task Force (USPTF) and the American Diabetes Association (ADA)—leading authorities in guideline development—have set forth guidance to primary care providers for opportunistic screening in high-risk diabetes populations that are asymptomatic. A comparison of the risk factors can be found in Table 2. Furthermore, social determinants of health and psycho-social factors are not reflected in either guideline.[35,66]

Table 2. adapted from Clinical Guidelines for Screening Asymptomatic Patients for Diabetes from the American Diabetes Association and United States Preventive Services Task Force.[25,57]

ADA Diabetes Guidelines 2016	USPSTF Diabetes Risk Guidelines 2015
Age ≥45	Age 40-70
Physical inactivity	Physical inactivity
First-degree relative with diabetes	Family history of diabetes
High-risk race/ethnicity	High-risk race/ethnicity: African Americans, American Indians or Alaskan Natives, Asian Americans, Hispanics or Latinos, or Native Hawaiians or Pacific Islanders)
Women with history of GDM or who delivered a baby >9 lb or were or polycystic ovarian syndrome (PCOS)	Women with history of gestational diabetes or PCOS
HDL-C <35mg/dL + TG >250 mg/dL	Hyperlipidemia (high cholesterol & high triglycerides)
Hypertension (≥140/90 mm Hg or on therapy)	Hypertension
A1C ≥5.7%, IGT, or IFG on previous testing	
Severe obesity	• Overweight and obesity • a high percentage of abdominal fat
History of CVD	NOTE: high risk races should be screened at a younger age or at a lower body mass index. Clinicians should consider screening earlier in persons with 1 or more of these characteristics.
--	Smoking

Several screening tools for diabetes risk assessment are based on the ADA or USPTF recommended variables and parameters; however, their validity and performance in identifying diabetes risk is varied.[102] In a study by Bullard et al., the ADA and USPTF criteria were applied to a sample from the National Health and Nutrition Examination Surveys (NHANES). Results showed that the ADA criteria had sensitivity, specificity, and positive predictive values of (88.8%, 13.5%, 47.7%) compared to using the USPTF (31%, 82.1%, 58.4%). Although the ADA criteria produced high sensitivity or few false negatives, the specificity was low indicating potential for false positives that do not need to be screened while the positive predictive value was poor indicating that probability of a positive test actually having a disease was inaccurate.

The USPTF had low sensitivity indicated more false negatives and high specificity, yet poor positive predictive value; in turn, the USPTF criteria's ability to screen for diabetes fails to properly identify asymptomatic patients. Furthermore, the age criteria set forth by both guidelines were ineffective in screening individuals who were high risk and <45 years of age.[49]

Another study by Kiefer et al. found that among those eligible (76%) based on the ADA guidelines, only 46.2% self reported to receipt of a diabetes screening. Of those who did not meet the ADA criteria, 0.4% had diabetes and 10.2% had prediabetes.[103] Due to the poor performance of existing diabetes screening tools, primary care providers lack confidence thereby underutilizing these tools.[67] Two objective measurements exist for the screening and diagnosis of diabetes: the glycated hemoglobin (HbA1c) biomarker test and oral glucose tolerance test (OGTT). The HbA1c is the gold standard and preferred as it is cost-effective in administration compared to the OGTT which requires a 2-hour, repeated measurement and patients to be fasting[35,104] Although the HbA1c test can be easily administered during routine patient visits, it is underutilized by primary care providers.

Sohler et al., found that only 21% of high-risk patients were screened using the HbA1c and 79% remaining undiagnosed. Among the patients with undiagnosed diabetes, 9% and 45% had HbA1c levels that were in diabetes and prediabetes ranges, respectively. Lowering the patient's age to <40 can also lead to detecting undiagnosed diabetes and prediabetes in asymptomatic patients.[105] Screening for prediabetes in tandem with lifestyle modifications has been

documented for its cost-effectiveness and ability to thwart the progression of diabetes even when compared to pharmaceutical intervention (metformin).[106,107]

Research groups have attempted to improve the precision of diabetes risk scores to identify undiagnosed diabetes. Although most have demonstrated moderate to good AUC, very little is known about their performance in different populations, particularly among Asian Americans.

The "Diabetes Risk Calculator" developed by Heikes et al., was based on an algorithm validated to appropriately classify the probability of belonging to one of the three groups identified using the NHANES dataset. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and ROC was highest for the undiagnosed diabetes group at 88%, 75%, 14%, 99.3%, and 0.85, respectively.[108]

Bang et al., developed an algorithm to identify undiagnosed diabetes using NHANES and validated it by comparing to cohorts from two separate studies. Although it had a good AUC of 0.83, it had only moderate performance in regards to sensitivity, specificity, PPV, and NPV, of 79%, 67%, 10%, 99%, and 0.83 respectively.[109]

To date, the only study evaluating a risk score for undiagnosed diabetes and prediabetes while examining gender and racial differences was conducted by Zhang et al. They applied the Finnish Diabetes Risk Score to a cross section of NHANES. However, the racial groups examined were Caucasian/White, African American/black,Hispanic/Latinos and did not include Asians. It had a good AUC of 0.75 for identifying undiagnosed diabetes in the general population, and similar AUC for the racial groups ranging from 0.67 to 0.72.[110]

Models and Algorithms Tailored for Asians

In Korea, it is estimated that 30% of the population does not know that they have diabetes. Using KHANES, a national survey, a model was developed and validated to become a screener for Koreans. Statistically significant variables associated with undiagnosed diabetes were: age, family history, hypertension, waist circumference, smoking and alcohol use. In detecting diabetes in 47% of high risk adults, the sensitivity, specificity and positive predictive values were 81%, 54%, and 6%, respectively; the positive likelihood ratio of 1.8 had a good AUC of 0.73. Given the

low specificity and PPV, it still showed better validation for Koreans compared to other U.S. and European-developed screening models.[79]

In Japan, Uemura et al. developed an algorithm (alternating decision tree) to identify patterns of variables linked to T2DM and uncovered the relationship of the inflammatory biomarker " high-sensitivity C-reactive protein" and increased prevalence of T2DM regardless of confounders (e.g., family history and BMI).[111]

Models and Algorithms for Undiagnosed Diabetes in Asians

Prediction models

Very few models have been developed to identify and predict undiagnosed diabetes in Asian populations. In addition, there are currently no models specifically developed for Asian Americans or studying the differences across Asian-American ethnic subgroups. Risk factors used in the models did not include any psycho social or social determinants of health (SDH) variables. However, only the study conducted by Zhang et al. introduced inadequate or excess sleep as a variable to their model.[110]

Zhang et al. developed a prediction model for T2DM with a large study population (n=12,285) comprised of residents of rural China. Once data was randomized into two groups to derive and validate the model, comparisons were made to the Finnish Diabetes Risk Score. However, it only had a slight improvement in AUC (0.66 compared to 0.64) but considered poor accuracy.[112]

A study by Ahn et al. validated the KRS diabetes risk scores using laboratory values in a South Korean population (n=3,029). The AUC was highest for the model using laboratory values (0.838) compared to using the KRS risk score alone. However, in the U.S., there are documented studies regarding the underutilization of screening using HbA1c which would impact the precision of this approach.[105] The sensitivity, specificity and AUC were less precise when the risk score was used alone to identify undiagnosed diabetes (81%, 58%, and 0.754) compared to the risk score related to predicting "future diabetes" (74%, 54%, 0.696).[113]

A study by Pongchaiyakul created a model using Bayesian analytic techniques from a dataset representing a Thai study population (n=4314). Bootstrapping methods were used to validate in

multiple groups of 150; however, they did not compare it to other populations. However, using only 3 risk factors (BMI, age, and systolic blood pressure) demonstrated a good AUC of 0.75.[81]

Screening Tools

A study by Dugee et al. developed a risk score for Mongolians with a study sample (n=1,018). The found that an existing risk score could be improved by incorporating exercise, healthy food intake, and hypertensive medication as factors which increased the final AUC to 0.77.[114]

The Madras Diabetes Research Foundation, spearheaded by Bhadoria et al., conducted a study of the Asian/Indian population (n=911). The diabetes risk score had a moderately good AUC of 0.736, but poor sensitivity (60.4%), decent specificity (70.7%), and low Youden index (0.31) indicating the lack of effectiveness of the risk score and the suboptimal threshold value for the cutoff of the score for undiagnosed diabetes.[115]

Li et al., aimed to identify undiagnosed “isolated post-load hyperglycemia (IPH)” in a Chinese population (n=1175). IPH is more sensitive in identifying diabetes compared to fasting plasma glucose (FPG) which is done traditionally instead of the lengthy oral glucose tolerance test (OGTT). Although the AUC was very good amongst all 4 risk scores developed with a range of 0.89 to 0.93, it still requires the collection of FPG, IPH, and HbA1c biomarkers—all of which are underutilized.[116]

Ku et al. studied the Finnish Diabetes Risk Score (FINDRISC) and its modifications tailored to Filipinos residing in the Philippines. Compared to the unaltered FINDRISC (AUC 0.74), the two modified versions of the risk score had similar AUC of 0.74 and 0.75.[117]

Chapter III
METHODS

INTRODUCTION

This is a cross-sectional study using secondary data from a publicly available dataset known as National Health and Nutrition Examination Survey (NHANES). The study aims to identify characteristics, predictors, and relationships of the factors associated with undiagnosed diabetes and prediabetes compared to their diagnosed counterparts in the Asian-American population.

Specific aims include: 1) identifying the associations and relationship of factors (i.e., social determinants of health, depression, and sleep) related to undiagnosed vs. diagnosed diabetes and prediabetes in Asians; 2) developing a predictive model of key factors related to undiagnosed diabetes and prediabetes.

The NHANES dataset including resources (i.e., codebooks, manuals, and analytic guides), methods (i.e., sampling and survey design), and data structure (i.e., components and constructs are described. In addition, procedures related to preparing the dataset includes: 1) abridged codebook development (with new or recoded variables), 2) identification of measures and covariates, 3) recoding of variables, 4) segmentation through subsetting, 5) defining diabetes status as an outcome, and 6) handling of missing data. Lastly, statistical methods for data analysis including descriptive and inferential statistics as well as multi-nomial logistic regression modelling will be discussed in this chapter.

STUDY POPULATION

The inclusion criteria for the study population consists of Asian-American adults, ages 20 years and older sampled through 3 cycles of the National Health and Nutrition Examination Survey (NHANES) from 2011-2016. Since 2011, Asian-Americans along with other racial groups (i.e. non-hispanic black and Hispanics) have been oversampled through the NHANES survey. Of 29,902 total population examined through three cycles of the NHANES (2011-2012, 2013-2014, 2015-2016), Asians comprised 14.83% (n=3,398). [118]

Sub-population analyses will include stratifying by diabetes status (dependent variable) into 4 categories: 1) undiagnosed diabetes, 2) diagnosed diabetes, 3) prediabetes, and 3) no diabetes or prediabetes as illustrated in Figure 5 below.

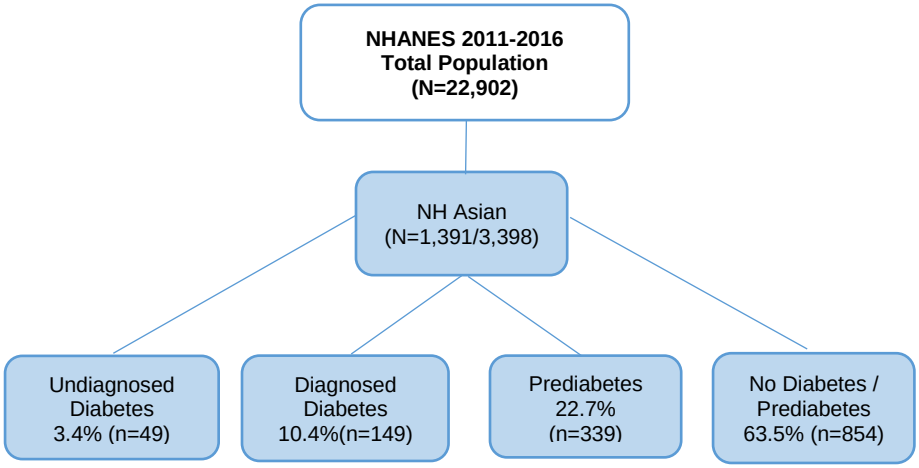


Figure 6. Flowchart of NHANES 2011-2016 study population

The study sample was limited to those with no missing data on glycated hemoglobin (HbA1c) which is one of two primary measures of glucose used to define and diagnose diabetes. Due to large missing data for the oral glucose tolerance test (OGTT) or plasma fasting glucose, this measure will not be used to define diabetes.

Women who self-reported that they were pregnant at the time of the assessment were excluded from the study sample. This is an important note as pregnant women may have gestational diabetes or have increased body mass index and be incorrectly classified.

DATASET: NHANES 2011-2016 (3 cycles)

The National Health and Nutrition Examination Survey (NHANES) is conducted annually and published in bi-annual cycles by the National Center for Health Statistics (NCHS) which is part of the Centers for Disease Control (CDC). It is comprised of individual and household interview questions and physical, lab, and dental assessments of ~5,000 individuals (non-institutionalized) in efforts to ascertain population health status and nutritional intake of a complex, stratified sample representing U.S. residents. The self-reported interview questions represent domains including: demographics, socioeconomic (SES), social determinants of health (SDH), disease

(i.e., infectious and chronic), behavior (i.e., nutrition, sleep, physical activity) and health. In addition, participants are asked for consent to maintain lab test samples in a biobank for future research. Although primarily used to determine disease prevalence and risk factors, the information garnered is available for use by epidemiological, health services researchers and institutions to "promote health and prevent diseases".[119]

Survey Methodology, Design, Sampling

NHANES utilizes a 4-stage, cluster sampling process that involves: 1) county-level grouping by characteristics (15 groups), 2) segmentation of counties (20-24 groups), 3) identification of households (~30), and 4) random sample of household members. Trained program personnel obtain consent, conduct interview questionnaires and physical/dental exams, and collect lab specimens on site in the NHANES "mobile examination center".

In order to ensure adequate sample size and improve the representation of underrepresented populations, groups such as Asians are over-sampled. This oversampling, provides reliable estimates of Asians with respect to age and gender categories. However, ethnic subgroups are not targeted in this oversampling which results in sample sizes too small for subgroup analyses. In addition, ethnicity data are not publicly available and requires special permission for on-site analyses at the CDC.[120]

Structure of NHANES Data

Data Elements

There are five elements to the data collected: 1) demographics, 2) dietary (i.e., nutritional intake), 3) physical and dental examination, 4) laboratory tests, and 5) interview questionnaire. The "demographics" data files consist of: 1) variables for its design (i.e., information on weights, stratifications, units of samples) and 2) demographic variables (i.e., race, age, sex, etc.). The "dietary" data files consist of nutritional intake of food, beverages, and additional supplements. The "examination" data files consist of data garnered from physical and dental exams (i.e., blood pressure, height and weight, etc.). The "laboratory" data files encompasses test results from the collection of specimens (i.e., urine, blood, skin, hair, environmental). Lastly, the self-reported responses to interview questions are enclosed in the "questionnaire" data files.[121]

Data Files, Code Books, Analytic Guidelines

Each data file contains variables relevant to each component within the aforementioned five elements. A manual for each section is available with details regarding a description of the variable and measure; inclusion criteria of sample; protocol for data collection, documentation, and processing; notes for data analysis; codebook with variable name, SAS label, text, sample targets (i.e., gender and age), and value descriptions for each code. In addition, a variable for the weights for the examination and interview are contained in the data file. The data codebook can be examined for the "interview and examination status" frequencies of participants who completed the interview only or both the interview and the physical, dental and lab assessments.

Furthermore, NHANES provides analytic guidelines. The analytic guidelines provides rationale for:1) publishing data in 2-year cycles (i.e., reduce variance estimates and improve anonymity of participants), 2) over-sampling and weighting to increase estimate's precision for under-represented, minority race populations. As of 2011, participants that identified as being non-black and non-hispanic Asians were categorized as "Asian" race. Missing data due to non-response and its impact (i.e., bias) was analyzed in the total population, Asians, elderly (age $\geq$60), and children (age 1-5). Appropriate weighting indicated that non-response bias was resolved after adjustments.[122]

PROCEDURES

Data File Preparation

After reviewing the documentation, technical notes, analytic guidelines, tutorial, the NHANES 2011-2012, 2013-2014, 2015-2016 data files and accompanying manuals were downloaded from the "Questionnaires, Datasets, and Related Documentation" tab located at the NHANES website:https://wwwn.cdc.gov/nchs/nhanes/Default.aspx. A "TEMP" folder was created where selected original datasets from 3 cycles pertaining to each of the variables of interest will be exported and stored. The new SAS datafiles created from the merged, exported data files is stored in a new "DATA" folder using the "PROC Copy in and out" statements. Using the "drop" and "keep" statements, the variables pertinent to the study will be kept in order to eliminate unnecessary data elements. The individual datasets that housed the variables from each cycle

were downloaded, merged, and appended for further data analysis. (See SAS code included in Appendix).

