Metabolic factors, genetics factors, and lifestyle in relation to diabetes: A cross-sectional study using NHANES 2017-March 2020 pre-pandemic

Ziyan Zhang*

Xi'an-jiaotong Liverpoor university, Suzhou, China

*Corresponding author: Ziyan.zhang19@student.xjtlu.edu.cn

Keywords: Diabetes Mellitus, Cross-sectional Study, National health and nutrition examination survey, Lifestyle, Metabolic Factors, Genetics factors, Adult aged over 20 years old.

Abstract: Background Diabetes mellitus (DM) is a disorder characterized by uncontrollably high blood glucose levels. Diabetes rates continue to climb as populations in some countries. The factors leading to diabetes are varied. Meanwhile, diabetes will lead to severe symptoms and is Highly associated with other diseases. The purpose of this study is to determine the prevalence of diabetes and its related factors in a representative sample of U.S. individuals aged 20 and above based on lifestyle, genetic factors, and metabolic factors.**Method** This cross-sectional study was conducted based on NHANES 2017-March 2020 pre-pandemic data. Criteria of diabetes were assessed by fasting plasma glucose and hemoglobin A1c. 12 independent variables were selected in the form of Demographics Data, Examination Data, Laboratory Data, and Questionnaire Data. Participants' baseline characteristics were summarized and then bivariable and multivariable binary logistic regression was performed to detect related factors using R version 4.1.2. A p-value of <0.05 was considered statistically significant.**Result** 2854 participants were involved in this study with 503 of them had diabetes. Middle-aged and elderly people are the population at high risk of diabetes. Mexican American are more likely to suffer from diabetes compare with Non-Hispanic White (AOR = 1.69; 95%CI:1.78,2.44). Low Cholesterol - High - Density Lipoprotein (HDL <40 mg/dL) (AOR = 1.69; 95%CI: 1.27,2.23), Close relative had diabetes (AOR = 1.69; 95%CI: 1.33,2.16), Insulin resistance (AOR = 5.37; 95%CI: 3.94,7.42), and Physical inactivity (AOR = 2.70; 95%CI: 2.13,3.48) were associated with diabetes significantly.**Conclusion** The prevalence of diabetes increases rapidly with age and some races are easier to be affected. HDL level, Close relative had diabetes, physical inactivity, and Insulin resistance were significantly associated with diabetes. People should visit a hospital on a frequent basis for checkups and maintain a healthy lifestyle.

1. Introduction

Diabetes mellitus (DM) is a condition in which blood glucose levels are uncontrollably high. Type 1 and 2 diabetes mellitus are the two most common subtypes, each having its own pathogenesis, presentation, and therapy. T1DM presents in children or adolescents, while T2DM is thought to affect middle-aged and older individuals who have long-term hyperglycemia as a result of poor lifestyle and nutritional choices [1]. It's worth noting that half of those surveyed (50.1%) were ignorant of their condition [2].

Diabetes affects approximately 8.9% of Europeans aged 20 to 79 as reported in 2019, [3] and 14.8% of Americans suffer from diabetes in 2021 National Health Statistics Reports. [4] According to World Health Organization (WHO), [5] Diabetes was the tenth largest cause of mortality in 2019, with an estimated 1.5 million fatalities caused directly by the disease. The factors leading to diabetes are varied, Obesity is a well-known risk factor for type 2 diabetes mellitus (T2DM) and is frequently associated with the disease. [6] Unhealthy lifestyle factors such as lack of physical exercise, sedentary behavior, and poor dieting are linked to the development of type 2 diabetes mellitus as well. [7] Low HDL cholesterol levels are consistently linked to an increased risk of type 2 diabetes in Haase et al's observational studies.[8] Type 2 diabetes has a greater link to family history and ancestry, and twin

studies have revealed that genetics plays a significant influence in type 2 diabetes development. [9] Type 2 diabetes in youth has been recognized as more frequent in indigenous minority populations of North America and accounts for 30 percent of new cases of diabetes.[10] In addition, insulin resistance is the most common cause of type 2 diabetes. [11] Meanwhile, diabetes will lead to severe symptoms and is Highly associated with other diseases. Patients in West Virginia's rural areas are at significant risk of atraumatic amputation.[12] Nearly two-thirds of people with T2DM also suffer from hypertension and elevated arterial blood pressure raises the chance of developing diabetes. [6] Sleep disturbances will arise since metabolic disorders and increased levels of glycated hemoglobin are caused by diabetes. [13]

Increased use of higher-cost new medicines, under the circumstances of an aging population and an increase in the incidence of type 2 diabetes, will place a considerable financial burden on the state in the future. [14] Because the pathogenesis of diabetes is complex and will bring great pain to people's bodies and minds. It is crucial to make prevention and timely treatment. The purpose of this study is to access the prevalence of diabetes and its associated factors from lifestyle, genetic factors, and metabolic factors in a representative sample of U.S. adults aged 20 and over.

