# Increased TG/HDL Ratio Is A Risk Factor for Insulin Resistance:: A Cross-Sectional Study From the US National Health and Nutrition Examination Survey, 2017–2018

**Rongpeng Gong**
Medical College of Qinghai University
**Zheng Li**
Endocrinology Department, Qinghai Provincial People's Hospital
**Ya Liu**
Medical College of Qinghai University
**Gang Luo**
Medical College of Qinghai University
**Lixin Yang**
Endocrinology Department, Qinghai Provincial People's Hospital
**Xiaoxing Wei** ( weixiaoxing@qhu.edu.cn )
Medical College of Qinghai University

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# Abstract

**Background:**

Some previous studies have suggested that elevated TG/HDL ratio is a risk factor for the development of insulin resistance.There is also evidence that TG/HDL ratios are ethnically diverse.Currently, there is still insufficient evidence on whether TG/HDL is a risk factor for the occurrence of insulin resistance in the US population. Therefore, we attempted to find out whether TG/HDL represents a risk factor for the occurrence of insulin resistance in the US population by studying the NHANES database (2017-2108).

**Methods:**

After adjusting the potential influencing factors, we used the method of multiple logistic regression to analyze the risk between TG/HDL and insulin resistance, and determined whether there was a linear relationship between TG/HDL and insulin resistance by smoothing curve fitting.At the same time, in order to verify the reliability of the results, we conducted a subgroup analysis.

**Results:**

We found that in the American population, increased TG/HDL ratio was a risk factor for insulin resistance (OR=2.47 (2.01,3.04)).At the same time, we found a saturation effect between TG/HDL ratio and insulin resistance.When the ratio was <0.84, the relationship between TG/HDL and the occurrence of insulin resistance was very significant (OR=21.24 (9.29,48.56)), and when the ratio was ≥0.84, the effect value was relatively reduced (OR=1.45(1.10,1.92)).

**Conclusions:**

In this study, we found that TG/HDL is negatively correlated with insulin resistance in the American population (except Hispanic Americans), and this effect is especially significant in people with higher education.


# Introduction

Insulin resistance is the insensitivity to insulin in insulin-dependent organ tissues. Its clinical manifestation is nonresponse to the sugar load, which leads to the metabolic disorder of fat, protein, and other carbohydrates in the body.

Previous studies have shown that metabolic disorders can cause systemic toxicity and chronic diseases such as thrombosis, oxidative peroxidation, endothelial dysfunction, even they can cause diabetes in severe cases. In a 2014 study (1), Paul Welsh et al. found that older adults without insulin resistance had a much lower incidence of diabetes than those with insulin resistance. At the same time, another 13-year follow-up study (2) showed that patients with insulin resistance also had a significantly increased risk of cardiovascular disease. Gianluca et al. (3) conducted a 15-year cohort study analysis. They found that

patients' mortality rate with insulin resistance was significantly different from those irrelevant to it in cancer cases. The mortality rate of cancer patients with insulin resistance was 5.6% higher than that of patients without insulin resistance. Therefore, insulin resistance (IR) can be considered a predictor of diabetes mellitus (DM), cardiovascular disease, and tumour.

As awareness of IR increases, we find that obesity often accompanies insulin resistance. Besides, smoking, hyperlipidemia, and hypertension have been affirmed and widely recognized as common risk factors for insulin resistance (IRRF). In Europe, a study of children found a 10.9% incidence of IR (4), suggesting that IR may occur with unrecognized IRRFs. Therefore, it is essential to find a model that can reduce the occurrence rate of IR.

At present, there are several methods to make a primary diagnosis of IR directly or indirectly (5). The gold standard diagnostic method is the high insulin regular blood sugar clamp test (HEC test), which is initially developed by DeFronzo(6). However, it is apparent defects, like high cost, fearful invasion, and long time required, so this method is not yet feasible in the clinical application (7).

Therefore, an easy mark of predicting IR helps clinicians identify whether patients have IR at an early stage and save patients' costs. Some studies have found that high triglyceridemia and low-density lipoprotein cholesterol plays a critical role in IR (8, 9), concluding the triglyceride/high-density lipoprotein cholesterol ratio as a simple clinical indicator of IR and a predictor of diabetes and coronary heart disease (10, 11). Various studies of potential clinical uses of triglyceride/HDL cholesterol ratios in adults and children have recently been investigated. Based on commonly used standardized measurements, the TG/HDL-C ratios index helps clinicians identify IR patients (10, 12–22). Based on data from the 2017–2018 National Health and Nutrition Examination Survey (NHANES), our study explored the role of the TG/HDL-C ratio in predicting IR in the general population. It suggests that early TG/HDL-C monitoring is of great significance in preventing insulin resistance and reducing the occurrence of chronic diseases related to insulin resistance.