Code Book Preparation

Upon reviewing the NHANES data manuals, a code book will be created using Microsoft Excel to enumerate the variables included in the study's data analyses including new variables that were defined using existing variables. It will include descriptions of the data variables, codes used, any re-coding (i.e., dummy variables for dichotomization) or calculations of continuous variables (i.e., BMI, age, HbA1c). The NHANES survey instruments and codebook were evaluated to identify key variables that would serve as plausible factors for undiagnosed diabetes compared to diagnosed diabetes or no diabetes.

Dataset subsetting and Weight-adjustment

Per NHANES analytic guidelines, data segmentation and subsetting is discouraged. Rather, subpopulation analyses of the NHANES dataset can be performed using the "DOMAIN" function in SAS to parse out observations related to the characteristics of the subpopulation of interest. A dichotomous (dummy) variable "includeASIAN" was created where "1" indicated that the subpopulation met the inclusion criteria defined as: 1) Asian race, 2) age $\geq$20 years, 3) exclusion of pregnant women, 4) complete data on all variables to be explored.

The 6-year weight variable was created by combining the 2-year weights from each of the three cycles and dividing by 3 to adjust for the 6 years included in the three, 2-year cycles. The variables "masked variance pseudo-PSU" and "masked variance pseudo-stratum" from the demographics datasets will be used to analyze the precision accurately in the estimation procedures.

Missing Data and Outliers

During the data cleaning step, all variables with a response labeled " refused" or " don't know" will be recoded as missing values using a "*". The spread across variables with >10% of missing data were checked. Moreover, complete case analysis method was used by deleting cases for which there are any missing variables of interest in addition to adjustment of weights will be

considered to handle the missing data. In addition, outliers were checked using univariate analysis for continuous variables (i.e., age, BMI, HbA1c).

Diabetes and Prediabetes Definition

Glycated Hemoglobin (HbA1c) is a biomarker—collected through a venipuncture blood draw—that represents an average of glucose levels over the course of the past two or three monthaf period. Diabetes is diagnosed based on the levels serving as cutoffs as shown in Figure 6. A level of ≥ 5.7% to < 6.5% is considered to be prediabetes while an A1c ≥6.5% is at diabetes level.

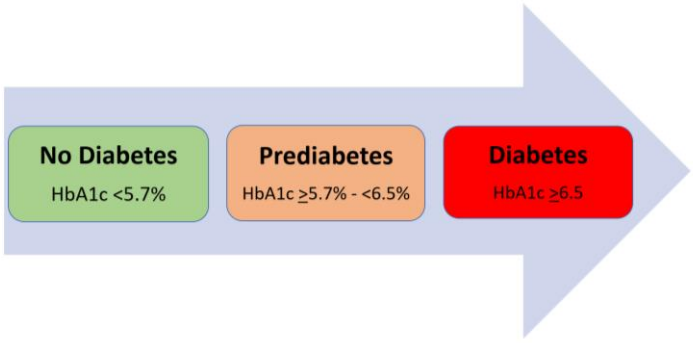


Figure 7. HbA1c cutoffs for diabetes levels.[25]

Furthermore, undiagnosed diabetes was determined by answering "no" to the following question on the NHANES diabetes questionnaire: "{Other than during pregnancy, {have you/has SP}/{Have you/Has SP}} ever been told by a doctor or health professional that {you have/{he/she/SP}(has} diabetes or sugar diabetes?". The data for this variable is located in the Diabetes (DIQ_H.xpt) data file.

NHANES Measures: Variable Selection

Covariates to be considered are based on constructs related to: 1) demographics, 2) social determinants of health (SDH), 3) depression, and 4) sleep duration. In addition, variables were chosen based on their availability across all 3 cycles.

Demographic Characteristics:

- Gender
- Age was used both as a continuous variable and re-coded into 3 categories: 1) 20-39, 2) 40-59, 3) 60+

Biomarkers, Physiological Assessments, Sleep:

- Glycated Hemoglobin A1C (HbA1c) was used as both continuous and re-coded into 3 levels: 1) normal, 2) prediabetes, and 3) diabetes.
- Body Mass Index (BMI) was used as both continuous and re-coded into 2 categories using Asian BMI cutoff ≥23: overweight/obese and normal.)
- Sleep duration (in hours) by self-report was used as both continuous and re-coded into 3 levels: 1) low=<7 hours, 2) normal=7-9 hours, and 3) high=>9 hours. The categories of sleep length of time (hours) is defined by the Sleep Foundation.

Social Determinants of Health Variables

- Language spoken (measure for acculturation) was classified into 3 categories: 1) only speaks or mostly speaks a language other than English, 2) speak both languages equally, 3) only speaks or mostly speaks English.
- Nativity was classified into 2 categories: U.S.-born or Foreign-born
- Education was classified into 4 categories: 1) less than high school, 2) high school graduate, 3) some college or Associates degree, 4) college graduate or higher education
- Marital status (proxy for social support) was classified into 2 categories: 1) married or living with partner, 2) divorced or single.
- Income-to-poverty ratio was classified into 5 categories: 1) <1.0 (<100% poverty threshold), 2) 1.1-1.4 (110-140% poverty threshold), 3) 1.5-1.9 (150%-190% poverty threshold), 4)2.0-3.0 (200%-300% poverty threshold), 5) >3.0 (>300% poverty threshold). Another variable was created to dichotomize the <100% vs. >100% poverty threshold. For reference, Medicaid eligibility is for anyone <138% poverty threshold.
- Health Insurance (proxy for healthcare access) was classified into 2 categories: 1) insured or 2) uninsured.
- Routine place to go for healthcare (proxy for healthcare access) was classified into 2 categories: 1) has routine place to go for healthcare or 2) does not have routine place to go for healthcare.

***Mental Health**

- depression (using PHQ-9 measure): consists of 4 severity levels including: 1) minimal (score=5-9), 2) minor depression (score=10-14),3) major depression, moderately severe (score=15-19) and major depression, severe (≥20) [123]

  *Although it was explored in the preliminary analysis, it was excluded from the final data analysis.

SAS 9.4

All data analyses were performed using SAS 9.4 software developed by SAS Institute Inc. in Cary, NC.

Institutional Review Board (IRB): (https://orra.rutgers.edu/humansubject)

Rutgers University's Office of Research Regulatory Affairs considers research on publicly available data as non-human research (NHR). An IRB application was submitted to the HealthSci IRB Newark through eIRB and approved for exemption: IRB#Pro20170001940. (See Appendix).

DATA ANALYSIS

The aforementioned measures were explored to determine its prevalence and the relationship of social determinants of health, depression, and sleep variables comparing these in undiagnosed and diagnosed diabetes and prediabetes subgroups. Models were weight-adjusted based on the variable with the lowest weight per NHANES guidelines.

Descriptive Statistics: Frequencies and Means

Data frequencies (i.e., counts and percentages) of each variable were generated prior to analysis to evaluate the distribution and outliers. For continuous variables (i.e., age, HbA1c, BMI, sleep duration), means and plots were generated with the confidence interval (CI), standard error (SE) and standard deviation (SD).[124] For categorical variables, "PROC SURVEYFREQ" was used to generate hypothesis tests for one-way and two-way tables while adjusting the variance estimates with respect to the complex survey design. The "DOMAIN" statement within the procedure was used in order to provide sub-population analyses of the sample meeting the study's inclusion/exclusion criteria.

Inferential Statistics: Chi Square

The Chi Square Test of Independence will be employed to test the association and strength of significant relationships between two categorical/nominal variables (i.e., between diabetes status and SDH, depression, sleep). This will produce a contingency table to quantify the differences in observed from expected counts while being mindful of deviations based on variations due to sampling and/or chance establishing concrete evidence for the alternative hypothesis. The Chi Square equation is listed below:

$X^2 = \Sigma [(ObC—ExC)^2 / ExC]$ where ObC= observed count at level r of variable 1 and level 3 of variable 2 and ExC = expected count at level r of variable 1 and level 3 of variable 2.

NHANES analytic guidelines recommends the SAS "proc surveyfreq * CHISQ" using an adjusted F-statistic. This adjusts the degrees of freedom (df) by subtracting the strata from the "primary sampling units (PSU)". The Rao-Scott square statistic was used as a conservative measure based on the NHANES analytic guidelines. It is based on the Pearson X^2 statistic but appropriately adjusts for the weighted frequencies. An F-value is also generated in the output to be used to determine if a null hypothesis that the proportion each response of the X2 is equal. [115]

Hypotheses for Chi Square tests include the following:

- ***H*0 (null hypothesis):** In the study population, diabetes status (4-level categorical variable) and one of the SDH, depression, overweight/obesity, sleep variables (categorical variable) are independent with no relationship between them.
- ***Ha* (alternative hypothesis):** In the study population, diabetes status (4-level categorical variable) and one of SDH, depression, overweight/obese BMI sleep variables (categorical variable) are dependent; thus there is a relationship between them.

Linear Regression

Linear regression models were used to assess the linear relationship and associations between a continuous, outcome/ dependent variable (i.e., age, BMI, and sleep duration) to a nominal or ordinal, independent variable (i.e., diabetes status: undiagnosed diabetes, diagnosed diabetes, prediabetes, normal as well as gender, nativity, marital status, education, language spoken, poverty, health insurance, routine healthcare provider, sleep levels, and obesity.

The equation of a simple linear regression model is stated below:

$$Y=\beta_0+\beta_1X_1+\varepsilon$$ [114]

The X_1 represents the predictor/independent variable and Y outcome/dependent variable (continuous). The intercept is denoted by β_0 whereas β_1 represents the slope (change in Y for each unit change of X). Lastly, the ε represents the difference—based on the linear line—in relation to when Y is plotted against X.

Upon conducting a univariate analyses of each independent variable, all significant variables were used in a Multiple Linear Regression model. Multiple Linear Regression models were used to evaluate potential confounders or covariates that can impact both the outcome/dependent variable and other predictor/independent variables. The formula of a multiple linear regression model which is stated below:

$$yi=\beta_0+\beta_1x_1,\ \beta_2x_2+\ldots+\beta_nX_n+\varepsilon$$ [114]

In order to contrast the difference in means between pairwise comparisons of the dependent/outcome variable (i.e., diabetes status categories: undiagnosed diabetes, diagnosed diabetes, prediabetes, normal), the "PROC SURVEYREG" statement paired with the "LS MEANS" function to test for statistically significant mean differences in continuous variables (i.e., age, BMI and sleep duration).

Multinomial Logistic Regression

Multinomial (otherwise known as polytomous) logistic regression allows for the dependent variable to be nominal/categorical with multiple categories as opposed to a binary variable used in binary logistic regression models. Variables of significance will be included in a multinomial logistic regression model to identify significant predictors of the nominal response variable, 4-category diabetes status variable (i.e., diagnosed diabetes, undiagnosed diabetes, prediabetes, no diabetes or prediabetes). The multinomial logistic regression model to predict the odds of having any of the diabetes status categories (dependent/categorical variable) in relation to demographic, SDH, depression level, and sleep level (independent variables). To avoid collinearity—when predictor variables are highly correlated and results in unreliable regression

coefficient estimates—among independent/predictor variables, potential confounding variables will be introduced into the model one at a time.

The first model introduced two demographic variables as independent/predictor variables in relation to the 4-category diabetes status (dependent) variable. Independent variables were initially entered in groups: 1) social determinants of health and clinical (i.e., BMI dummy variable and sleep levels). Unadjusted models were initially developed.

To adjust for confounders, a separate adjusted model without demographics (i.e., age, gender) was tested. then a separate model that was adjusted for age and gender. Lastly, the final model included the statistically significant variables.

Adjustments using variables "SDMVSTRA" for the strata and "SDMVPSU" for cluster—located in the demographics data file—relates to how participants were sampled for the survey's design.[115] Next, the 6-year weight variable created was applied with the "DOMAIN" statement in the modelling procedure. The model's dependent variable will be the diabetes status (event=odds of undiagnosed diabetes code). Lastly, calculation of confidence limits around the parameters and variance adjustments (none) will be included. NHANES recommends using the SAS procedure "PROC SURVEYLOGISTIC", "PROC SURVEYMEANS' rather than "PROC logistic" due to the complexity of the survey data. The "PROC SURVEYLOGISTIC" procedure lacks the ability to use stepwise selection or restrict the output to statistically significant predictors and their ranking. Instead, it uses the Taylor Series Linearization (TSL) as the default to factor in the complex design of the NHANES sample (i.e., clustering, stratification, weighting). The variances from each stratum are computed and then combined. [115]

Chapter IV
RESULTS

INTRODUCTION

Variables of interest that were available across all 3 cycles of NHANES 2011-2016 included: demographics (i.e., gender, age, marital status), social determinants (i.e., acculturation, nativity, education, income-to-poverty ratio, healthcare provider and health insurance status), clinical biomarkers (i.e., body mass index and glycated hemoglobin), and depression. The sleep dataset was unavailable at the time of the preliminary analyses; however, it became available for the final analysis in addition to demographic, social determinants of health and depression variables which were studied in relation to undiagnosed diabetes and prediabetes status. A complete case analysis was performed to eliminate cases with missing data on any of the variables explored. Lastly, all percentages reflect the recommended weights applied.

Data analyses performed include descriptive statistics, means and totals analysis, chi square test of independence, multiple linear regression of continuous variables (i.e., age, HbA1c, BMI, and sleep duration) regressed on the 4-level diabetes response (outcome) variable (i.e., diagnosed diabetes, undiagnosed diabetes, prediabetes, and no diabetes or prediabetes, and multinomial logistic regression with the 4-level response.

PRELIMINARY FINDINGS

STUDY SAMPLE: INCLUSION/EXCLUSION CRITERIA

Data on depression and marital status are collected only on a subset of the population who are 18+ years of age. In addition, educational attainment is structured differently for those 20+ years of age compared to those who are <20 years old; therefore, the study sample was limited to those meeting the following inclusion criteria: 1) not pregnant at the time of survey (self-report), 2) age 20 years and older, 3) non-Hispanic Asian race, and 4) complete data on all variables studied. The study sample for the preliminary analysis that met the inclusion criteria included (n=1,391) non-hispanic Asian participants (Asians) representing a weighted frequency of

8,641,037 of the Asian population in the U.S. Of the 1,391 Asians in the sample, 15% (207/1391) identified as being U.S.-born and 85% (1,184/1,391) as foreign-born (Table 1).

TABLE 3. Weighted sociodemographic characteristics of study population by nativity, NHANES 2011-2016

Characteristic	**Asians (U.S.-born)** (n=207) (15%)	**Asians (Foreign-born)** (n=1,184) (85%)
AGE CATEGORY (YEARS)	**Mean**=36.25 / **SE**=1.59 CI (33.05 to 39.46)	**Mean**=45.94 / **SE**=0.9414 CI (44.04 to 47.83)
20-39	10.4% (137/1391)	33.3% (427/1391)
40-59	3.0% (41/1391)	32.1% (457/1391)
60+	1.8% (29/1391)	19.4% (300/1391)
GENDER		
Male	7.3% (108/1391)	41.0%(599/1391)
Female	7.8% (99/1391)	43.9% (585/1391)
EDUCATION		
<High School	0.2% (3/1391)	12.5% (183/1391)
High School grad	1.3% (17/1391)	9.9% (149/1391)
Some College or AAS	4.9% (65/1391)	15.2% (219/1391)
College grad or above	8.8% (122/1391)	47.2% (633/1391)
MARITAL STATUS		
Married or Living with partner	6.6% (91/1391)	62.0% (865/1391)
Single, Divorced, Widowed	8.5% (116/1391)	22.9%(319/1391)

DESCRIPTIVE STATISTICS

Demographics: Population Characteristics

The overall mean age for Asians was 44.47, SE=0.84 (42.79 to 46.16). When stratified by nativity, the mean age for U.S.-born Asians was 36.25, SE=1.59 (33.05 to 39.46) significantly younger (p=0.003) than foreign-born Asians was 45.94 SE=0.9414 (44.04 to 47.83) . See table 1.

Of total Asians (n=1,391), gender was fairly evenly distributed with males and females comprising 50.8% (707/1391) and 49.2% (684/1391), respectively. Even after stratifying by nativity, the gender distribution remained comparable with 52.2% (108/207) U.S.-born males, 47.8% (99/207) females, 50.6%(599/1184) foreign-born males, and 49.4%(585/1184) females.