2. Method

2.1. Study population

The National Health and Nutrition Examination Survey (NHANES) is a series of studies aimed at determining the health and nutritional status of Americans, including adults and children. National Center for Health Statistics (NCHS) collected the data from 30 locations across the united states. Therefore, the national representative could be guaranteed. The survey data are released once every two years. In our study, the datasets were obtained from NHANES 2017-March 2020 pre-pandemic data [15], which is the combination of NHANES 2017-2018 and 2019-March 2020 data. The types of data used in this article include Demographics Data, Examination Data, Laboratory Data, and Questionnaire Data. In addition, people in pregnancy status were not involved in the study population. Due to the fact that required information was stored in different parts of the NHANES program, specific variables columns were projected and joined into a new table according to their sole Respondent sequence number (SEQN). Considering that some variables in some respondents were missing or respondents refused to provide information in the questionnaire stage. The final sample contained the participants who had complete data in all variables. After filtrating the data step by step. The sample size was set at 2854(N= 2854)

2.2 Identification of diabetes

According to National Health Statistics Reports [4], Fasting plasma glucose and hemoglobin A1c were measured in the venous blood samples of participants using standardized protocols, then collected in the mobile examination center (MEC). Either participant had a fasting plasma glucose greater than or equal to 126 mg/dL or had a hemoglobin A1c greater than or equal to 6.5% would be defined as diabetes, which are the Criteria from the American Diabetes Association (ADA)[9].

2.2 Covariates

In this study, Gender, Age, Race, and income level were selected as Covariates to control the potential confounding effects. Age was divided into four parts (20-35, 36 - 50, 51-65, >66) based on the sample distribution and income level was categorized as poor (ratio of family income to poverty <=1) and non-poor (ratio of family income to poverty >1). The detailed information on race has been shown in table 1. All the Covariates could be acquired from NHANES 2017-March 2020 Pre-Pandemic Demographics Data.

2.4 Selection of independent variable

7 common factors were chosen from metabolic (body mass, insulin resistance, blood pressure conditions, Cholesterol - High - Density Lipoprotein concentration) aspect, lifestyle aspect (diet habit,

physical inactivity, sleep time), and 1 genetic factor (relative have diabetes) were involved in this study. The selection criterion is based on reviewing variables from previously published articles [8-9,16] that have an association with diabetes more or less and universally exist in human society. For Detailed data collection operations, please refer to NHANES 2017-2018 Procedure Manuals [8]and NHANES 2019-2020 Procedure Manuals [17].

2.5 Data processing and classification

Body mass index (BMI), fasting serum insulin (mU/l), Blood Pressure, and HDL level has been collected from NHANES 2017-March 2020 Pre-Pandemic laboratory and examination Data. Where Body mass index (BMI) is an internationally used measure of fat, thinness, and health. A healthy weight range comes with a BMI value between 18.5 and 25, with less than 18.5 being underweight, over 25 being overweight and more than 30 obese. fasting serum insulin (mU/l) has been used to calculate insulin resistance score (HOMA-IR) using a specific formula: fasting plasma glucose (mmol/l) times fasting serum insulin (mU/l) divided by 22.5 given by ADA. [9] A HOMA-IR index of more than 2.5 was used to define insulin resistance. Cholesterol - High - Density Lipoprotein (HDL) was categorized as <=40, 40-60, >=60. Blood Pressure (Oscillometric Measurement), which is the standard for determining whether respondents had high blood pressure. Here, the values of diastolic and systolic blood pressure were taken from the mean of three detections. Standard from American Heart Association [18] was used to measure the blood pressure level, please refer to the criterion in appendix 1. Another four variables have been extracted from NHANES 2017-March 2020 Pre-Pandemic questionnaire data. Average sleep time was computed using the formula: sleep hours in weekdays * 5/7 + sleep hours in weekdays * 2/7. It is classified as less than 6 hours,6-9 hours, and more than 9 hours per day. Both Close relatives had diabetes and physical inactivity have two categories (yes, no) and there is five grade for diet factors (Excellent, very good, Good, Fair, Poor). Respondents were asked several questions by doctors to determine how healthy their diets is.