# Methods

### Study design and study population

The data for this study comes from the CDC's National Center for Health Statistics (NCHS) cross-sectional study of NHANES(http://www.cdc.gov/nchs/nhanes/). Sample source of NHANES: after a complex, stratified, multi-stage design, a resident sample with a representative national population sample (23). The NHANES program began in the early 1960s as a series of surveys of different populations or health topics. The NHANES study program is described in detail elsewhere (National Center for Environmental Health, Centers for Disease Control and Prevention). The NHANES protocol has been reviewed and approved by the NCHS Research Ethics Committee. All participants provided written informed consent before participation. The survey is unique in its combination of interviews and medical examinations.

In this study, in order to ensure the reliability of the results. We selected the NHANES data volume for the latest period (2017-2018). On the basis of the 9,254 people who participated in the NHANES survey during this midweek, we included and excluded them according to the following criteria.We will include those who meet the following conditions: 1. Adults ≥18 years old.2. Have insulin test data.3. Data of general biochemical examination and sample questionnaire are available.Exclusion criteria: those who do not meet the above conditions will be excluded. We performed multiple interpolation for the remaining missing data. A total of 2,632 participants were enrolled in the study.figure 1

### Data collection and measurement

All the information is collected by specially trained investigators.These data include general demographic data (gender, age, race, education, etc.), health behaviors, physical examinations (height, waist circumference, etc.), and biochemical indicators (ALT, HDL, TG, etc.). The determination of insulin was performed on a TOSOH AIA system analyzer using AIA- PACK method. All tests are conducted through quality control to ensure that all inspection results are true and valid

### Assessment criteria

### Smoking

In this study, smokers were divided into two classes because fewer people quit smoking. Smoker: current smokers who have smoked more than 100 cigarettes are defined as smokers. Non-smokers: those who do not meet the requirements of smokers are defined as non-smokers.

### hypertension

For this study, we used a relatively rigorous standard, the 2017 American College of Cardiology/American Heart Association Blood Pressure Guidelines. Patients with >130/80 or normal blood pressure and taking hypertensive medication were considered hypertensive participants..

### Diabetes

NHANES defined diabetes by questionnaire collection, fasting blood glucose (FPG) and glycated hemoglobin (HbA1c). In this study, we defined diabetes as having fasting blood glucose ≥12.6 mg/dL or A1c ≥6.5%(48 mmol/mL) and reporting that they had diabetes and were taking medication according to the 2015 American Diabetes Association criteria.

### Statistical analysis

In this study, continuous variables of patients' baseline characteristics were expressed as mean ± standard deviation (normal distribution) or median Q1-Q3 (skewed distribution). Classification variables are expressed as counts and percentages. We used the chi-square test to analyze the categorical variables during the comparison between groups, and used the analysis of variance (normal distribution) or the Kruskal-Wallis test (non-normal distribution) for continuous variables.Multivariate logistic

regression model was used to analyze the relationship between vitamin D3 content and the risk of insulin resistance. We calculated rough odds ratios (OR) and adjusted odds ratios (OR) with confidence intervals (CI) of 95%.

We included covariates of factors that contributed more than 10% to the development of insulin resistance, or important factors based on published studies in recent years.We incorporated these covariables into the final adjustment model as potential mixing factors.Model 1 has not been adjusted.Model 2 adjusts for age, sex, race, and education.Model 3 added adjustments for income, smoking, hypertension, diabetes, BMI and waist circumference on the basis of Model 2.

We examined interactions and stratified analyses by race, smoking, hypertension, and diabetes.To explore the risk of insulin resistance in different TG/HDL ratios. We divided the ratio of TG/HDL into two groups according to the inflection point of saturation effect, and evaluated the relationship between TG/HDL and the occurrence of insulin resistance on the basis of adjusting for confounding factors.The R statistical software package, version 3.4.3(http://www.R-project.org), was used to conduct multiple interpolation for the missing data, and then statistical analysis was performed.Bilateral significance level test was used, and $P<0.05$ was evaluated as statistically significant.

### Consent to participate

All participants provided written informed consent, and the study was approved by the NCHS Research Ethics Review Board(https://wwwn.cdc.gov/nchs/nhanes/default.aspx)

### Patient and public involvement

Patients and the public were not involved in developing the study question or measuring the outcome, study design or recruitment, and study's conduct. There are no plans to disseminate the results directly to participants.