The majority of total Asians 68.7% were married or living with a partner; however, when stratifying by nativity, it was mostly foreign-born Asians who were married or living with a partner 73.1%(865/1184) compared to U.S.-born Asians 44.0% (91/207).

Educational attainment of “some college or associate’s degree” and “college graduate or above” was 74.7% (1039/1391) overall. When stratifying by nativity, U.S.-born had higher percentage of educational attainment at 90.3% (187/207) compared to those who were foreign-born 72.0% (852/1184).

Social Determinants of Health

Language spoken is a proxy for acculturation. Of total Asians, 54.2% (754/1391) either “only spoke a language other than English” or “spoke more of the non-English language”, 8.0% (111/1391) spoke both English and another language equally well, and 37.8% (526/1391) spoke “only spoke English” or “spoke more English”. When stratifying the sample by nativity, it was mostly those who were foreign-born 62.0% (734/1184) that either “only spoke a language other than English” or “spoke more of the non-English language” compared to U.S.-born Asians 9.7% (20/207).

Of total Asians, the majority were insured 84.1% (1170/1391) and 15.9% (221/1391) were uninsured. This distribution was consistent when stratifying by nativity with 84.5% (175/207) of U.S.-born and 84.0% (995/1184) of foreign-born being insured.

A majority of total Asians 80.4% (1119/1391) reported having a routine place to go for healthcare while 19.6% (272/1391) did not. When stratifying by nativity, U.S.-born had a higher percentage of not having a routine place to go for healthcare at 27.5% (57/207) compared to those who are foreign-born 18.2% (215/1184).

Of total Asians,14.3% (209/1391) had <1.0 income-to-poverty ratio which is equivalent to living below the 100% poverty threshold as defined by the Census.[125] When stratifying by nativity, both foreign-born and U.S.-born had 15.0% of people within each category living below the 100% poverty threshold.

TABLE 4. Weighted social determinants of health characteristics of study population, NHANES 2011-2016

Characteristic	Asians (U.S.-born) (n=207) (15%)	Asians (Foreign-born) (n=1,184) (85%)
ACCULTURATION		
Non-English language (only or more)	1.4% (20/1391)	52.0% (734/1391)
Both English and non-English (equally)	0.3% (5/1391)	7.4% (106/1391)
English (only or more)	13.4% (182/1391)	25.5%(344/1391)
HEALTH INSURANCE		
Yes, insured	12.8% (175/1391)	72.6% (995/1391)
No, uninsured	2.3% (32/1391)	12.3% (189/1391)
REGULAR HEALTH PROVIDER		
Yes	10.7% (150/1391)	69.3% (969/1391)
No	4.4% (57/1391)	15.6% (215/1391)
POVERTY		
<100%	2.3% (31/1391)	12.0% (178/1391)
≥100%	12.8% (176/1391)	72.9% (1006/1391)

Overweight/Obesity

Using the recommended Asian body mass index (BMI) cutoff of ≥ 23[35] for overweight/obesity, 64.4% (900/1391) of total Asians were considered overweight or obese, 54.7% (768/1391) of whom were foreign-born. Even when stratifying by nativity, the distribution of overweight/obese individuals remained comparable at 64.9% (768/1184) among foreign-born and 63.8% (132/207) among U.S.-born. Means analysis of BMI showed very little difference between U.S. born $\bar{x}$=25.15, SE=0.4171 (CI: 24.31 to 25.99) and foreign-born $\bar{x}$=24.75, SE=0.1540 (CI: 24.44 to 25.06) (Table 4). There was a marked difference in BMI means when comparing total Asians $\bar{x}$=24.81, SE=0.1457 (CI:24.52 to 25.10) to all other races $\bar{x}$=27.04, SE=0.1024, (CI:26.84 to 27.25) (Table 5).

TABLE 5. Weighted overweight/obesity and clinical characteristics of study population, NHANES 2011-2016

CHARACTERISTIC	Asians (U.S.-born) (n=207) (15%)	Asians (Foreign-born) (n=1,184) (85%)
	Mean BMI=25.15 SE=0.4171 95% CI =24.31 to 25.99	**Mean BMI=24.75 SE=0.1540 95% CI =24.44 to 25.06**
OVERWEIGHT/OBESE (Asian BMI criteria ≥ 23)		
Yes	9.7% (132/1391)	54.7% (768/1391)
No	5.4% (75/1391)	30.2% (416/1391)
GLYCOHEMOGLOBIN: HbA1C (%)		
	Mean HbA1c=5.43 SE=0.0295 95% CI=5.37 to 5.49	**Mean HbA1c=5.74 SE=0.0425 95% CI=5.66 to 5.83**
Diabetes level	0.6% (8 /1391)	9.2% (137/1391)
Prediabetes level	2.4% (36/1391)	23.6% (349/1391)
Normal	12.1% (163/1391)	52.0% (698/1391)
DIABETES STATUS		
Undiagnosed Diabetes	0.2% (2/1391)	3.2% (47/1391)
Diagnosed Diabetes	0.9% (12/1391)	9.5% (137/1391)
Prediabetes	2% (30/1391)	20.7% (309/1391)
Normal	12.1% (163/1391)	51.4% (691/1391)
DEPRESSION		
None/Minimal (<5)	12.2% (167/1391)	71.6 % (1003/1391)
Mild (5-9)	2.4% (32/1391)	10.7% (145/1391)
Moderate (10-14)	0.5% (8/1391)	2.1%(28/1391)
Moderately Severe (15-19)	0% (0/1391)	0.2% (3/1391)
Severe (≥20)	0% (0/1391)	0.3% (5/1391)

Glycohemoglobin: HbA1C (%) and Diabetes Status

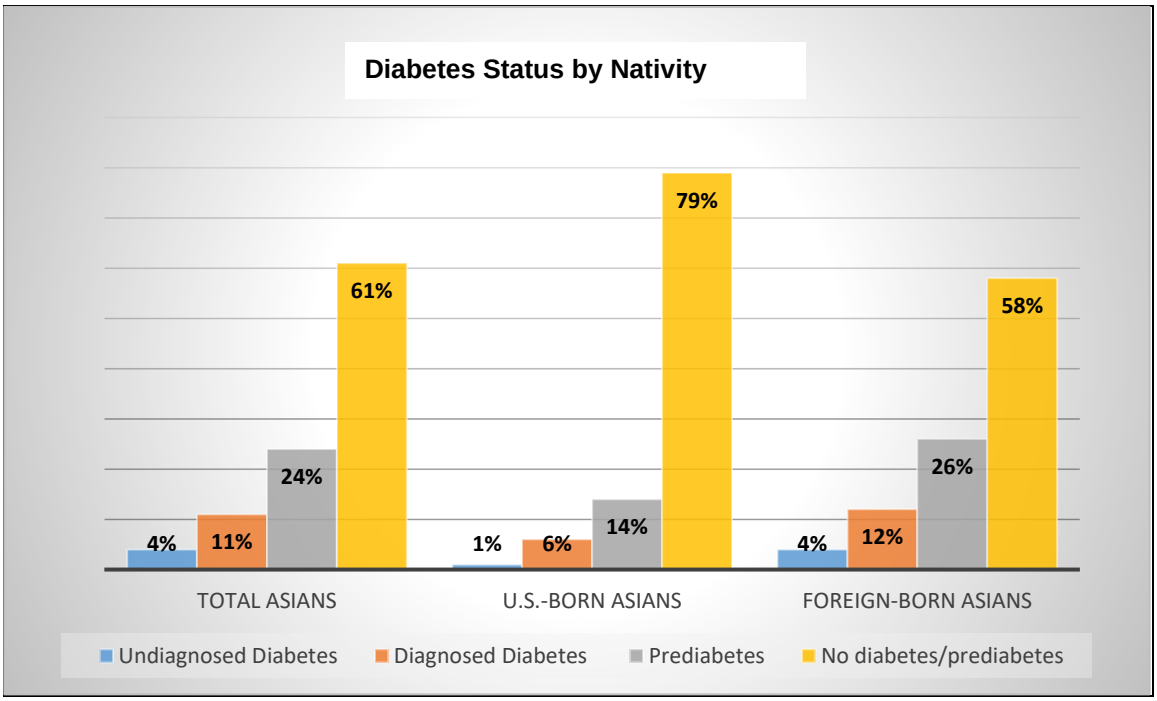
Prior to applying the diabetes status definition, HbA1c means analysis of total Asians to other race showed that Asians had a higher HbA1c $\bar{x}$=5.69, SE=0.0362 (CI:5.62 to 5.77) compared to other races $\bar{x}$=5.59, SE=0.0136 (CI:5.57 to 5.62) (Table 6). HbA1c means analysis of Asians by nativity showed that foreign-born Asians had a higher HbA1c $\bar{x}$=5.74, SE=0.0425 (CI:5.66 to 5.83) compared to U.S.-born Asians $\bar{x}$=5.43, SE=0.0295 (CI:5.37 to 5.49) (Table 7).

Of total Asians, 9.8% (145/1391) have diabetes-level HbA1c, 26.0% (385/1391) have prediabetes-level HbA1c, and 64.1% (861/1391) have normal HbA1c. When stratifying by nativity, foreign-born have higher percentage of diabetes-level HbA1c 11.6% (137/1184) compared to

U.S.-born Asians 3.9% (8/207). In addition, foreign-born Asians also have a higher percentage of prediabetes-level HbA1c 29.5% (349/1184) compared to U.S.-born Asians17.4% (36/207)(Table3).

After applying the diabetes status definition to categorize undiagnosed diabetes, diagnosed diabetes, prediabetes and no diabetes/prediabetes, the results showed differences between foreign-born and U.S.-born Asians. Of total Asians, 24.4% had prediabetes and 14.3% (198/1391) had diabetes of which 24.7% (49/198) were undiagnosed. When stratifying by nativity, foreign-born Asians had 26.1% (309/1184) had prediabetes and 15.5% (184/1184) had diabetes of which 25.5% (47/184) was undiagnosed. Of U.S.-born Asians, 14.5% (30/207) had prediabetes and 6.7%(14/207) had diabetes of which 14.3% (2/14) were undiagnosed (Figure 7).

Figure 8. Diabetes Status by Nativity (%)



CHI SQUARE TEST OF INDEPENDENCE

There was a statistically significant association to diabetes status—whether being diagnosed, undiagnosed, having prediabetes or having no diabetes/prediabetes—and age ($p<0.001$), nativity ($p<0.001$), educational attainment ($p<0.001$) and language spoken (proxy for acculturation) ($p<0.0364$). However, the following variables were not found to have a statistically significant association to diabetes status at any level: BMI ($p=0.082$), gender ($p=0.425$), marital status ($p=0.405$), poverty ($p=0.037$), health insurance ($p=0.1013$), regular health provider ($p=0.1013$) The alpha for the p-value was set at 0.05.

Depression

Of total Asians, the vast majority 96.9% (1347/1391) had minimal or mild depression, very few had moderate depression 2.6% (36/1391). There were no marked differences when stratifying by nativity. This is significantly less than the estimated depression prevalence of Asian Americans which is between 4.5% and 11.3%. [126]

FINAL DATA ANALYSIS

STUDY SAMPLE: INCLUSION/EXCLUSION CRITERIA

Data on HbA1c, sleep, and marital status are collected only on a subset of the population who are 18+ years of age. In addition, educational attainment is structured differently for those 20+ years of age compared to those who are <20 years old; therefore, the study sample was limited to those meeting the following inclusion criteria: 1) not pregnant at the time of survey (self-report), 2) age 20 years and older, 3) non-Hispanic Asian race, and 4) complete data on all variables studied. The study sample in the final analysis that met the inclusion criteria included (n=1,685) non-hispanic Asian participants (Asians) representing a weighted frequency of 10,445,882 of the Asian population in the U.S. Of the 1,685 Asians in the sample, 13.2% (222/1,685) identified as being U.S.-born and 86.8% (1,463/1685) as foreign-born (Table 7).

Sleep duration (hours) data became available on March 2018; it was incorporated into the final analysis. Due to the low prevalence of depression, the depression variable was removed resulting in an additional sample of 294 to the 1,391 previously reported in the preliminary analysis. Of the total NHANES population (n=29,902), the inclusion/exclusion criteria were applied resulting in the final study sample of (n=1,685).

STUDY SAMPLE: INCLUSION/EXCLUSION CRITERIA

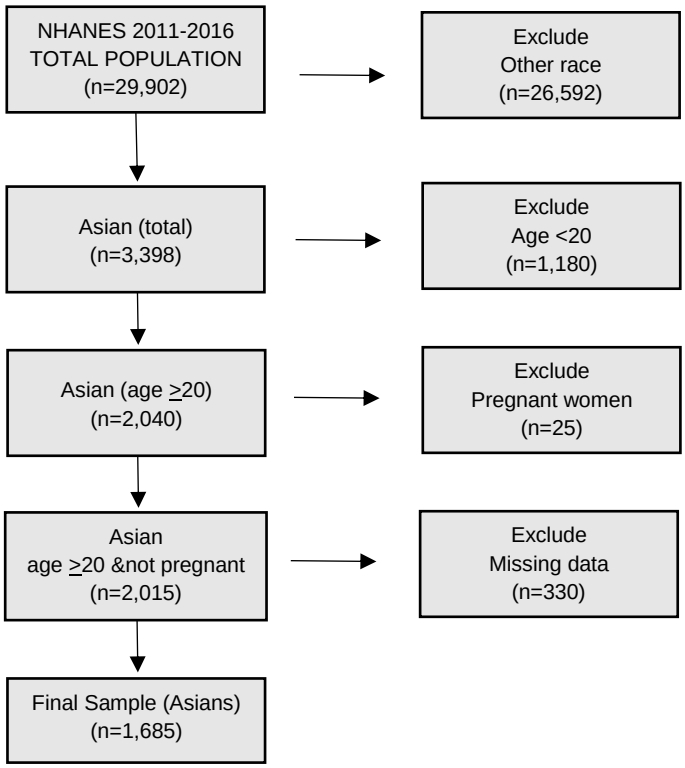


Figure 9. Flowchart of study population with inclusion/exclusion criteria

DESCRIPTIVE STATISTICS

Demographics: Population Characteristics

Sociodemographic variables including age, gender, education, and marital status were analyzed to evaluate characteristics among all Asians and to determine if there were differences between U.S.-born and foreign-born Asians. Upon stratifying by nativity, key differences emerged between U.S.-born and foreign-born Asians included in the study sample in terms of age, education, and marital status.

Of total Asians (n=1,685) included in this study, the overall mean age was 44.6, SE=0.76 (43.04 to 46.11). When stratified by nativity, the mean age for U.S.-born Asians was 36.0, SE=1.49 (CI: 32.99 to 38.99) which is significantly younger (p=0.003) than foreign-born Asians who had a mean age of 45.9, SE=0.85 (CI:44.21 to 47.61). Approximately 61% of foreign-born Asians are older >40 years old compared to ~31% of U.S. born Asians in the same age

categories. There are 2 times as many foreign-born Asians who are > 60 years old compared to U.S.-born Asians. When examining the mean age differences across diabetes status, it was lower for those with undiagnosed diabetes than diagnosed diabetes (Figure , Table).