2.6 Statistical analysis.

Descriptive statistics were used to summarize the baseline characteristics. For continuous variables, participants' baseline characteristics were presented as means with SDs, and for categorical variables, as numbers with proportions. Studnet t-test for continuous variables and the chi-square test for categorical variables were used to examine the differences in baseline characteristics. Logistic regression analysis was used to calculate Both Crude Odds Ratio (COR) and Adjusted Odds Ratio (AOR), Variables with $p \leq 0.20$ were chosen for multivariable logistic regression analysis during bivariable analysis [19]. 95% confidence intervals (CIs) for the association between diabetes and variable. The result of the calculation is reserved for two decimal places and proportions for one decimal. $P < 0.05$ was considered statistically significant. All data were analyzed using R version 4.1.2.

3. Result

3.1Baseline Characteristics

Table 1 summarized the baseline characteristics of the sample by diabetes status. 2854 participants were included in this study, 503(17.6%) of whom had diabetes. The proportion of males (48.9%) was slightly lower than that of females (51.1%). diabetics were older and more obese than non-diabetics. More than half (56.2%) of diabetics had high blood pressure. Insulin resistance and physical inactivity are two factors that are common in diabetics, accounting for 87.4% and 73.0% respectively. From the genetic point of view, almost Two-thirds of the diabetics had a close relative with diabetes. In addition, there exist statistically significant differences in participants with different races, average sleep time, household income level, Cholesterol-High-Density Lipoprotein (HDL) level, and diet habits.

Table 1. Characteristics of participants by diabetes status.

	Non-diabetes	Diabetes	Total(N=2854)	P-value
No. of participants	2351(82.4%)	503(17.6%)	2854	
Age				<0.001
20-35	680(28.9%)	19(4.8%)	699(24.5%)	
36-50	596(25.4%)	100(19.9%)	696(24.4%)	
51-65	637(27.1%)	213(45.9%)	850(29.8%)	
66+	438(18.6%)	171(40.0%)	609(21.3%)	
Gender				0.2142
male	1136(48.3%)	259(51.5%)	1395(48.9%)	
female	1215(51.7%)	244(48.5%)	1459(51.1%)	
Race				0.01582
Mexican American	277(11.8%)	83(16.5%)	360(12.6%)	
Other Hispanic	225(9.6%)	53(10.5%)	278(9.7%)	
Non-Hispanic White	880(37.4%)	162(32.2%)	1042(36.5%)	
Non-Hispanic Black	559(23.8%)	132(26.2%)	691(24.2%)	
Non-Hispanic Asian	279(11.9%)	49(9.7%)	328(11.5%)	
Other Race- Including Multi-Racial	131(5.6%)	24(4.8%)	155(5.4%)	
Is insulin resistance	1055(44.9%)	438(87.4%)	1493(52.3%)	<0.001
Average sleep time				<0.001
<= 6 h per day	262(11.4%)	79(15.7%)	341(11.9%)	
6-9 h per day	1659(70.6%)	308(61.2%)	1946(68.2%)	
>=9 h per day	433(18.4%)	116(23.1%)	549(19.2%)	
Physical inactivity	1056(44.9%)	367(73.0%)	1420(49.8)	<0.001
Close relative had diabetes	873(37.1%)	335(66.7%)	1208(42.3%)	<0.001
Diet				<0.001
Excellent	173(7.4%)	21(4.2%)	194(6.8%)	
very good	507(21.6%)	79(15.8%)	586(20.5%)	
Good	922(39.2%)	213(42.3%)	1135(39.8%)	
Fair	589(25.0%)	153(30.4%)	742(26.0%)	
Poor	160(6.8%)	37(7.4%)	197(6.9%)	
Blood pressure level				<0.001
Normal	1123(47.8%)	151(30.0%)	1274(44.6%)	
Elevated	287(12.2%)	69(13.7%)	356(12.5%)	
High blood pressure(stage1)	496(21.1%)	127(25.2%)	623(21.8%)	
High blood pressure(stage2)	445(18.9%)	156(31.0%)	601(21.1%)	
Income level				0.58
Poor	426(18.1%)	97(19.2%)	523(18.3%)	
Non-poor	1925(81.9%)	406(80.7%)	2331(81.7%)	
Fasting glucose, mg/dL	101.30(9.91)	169.79(62.10)	113.37(37.96)	<0.001
Glycohemoglobin,%	5.49(0.39)	7.65(1.78)	5.87(1.17)	<0.001
Fasting serum insulin (mU/l)	12.04(13.88)	25.34(43.27)	14.39(22.67)	<0.001
HOMA-IR index	3.07(3.62)	10.35(17.49)	4.36(8.50)	<0.001
Cholesterol - High - Density Lipoprotein(HDL),mg/dL	54.77(15.87)	47.27(14.17)	53.45(15.84)	<0.001
Systolic blood pressure, mmHg	122.22(17.99)	129.76(20.64)	123.55(18.70)	<0.001
Diastolic blood pressure, mmHg	74.32(11.31)	74.78(11.68)	74.40(11.37)	0.4145
Body mass index, kg/m2	29.28(7.01)	33.36(8.20)	30.00(7.40)	<0.001