## Results

In our study, 2331 participants from the NHANES (2013–2014) database were eventually included(figure 1). In our study population, the mean age of all participants was 50.0 ± 18.3 years, and the age of participants with insulin resistance (51.7 ± 17.2) was slightly higher than that of participants without insulin resistance (49.4 ± 18.7).There was no difference in the incidence of insulin resistance by sex or smoking.In this study, non-Hispanic whites with insulin resistance accounted for a large proportion (170/588, 28.9%). The waist circumference of the insulin resistant population (113.9 ± 16.7) was significantly higher than that of the participants without insulin resistance (96.1 ± 15.5). Meanwhile, the TG/HDL ratio was also higher than that of the participants without insulin resistance (1.17 (0.81,1.80)).Table 1

Table 1
Baseline characteristics of the study participants

| Characteristics | All participants(N = 2331) | Patients with Insulin resistance(N = 588) | Patients without Insulin resistance(N = 1743) | *P*-value |
|---|---|---|---|---|
| **Demographic** | | | | |
| Age(years),mean ± SD | 50.0 ± 18.3 | 51.7 ± 17.2 | 49.4 ± 18.7 | 0.011 |
| sex | | | | 0.403 |
| male,no.(%) | 1109 (47.6) | 289 (49.1) | 820 (47) | |
| female,no.(%) | 1222 (52.4) | 299 (50.9) | 923 (53) | |
| BMI(kg/m2),mean ± SD | 29.8 ± 7.4 | 35.3 ± 7.7 | 27.9 ± 6.3 | < 0.001 |
| smoker | | | | 0.096 |
| no-smoker | 1386 (59.5) | 332 (56.5) | 1054 (60.5) | |
| smoker,no.(%) | 945 (40.5) | 256 (43.5) | 689 (39.5) | |
| Waist(cm),mean ± SD | 100.6 ± 17.6 | 113.9 ± 16.7 | 96.1 ± 15.5 | < 0.001 |
| race | | | | < 0.001 |
| Mexican American | 349 (15.0) | 128 (21.8) | 221 (12.7) | |
| Other Hispanic | 220 ( 9.4) | 65 (11.1) | 155 (8.9) | |
| Non-Hispanic White | 786 (33.7) | 170 (28.9) | 616 (35.3) | |
| Non-Hispanic Black | 516 (22.1) | 125 (21.3) | 391 (22.4) | |
| Other Race - Including Multi-Racial | 460 (19.7) | 100 (17) | 360 (20.7) | |
| education, no.(%) | | | | < 0.001 |
| Less than college, no.(%) | 1777 (76.2) | 484 (82.3) | 1293 (74.2) | |
| College graduate or above, no.(%) | 554 (23.8) | 104 (17.7) | 450 (25.8) | |
| **Clinical characteristics** | | | | |

| Characteristics | All participants(N = 2331) | Patients with Insulin resistance(N = 588) | Patients without Insulin resistance(N = 1743) | *P*-value |
|---|---|---|---|---|
| Hypertension, no. (%) | 1196 (51.3) | 361 (61.4) | 835 (47.9) | < 0.001 |
| Diabetes mellitus, no.(%) | 474 (20.3) | 268 (45.6) | 206 (11.8) | < 0.001 |
| **Serum biomarkers** | | | | |
| TG/HDL,median(Q1-Q3) | 0.77 (0.46, 1.29) | 1.17 (0.81, 1.80) | 0.64 (0.40, 1.09) | < 0.001 |
| TG/HDL group | | | | < 0.001 |
| < 0.84, no.(%) | 1274 (54.7) | 163 (27.7) | 1111 (63.7) | |
| >=0.84, no.(%) | 1057 (45.3) | 425 (72.3) | 632 (36.3) | |
| Abbreviations: BMI,body mass index; TG,Triglyceride;HDL,high-density lipoprotein | | | | |

We used univariate analysis to observe the effects of age, gender, race, BMI, waist circumference and other factors on the occurrence of insulin resistance without further adjustment.Hispanics (OR = 0.72 (0.5,1.04) P = 0.081,CI:95%)) and Mexican Americans had a similar risk of insulin resistance, but the other races had a lower risk of insulin resistance than Mexican Americans.BMI, waist circumference, smoking, hypertension, diabetes, TG/HDL and other factors are risk factors for the development of insulin resistance.Higher education level (OR = 0.62 (0.49,0.78)CI:95%)) was a protective factor for the development of insulin resistance.When the TG/HDL ratio was ≥ 0.84, the effect value was more obvious than < 0.84 (OR = 4.58 (3.73,5.63),CI:95%)).(Table 2)