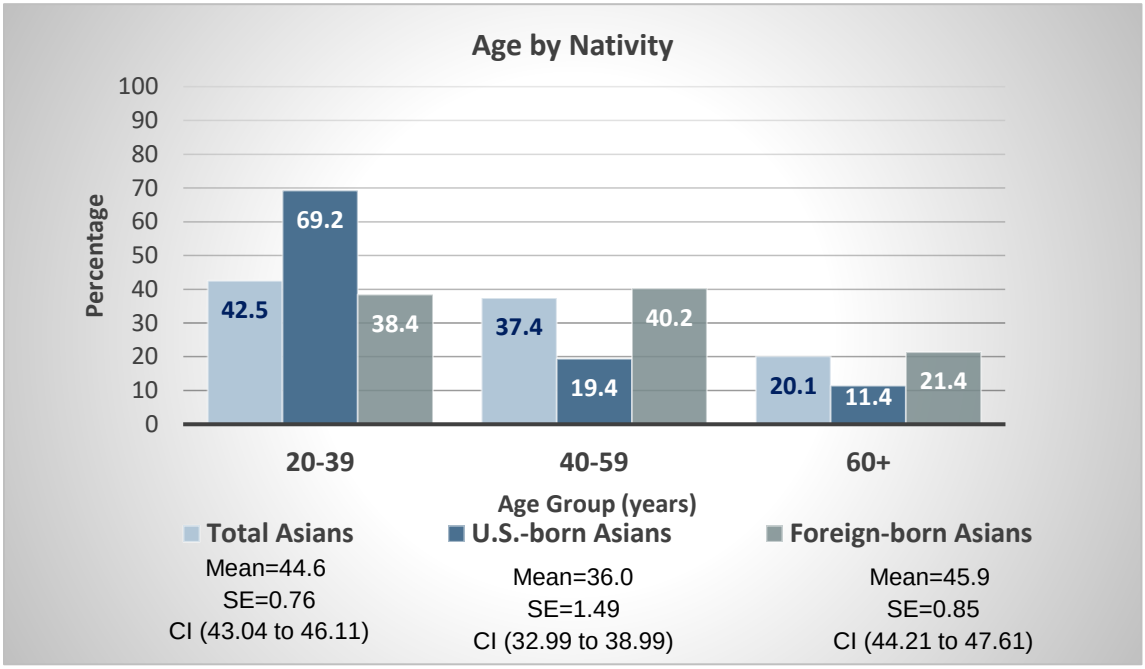


Figure 10. Age by Nativity

TABLE 6. Weighted mean age by diabetes status, NHANES 2011-2016

Diabetes Status of Total Asians	Mean Age	SE	95% CL
Undiagnosed Diabetes (n=61)	54.8	1.85	(51.03 to 58.48)
Diagnosed Diabetes (n=177)	60.0	1.55	(56.89 to 63.13)
Prediabetes (n=402)	52.9	0.75	(51.40 to 54.42)
Normal (n=1045)	38.7	0.60	(37.44 to 39.87)

However, the gender composition remained the same regardless of stratification. The weighted gender composition was evenly distributed with males and females comprising 46.6% (827/1685) and 53.4% (858/1685), respectively. After stratifying by nativity, the gender composition remained comparable to that of the total Asian population with 51.1% (116/222) U.S.-born males, 48.9% (106/222) females, 46.2% (711/1463) foreign-born males, and 53.8% (752/1463) females.

TABLE 7. Weighted sociodemographic characteristics of study population by nativity, NHANES 2011-2016

Characteristic	Total Population n=1685	Asians (U.S.-born) n=222 (13.2%)	Asians (Foreign-born) n=1,463 (86.8%)
AGE CATEGORY (YEARS)	**Mean=44.6 SE=0.76 CI (43.04 to 46.11)**	**Mean=36.0 SE=1.49 CI (32.99 to 38.99)**	**Mean=45.9 / SE=0.85 CI (44.21 to 47.61)**
20-39	667 (42.5%)	148 (69.2%)	519 (38.4%)
40-59	646 (37.4%)	44 (19.4%)	602 (40.2%)
60+	372 (20.1%)	30 (11.4%)	342 (21.4%)
GENDER			
Male	827(46.6%)	116 (51.1%)	711 (46.2%)
Female	858 (53.4%)	106 (48.9%)	752 (53.8%)
EDUCATION			
<High School	243 (13.5%)	3 (1.2%)	240 (15.4%)
High School grad	221 (12.3%)	18 (8.2%)	203 (12.9%)
Some College or AAS	356 (20.9%)	72 (33.5%)	284 (18.9%)
College grad or above	865 (53.3%)	129 (57.1%)	736 (52.8%)
MARITAL STATUS			
Married or Living with partner	1198 (70.8%)	101 (45.1%)	1097 (74.7%)
Single, Divorced, or Widowed	487 (29.2%)	121 (54.9%)	366 (25.3%)

Social Determinants of Health

Marital status, often used as a demographic variable, was used in this study as a proxy measure of social support. The majority of total Asians 70.8% (1198/1685) were married or living with a partner while 29.2% (487/1685) were single, divorced, or widowed; however, when stratifying by nativity, it was mostly foreign-born Asians who were married or living with a partner 74.7% (1097/1463) compared to U.S.-born Asians 45.1% (101/222).

Educational attainment of “some college or associate’s degree” or “college graduate or above” was 74.2% (1221/1685) overall. When stratifying by nativity, U.S.-born had a higher percentage of educational attainment of “some college or associate’s degree” or “college graduate or above” at 90.6% (201/222) compared to those who were foreign-born 71.7% (1020/1463).

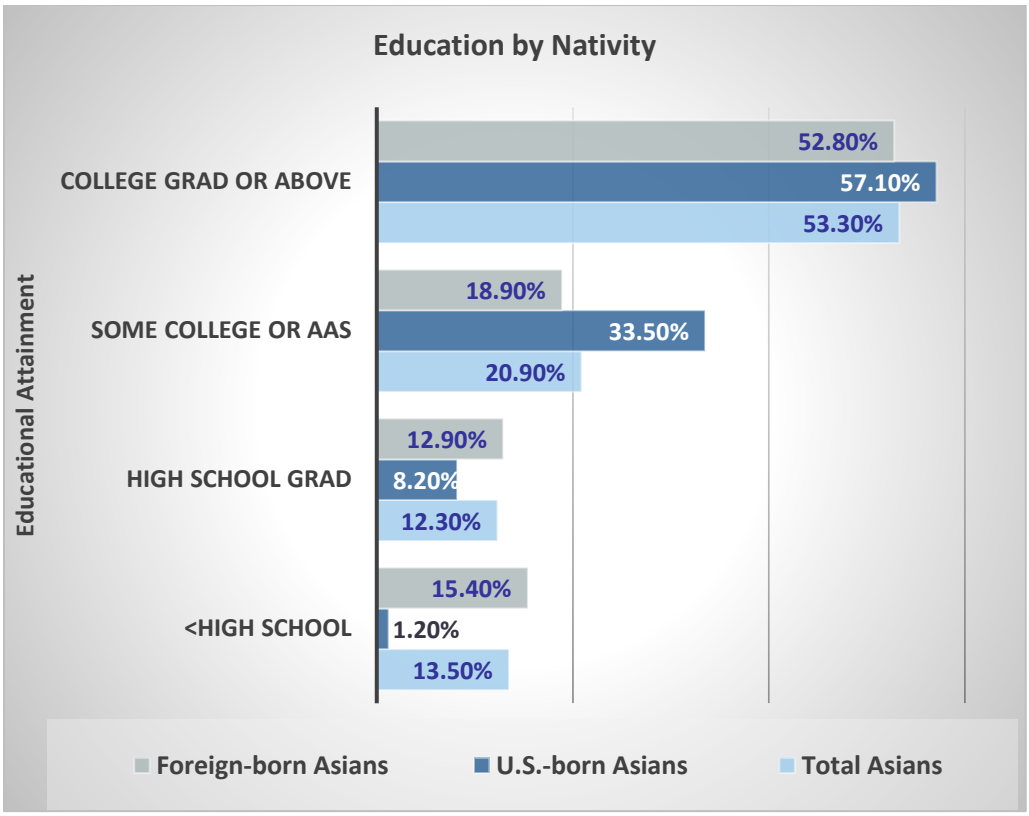


Figure 11. Educational Attainment by Nativity

Language spoken was used as a proxy for acculturation. Of total Asians, 56.0% (962/1685) either “only spoke a language other than English” or “spoke more of the non-English language”, 8.3% (141/1685) spoke both English and another language equally well, and 35.7% (582/1685) spoke “only spoke English” or “spoke more English”. When stratifying the sample by nativity, it was mostly those who were foreign-born 63.2% (939/1463) that either “only spoke a language other than English” or “spoke more of the non-English language” compared to U.S.-born Asians 10.0% (23/222). The majority of U.S.-born Asians “spoke only or more English” at 86.3% (191/222) compared to Foreign-born Asians 27.8% (391/1463).

Of total Asians, the majority were insured 85.1% (1412/1685) while 14.9% (273/1685) were uninsured. It was consistent when stratifying by nativity with 84.9% (188/222) of U.S.-born and 85.2% (1224/1463) of foreign-born being insured.

A majority of total Asians 80.1% (1356/1685) reported having a “routine place to go for healthcare” while 19.9% (329/1685) did not. When stratifying by nativity, U.S.-born had a higher

percentage of not having a “routine place to go for healthcare” at 29.4% (62/222) compared to those who are foreign-born 18.4% (267/1463).

TABLE 8. Weighted social determinants of health characteristics of study population, NHANES 2011-2016

Characteristic	Total Population n=1685	Asians (U.S.-born) (n=222) (13.2%)	Asians (Foreign-born) (n=1,463) (86.8%)
LANGUAGE SPOKEN (proxy of acculturation)			
Non-English language (only or more)	962 (56.0%)	23 (10.0%)	939 (63.2%)
Both English and non-English (equally)	141 (8.3%)	8 (3.7%)	133 (9.0%)
English (only or more)	582 (35.7%)	191 (86.3%)	391 (27.8%)
HEALTH INSURANCE			
Yes, insured	1412 (85.1%)	188 (84.9%)	1224 (85.2%)
No, uninsured	273 (14.9%)	34 (15.1%)	239 (14.8%)
REGULAR HEALTH PROVIDER			
Yes	1356 (80.1%)	160 (70.6%)	1196 (81.6%)
No	329 (19.9%)	62 (29.4%)	267 (18.4%)
POVERTY			
<100%	253 (14.0%)	32 (14.3%)	221 (14.0%)
≥100%	1432 (86.0%)	190 (85.7%)	1242 (86.0%)

Of total Asians,14.0% (253/1685) had <1.0 income-to-poverty ratio which is equivalent to living below the 100% poverty threshold as defined by the Census.[125] This rate remained consistent even when stratifying by nativity with foreign-born 14.0% (221/1463) and U.S.-born 14.3% (32/222) were living below the 100% poverty threshold.

Overweight/Obesity

Using the recommended Asian body mass index (BMI) cutoff of ≥ 23[35] for overweight/obesity, 63.3% (1070/1685) of total Asians were considered overweight or obese while 36.7% (615/1685) had a normal BMI. Even when stratifying by nativity, the distribution of overweight/obese individuals remained comparable at 63.1% (928/1463) among foreign-born and 64.7% (142/222) among U.S.-born. Means analysis of BMI showed very little difference between U.S. born $\bar{x}$=25.2, SE=0.3826 (CI:24.4 to 26.00) and foreign-born $\bar{x}$=24.75, SE=0.1308 (CI: 24.41 to 24.94).

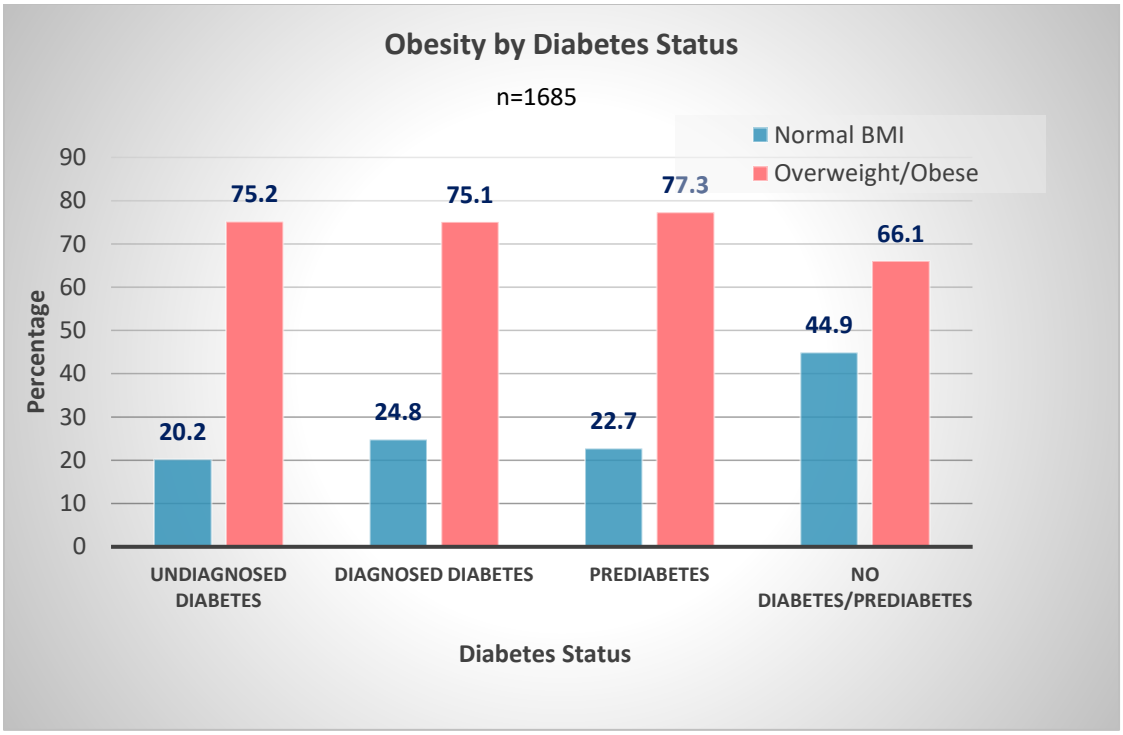


Figure 12. Obesity by Diabetes Status

Amongst Asian Americans with undiagnosed and diagnosed diabetes, 75% were overweight or obese with a BMI ≥23*, 77% with Prediabetes were overweight or obese, and 66% of those who did not have diabetes or prediabetes were overweight or obese.

TABLE 9. Weighted mean BMI, NHANES 2011-2016

Nativity	N	Mean	SE	95% CL for Mean	
Foreign-born Asians	1463	24.7	0.130775	24.41	24.94
US-born Asians	222	25.2	0.382588	24.4	26.00

There were no statistically significant differences in mean BMI between diagnosed diabetes and undiagnosed diabetes or diagnosed diabetes and prediabetes or when adjusting for nativity. Compared to those with No diabetes or prediabetes, the mean BMI for those with diagnosed diabetes is 2.68 higher, undiagnosed diabetes is 2.79 higher, and prediabetes is 2.42 higher.

Table 10. Diabetes Status by BMI for Total Population

Obesity	**Undiagnosed diabetes** n=61 (3.5%)	**Diagnosed diabetes** n=177 (10.1%)	**Prediabetes** n=402 (22.4%)	**No prediabetes or diabetes** n=1045 (64.0%)
Normal BMI (n=615)	14 (20.2%)	36 (24.8%)	97 (22.7%)	468 (44.9%)
Overweight/Obese BMI (n=1070)	47 (75.2%)	141 (79.8%)	305 (77.3%)	577 (55.1%)

TABLE 11. Weighted overweight/obesity and clinical characteristics of study population

CHARACTERISTIC	Total Population n=1685	Asians (U.S.-born) n=222 (13.2%)	Asians (Foreign-born) n=1,463 (86.8%)
OVERWEIGHT/OBESE (Asian overweight/obese BMI criteria ≥ 23)			
Yes	1070 (63.3%)	142 (64.7%)	928 (63.1%)
No	615 (36.7%)	80 (35.3%)	535 (36.9%)
GLYCOHEMOGLOBIN: HbA1C (%)			
Diabetes level	179 (10.1%)	8 (3.8%)	171 (11.1%)
Prediabetes level	452 (25.3%)	37 (15.4%)	415 (26.8%)
Normal	1054 (64.6%)	177 (80.8%)	877 (62.1%)
DIABETES STATUS			
Undiagnosed Diabetes*	61 (3.5%)	2 (1.1%)	59 (3.9%)*
Diagnosed Diabetes	177 (10.2%)	12 (5.4%)	165 (10.9%)*
Prediabetes*	402 (22.3%)	31 (12.7%)	371 (23.8%)*
Normal	1045 (64.0%)	177 (80.8%)	868 (61.4%)
SLEEP			
Low (<7 hrs.)	523 (29.4%)	77 (34.1%)	446 (28.7%)
Normal (7-9 hrs.)	1106 (67.1%)	139 (63.3%)	967 (67.7%)
High (>9 hrs.)	56 (3.5%)	6 (2.6%)	50 (3.6%)

Glycohemoglobin: HbA1C (%) and Diabetes Status

Prior to applying the diabetes status definition, the weighted frequencies of glycohemoglobin HbA1c levels were at diabetes level for 10.1% and 25.3% prediabetes level amongst the overall Asian study population. HbA1c means analysis of Asians by nativity showed that foreign-born Asians had a higher HbA1c $\bar{x}$=5.7, SE=0.03 (CI: 5.36 to 5.48) compared U.S.-born Asians $\bar{x}$=5.4, SE=0.04 (CI: 5.66 to 5.81) (Table 11).

TABLE 12. Weighted HbA1c Means by Nativity

	Mean HbA1c	SE	95% CL
U.S. born (n=222)	5.4	0.04	(5.66 to 5.81)
Foreign-born (n=1463)	5.7	0.03	(5.36 to 5.48)
Total Population (n=1685)	5.7	0.03	(5.62 to 5.76)

Of total Asians, 10.1% (179/1685) have diabetes-level HbA1c, 25.3% have prediabetes-level HbA1c, and 64.6% have normal HbA1c. When stratifying by nativity, foreign-born have higher percentage of diabetes-level HbA1c 11.1% compared to U.S.-born Asians 3.8%. In addition, foreign-born Asians also have a higher percentage of prediabetes-level HbA1c 26.8% compared to U.S.-born Asians16.4%.