The data is expressed as a mean (SD) or a number (n) (percent). Because of rounding, percentages may not add up to 100 percent. p values are based on T-test for continuous variables or $\chi 2$ test for categorical variables.

3.2Factors associated with diabetes

After bivariable analysis, there are 11 variables (gender, age, race, insulin resistance, a close relative had diabetes, blood pressure level, HDL level, average sleep time, diet, BMI index, physical inactivity) exclude income level (COR: 1.08; 95%CI =0.84-1.37; P-value =0.54) become candidates for the final model.

view 20-35 years olds as a reference, The possibility of people aged 36-50years old(AOR=5.43;95% CI=3.27-9.46), people aged 51-65 years old (AOR=11.27; 95% CI=6.91-19.40)and people aged more than 66 years old (AOR=15.53, 95% CI=9.27-27.33) get diabetes increase 5.43,11.27 and 15.53 times respectively. The odds of developing diabetes among people who had Insulin resistance was 5.37 times higher when compared with those without insulin resistance(AOR=5.37; 95% CI=3.94,7.42). If people have Close relatives who had diabetes, they were 1.69 times more likely to be diabetes (AOR=1.69; 95% CI=1.33,2.16). Compared with people with HDL level between 40-60 mg/dL, the odds of people with HDL level > 60 mg/dL was 30% less likely to get diabetes(AOR=0.7; 95% CI=1.27-2.23), but for those who had a HDL level < 40 mg/dL,There was 169% more likely to be diabetics by contrast(AOR=1.69; 95% CI=0.50-0.96). The possibility of people developing diabetes with adequate physical activity was 37% of those who were inactive (AOR=0.37; 95% CI=0.29-0.47). In addition, Mexican-Americans have higher rates of diabetes than non-Hispanic whites (AOR=0.59; 95% CI=0.41-0.85).

However, Blood pressure level, Average sleep time, Diet, and Body mass index were not significantly associated with outcome variables in the final multivariable logistic regression model.

Table.2.Factors assicaited with diabetes

variable	Category	Crude OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Gender	male	1.14(0.94,1.38)	0.197	1.09(0.86,1.39)	0.465
	female	1		1	
Age	20-35	1	<0.001	1	<0.001
	36-50	6.00(3.72,10.22)	<0.001	5.43(3.27, 9.46)	<0.001
	51-65	11.97(7.59,20.00)	<0.001	11.27(6.91,19.40)	<0.001
	66+	13.97(8.79, 23.50)	<0.001	15.53(9.27,27.33)	<0.001
Race					
	Mexican American	1		1	
	Other Hispanic	0.79(0.53,1.15)	0.223	0.67(0.42,1.05)	0.080
	Non-Hispanic White	0.61(0.46,0.83)	0.001	0.59(0.41,0.85)	0.004
	Non-Hispanic Black	0.79(0.58,1.08)	0.132	0.79(0.54,1.15)	0.214
	Non-Hispanic Asian	0.59(0.39,0.86)	0.007	0.81(0.50,1.30)	0.383
	Other Race-Including Multi-Racial	0.61(0.36,0.99)	0.053	0.75(0.41, 1.35)	0.353