Table 2
Univariate analysis for Insulin resistance

| Covariate | OR(95%CI) | *P*-value |
|---|---|---|
| Age(years),mean ± SD | 1.0066 (1.0015,1.0118) | 0.012 |
| BMI(kg/m2),mean ± SD | 1.16 (1.14, 1.18) | < 0.0001 |
| Waist(cm),mean ± SD | 1.07 (1.07, 1.08) | < 0.0001 |
| RACE: | | |
| Mexican American | 1 | |
| Other Hispanic | 0.72 (0.5,1.04) | 0.081 |
| Non-Hispanic White | 0.48 (0.36,0.63) | < 0.001 |
| Non-Hispanic Black | 0.55 (0.41,0.74) | < 0.001 |
| Other Race - Including Multi-Racial | 0.48 (0.35,0.65) | < 0.001 |
| sex | | |
| male | 1 | |
| Female | 0.92 (0.76,1.11) | 0.377 |
| education | | |
| Less than college, no.(%) | 1 | |
| College graduate or above, no.(%) | 0.62 (0.49, 0.78) | < 0.0001 |
| smoker | | |
| never smoker | 1 | |
| smoker,no.(%) | 1.18 (0.98,1.43) | 0.087 |
| TG/HDL,median(Q1-Q3) | 2.14 (1.89, 2.42) | < 0.001 |
| Hypertension | | |
| NO,no.(%) | 1 | |
| YES,no.(%) | 1.73 (1.43,2.09) | < 0.001 |
| Diabetes mellitus, no.(%) | | |
| NO,no.(%) | 1 | |
| Yes,no.(%) | 6.25 (5.03,7.77) | < 0.001 |
| TG/HDL group | | |
| < 0.84, no.(%) | 1 | |

| Covariate | OR(95%CI) | *P*-value |
|---|---|---|
| >=0.84, no.(%) | 4.58 (3.73,5.63) | < 0.001 |

Table 3 shows the relationship between TG/HDL and the risk of insulin resistance after adjusting for potential confounders. We built three regression models. Model one adjusted for nothing, and Model two adjusted for age, sex, race, and education. Model 3 added smoking, diabetes, hypertension, BMI and waist circumference on the basis of model 2. The results show that both the unadjusted model I and the fully adjusted model III. TG/HDL were significantly different from insulin resistance. In the unadjusted model, the TG/HDL ratio and the risk of insulin resistance were extremely significant (OR = 2.14(1.82,2.42), P < 0.001,CI:95%)), as were the fully adjusted effect values (1.73 (1.50, 1.99), P < 0.001, CI:95%)). Each increase in the TG/HDL ratio was associated with a 73% increase in the risk of insulin resistance. The TG/HDL > 0.84 group was more significant (OR = 2.97(2.31,3.82), P < 0.001,CI:95%).

**Table 3**. The association between TG/HDL and insulin resistance in a multiple regression model

| Outcome | Non-adjusted Model | | Model1 | | Model2 | |
|---|---|---|---|---|---|---|
| | OR(95%CI) | *P*-value | OR(95%CI) | *P*-value | OR(95%CI) | *P*-value |
| TG/HDL | 2.14 (1.89, 2.42) | <0.0001 | 2.20 (1.94, 2.51) | <0.0001 | 1.73 (1.50, 1.99) | <0.0001 |
| TG/HDL group | | | | | | |
| <0.84 | 1 | | 1 | | 1 | |
| >=0.84 | 4.44 (3.61, 5.46) | <0.0001 | 4.71 (3.78, 5.86) | <0.0001 | 2.97 (2.31, 3.82) | <0.0001 |
| Non-adjusted model adjust for: None.Adjust I model adjust for: Gender; age; race; education. Adjust II model adjust for: Adjust model I +bmi; wasit; Diabetes; Hypertension; Smoking; | | | | | | |

We plotted a smooth curve fitting to analyze the association between TG/HDL and insulin resistance(figure 2). It was found that there was a nonlinear relationship between TG/HDL and insulin resistance, and there was a saturation effect. Through threshold effect analysis, we found that when TG/HDL reached 0.84, the risk of insulin resistance gradually leveled off. When the TG/HDL < 0.84, the TG/HDL ratio was significantly associated with the risk of insulin resistance (OR = 21.24(9.29,48.56), P < 0.001, CI: 95%). When the TG/HDL was < 0.84, the risk of insulin resistance increased by an average of 20.24 times with each increase of one unit. The clinical significance of this is extremely significant, and we can consider it to be a good indicator for predicting the occurrence of insulin resistance. When TG/HDL ≥ 0.84, the effect value was relatively stable (OR = 1.45(1.10,1.92), P = 0.0086, CI: 95%)Table 4.