An analysis of the HbA1c means by diabetes status shows that those with undiagnosed diabetes have a higher mean HbA1c $\bar{x}$=7.6, SE=0.17 (CI:7.25 to 7.92) compared to those with diagnosed diabetes $\bar{x}$=7.2, SE=0.12 (6.94 to 7.44).

TABLE 13. HbA1c Means by Diabetes Status

	Mean HbA1c	SE	95% CL
Undiagnosed Diabetes	7.6	0.17	(7.25 to 7.92)
Diagnosed Diabetes	7.2	0.12	(6.94 to 7.44)
Prediabetes	5.92	0.01	(5.90 to 5.94)
Normal	5.3	0.01	(5.26 to 5.29)

When comparing HbA1c levels by diabetes status, only 1% of those with normal HbA1c have diagnosed diabetes. Of those with prediabetes-level HbA1c, 11.7% have diagnosed diabetes. Only 6.3% of those with diagnosed diabetes, 29.2% have normal HbA1c and 64.5% continue to have diabetes-level HbA1c. Of those with diabetes-level HbA1c, 35% have undiagnosed diabetes and 65% have diagnosed diabetes.

TABLE 14. HbA1c Levels by Diabetes Status

HbA1c Level	Diabetes Status	Frequency	Percent	Row Percent	Column Percent
Normal A1c	**Diagnosed Diabetes**	9	0.6375	0.9866	6.28
	Undiagnosed Diabetes	0	.	.	.
	Prediabetes	0	.	.	.
	No diabetes/prediabetes	1045	63.9832	99.01	100.00
	Total	1054	64.6207	100.00	
Prediabetes A1c	**Diagnosed Diabetes**	50	2.9636	11.71	29.20
	Undiagnosed Diabetes	0	.	.	.
	Prediabetes	402	22.3397	88.29	100.00
	No diabetes/prediabetes	0	.	.	.
	Total	452	25.3033	100.00	
Diabetes A1c	**Diagnosed Diabetes**	118	6.5482	65.0	64.5
	Undiagnosed Diabetes	61	3.5278	35.0	100.0
	Prediabetes	0	.	.	.
	No diabetes/prediabetes	0	.	.	.
	Total	179	10.0760	100.00	

More alarming are the corresponding HbA1c levels—in the diabetes and prediabetes range—amongst those with diagnosed diabetes. Approximately 94% have an HbA1c in the prediabetes to diabetes range, ~69% of which are at diabetes level. Based on this analysis, only 6.3% of those with diagnosed diabetes have their glucose under control.

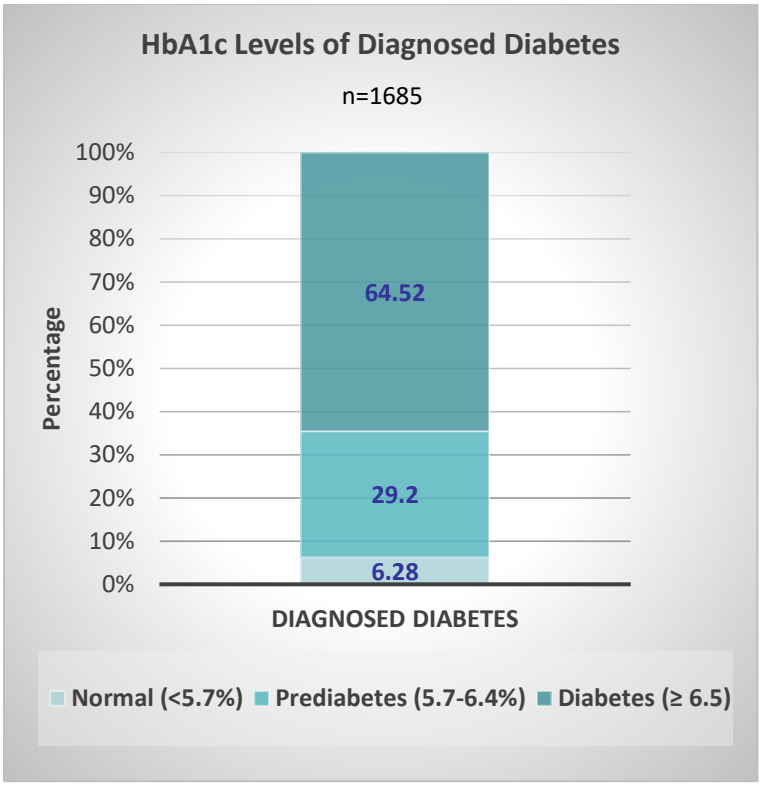


FIGURE 13. HbA1c Levels for Asian-Americans with Diagnosed Diabetes

After applying the diabetes status definition to categorize undiagnosed diabetes, diagnosed diabetes, prediabetes and no diabetes/prediabetes, the results showed differences between foreign-born and U.S.-born Asians. In the total Asian American population, 3.5% had undiagnosed diabetes, 10.2% had diagnosed diabetes, 22.3% had prediabetes, and 64.0% had no diabetes/prediabetes.

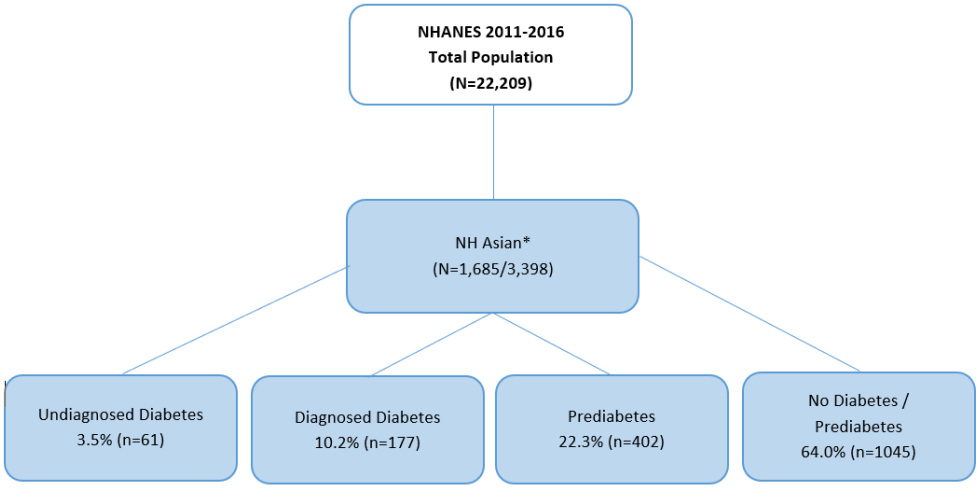


Figure 14. Flowchart of Diabetes Status

When stratifying by nativity, the results were drastically different. Amongst U.S.-born Asian Americans, 1.1% had undiagnosed diabetes compared to 3.9% in foreign-born. The prevalence of diagnosed diabetes in those foreign-born was 10.9% which is double the proportion compared to U.S.-born Asians at 5.4%. Prediabetes rates were also higher amongst foreign-born (23.8%) compared to 12.7% in those who are U.S.-born. When analyzing the percentage undiagnosed from overall diabetes prevalence, 13.6% were undiagnosed amongst U.S.-born Asian Americans compared to 26.4% undiagnosed diabetes (Figure).

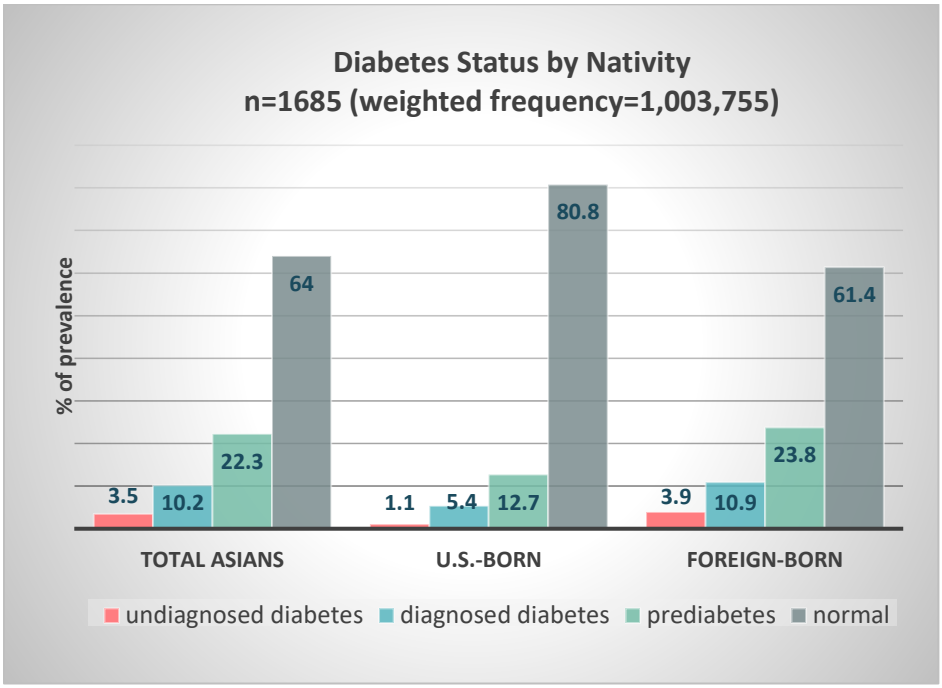


Figure 15. Diabetes Status by Nativity

Sleep

Of total Asians, there were no differences in diabetes status and mean sleep duration.

TABLE 15. Weighted mean sleep duration (hours), NHANES 2011-2016

Diabetes Status	N	Mean	SE	95% CL for Mean	
Diagnosed Diabetes	177	7.246005	0.13	6.99	7.51
Undiagnosed Diabetes	61	7.389205	0.23	6.92	7.86
Prediabetes	402	7.018170	0.06	6.90	7.13
No diabetes/prediabetes	1045	7.125678	0.05	7.028	7.22

Foreign-born Asians had low (30%), normal (62.2%) or high (7.8%) sleep levels. When comparing to U.S.-born Asians, they had lower proportion of individuals who had low sleep levels (30.3% vs. 39.2%). Interestingly, none of the U.S.-born Asians reported having a high level of sleep (>9 hours). (Table 15).

TABLE 16. Weighted Sleep levels by Nativity, NHANES 2011-2016

Sleep Level	Nativity	Frequency	Percent	Column Percent
Low=<7hours	'Foreign born Asians'	57	28.50	30.03
	'US born Asians'	3	1.98	39.15
	Total	60	30.49	
Normal: 7-9 hours	'Foreign born Asians'	102	59.04	62.19
	'US born Asians'	5	3.08	60.85
	Total	107	62.13	
High: >9 hours	'Foreign born Asians'	12	7.39	7.78
	'US born Asians'	0	.	.
	Total	12	7.39	

Among Asian Americans with undiagnosed diabetes, ~31% had low sleep and ~12% had high sleep. Normal sleep levels were higher in those who had diagnosed diabetes (~66%), prediabetes (~65%) , and no diabetes/prediabetes (~68.29%).

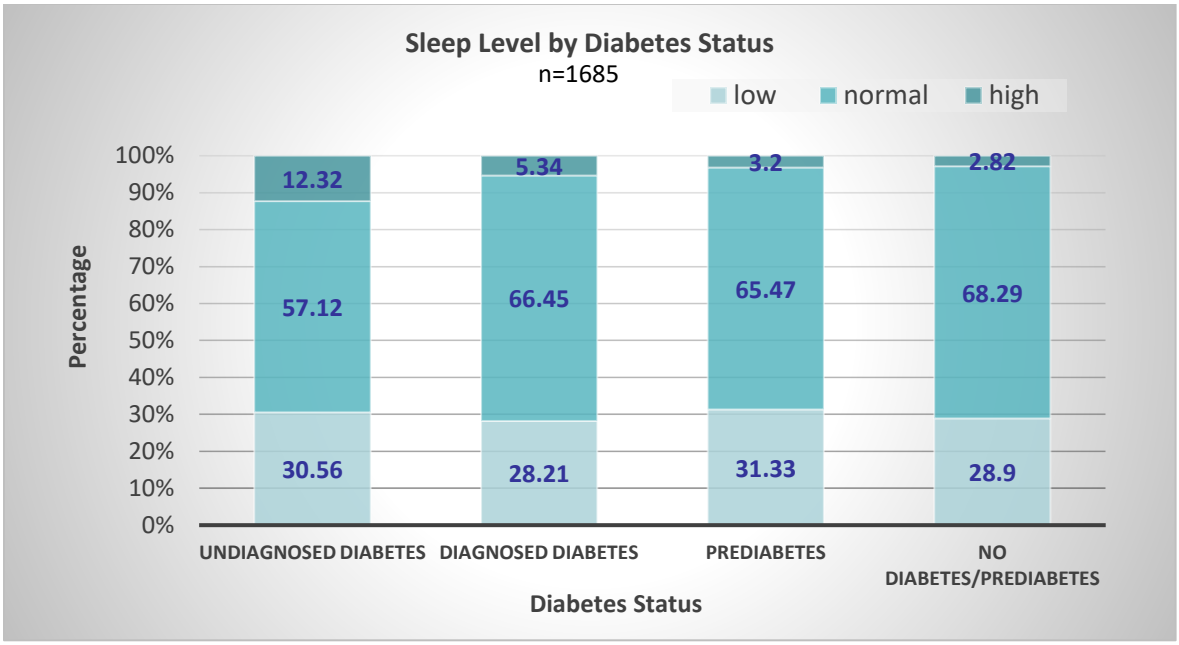


Figure 16. Diabetes Status by Nativity

CHI SQUARE TEST OF INDEPENDENCE

There was a statistically significant association to diabetes status—whether being diagnosed, undiagnosed, having prediabetes or having no diabetes/prediabetes—in differences related to age group ($p<0.001$), nativity ($p<0.001$), educational attainment ($p<0.001$), BMI ($p<0.001$), marital status ($p=0.001$), poverty ($p=0.009$), and language spoken (proxy for acculturation) ($p=0.010$), binary sleep duration ($p<0.001$), and 3- level sleep duration ($p=0.0335$). However, the following variables were not found to have a statistically significant association to diabetes status at any level: gender ($p=0.135$), health insurance ($p=0.251$), (Table 8). The "cutoff" point for the p-value was set at an alpha of 0.05.

Of those who had undiagnosed diabetes, 95.7% were foreign-born, 83.3% were 40 years and older, 80.3% were married or living with a partner, 67.6% spoke mostly a foreign language—a measure of acculturation. Interestingly, an inverse relationship emerged where those who had a higher income-to-poverty ratio and greater routine healthcare access have undiagnosed diabetes.

Of those who had diagnosed diabetes, 92.8% were foreign-born, 92.0% were 40 years and older, 76.6% were married or living with a partner, 72.5% spoke mostly a foreign language—a measure of acculturation. Interestingly, an inverse relationship emerged where those who had a higher income-to-poverty ratio and greater routine healthcare access have diagnosed diabetes at 77.6% and 95.4%, respectively.

Of those who had prediabetes, 92.4% were foreign-born, 66.2% were 40 years and older, 77.7% were married or living with a partner, 58.5% spoke mostly a foreign language—a measure of acculturation. Interestingly, an inverse relationship emerged where those who had a higher income-to-poverty ratio and greater routine healthcare access have diagnosed diabetes at 87.2% and 75.4%, respectively.

All three age groups have significantly different estimated diabetes status, $F=80.0$, $df=6$, $p<.0001$. Amongst those ages 20-39, 3.3% have diabetes (1.4% of which are undiagnosed) and 9.7% with prediabetes. The diabetes and prediabetes rates are higher amongst those ages 40-59 than in the younger age group where 13.7% have diabetes (3.9% of which are undiagnosed) and 28.6% have prediabetes. Lastly, those ages 60 years and older 35.8% have diabetes (7.5%

of which are undiagnosed) and 37.7% have prediabetes. The proportion of diabetes—both diagnosed and undiagnosed—and prediabetes increases with age.

When examining nativity and diabetes status, foreign-born Asians have significantly higher estimated diagnosed and undiagnosed diabetes and prediabetes, F=10.12, df=3, p<.0001. Amongst U.S.-born Asians, 6.5% have diabetes (1.1% are undiagnosed) and 12.7% have prediabetes. However, amongst foreign-born Asians, 14.8% have diabetes (3.9% of which are undiagnosed) and 23.8% have prediabetes.