Insulin resistance	Yes	8.28(6.35,10.96)	<0.001	5.37(3.94,7.42)	<0.001
	No	1		1	
Close relative had diabetes	Yes	3.38(2.76,4.14)	<0.001	1.69(1.33,2.16)	<0.001
	No	1		1	
Blood pressure level	Normal	1		1	
	Elevated	1.79	<0.001	1.09(0.76,1.58)	0.630
	High blood pressure(stage 1)	1.90	<0.001	1.14(0.84, 1.54)	0.406
	High blood pressure(stage 2)	2.61	<0.001	1.27(0.94,1.71)	0.121
Cholesterol - High - Density Lipoprotein(HDL),mg/dL	40-60	1			
	<40	2.02(1.60 ,2.54)	<0.001	1.69(1.27,2.23)	0.03
	>60	0.45(0.34,0.60)	<0.001	0.70(0.50, 0.96)	<0.001
Average sleep time	6-9 h per day	1		1	
	<= 6 h per day	1.62(1.22,2.14)	<0.001	1.28(0.92,1.77)	0.145
	>=9 h per day	1.44(1.13,1.82)	0.002	1.30(0.98,1.73)	0.066
Diet	Excellent	0.47(0.28, 0.74)	0.002	0.70(0.39,1.21)	0.213
	very good	0.60(0.44, 0.80)	<0.001	0.79(0.78, 1.35)	0.197
	Good	0.89(0.71, 1.12)	0.322	1.03(0.55,1.13)	0.855
	Fair	1		1	
	Poor	0.89(0.59, 1.32)	0.568	1.02(0.64, 1.60)	0.944
Body mass index, kg/m2	=18.5-25	1		1	
	<18.5	0.76(0.12, 2.62)	0.718	1.13(0.17,4.38)	0.882
	=25-30	2.23(1.60, 3.14)	<0.001	0.88(0.59,1.31)	0.520
	>=30	4.14(3.06,5.71)	<0.001	1.05(0.70,1.58)	0.818
Physical inactivity	YES	1		1	
	NO	0.30(0.24,0.37)	<0.001	0.37(0.29,0.47)	<0.001

CI: Confidence Interval; 1: Reference

4. Discussion

This cross-sectional study was conducted to evaluate the associated metabolic factors, lifestyle, and genetic factors of diabetes among US adults in recent years (2017-2020 Pre-Pandemic). The result display that in a sample size of 2854 adults, 17.6% had diabetes. This might be slightly different from the real situation due to the detection methods. For example, in Matsunaga, Hurwitz, and Li's study, a diabetes status variable was created based on individuals' replies to diabetes questionnaires. [20]

Apparently, the prevalence of diabetes increases rapidly with age, especially when people are over the age of 51. This is in line with earlier findings. [21] Moreover, the mean (SD) age at diabetes diagnosis is 54.60 ± 9.48 years as reported by Hu et al. [22] Middle-aged and elderly people are still the population at high risk of diabetes.

The risk of diabetes is closely related to insulin resistance in this study. More than 85% of people with diabetes have insulin resistance. Insulin resistance hinders glucose disposal, leading to an increase in beta-cell insulin synthesis and hyperinsulinemia as a compensatory response. [23] Type 2 diabetes is the most common result of insulin resistance since insulin is a key factor in regulating blood sugar (glucose) in the body. [11] Physical activity and Weight loss are two valid methods to reverse Insulin Resistance because they make insulin sensitive. [24]

People who had close relatives had diabetes in the family is easier to suffer from diabetes than normal. The mechanism behind it is not fully understood. [25] It could be that families often share similar living habits and environments, and this is where issues occur [26], or result from genetics, Denton and Fernandez's research found that children in normal weight with a family history of diabetes have higher fasting insulin. [27] It has been known that Individuals from Hispanic populations are at a higher risk of acquiring T2D than those from European populations. [28] This is also the case in our research, the difference between Mexican American and Non-Hispanic White is significant and the 2020 National Diabetes Statistics Report support this point. [29]

Another Metabolic factor that has a significant association with diabetes in this study is HDL level. Generally, the higher the HDL levels, the lower the possibility of developing diabetes. HDL is known to be inversely connected to cardiovascular disease due to its antiatherogenic properties. Diabetes mellitus, however, can cause HDL particles to undergo a variety of structural changes, resulting in major changes in their function. [30]