**Table 4** Threshold effect analysis of TG/HDL-C on insulin resistance

| Outcome | OR(95%CI) | *P*-value |
|---|---|---|
| One-linear regression modle | 1.73 (1.50, 1.99) | <0.0001 |
| Two-piecewise linear regression model | | |
| TG/HDL-C<0.84 | 21.24 (9.29, 48.56) | <0.0001 |
| TG/HDL-C>=0.84 | 1.45 (1.10, 1.92) | 0.0086 |
| Adjust I model adjust for: Gender; age; race; education. Adjust II model adjust for: Adjust model I +bmi; wasit; Diabetes; Hypertension; Smoking; | | |

The interactions and layering analysis are shown in Fig. 3. An increase in TG/HDL ratio was associated with an increase in the risk of insulin resistance in any group except Hispanics, where TG/HDL was not significantly associated with the risk of insulin resistance. Especially not Hispanic black (OR = 2.65 (1.75, 4), P < 0.001, 95% CI:) and Mexican americans (OR = 1.42 (1.12, 1.8), P < 0.001, 95% CI:) is more obvious. We also saw that the interaction between TG/HDL and insulin resistance was more significant in highly educated people (OR = 1.64 (1.25, 2.14),P < 0.001,CI:95%) and non-smoking people (OR = 1.33(1.15,1.53),P < 0.001,CI:95%).

# Discussion

In this study, we used the NHANES (2017–2018) database to study the association between TG/HDL and insulin resistance. The current results show that in the American adult population, TG/HDL ratio is closely related to the occurrence of insulin resistance. We found that when TG/HDL < 0.84, the effect value between TG/HDL ratio and insulin resistance was significant.

When TG/HDL ≥ 0.84, it gradually leveled off. Remarkably, we observed an even more significant association in the highly educated population; Also, interestingly, we did not see an association between TG/HDL and insulin resistance in the Hispanic population.However, no such difference was found in previous studies.

Previous studies seem to have looked elsewhere. A research on the mechanism of elevated TG/HDL ratio is reported, and TG/HDL ratio increases may be the trap of adipose tissue, in the case of insulin resistance will keep a small amount of fatty acids (28), the relative increase of free fatty acids to the liver, to synthesize more triglycerides and more contains very low density lipoprotein (VLDL). In addition.The triglycerides that are rich in very low density lipoprotein and the cholesterol esters that are rich in high density lipoprotein are more likely to exchange at higher triglyceride concentrations to form high density lipoprotein that is rich in triglycerides. Therefore, people with insulin resistance are more likely to have high TG/HDL, high TG, and low HDL. Meanwhile, another study on TG/HDL found that people with high TG/HDL were more likely to develop diabetes and promoted atherosclerotic dilation in prediabetic and newly diagnosed type 2 diabetes (29).This is consistent with our findings, because insulin resistance is

the most typical feature and early pathological mechanism of type 2 diabetes.Murguia-Romero et al. examined over 2000 healthy young subjects and determined that the TG/HDL-C ratio could be used to identify IR and increased cardiometabolic risk.There is also evidence that elevated TG/HDL-C is associated with atherosclerotic disease and cardiovascular disease related morbidity and mortality (12, 30).It can also predict long-term mortality in high-risk patients (31).Our results therefore have implications for the prevention of diabetes, cardiovascular disease, cancer and other new developments.

In this study, we adjusted for confounding factors with waist circumference, as previous studies have shown a close association between waist circumference level and the occurrence of insulin resistance (32). In addition, for the first time, we included education level in the covariate and subgroup stratification analysis, because in our restudy, we found that people with higher education had a significantly lower risk of developing insulin resistance compared to people without higher education. We speculate that this may be due to the perception of the disease. People with higher education are more likely to be aware of the risk factors for chronic diseases and to pay more attention to their physical health in their daily lives.However, the specific existence and the differences between the two need further study. Meanwhile, in the population represented in this sample, we concluded that TG/HDL was not significantly associated with insulin resistance, except in the Hispanic population.In other populations and subgroups, the elevated TG/HDL ratio is a good indicator of the risk of insulin resistance..

It is worth mentioning that our study has several advantages. First of all, our study is the first to use a nationally representative sample to analyze the relationship between TG/HDL in the American population, enhancing the general applicability and reliability of the results in the American population. Secondly, our study is the first to consider the effect of education level on insulin resistance, provide for the first time the effect of interaction between TG/HDL and education level on insulin resistance, and find that higher education level is a protective factor of insulin resistance.