When examining marital status differences in diabetes status, those who are married or living with a partner had a significantly higher estimate of diagnosed and undiagnosed diabetes and prediabetes, F=5.5, df=3, p=.0009. Amongst those who are not married or not living with a partner, 10.5% have diabetes (2.4% of which is undiagnosed) and 17.0% have prediabetes. These rates were higher amongst those who are married or living with a partner with 15.0% having diabetes (4.0% of which are undiagnosed) and 24.5% with prediabetes.

Those with less educational attainment compared to their counterparts with higher education have significantly different estimated diabetes status, F=21.4, df=3, p=<.0001. Amongst those with some college, Associates degree, College graduate or above, 10.5% have diabetes (2.7% which are undiagnosed) and 20.2% have prediabetes. These rates are higher amongst those who graduated high school or had less than high school education, 22.8% have diabetes (6.0% of which are undiagnosed) and 28.5% with prediabetes.

A significant difference in estimated diabetes status when examining level of acculturation, F=5.4, df=3, p=0.0010. Amongst those who were more acculturated and spoke mostly English or equally as well as a foreign language, 10.1% have diabetes (2.6% of which are undiagnosed) and 21.1% have prediabetes. However, those who are less acculturated and spoke mostly non-English, 16.5% have diabetes (4.3% of which are undiagnosed) and 23.3% have prediabetes.

When examining poverty, there is a significantly different estimated diabetes status, F=3.8, df=3 , p=0.0094. Amongst those whose income was greater than 100% of the poverty level, 12.7% have diabetes (3.5% of which are undiagnosed) and 22.5% have prediabetes. The rates are higher amongst those whose income was less than 100% of the poverty level with

20% have diabetes (3.8% of which are undiagnosed) and 21.5% have prediabetes.

Having a regular healthcare access has significantly different estimated diabetes status, F= 21.0, df=3, *p*<.0001. Amongst those who had one or more routine places to go for healthcare, 15.4% have diabetes (3.4% of which are undiagnosed) and 24.3% have prediabetes. Interestingly, lower rates were observed for those who did not have a place to go for healthcare. Of those without a regular health provider, 6.5% have diabetes (4.2% of which are undiagnosed) and 14.2% have prediabetes.

Table 17. Association of sociodemographic variables and Undiagnosed Diabetes, Diagnosed Diabetes and Prediabetes among Asian adults (20+ years old)*

	Undiagnosed Diabetes n=61 (%)	Diagnosed Diabetes n=177 (%)	Prediabetes n=402 (%)	Normal n=1045 (%)	F-statistic	df	*p*-value*
Nativity							
U.S.-born	2 (4.3%)	12 (7.2%)	31 (7.6%)	177 (17.0%)	10.11	3	<.001*
Foreign-born	59 (95.7%)	165 (92.8%)	371 (92.4%)	868 (83.0%)	10.11	3	<.001*
Gender							
Male	36 (55.9%)	92 (51.1%)	205 (51.3%)	494 (28.8%)	1.85	3	0.135
Female	25 (44.1%)	85 (48.9%)	197 (%48.7)	551 (35.2%)	1.85	3	0.135
Age							
20-39	9 (16.7%)	12 (8.0%)	68 (18.4%)	578 (57.9%)	80	6	<.001*
40-59	25 (40.9%)	64 (36.0%)	192 (47.8%)	365 (33.8%)	80	6	<.001*
60+	27 (42.4%)	101 (56.0%)	142 (33.8%)	102 (8.3%)	80	6	<.001*

Rao-Scott F-adjusted chi-square statistic
* denotes statistical significance

Table 18. Association of Social Determinants of Health and Undiagnosed Diabetes, Diagnosed Diabetes and Prediabetes among Asian adults (20+ years old)*

	Undiagnosed Diabetes n=61 (%)	Diagnosed Diabetes n=177 (%)	Prediabetes n=402 (%)	Normal n=1045 (%)	F-value	df	*p*-value*
Marital Status							
Married or living with partner	50 (80.3%)	134 (76.7%)	312 (77.7%)	702 (66.8%)	5.51	3	0.001*
Divorced or single	11 (19.7%)	43 (23.3%)	90 (22.3%)	343 (33.2%)	5.51	3	0.001*
Education							
<High School	13 (20.7%)	52 (28.4%)	80 (19.8%)	98 (8.6%)	8.90	9	<.001*
High School grad	15 (23.5%)	25 (14.3%)	59 (13.1%)	122 (11.1%)	8.90	9	<.001*
Some College or AAS	11 (18.1%)	31 (17.9%)	87 (21.4%)	227 (21.3%)	8.90	9	<.001*
College grad or above	22 (37.7%)	69 (39.5%)	176 (45.7%)	598 (59.1%)	8.90	9	<.001*
Language Spoken (proxy for acculturation)							
Non-English language (only or mostly)	43 (67.6%)	121 (67.5%)	241 (58.5%)	557 (52.7%)	2.79	6	.010*
Both English and non-English (equally)	2 (3.8%)	9 (5.0%)	32 (7.6%)	98 (9.3%)	2.79	6	.010*
English (only or mostly)	16 (28.6%)	47 (27.5%)	129 (33.9%)	390 (38.0%)	2.79	6	.010*
Poverty							
<100%	10 (15.0%)	43 (22.4%)	58 (13.5%)	142 (12.8%)	3.83	3	0.009*
≥100%	51 (85.0%)	134 (77.6%)	344 (86.5%)	903 (87.2%)	3.83	3	0.009*
Health Insurance							
Yes, Insured	46 (77.2%)	151 (87.2%)	342 (86.9%)	873 (84.6%)	1.37	3	.251
No, Uninsured	15 (22.8%)	26 (12.8%)	60 (13.1%)	172 (15.4%)	1.37	3	.251
Routine place to go for healthcare (proxy for healthcare access)							
Yes	46 (76.6%)	167 (95.4%)	350 (87.3%)	793 (75.4%)	20.99	3	<.001*
No	15 (23.4%)	10 (4.6%)	52 (12.7%)	252 (24.6%)	20.99	3	<.001*

Rao-Scott F-adjusted chi-square statistic
* denotes statistical significance

Obesity has significantly different estimated diabetes status, F=21.8, df=3, *p*<.0001. Amongst those who are not overweight or obese, 8.0% have diabetes (2.4% of which are undiagnosed) and 13.8% have prediabetes. Those who are overweight or obese have diabetes rate of 17.0% (4.2% of which are undiagnosed) and 27.3% have prediabetes.

Levels of sleep duration have significantly different estimated diabetes status, F=2.3, df=6, *p*=0.0335. Those who had low sleep duration of less than seven hours had significantly higher rate of prediabetes (23.8%%) compared to those who had normal (21.8%) or high (20.5%) sleep duration. However, those with high sleep duration of more than 9 hours had a higher rate of diabetes—27.9% of which 12.4% is undiagnosed diabetes—compared to those who had lower sleep duration. Similarly, those who had normal sleep duration of seven to nine hours had a diabetes rate of 13.1% (of which 3.0% is undiagnosed) comparable to those who had low sleep duration and a diabetes rate of 13.4% (3.7%).

Table 19. Association of Clinical Factors and Undiagnosed Diabetes, Diagnosed Diabetes and Prediabetes among Asian adults (20+ years old)*

	Undiagnosed Diabetes n=61 (%)	Diagnosed Diabetes n=177 (%)	Prediabetes n=402 (%)	Normal n=1045 (%)	F-statistic	df	*p*-value*
Body Mass Index (BMI)							
Normal	14 (24.8%)	36 (20.2%)	97 (22.7%)	468 (44.9%)	21.84	3	<.001*
Overweight/Obese	47 (75.2%)	141 (79.8%	305 (77.3%)	577 (55.1%)	21.84	3	<.001*
Sleep Duration (Hours slept)							
Low (<7 hours)	22 (30.6%)	55 (28.2%)	131 (31.3%)	315 (28.9%)	2.28	6	.033*
Normal (7-9 hours)	32 (57.1%)	113 (66.5%)	260 (65.5%)	701 (68.3%)	2.28	6	.033*
High (>9 hours)	7 (12.3%)	9 (5.3%)	11 (3.2%)	29 (2.8%)	2.28	6	.033*

Rao-Scott F-adjusted chi-square statistic
* denotes statistical significance

LINEAR REGRESSION

Initially, each Simple Linear Regression model consisted of one outcome (dependent) variable (i.e., age, HbA1c, sleep, BMI) regressed onto diabetes status (i.e., undiagnosed diabetes, diagnosed diabetes, prediabetes). This would answer the question: Are there differences in diabetes status with age, HbA1c, sleep, and BMI? The only linear regression model with statistical significance was of differences in diabetes status with age (continuous) based on the diffogram (Figure 10). Each line represents the pairwise differences between the diabetes status LS-means; a longer line represents the confidence interval. The LS-mean is significantly different if the line does not cross the 45-degree line. The analysis of mean contrasts results shows that mean age difference of diagnosed diabetes and undiagnosed diabetes is statistically significant (p=<.0001). Those with diagnosed diabetes were significantly older than those with undiagnosed diabetes (5 yrs. older), prediabetes (7 yrs. Older), no diabetes/prediabetes (21 yrs. older) Those with prediabetes were younger but not statistically different than those with undiagnosed diabetes. No differences were observed in the association of diabetes status and HbA1c, sleep, BMI .

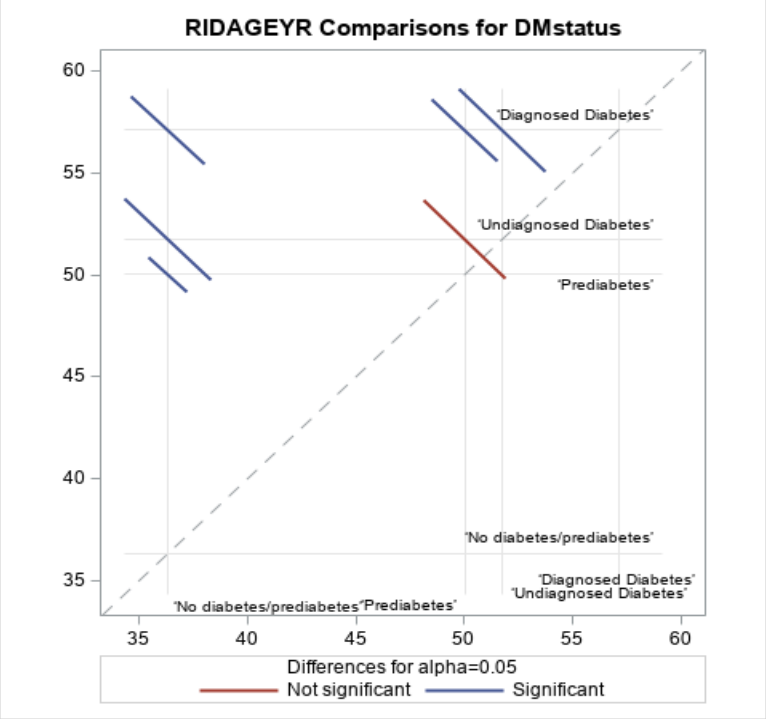


Figure 17. Linear Regression Model of Age differences by Diabetes Status

MULTINOMIAL LOGISTIC REGRESSION MODELS

Prior to adding grouped variables, each categorical independent/predictor variable was modeled with the outcome/dependent variable of diabetes status (i.e., undiagnosed diabetes, diagnosed diabetes, prediabetes, and normal). Undiagnosed diabetes was used as the reference outcome category for the analysis. Due to the categorical, nominal levels of the independent variables, the reference categories for each independent variable are also noted in the table.

Of all the univariate multinomial logistic regression analyses, the independent variables that were significant included: gender, nativity, marital status, education, regular health provider, When comparing gender, females were 1.6 times more likely than males to have no diabetes/prediabetes compared to undiagnosed diabetes (p=0.0377), OR:1.550 (CI:1.026 to 2.340).

When comparing nativity, foreign-born Asians are 0.2 times more likely than U.S.-born Asians to have no diabetes/prediabetes compared to undiagnosed diabetes nativity foreign-born Asians (p=0.0405), OR: 0.222 (CI: 0.053 to 0.935).

When comparing marital status, those who are married or living with partner are 0.5 times more likely than those single or divorced for having no diabetes/prediabetes compared to having undiagnosed diabetes (p=0.0361) OR: 0.494 (CI:0.256 to 0.953).

When comparing education, higher educational attainment was associated with having no diabetes/prediabetes compared to undiagnosed or diagnosed diabetes. Of note is when comparing those who are college graduates or above to high school graduates, they are 3.3 times more likely to have no diabetes/prediabetes compared to undiagnosed diabetes (p=0.0031) OR: 3.337, (CI: 1.534 to 7.261). In addition, those who had some college or AAS degree when compared to high school graduates were 2.5 times more likely to have no diabetes/prediabetes compared to having undiagnosed diabetes (p=0.0453), OR: 2.497 (CI:1.020 to 6.112). The only exception was those who had less than high school education compared to those who were high school graduates were 2.3 times more likely to have diagnosed diabetes compared to undiagnosed diabetes. (p=0.0303), OR: 2.259 (CI:1.084 to 4.705).

Those who did not have a regular healthcare provider were 0.5 times more likely than those who had a regular healthcare provider to have prediabetes compared to having undiagnosed diabetes. (p=0.0061), OR: 0.475 (CI: 0.282 to 0.800). The exception to this was when comparing those who did not have a regular healthcare provider were 0.2 times more likely than those who had a regular healthcare provider to have diagnosed diabetes compared to having undiagnosed diabetes. (p= 0.0003), OR: 0.157 (CI: 0.060 to 0.410).

Those having overweight/obese BMI≥23 (Asian cutoff) were 0.4 times more likely than those with normal BMI to have no diabetes/prediabetes compared to undiagnosed diabetes. (p=0.0126), OR 0.406 (CI:0.201 to 0.817).

When comparing sleep levels, those who had high level of sleep (>9 hours) were 0.2 times more likely than those who had normal level of sleep (7-9 hours) to have no diabetes/prediabetes compared to having undiagnosed diabetes (p=0.0036), OR: 0.191,(CI:0.064 to 0.567). In addition, those who had a high level of sleep were 0.1 times more likely than those who had normal level of sleep to have prediabetes compared to undiagnosed diabetes (p=0.0217), OR:0.065 (CI:0.065 to 0.797).

However, there were no significant associations for age, poverty, health insurance, language spoken (proxy for acculturation).

Upon completing the univariate analyses of multinomial logistic regression, five models were developed including the Social Determinants of Health (SDOH) variables (i.e., nativity, acculturation, education, marital status, poverty, health insurance, routine health care provider) and clinical variables (i.e., obese BMI and sleep).

Model #1: Social Determinants of Health variables (unadjusted)

Education and having a regular healthcare provider were the only significant predictors of diabetes status (i.e., undiagnosed diabetes, diagnosed diabetes, prediabetes, no diabetes/prediabetes).

Those whose educational attainment was college graduate or above when compared to high school graduates were 3.0 times more likely to have no diabetes/prediabetes compared to having undiagnosed diabetes (p=0.0187), OR: 2.987 (CI: 1.288 – 6.930).

Those who did not have a regular healthcare provider were 0.2 times more likely than those who had a regular healthcare provider to have diagnosed diabetes than undiagnosed diabetes (p=0.0010), OR: 0.168, (CI: 0.061 – 0.466). Those who did not have a regular healthcare provider were 0.5 times more likely than those who had a regular healthcare provider to have prediabetes than undiagnosed diabetes (p=0.0360), OR: 0.542, (CI: 0.307 – 0.959).

Model #2: Social Determinants of Health variables (adjusted for age and gender)

The second model adjusted the SDOH model with age and gender which are known to be confounders based on our initial univariate regression models.

Those whose educational attainment was college graduate or above when compared to high school graduates were 3.0 times more likely to have no diabetes/prediabetes compared to having undiagnosed diabetes (p=0.0187), OR: 2.987 (CI:1.288 – 6.930) .

Those who did not have a regular healthcare provider were 0.2 times more likely than those who had a regular healthcare provider to have diagnosed diabetes than undiagnosed diabetes (p=0.0032), OR: 0.194 (CI: 0.067 – 0.560).