Finally, people who are Physical inactive have a higher risk of developing diabetes. This is in line with earlier findings from several research. Physical inactivity will generate a series of adverse reactions including high Cardiovascular risk factors and obesity. [31] Regular physical exercise can not only prevent T2DM from developing, but it can also enhance the benefits of anti-diabetic pharmacological therapy, resulting in better glycaemic control. [32]

5. Limitation

Some data in this study were collected in the form of a questionnaire. Although it is easy to acquire and low-cost, its reliability is far from Laboratory data and examination data. Meanwhile, some responders would answer some questions and refuse to answer others in most case, which influence the integrity of data. We have to delete the sample which was short of one or more variables. It is regretful to fail to include more variables in this study such as smoking and drinking since some data in NHANES 2017-March 2020 pre-pandemic cycle had low response rates which would lead to a small sample. Meanwhile, It is a Cross-Sectional Study, some weaknesses are inevitable, including the inability to form a causal inference, study the temporal relationship between outcomes and risk factors, and research is prone to sample bias [33].

6. Conclusions

Current study has presented Logistic regression to identify associated factors from three aspects (metabolic factors, lifestyle, and genetic aspect) based on NHANES 2017-March 2020 pre-pandemic data. The findings from the current study indicate that people with insulin resistance have an extremely

high risk of developing diabetes. Family history of DM and physical inactivity were significantly associated with diabetes. HDL concentration was negatively correlated with the prevalence of diabetes mellitus. In addition, diabetes mellitus presents a distinct age distribution, and some races are more likely to develop diabetes. However, some variables become insignificant when mixed with multiple factors, and the connection of them with diabetes require further studies. Overall, people ought to go to a hospital to check regularly and keep a healthy lifestyle.

References

[1] Sapra A, Bhandari P, Wilhite (Hughes) A. Diabetes Mellitus (Nursing). 2021 Sep 18. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 33760470.

[2] Mahe, G., Brodmann, M., Capodanno, D., Ceriello, A., Cuisset, T., Delgado, V., Espinola-Klein, C., Johnson, T., Sprynger, M., Sattar, N., Schnell, O. and Valensi, P., 2022. Current management and screening of peripheral and coronary artery disease in people with diabetes mellitus in Europe. The PADDIA/CADDIA survey. *Diabetes Research and Clinical Practice*, 184, p.109214.

[3] Elek, P. and Bíró, A., 2021. Regional differences in diabetes across Europe – regression and causal forest analyses. *Economics & Human Biology*, 40, p.100948.

[4] Stierman, B., D, M., P.H, M., Afful, J. and S, M., 2022. National Health and Nutrition Examination Survey 2017–March 2020 Prepandemic Data Files—Development of Files and Prevalence Estimates for Selected Health Outcomes. *National Health Statistics Reports*, [online] 158, p.19. Available at: <https://www.cdc.gov/nchs/data/nhsr/nhsr158-508.pdf> [Accessed 27 January 2022].

[5] Who.int. 2022. *Diabetes*. [online] Available at: <https://www.who.int/news-room/fact-sheets/detail/diabetes> [Accessed 13 February 2022].

[6] Yu, Z., Nan, F., Wang, L., Jiang, H., Chen, W. and Jiang, Y., 2020. Effects of high-protein diet on glycemic control, insulin resistance and blood pressure in type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials. *Clinical Nutrition*, 39(6), pp.1724-1734.

[7] Buss, V., Varnfield, M., Harris, M. and Barr, M., 2021. Validation of a lifestyle-based risk score for type 2 diabetes mellitus in Australian adults. *Preventive Medicine Reports*, 24, p.101647.

[8] Haase, C., Tybjærg-Hansen, A., Nordestgaard, B. and Frikke-Schmidt, R., 2015. HDL Cholesterol and Risk of Type 2 Diabetes: A Mendelian Randomization Study. *Diabetes*, 64(9), pp.3328-3333.

[9] Diabetes.org. 2022. *American Diabetes Association | Research, Education, Advocacy*. [online] Available at: <https://www.diabetes.org/> [Accessed 27 January 2022].

[10] Rosenbloom, A., Joe, J., Young, R. and Winter, W., 1999. Emerging epidemic of type 2 diabetes in youth. *Diabetes Care*, 22(2), pp.345-354.