However, this study still has some shortcomings in a certain sense. The sample we used was a cross-sectional survey from the NHANES database. Therefore, further studies are needed to further clarify the relationship between TG/HDL and insulin resistance in the US population. At the same time, the use of HOMA-IR as an alternative method for the diagnosis of insulin resistance has certain limitations in its repeatability and reliability. Finally, we did not assess the genetic impact on the development of insulin resistance risk

# Conclusion

In conclusion, in our study, TG/HDL was found to be highly correlated with insulin resistance in all the American population except the Hispanic population, and the effect was more significant in the people with higher education. As the ratio of TG/HDL increases continuously, the risk of insulin resistance also increases continuously, and becomes relatively flat after reaching 0.84. However, since this study was a cross-sectional study, more evidence is needed to further investigate the risk factors for insulin resistance in the American population.

# Abbreviations

TG/HDL-C
triglyceride/ high-density lipoprotein
IR
insulin resistance CI:confidence interval OR:odds ratio
BMI,body mass index; BUN, blood urea nitrogen;LDH,Lactate dehydrogenase;TBIL,total bilirubin;TG,Triglyceride;HDL,high-density lipoprotein ALT
Alanine aminotransferase
ALP
alkaline phosphatase AST:Aspartate aminotransferase

# Declarations

### Authors' contributions

Rongpeng Gong and Xiaoxing Wei conceived the idea; Rongpeng Gong and Ya Liu wrote the manuscript; Zheng Li and Lixin Yang collected and read the literature and revised the article; Xiaoxing Wei read through and corrected the manuscript. All authors read and approved the final manuscript. Rongpeng Gong is the first author and Xiaoxing Wei is the corresponding author of this paper.

### Author details

Rongpeng Gong and Xiaoxing Wei are from Medical College of Qinghai University, Xining 810016, P. R. China.

Zheng Li and Lixin Yang are from Endocrinology Department of Qinghai Provincial People's Hospital. 810016, P. R. China.

### Competing interests

The authors declare that they have no competing interests.

### Availability of data and materials

Not applicable.

### Consent for publication

Not applicable

### Ethics approval and consent to participate

All participants provided written informed consent, and the study was approved by the NCHS Research Ethics Review Board(https://wwwn.cdc.gov/nchs/nhanes/default.aspx)