Table 20. Multinomial Logistic Regression Model #1 of Social Determinants of Health Independent Variables (unadjusted)

Independent Variables	Diagnosed Diabetes		Prediabetes		Normal	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Nativity						
U.S.-born	Ref		Ref		Ref	
Foreign-born	0.498 (0.097 - 2.56)	0.3961	0.578 (0.131 - 2.556)	0.4616	0.273 (0.058-1.275)	0.0966
Education						
Less than high school	2.004 (0.933 – 4.306)	0.3018	1.704 (0.615 – 4.725)	0.7781	1.011 (0.375 – 2.727)	0.1983
High school graduate	Ref		Ref		Ref	
Some college or AAS	1.589 (0.527 – 4.794)	0.9008	1.834 (0.704 – 4.777)	0.5656	1.929 (0.763 – 4.878)	0.4229
College graduate or above	1.694 (0.705-4071)	0.6735	1.861 (0.802 – 4.320)	0.5119	2.987 (1.288 – 6.930)	0.0187*
Poverty						
>100% poverty	0.597 (0.311 – 1.147)	0.1188	0.973 (0.505 – 1.876)	0.9337	0.774 (0.359 – 1.666)	0.5040
≤100% poverty	Ref		Ref		Ref	
Language spoken						
Speak both languages equally	1.256 (0.288 – 5.472)	0.6544	2.028 (0.395 – 10.413)	0.4162	2.245 (0.428 – 11.790)	0.2820
Speak only or mostly English	0.828 (0.385 – 1.779)	0.5216	1.082 (0.525 – 2.231)	0.5950	0.834 (0.378 – 1.840)	0.2817
Speak only or mostly non-English	Ref		Ref		Ref	
Marital Status						
Married of living with partner	0.778 (0.368 – 1.643)	0.5023	0.851 (0.388 – 1.870)	0.6827	0.583 (0.284 – 1.195)	0.1373
Not married or not living with partner	Ref		Ref		Ref	
Health Insurance						
Insured	1.428 (0.570 – 3.581)	0.4393	1.475 (0.557 – 3.909)	0.4265	1.420 (0.541 – 3.729)	0.4682
Uninsured	Ref		Ref		Ref	
Routine place for healthcare						
Yes	Ref		Ref		Ref	
No	0.168 (0.061 – 0.466)	0.0010*	0.542 (0.307 – 0.959)	0.0360 *	1.065 (0.634 – 1.788)	0.8089

CI-Confidence Intervals. OR-odds ratio Ref-Reference
Note: The OR reflects the ratio of the probability of being in one of the diabetes status categories relative to the baseline/reference variable category of “Undiagnosed Diabetes”.

Table 21. Multinomial Logistic Regression Model #2 of Social Determinants of Health Independent Variables (adjusted for age and gender)

Independent Variables	Diagnosed Diabetes		Prediabetes		Normal	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Nativity						
U.S.-born	Ref		Ref		Ref	
Foreign-born	0.453 (0.082 – 2.518)	0.3580	0.548 (0.117 – 2.577)	0.4383	0.304 (0.062 – 1.493)	0.1388
Education						
Less than high school	1.794 (0.793 – 4.057)	0.5412	1.789 (0.631 – 5.079)	0.6651	1.571 (0.575 – 4.293)	0.9582
High school graduate	Ref		Ref		Ref	
Some college or AAS	1.609 (0.529 – 4.896)	0.8564	1.757 (0.691 – 4.466)	0.6490	1.508 (0.628 – 3.619)	0.9245
College graduate or above	1.808 (0.762 – 4.292)	0.4673	1.830 (0.799 – 4.189)	0.5500	2.395 (1.076 – 5.330)	0.1167
Poverty						
>100% poverty	0.649 (0.339 – 1.244)	0.1878	0.988 (0.514 – 1.902)	0.9718	0.794 (0.363 – 1.738)	0.5564
≤100% poverty	Ref		Ref		Ref	
Language spoken						
Speak both languages equally	1.287 (0.279 – 5.947)	0.6363	1.888 (0.373 – 9.558)	0.4331	1.801 (0.363 – 8.952)	0.3479
Speak only or mostly English	0.820 (0.369 – 1.824)	0.5014	1.002 (0.478 – 2.101)	0.5372	0.726 (0.332 – 1.586)	0.2346
Speak only or mostly non-English	Ref		Ref		Ref	
Marital Status						
Married of living with partner	0.826 (0.363 – 1.880)	0.6421	0.855 (0.386 – 1.893)	0.6940	0.764 (0.378 – 1.541)	0.4439
Not married or not living with partner	Ref		Ref		Ref	
Health Insurance						
Uninsured	0.844 (0.313 – 2.278)	0.7334	0.688 (0.254 – 1.861)	0.4535	0.629 (0.239 – 1.652)	0.3387
Insured	Ref		Ref		Ref	
Routine place for healthcare						
Yes	Ref		Ref		Ref	
No	0.194 (0.067 – 0.560)	0.0032*	0.542 (0.279 – 1.050)	0.0688	0.787 (0.423 -1.467)	0.4439

CI-Confidence Intervals. OR-odds ratio Ref-Reference
Note: The OR reflects the ratio of the probability of being in one of the diabetes status categories relative to the baseline/reference variable category of “Undiagnosed Diabetes”.

Model #3: Clinical variables (unadjusted)

The third model included the clinical variables: BMI status and sleep level as independent, predictor variables. There were statistically significant predictors of diabetes status.

When comparing those who had overweight/obese BMI to normal BMI, they were 0.4 times more likely to have no diabetes/prediabetes than undiagnosed diabetes (p=0.0119), OR=0.405 (CI: 0.202 – 0.812)

Higher level of sleep duration was associated with lower diabetes status compared to those who had normal sleep. Those who had a high level of sleep (>9 hours) compared to those who had normal level (7-9 hours) were 0.2 times more likely to have prediabetes than undiagnosed diabetes (p=0.0214), OR: 0.227 (CI: 0.065 – 0.795). Additionally, those who had high level sleep compared to those who had normal level sleep were 0.2 times more likely to have no diabetes/prediabetes than undiagnosed diabetes (p=0.0055), OR: 0.190 (CI:0.060 – 0.598).

Table 22: Multinomial Logistic Regression Model#3 of Clinical Indicators (Unadjusted)

Independent Variables	Diagnosed Diabetes		Prediabetes		Normal	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Obesity						
Overweight/obese BMI≥23	1.311 (0.500 – 3.434)	0.5746	1.119 (0.558 – 2.245)	0.7464	0.405 (0.202 – 0.812)	0.0119*
Normal BMI<23	Ref		Ref		Ref	
Sleep Duration						
Low: <7hours	0.782 (0.403 – 1.518)	0.4603	0.889 (0.436 – 1.811)	0.7408	0.840 (0.434 – 1.623)	0.5959
Normal: 7-9 hours	Ref		Ref		Ref	
High: >9 hours	0.373 (0.111 – 1.257)	0.1090	0.227 (0.065 – 0.795)	0.0214*	0.190 (0.060 – 0.598)	0.0055*

CI-Confidence Intervals. OR-odds ratio Ref-Reference
Note: The OR reflects the ratio of the probability of being in one of the diabetes status categories relative to the baseline/reference variable category of "Undiagnosed Diabetes".
* denotes statistical significance

Model #4: Final model with Social Determinants of Health and Clinical variables

The final, unadjusted model included that previously demonstrated statistical significance such as education, regular healthcare provider, overweight/obese BMI, and sleep levels combined with potential confounders such as nativity and marital status.

Education, having a regular healthcare provider, BMI, and sleep duration were the only significant predictors of diabetes status (i.e., undiagnosed diabetes, diagnosed diabetes, prediabetes, no diabetes/prediabetes).

Those whose educational attainment was college graduate or above compared to high school graduates were 3.2 times more likely to have no diabetes/prediabetes than undiagnosed diabetes (p=0.0056), OR: 3.157 (CI: 1.423 – 7.005). Those whose educational attainment was less than high school compared to high school graduates were 2.3 times more likely to have diagnosed diabetes than undiagnosed diabetes (p=0.0336), OR: 2.331 (CI: 1.071 – 5.074).

Those who did not have a had a regular healthcare provider were 0.5 times more likely than those who did not have a regular healthcare provider to have prediabetes than undiagnosed diabetes (p=0.0080), OR: 0.479 (CI:0.281 – 0.818). Those who did not have regular healthcare provider were 0.2 times more likely than those who had a regular healthcare provider to have diagnosed diabetes than undiagnosed diabetes (p=0.0004), OR: 0.158 (CI:0.059 – 0.422).

When comparing those who had overweight/obese BMI to normal BMI, they were 0.4 times more likely to have no diabetes/prediabetes than undiagnosed diabetes (p=0.0146), OR=0.409 (CI: 0.202 – 0.831) .

Higher level of sleep duration was associated with lower diabetes status compared to those who had normal sleep. Those who had a high level of sleep (>9 hours) compared to those who had normal level (7-9 hours) were 0.2 times more likely to have prediabetes than undiagnosed diabetes (p=0.0231), OR: 0.214 (CI: 0.057 – 0.802). Additionally, those who had high level sleep compared to those who had normal level sleep were 0.2 times more likely to have no diabetes/prediabetes than undiagnosed diabetes (p=0.0168), OR: 0.196 (CI: 0.052 – 0.735)

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Table 23: Multinomial Logistic Regression Model #4 Final Model (Unadjusted)

Independent Variables	Diagnosed Diabetes		Prediabetes		Normal	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Nativity						
U.S.-born	Ref		Ref		Ref	
Foreign-born	0.552 (0.110 – 2.775)	0.4627	0.598 (0.146 – 2.449)	0.4665	0.287 (0.067 – 1.235)	0.0919
Education						
Less than high school	2.331 (1.071 – 5.074)	0.0336*	1.884 (0.703 – 5.047)	0.2022	1.067 (0.408 – 2.794)	0.8920
High school graduate	Ref		Ref		Ref	
Some college or AAS	1.475 (0.478 – 4.554)	0.4909	1.983 (0.759 – 5.180)	0.1579	2.077 (0.812 – 5.314)	0.1241
College graduate or above	1.564 (0.668 – 3.662)	0.2955	2.046 (0.926 – 4.520)	0.0756	3.157 (1.423 – 7.005)	0.0056*
Marital Status						
Married of living with partner	0.697 (0.319 – 1.524)	0.3583	0.753 (0.355 – 1.599)	0.4529	0.534 (0.266 – 1.073)	0.0768
Not married or not living with partner	Ref		Ref		Ref	
Routine place for healthcare						
Yes	Ref		Ref		Ref	
No	0.158 (0.059 – 0.422)	0.0004*	0.479 (0.281 – 0.818)	0.0080*	0.969 (0.581 – 1.614)	0.9005
Obesity						
Overweight/obese BMI≥23	1.291 (0.489 – 3.409)	0.5986	1.116 (0.559 – 2.230)	0.7505	0.409 (0.202 – 0.831)	0.0146*
Normal BMI<23	Ref		Ref		Ref	
Sleep Duration						
Low: <7hours	0.789 (0.410 – 1.517)	0.4694	0.899 (0.434 – 1.860)	0.6471	0.857 (0.436 – 1.684)	0.7688
Normal: 7-9 hours	Ref		Ref		Ref	
High: >9 hours	0.306 (0.087 – 1.078)	0.0647	0.214 (0.057 – 0.802)	0.0231	0.196 (0.052 – 0.735)	0.0168*

Model #5: Final model with Social Determinants of Health and Clinical variables (Adjusted)

The final model was adjusted with age and gender and included only the variables that demonstrated statistical significance such as education, regular healthcare provider, overweight/obese BMI, and sleep levels.

The odds ratio slightly decreased from the unadjusted model. Those whose educational attainment was college graduate or above compared to high school graduates were 2.5 times more likely to have no diabetes/prediabetes than undiagnosed diabetes (p=0.0148), OR: 2.524 (CI: 1.209 – 5.269). However, college graduate educational attainment and diagnosed diabetes no longer was significant in the adjusted model.

Those who did not have a had a regular healthcare provider were 0.5 times more likely than those who did not have a regular healthcare provider to have prediabetes than undiagnosed diabetes (p=0.0174), OR: 0.460 (CI:0.244 – 0.867). Those who did not have regular healthcare provider were 0.2 times more likely than those who had a regular healthcare provider to have diagnosed diabetes than undiagnosed diabetes (p=0.0017), OR: 0.188 (CI:0.069 – 0.516).

When comparing those who had overweight/obese BMI to normal BMI, they were 0.4 times more likely to have no diabetes/prediabetes than undiagnosed diabetes (p=0.0158), OR=0.426 (CI: 0.214 – 0.845).

Higher level of sleep duration was associated with lower diabetes status compared to those who had normal sleep. Those who had a high level of sleep (>9 hours) compared to those who had normal level (7-9 hours) were 0.2 times more likely to have prediabetes than undiagnosed diabetes (p=0.0261), OR: 0.225 (CI: 0.061 – 0.831). Additionally, those who had high level sleep compared to those who had normal level sleep were 0.2 times more likely to have no diabetes/prediabetes than undiagnosed diabetes (p=0.0190), OR: 0.223 (CI: 0.064 – 0.772).

Overall, the final model did not change significantly with the adjustment of age and gender. The only variable that was slightly affected was education.

Table 24: Multinomial Logistic Regression Model #5 Final Model
(Adjusted for Age and Gender)

Independent Variables	Diagnosed Diabetes		Prediabetes		Normal	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Education						
Less than high school	2.150 (0.952 – 4.855)	0.0648	2.008 (0.730 – 5.520)	0.1722	1.651 (0.615 – 4.429)	0.3122
High school graduate	Ref		Ref		Ref	
Some college or AAS	1.620 (0.540 – 4.858)	0.3811	1.973 (0.797)	0.1384	1.781 (0.761 – 4.166)	0.1783
College graduate or above	1.736 (0746 – 4.041)	0.1954	1.991 (0.916 – 4.329)	0.0809	2.524 (1.209 – 5.269)	0.0148*
Routine place for healthcare						
Yes	Ref		Ref		Ref	
No	0.188 (0.069 – 0.516)	0.0017*	0.460 (0.244 – 0.867)	0.0174*	0.672 (0.351 – 1.289)	0.2260
Obesity						
Overweight/obese BMI≥23	1.380 (0.530 – 3.591)	0.5011	1.149 (0.569 – 2.319)	0.6935	0.426 (0.214 – 0.845)	0.0158*
Normal BMI<23	Ref		Ref		Ref	
Sleep Duration						
Low: <7hours	0.792 (0.420 – 1.495)	0.4646	0.922 (0.451 – 1.884)	0.8203	1.038 (0.527 – 2.045)	0.9118
Normal: 7-9 hours	Ref		Ref		Ref	
High: >9 hours	0.287 (0.081 – 1.010)	0.0517	0.225 (0.061 – 0.831)	0.0261*	0.223 (0.064 – 0.772)	0.0190*

Chapter V.
SUMMARY OF FINDINGS AND DISCUSSION

Prevalence of Diabetes in Asians: Foreign-born vs. U.S.-born

In the Asian-American population studied, the overall diabetes prevalence of 10.2% was higher than previous estimates of 8% for Asian Americans. When stratifying by nativity, marked differences in prevalence were observed in diabetes—both diagnosed and undiagnosed—as well as prediabetes. Foreign-born Asians had two times greater prevalence of diagnosed diabetes and prediabetes and nearly four times greater of undiagnosed diabetes (23.8% vs. 12.7%) when compared to their U.S.-born counterparts. The proportion of diabetes that was undiagnosed was also two times higher in foreign-born Asian-Americans (26.4%) compared to 13.6% amongst U.S.-born Asian Americans.

Factors Associated with Undiagnosed Diabetes and Prediabetes

Differences in demographic characteristics were seen between those foreign-born and U.S.-born. Foreign-born Asian-Americans had a higher mean age, more likely to be married or living with a partner (75.0% vs. 45.0%), and more likely to speak a non-English language (62.0% vs. 9.7%).

The gender composition and having health insurance was comparable between the two sub-populations. Interestingly, an extremely high percentage of both U.S.-born Asians and foreign-born Asians had health insurance (~84.0%).

Role of Social Determinants

Of the Social Determinants of Health studied, the chi square test showed associations between nativity (p<.001), language spoken proxy for acculturation (p=0.010), education (p<.001), marital status (p=0.001), poverty (p=0.009), having a regular healthcare provider (p<.001) with the 4-category diabetes status (i.e., undiagnosed diabetes, diagnosed diabetes, prediabetes, normal) variable.

An income-to-poverty ratio of <1.0 which is equivalent of 100% below poverty level affected ~14.0% of Asians regardless of nativity.

However, educational attainment was higher amongst U.S.-born compared to those who were foreign-born (90.3% vs. 72.0%). U.S.-born Asians (90.6%) have higher educational attainment with some college or above compared to 71.7% of foreign-born Asians.
28.3% of Foreign-born Asians are HS graduates or less compared to 9.4% of U.S.-born

Although the majority of Asians (80.4%) had a regular healthcare provider, U.S.-born had a higher percentage of not having a routine place to go for healthcare at 27.5% (57/207) compared to those who are foreign-born 18.2% (215/1184).

Even when stratifying by nativity, overweight/obese individuals remained comparable at ~63% while the mean BMI remained the same at $\bar{x}$ = ~25.