[11] Freeman AM, Pennings N. Insulin Resistance. 2021 Jul 10. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 29939616.

[12] Danielle Minc, S., Budi, S., Thibault, D., Misra, R., Armstrong, D., Stephen Smith, G. and Marone, L., 2021. Opportunities for diabetes and peripheral artery disease-related lower limb amputation prevention in an Appalachian state: A longitudinal analysis. *Preventive Medicine Reports*, 23, p.101505.

[13] Campos-Romero, S., Barrios Araya, S., Masalan-Apip, M., Guajardo Tobar, V., Arias-Ortiz, N. and Bobadilla-Beiza, L., 2022. Sleep quality in people with type 2 diabetes controlled at the primary level and its association with sociodemographic and clinical characteristics. *Enfermería Clínica (English Edition)*, 32(1), pp.45-53.

[14] Smith, A., Kennedy, C., Clarke, S. and Barry, M., 2022. Utilisation and expenditure on glucose-lowering drugs used for the treatment of type 2 diabetes mellitus in Ireland, a repeated cross-sectional study. *Diabetes Epidemiology and Management*, 5, p.100038.

[15] Wwwn.cdc.gov. 2022. *NHANES Questionnaires, Datasets, and Related Documentation*. [online] Available at: <https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/default.aspx?cycle=2017-2020> [Accessed 26 January 2022].

[16] Wang, T., Zhao, Z., Wang, G., Li, Q., Xu, Y., Li, M., Hu, R., Chen, G., Su, Q., Mu, Y., Tang, X., Yan, L., Qin, G., Wan, Q., Gao, Z., Yu, X., Shen, F., Luo, Z., Qin, Y., Chen, L., Huo, Y., Zeng, T., Chen, L., Ye, Z., Zhang, Y., Liu, C., Wang, Y., Wu, S., Yang, T., Deng, H., Zhao, J., Shi, L., Xu, Y., Xu, M., Chen, Y., Wang, S., Lu, J., Bi, Y., Ning, G. and Wang, W., 2021. Age-related disparities in diabetes risk attributable to modifiable risk factor profiles in Chinese adults: a nationwide, population-based, cohort study. *The Lancet Healthy Longevity*, 2(10), pp.e618-e628.

[17] Wwwn.cdc.gov. 2022. *NHANES 2019-2020 Procedure Manuals*. [online] Available at: <https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/manuals.aspx?BeginYear=2019> [Accessed 1 February 2022].

[18] www.heart.org. 2022. *Understanding Blood Pressure Readings*. [online] Available at: <https://www.heart.org/en/health-topics/high-blood-pressure/understanding-blood-pressure-readings> [Accessed 5 February 2022].

[19] Chanie, E., Dagne, Z., Jimma, M., Eyayu, T., Nebiyu, S., Wondifraw, E., GebreEyesus, F., Yemata, G. and Melkie, A., 2021. The effect of timely initiation of complementary feeding and vitamin A supplementation on acute malnutrition among children aged 6–59 months attending Hamusit Health Centre, Northwest Ethiopia, 2021: A cross-sectional study. *Heliyon*, 7(11), p.e08449.

[20] Matsunaga, M., Hurwitz, E. and Li, D., 2021. Adequate intake of plant protein foods and moderate intake of animal protein foods are inversely associated with C-reactive protein in US adults with diabetes: A cross-sectional study with National Health and Nutrition Examination Survey. *N utrition*, 89, p.111276.

[21] Bonora, E., Cataudella, S., Marchesini, G., Miccoli, R., Vaccaro, O., Fadini, G., Martini, N. and Rossi, E., 2021. Initial treatment of diabetes in Italy. A nationwide population-based study from of the ARNO Diabetes Observatory. *Nutrition, Metabolism and Cardiovascular Diseases*, 31(9), pp.2661-2668.

[22] Hu, C., Lin, L., Zhu, Y., Zhang, Y., Wang, S., Zhang, J., Qi, H., Li, M., Zhu, Y., Huo, Y., Wan, Q., Qin, Y., Hu, R., Shi, L., Su, Q., Yu, X., Yan, L., Qin, G., Tang, X., Chen, G., Xu, M., Xu, Y., Wang, T., Zhao, Z., Gao, Z., Wang, G., Shen, F., Luo, Z., Chen, L., Li, Q., Ye, Z., Zhang, Y., Liu, C., Wang, Y., Yang, T., Deng, H., Chen, L., Zeng, T., Li, D., Zhao, J., Mu, Y., Bi, Y., Wang, W., Ning, G., Wu, S., Chen, Y. and Lu, J., 2021. Association Between Age at Diagnosis of Type 2 Diabetes and Cardiovascular Diseases: A Nationwide, Population-Based, Cohort Study. *Frontiers in Endocrinology*, 12.

[23] Freeman AM, Pennings N. Insulin Resistance. 2021 Jul 10. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 29939616.

[24] Centers for Disease Control and Prevention. 2022. *The Insulin Resistance–Diabetes Connection*. [online] Available at: <https://www.cdc.gov/diabetes/basics/insulin-resistance.html> [Accessed 11 February 2022].

[25] Aslam, M., Mishra, B., Goyal, S., Siddiqui, A. and Madhu, S., 2021. Family history of diabetes determines the association of HOMA-IR with fasting and postprandial triglycerides in individuals with normal glucose tolerance. *Journal of Clinical Lipidology*, 15(1), pp.227-234.

[26] Sakurai, M., Nakamura, K., Miura, K., Takamura, T., Yoshita, K., Sasaki, S., Nagasawa, S., Morikawa, Y., Ishizaki, M., Kido, T., Naruse, Y., Suwazono, Y. and Nakagawa, H., 2013. Family history of diabetes, lifestyle factors, and the 7-year incident risk of type 2 diabetes mellitus in middle-aged Japanese men and women. *Journal of Diabetes Investigation*, 4(3), pp.261-268.

[27] Denton, J. and Fernandez, J., 2021. The role of family history of diabetes as a predictor of insulin activity in a sample of diverse, normal weight children. *Endocrine and Metabolic Science*, 3, p.100090.

[28] Polfus, L., Darst, B., Highland, H., Sheng, X., Ng, M., Below, J., Petty, L., Bien, S., Sim, X., Wang, W., Fontanillas, P., Patel, Y., Preuss, M., Schurmann, C., Du, Z., Lu, Y., Rhie, S., Mercader, J., Tusie-Luna, T., González-Villalpando, C., Orozco, L., Spracklen, C., Cade, B., Jensen, R., Sun, M., Joo, Y., An, P., Yanek, L., Bielak, L., Tajuddin, S., Nicolas, A., Chen, G., Raffield, L., Guo, X., Chen, W., Nadkarni, G., Graff, M., Tao, R., Pankow, J., Daviglus, M., Qi, Q., Boerwinkle, E., Liu, S., Phillips, L., Peters, U., Carlson, C., Wikens, L., Le Marchand, L., North, K., Buyske, S., Kooperberg, C., Loos, R., Stram, D. and Haiman, C., 2021. Genetic discovery and risk characterization in type 2 diabetes across diverse populations. *Human Genetics and Genomics Advances*, 2(2), p.100029.

[29] Cdc.gov. 2022. *National Diabetes Statistics Report 2020 Estimates of Diabetes and Its Burden in the United States*. [online] Available at: <https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf> [Accessed 11 February 2022].

[30] Farbstein, D. and Levy, A., 2012. HDL dysfunction in diabetes: causes and possible treatments. Expert *Review of Cardiovascular Therapy*, 10(3), pp.353-361.

[31] Colberg, S., Sigal, R., Yardley, J., Riddell, M., Dunstan, D., Dempsey, P., Horton, E., Castorino, K. and Tate, D., 2016. Physical Activity/Exercise and Diabetes: A Position Statement of the American Diabetes Association. *Diabetes Care*, 39(11), pp.2065-2079.

[32] Anjana, R. and Mohan, V., 2016. Diabetes and physical activity. *Indian Journal of Medical Research*, 143(4), p.530.

[33] Wang, X. and Cheng, Z., 2020. Cross-Sectional Studies. *Chest*, 158(1), pp.S65-S71.

Appendix1

1. Healthy and unhealthy blood pressure ranges (mmHg)

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)	and/or	DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	AND	LESS THAN 80
ELEVATED	120-129	AND	LESS THAN 80
HIGH BLOOD PRESSURE(STAGE1)	130-149	OR	80-89
HIGH BLOOD PRESSURE(STAGE2)	140 OR HIGHER	OR	90 OR HIGHER