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# Figures

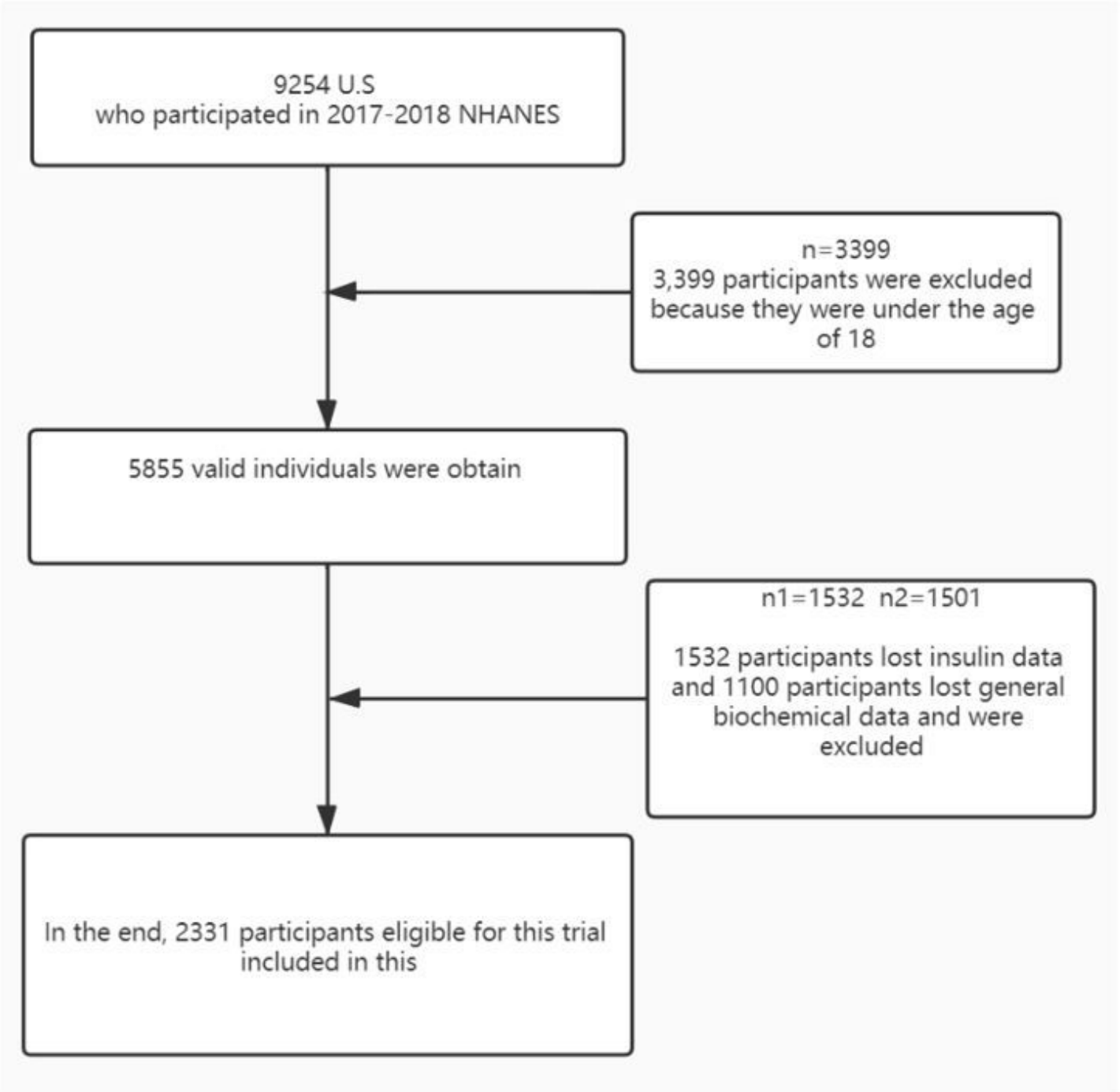
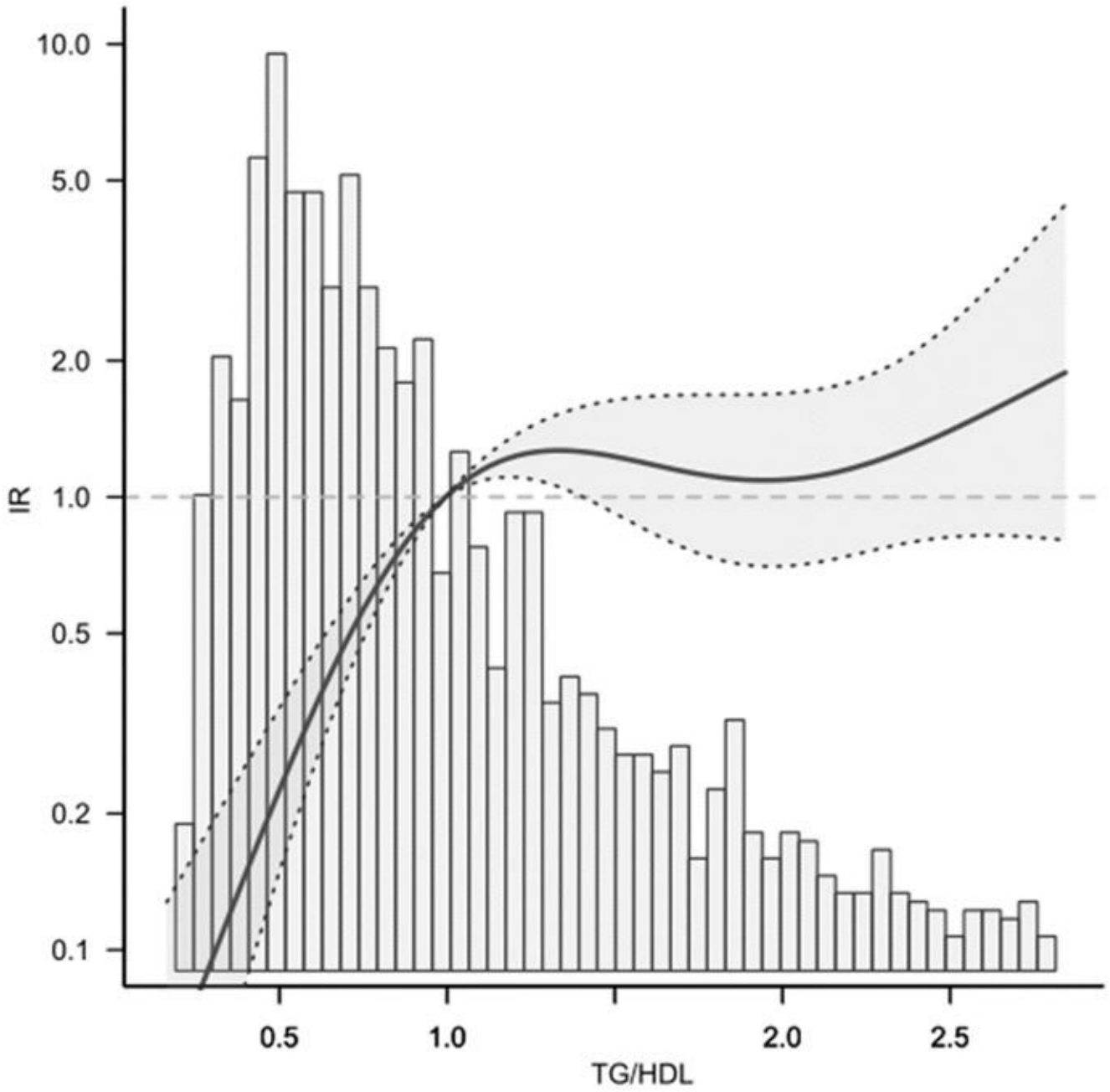


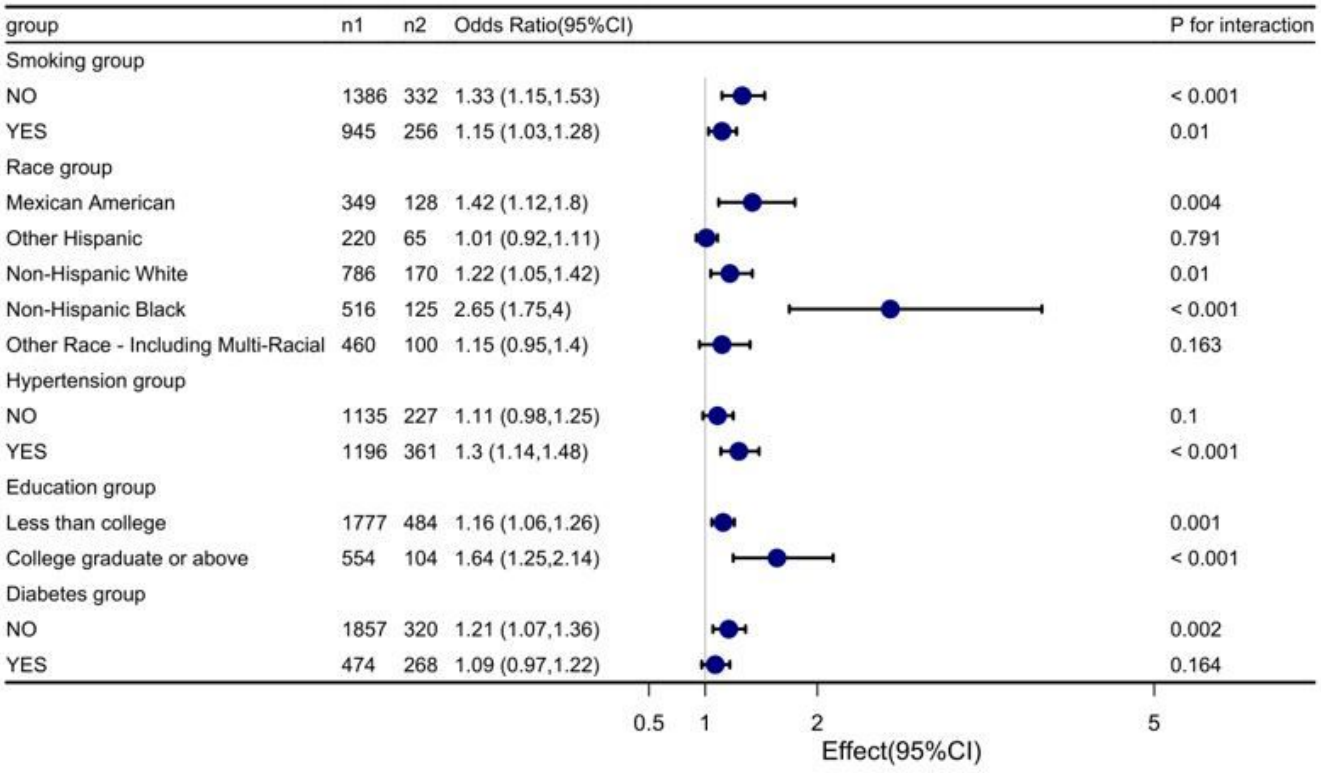

**Figure 1**

Flowchart of patient selection.




## Figure 2

Association between TG/HDL-C and IR. Notes: The two blue lines represent estimates and their corresponding 95% confidence intervals.




## Figure 3

Association of triglycerides to high-density lipoprotein-cholesterol ratio with risk of incident