Asians had a higher HbA1c mean $\bar{x}$=5.7, SE=0.03 (CI: 5.36 to 5.48) compared U.S.-born Asians $\bar{x}$=5.4, SE=0.04 (CI: 5.66 to 5.81). Of total Asians, 10.1% have diabetes-level HbA1c, 25.3% have prediabetes-level HbA1c, and 64.6% have normal HbA1c. Foreign-born have higher percentage of diabetes (11.1%) and prediabetes-level HbA1c (26.8%) compared to U.S.-born Asians 3.8%. and 16.4%, respectively. More alarmingly, Asian-Americans with undiagnosed diabetes had a higher mean HbA1c $\bar{x}$=7.6, SE=0.17 (CI:7.25 to 7.92) compared to those with diagnosed diabetes $\bar{x}$=7.2, SE=0.12 (6.94 to 7.44).

Those with undiagnosed diabetes were more likely to be foreign-born (95.7%), 40 years and older (83.3%), married or living with a partner, (80.3%), and 67.6% spoke mostly a foreign language—a measure of acculturation. Although undiagnosed diabetes is generally prevalent in populations with lower socio-economic status and minority populations. Amongst Asians, however, poverty and uninsured health status was lower and insignificant. According to U.S. national estimates of diabetes prevalence was higher in men than women, (36.6% vs. 23.9%), respectively; however, the gender composition was comparable amongst Asian Americans.[4]

Education, acculturation, and having a healthcare provider were factors found to be either significantly associated with and/or a predictor of undiagnosed diabetes and prediabetes.

This shows an opportunity for healthcare providers to tailor their communications for the appropriate cultural, linguistic, and health literacy level. Those who mostly spoke a foreign language (proxy of acculturation) was found to be associated with undiagnosed diabetes and prediabetes. Ledford et al. studied the influence of race on key dimensions of diabetes knowledge and awareness, health literacy, severity of diabetes, and duration of diabetes by comparing two sites in different states within a health system. The study discovered that Asian-Americans were less likely to have diabetes knowledge and awareness as well as the duration of diabetes. There were regional differences in understanding the severity of diabetes.[127]

A study by King et al. found that barriers in the effective translation of the diabetes resources, namely the Diabetes Prevention Program, for the various Asian languages. The study also found other challenges such as cultural beliefs, nutrition, and social support. In addition, Asians also relied on "self-care" through complementary alternative medicine and "traditional medicine" in combination with western medicine.[128]

National Academies of Medicine (IOM) drafted document proposing SDOH capture for Stage 3 meaningful use EHRs (Appendix). The American Medical Association (AMA) in collaboration with United Health Care insurance company has proposed ICD-10 codes specifically to capture social determinants of health for documentation of "referrals of social services". If approved, the addendum will go into effect on October 1, 2020.[129]

Risk Perception and Awareness of Diabetes Risk Factors

Cultural nuances in diabetes risk perception can yield valuable insight into addressing diabetes prevention needs. In Singapore, a small qualitative study found 4 key themes in those managing diabetes: 1) genetic predisposition and fatalism, 2) difficulty of management, 3) lack of knowledge about diabetes, and 4) need for medical provider's guidance and intervention. [130]

Knowledge and awareness of diabetes risk was lower in minorities and those of lower socioeconomic status. Lower risk perception was significantly associated with diabetes prevention and receipt of preventive screening.[44, 45] This concurs with the ~90% of Americans who do not know they have prediabetes.

Prediabetes is a risk factor for diabetes and an optimal time for intervention to prevent the onset of diabetes. However, lack of routine screening and early intervention may exacerbate the condition.

Interventions for Population Health Management and Public Health

Given that medical providers use the United States Preventive Task Force (USPTF) guidelines to screen asymptomatic populations, general risk factors (i.e., obesity) may not be suitable for measuring risk amongst Asians.

When comparing those with less than high school education, the prevalence of diabetes amongst U.S. adults was higher than Asians (12.6% vs. ~3.9%). However, diabetes prevalence was comparable to U.S. adults amongst those attaining higher education (7.9% vs. 7.2%).[4]

Based on this study and previous studies, body mass index (BMI)—even with the lowered Asian overweight/obese BMI cutoff of 23—is not an accurate risk factor or predictor of diabetes. Therefore, alternative risk factors and objective measurements must be evaluated to address diabetes prevention in an asymptomatic population. A need for routine preventive screenings using HbA1c and establishing a baseline measurement will aid in tracking the trajectory and trend results leading to earlier prediabetes and diabetes diagnoses.

Diabetes Diagnosis: Tests and Variability

Although HbA1c is recommended by the ADA to screen for diabetes, other tests associated with diabetes diagnosis have been documented to show varying levels of predictive accuracy across ethnic subgroups. In a study of Asian-American Indians, the HbA1c and Fasting Plasma Glucose (FPG) of accurately screening for diabetes.[131] Therefore, ethic differences have been well documented to affect disease risk estimates.[132]

Other than BMI and HbA1c screenings, the relationship between sleep duration and diabetes is well-established. Although a longitudinal study in Japan showed shorter sleep duration to the progression to diabetes, this has yet to be studied amongst Asian Americans.[133] In this study, higher sleep duration was a predictor of no diabetes/prediabetes compared to undiagnosed diabetes. As a self-reported measure, this can be a way to measure diabetes risk.

Cultural Factors: Traditional Medicine and Perception of Clinical Providers

Among the confounders to healthcare seeking patterns include the use of traditional medicine (TM) and complementary alternative medicine (CAM). Globally, the World Health Organization (WHO) reported its highest use in India (11.7%) vs. China (<3%). In U.S., a study using the National Health Interview Survey (NHIS) data estimated that 16% of Asian Americans used CAM or TM. Mind/body therapies were used primarily by Asian Indians (31%) than by Chinese (21%) and Filipinos (22%) while traditional medicine was used by Chinese (32%), Filipinos (26%), and Asian Indians (19%).[134]

Asian Americans were less likely to report that their doctors discussed mental health or lifestyle modifications with them. They reported their doctors lack understanding of their culture and values. Furthermore, they reported too little time spent with their provider during a visit, felt ignored by provider with lack of listening or allowing patients to participate in care planning.[135]

Public Health Informatics

Currently, among government-wide surveillance databases, diabetes registries exist at the state and local city levels. However, there is less known about prediabetes and those at risk to target prevention efforts to promote strategic, opportunistic screenings. Issues of data interoperability and sharing as well as documentation failure leads to fragmented electronic health records and appropriate identification.

Health policy, public and population health indicators and MD guidelines have yet to be explored on the earliest possible detection and screening of diabetes and prediabetes and whether this is a cost-savings approach to care. Inclusion in other measures of meaningful use and Healthcare Effectiveness Data and Information Set (HEDIS)—collected by the National Committee for Quality Assurance (NCQA) from insurance companies—can potentially set forth a goal to encourage screening. However, the question of interventions to provide patients to promote self-efficacy and management of their lifestyles in the confines of their social determinants and extrinsic/external environments will need to be studied.

Diabetes prevention interventions including the NDPP model of education have yet to explore the timeliness of screening (prediabetes diagnosis by MD needed) and further implications of

technology platforms and cell phone apps to deliver content to underserved communities where cell phones / smart phone usage may be less due to tech literacy, cost of data, etc.

The final multinomial logistic regression model in this study—adjusted with age and gender—included only the variables that demonstrated statistical significance such as education, regular healthcare provider, overweight/obese BMI, and sleep levels. However, the two social determinants of health variables that were predictor were predictors of either undiagnosed diabetes or prediabetes were education and having a regular medical provider.

Chapter VI.
LIMITATIONS AND CONCLUSIONS

LIMITATIONS

There are six limitations to this study. The first limitation, although there was an oversampling of the Asian population for the NHANES study, the overall subsample of those with undiagnosed diabetes was relatively small. The status of whether diabetes was defined as “diagnosed” or “undiagnosed” was based on a self-report. Further, there was no confirmatory test to assess whether the initial HbA1c test was accurate in diagnosing diabetes. The second limitation was the inability to differentiate between type-1 diabetes and type-2 diabetes. In addition, there are several studies finding that HbA1c may not be a sensitive measure for certain Asian ethnic subgroups. Due to protecting the anonymity of subjects participating in NHANES, data were not publicly available to stratify by ethnic subgroups and geographic differences.

The fourth limitation was missing data which may impact the overall precision in estimates as well as potential selection bias due to exclusion. Several variables which may have enriched this study were either unavailable across all cycles (e.g., OGTT, FPG, dietary, etc.) or had >20% of missing data (e.g., family history, medication, dietary supplements, physical activity).

The fifth limitation was not knowing the HbA1c, BMI, and sleep duration at the time of diabetes diagnosis for those who were in the diagnosed diabetes category. The lower means of these risk factors may have resulted from an appropriate intervention—whether lifestyle changes or medication—resulting in effective management and control of their HbA1c.

Lastly, due to the cross-sectional design, there was no longitudinal data to show the progression of those who had undiagnosed diabetes to later be diagnosed by their medical providers.

Mental Health

Depression, a known risk factor to diabetes, was extremely low compared to the U.S. national prevalence of 7.1% for adults ages 18+. It is well established in the literature that depression rates may be lower amongst Asians due to the cultural and social stigma for seeking help for

mental disorders, resulting in an underdiagnosis of depression.[136] Therefore, this risk factor was excluded as a predictor variable from the final data analyses.

CONCLUSION

Diabetes is a complex, costly, and debilitating condition that can pose a significant threat to both health and quality of life. These risks and economic burden can potentially be reduced through opportunistic screening and early intervention. Knowledge of the factors associated with undiagnosed diabetes and prediabetes can help target the appropriate population and assist with tailoring their intervention. Social determinants of health and socio-economic status (SES) factors can assist with identifying key characteristics of an asymptomatic population such as Asians who have undiagnosed diabetes or prediabetes yet do not have a high BMI. Differences in key characteristics such as nativity, age, education, marital status, acculturation, regular healthcare provider and sleep duration are potential factors that need to be considered when developing interventions or preventive strategies for Asian Americans were associated with undiagnosed diabetes and prediabetes when further stratified. Findings can promote the collection of these data through insurer, provider and health system's EHR as well as public health surveillance systems. These factors need to be explored further to understand the contributors and influential factors aimed to help develop diabetes prevention strategies, programs, and surveillance of Asian Americans. These findings can also increase a primary care provider's awareness of looking at other attributes other than BMI when initiating diabetes screenings.

Although patients at risk for diabetes can benefit from early diagnosis, disease awareness is the first step towards behavior modification. This is particularly important when thinking about how challenging it is to affect lifestyle changes such as diet and exercise. Of distinction, is that adequate sleep (not too much or too little), is a health behavior that is understudied and referenced with other modifiable lifestyle behaviors.

Future research will need to explore the precision of diabetes diagnostic methods (i.e., HbA1c, OGTT, and PFG) among ethnic subgroups. In addition, the impact of collecting baseline HbA1c and subsequent testing to establish a trajectory may yield important information on the best time

for a primary care provider to intervene. Moreover, additional research on specific ethnic subgroups will yield a more customized approach to care.

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APPENDIX A. Social and Behavioral Domains and Measures:
Recommendations by the Health and Medicine Division (HMD) of the National Academies of Sciences (formerly known as the Institute of Medicine)[6]

Social and Behavioral Domains and Measures.

Domain	Measure*	Frequency
Race or ethnic group†	1. What is your race? 2. Are you of Hispanic, Latino, or Spanish origin?	At entry
Education	1. What is the highest level of school you have completed? 2. What is the highest degree you earned?	At entry
Financial-resource strain	How hard is it for you to pay for the very basics like food, housing, medical care, and heat?	Screen and follow up
Stress	Stress means a situation in which a person feels tense, restless, nervous, or anxious, or is unable to sleep at night because his or her mind is troubled all the time. Do you feel this kind of stress these days?	Screen and follow up
Depression	Over the past 2 weeks, how often have you been bothered by 1. Little interest or pleasure in doing things? 2. Feeling down, depressed, or hopeless?	Screen and follow up
Physical activity	1. On average, how many days per week do you engage in moderate to strenuous exercise (like walking fast, running, jogging, dancing, swimming, biking, or other activities that cause a light or heavy sweat)? 2. On average, how many minutes do you engage in exercise at this level?	Screen and follow up
Tobacco use†	1. Have you smoked at least 100 cigarettes in your entire life? If yes: 2. Do you now smoke cigarettes every day, some days, or not at all?	Screen and follow up
Alcohol use†	1. How often do you have a drink containing alcohol? 2. How many standard drinks containing alcohol do you have on a typical day? 3. How often do you have six or more drinks on one occasion?	Screen and follow up
Social connection or isolation	1. In a typical week, how many times do you talk on the telephone with family, friends, or neighbors? 2. How often do you get together with friends or relatives? 3. How often do you attend church or religious services? 4. How often do you attend meetings of the clubs or organizations you belong to?	Screen and follow up
Intimate-partner violence	1. Within the last year, have you been humiliated or emotionally abused in other ways by your partner or ex-partner? 2. Within the last year, have you been afraid of your partner or ex-partner? 3. Within the last year, have you been raped or forced to have any kind of sexual activity by your partner or ex-partner? 4. Within the last year, have you been kicked, hit, slapped, or otherwise physically hurt by your partner or ex-partner?	Screen and follow up
Residential address†	What is your current address?	Verify at every visit
Census-tract median income	Geocoded	Update on address change

* Wording is taken from existing measures; standard response categories are available. Psychometric testing of the full panel, including ordering and wording, has not yet been conducted.
† This domain is already widely included in clinical practice.

Source: Adler, N. E., & Stead, W. W. (2015). Patients in context--EHR capture of social and behavioral determinants of health. N Engl J Med, 372(8), 698-701. doi:10.1056/NEJMp1413945.

APPENDIX B. Rutgers IRB Exemption Approval Letter

From: eIRB@ored.rutgers.edu
Sent: Thursday, December 7, 2017 2:40 PM
To: Euny Lee
Cc: bonhomvr@rutgers.edu
Subject: Rutgers University eIRB: Study Approved

RUTGERS eIRB

Arts & Sciences IRB - New Brunswick
335 George Street
Suite 3100, 3rd Floor
New Brunswick, NJ 08901
Phone: 732-235-2866

Health Sciences IRB - New Brunswick/Piscataway
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Health Sciences IRB - Newark
65 Bergen Street
Suite 511, 5th Floor
Newark, NJ 07107
Phone: 973-972-3608

DHHS Federal Wide Assurance Identifier: FWA00003913
IRB Chair Person: Cheryl Kennedy
IRB Director: Carlotta Rodriguez
Effective Date: 12/7/2017
Approval Date: 12/4/2017

eIRB Notice of Approval for Initial Submission # Pro20170001940

STUDY PROFILE

Study ID: Pro20170001940
Title: Factors Related to Undiagnosed Diabetes in Asian Americans

Principal Investigator:	Euny Lee
Risk Determination:	Minimal Risk
Review Type:	Non-Human Determination

CURRENT SUBMISSION STATUS

Submission Type:	Request for Determination of Non-Human Subject	**Submission Status:**	Approved

	Research (including Quality Assurance/Quality Improvement Only)				
Approval Date:	12/4/2017				
Pregnancy Code:	Not Applicable	**Pediatric Code:**	Not Applicable	**Prisoner Code:**	Not Applicable

ALL APPROVED INVESTIGATOR(S) MUST COMPLY WITH THE FOLLOWING:

1. Conduct the research in accordance with the protocol, applicable laws and regulations, and the principles of research ethics as set forth in the Belmont Report.
2. **Amendments/Modifications/Revisions**: If you wish to change any aspect of this study, including but not limited to, study procedures, consent form(s), investigators, advertisements, the protocol document, investigator drug brochure, or accrual goals, you are required to obtain IRB review and approval prior to implementation of these changes unless necessary to eliminate apparent immediate hazards to subjects.
3. **Unanticipated Problems**: Unanticipated problems involving risk to subjects or others must be reported to the IRB Office (45 CFR 46, 21 CFR 312, 812) as required, in the appropriate time as specified in the attachment online at: https://orra.rutgers.edu/hspp
4. **Protocol Deviations and Violations**: Deviations from/violations of the approved study protocol must be reported to the IRB Office (45 CFR 46, 21 CFR 312, 812) as required, in the appropriate time as specified in the attachment online at: https://orra.rutgers.edu/hspp
5. **Completion of Study:** Notify the IRB when your study has been stopped for any reason. Neither study closure by the sponsor or the investigator removes the obligation for submission of a timely final report.
6. The Investigator(s) did not participate in the review, discussion, or vote of this protocol.

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Study.PI Name:
Study.Co-Investigators: