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The Association between Nonalcoholic Fatty Liver Disease and Bone Mineral Density -- Results from the Third National Health and Nutrition Examination Survey (NHANES III)

By

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Master of Public Health

Epidemiology

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Doctor of Philosophy (Medicine), the University of Tokyo, 2014

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An abstract of

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Abstract

The Association between Nonalcoholic Fatty Liver Disease and Bone Mineral Density -- Results from the Third National Health and Nutrition Examination Survey (NHANES III)

By Toshihiro Umehara

Background

Previous studies have suggested that nonalcoholic fatty liver disease (NAFLD) is associated with lower bone mineral density (BMD), but data are limited especially in Western countries.

Methods

The cross-sectional study was conducted to assess the association between NAFLD and BMD. In this study, the author used the National Health and Nutrition Survey (NHANES) III dataset, and examined the association in the United States population.

Results

6,126 participants from 40 to 75 year old were selected after excluding people with hepatitis virus serology, elevated alcohol consumption, or decreased renal function, and pregnant women. The exposure, NAFLD, was defined as having moderate to severe hepatic steatosis. The prevalence of NAFLD was 24.9% among the selected participants. Multivariate linear regression with the outcome of BMD was conducted. After controlling for gender/menopausal status, race, age and BMI, the final model did not show a statistically significant NAFLD effect on BMD (beta coefficient: -0.007, 95%CI: -0.016, 0.003).

In the secondary analysis, using serum alanine aminotransferase (ALT) level, NAFLD group was further categorized into high ALT NAFLD group and normal ALT NAFLD group. These two groups were used as exposures, and non-NAFLD group was used as a reference group. After controlling for gender/menopausal status, race, age and BMI, the final model showed that high ALT NAFLD has statistically significant negative effect on BMD (beta coefficient: -0.051, 95% CI: -0.081, -0.020) at the overall average BMI level, 27 kg/m2. The interaction term between high ALT NAFLD and BMI showed statistically significant positive coefficient (beta coefficient: 0.004, 95% CI: 0.001, 0.007), which suggests the high ALT NAFLD negative effect is attenuated among higher BMI people.

Conclusions

The primary analysis did not support the hypothesis that NAFLD has an association with lower BMD. The secondary analysis suggested the possible relationship between NAFLD and lower BMD among people with low to normal BMI.

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Background/Literature Review

In this study, I focused on two chronic health conditions, low bone mineral density and nonalcoholic fatty liver (NAFLD). These days, chronic health conditions have been attracting more attentions in public health, as the population lives longer and ages. Historically communicable diseases or infectious diseases were the main concerns, contributing to the mortality and morbidity. After the end of 19th century, developing the knowledge and treatments for infectious diseases has contributed to the steep declines in mortality from infectious diseases (1). As a result people live longer but people became suffering from different diseases, such as cancers, heart diseases, diabetes, and dementia (2). Low bone mineral density and NAFLD are not directly related to a life-threatening conditions, and they have not attracted so much attention. However, low bone mineral density can increase the rate of bone fracture, which decrease the patients' quality of life. The number of people with NAFLD is increasing as obesity is becoming more prevalent. Therefore, these two factors can have a great impact on public health, and considering the association can give us a better strategy for prevention and therapy, and must be beneficial for the future researches.

Bone Mineral Density

Bone mineral density (BMD) is widely used to diagnose osteoporosis (3). Osteoporosis is a disease “characterized by low bone mass, deterioration of bone tissue and disruption of bone architecture, compromised bone strength and an increase in the risk of fracture.” (3) Wright reported 10.2 million Americans aged 50 years and older are affected by osteoporosis in 2013 (4).

Maintaining BMD level is beneficial to protect against incidents of bone fractures. Prospective cohort studies have demonstrated that people with low bone mineral density of femur (5, 6), lumber spine (5, 7), radius (6, 8) or forearm (9) have higher risk of bone fracture. Meta-analysis reported -1 S.D. BMD people have 1.5 to 2.6 times as high risk of bone fracture (10).

In the industrialized countries, the number of people with osteoporosis or low bone mineral density is increasing, as population is aging. “It is anticipated that the number of fractures will grow proportionally.” (3) “Annually, two million fractures are attributed to osteoporosis, causing more than 432,000 hospital admissions, almost 2.5 million medical office visits and about 180,000 nursing home

admissions in the U.S." (3) Therefore, keeping bone mineral density is also beneficial from the view of public health and healthcare economy.

NAFLD

NAFLD is a disease characterized by an excessive fat deposition in liver caused by non-alcohol factors. Fatty liver can be caused by excessive use of alcohol, steatogenic medication, hepatitis virus, autoimmune or hereditary disorders, but when the patient does not have those underlying liver conditions, the fatty liver is diagnosed as NAFLD (11). According to the clinical guideline, the diagnosis requires "(a) there is evidence of hepatic steatosis, either by imaging or by histology and (b) there are no causes for secondary hepatic fat accumulation such as significant alcohol consumption, use of steatogenic medication of hereditary disorders." (11)

NAFLD often follows a benign course, but there are some comorbidities involving with NAFLD. Majority of NAFLD cases can be observed in patients with metabolically abnormal conditions, such as obesity, diabetes mellitus and dyslipidemia. Obesity, type2 diabetes, dyslipidemia and metabolic syndrome are

reported to be closely related to NAFLD (11). Kotronen reported type2 diabetic patients have 80% more liver fat than non-diabetic people after adjusting for age, weight and gender (12). Framingham Heart Study also reported the relationship of fatty liver with dyslipidemia and dysglycemia (13). NAFLD and these factors are also related to the development of cardiovascular diseases, and some types of cancers.

Previous studies reported that prevalence of NAFLD is about 25% to 45% (14). Among general population, the number of NAFLD patients is increasing along with the increase of obese people and people with diabetes. Therefore the effect of NAFLD on public health can be large.

Possible relationship between NAFLD and bone mineral density

Previous epidemiological studies from Asia have suggested that NAFLD has an association with low bone mineral density. Moon et al. reported the association among postmenopausal women in Korea (15). They found a significant association between lumber BMD and NAFLD, even after adjusting for age, body mass index, serum alanine aminotransferase (ALT), smoking status, and alcohol consumption

(β coefficient -0.066, 95%CI: -0.105 to -0.027). Cui et al. also reported a statistically significant negative association both among men and among postmenopausal women in China (16). The association was observed, even after adjusting for weight, BMI, waist, HDL, and ALT. This relationship became non-significant when adding the indicator variable of insulin resistance (HOMA-IR), which suggests the important role of insulin resistance for this NALFD-BMD association.

Some other articles also support the importance of insulin resistance or metabolic syndrome in this relationship. Meta-analysis showed that control groups without metabolic syndrome has higher BMD after adjusting covariates (17). As widely known, insulin resistance or metabolic syndrome has a close relationship with NAFLD (14, 18). Therefore, these findings suggest insulin resistance or metabolic syndrome can intervene the NAFLD-BMD relationship.

NAFLD liver can also increase and release bone-influencing proteins. Tumor necrosis factor (TNF-alpha) (19-22), osteopontin (OPN) (23, 24), osteoprotegerin (OPG) (25) , and fetuin-A (26, 27) have been shown for their levels to change in NAFLD liver, and have been shown to have an effect on bone formation and bone

resorption.

Vitamin D is another possible factor intervening this relationship. Vitamin D, which was previously thought to be important for skeletal health, is reported to have relationship with adiponectin and other inflammatory cytokines, such as IL-6 and IL-1β (28, 29). Hao reported a negative relationship between vitamin D and NAFLD (30). Also, vitamin D insufficiency and deficiency are much more prevalent than previously thought, and can have an influence on general population (31).

Thus, there are some epidemiological reports about the relationship between NAFLD and BMD, and also possible underlying mechanisms. However, there are not enough reports about this relationship, especially from Western countries. In this study, I assessed this relationship between NAFLD and BMD in the U.S. population by using national health and nutrition survey data.

Methods

Study Design

Cross-sectional analysis was conducted for the dataset from the National Health and Nutrition Survey (NHANES) III (32). The main purpose of this study is to assess the hypothesis that there is a negative association between NAFLD and BMD in the population of the United States. BMD was used as an outcome, and NAFLD status was used as an exposure variable. Gender, menopausal status, age, BMI and race were controlled for as confounders. I assessed the residual relationship between NAFLD and BMD (Fig 1).

Study Population

I included men and women from 40 to 75 years old. People who meet the following exclusion criteria are excluded (Fig 2)

(1) People with hepatitis B or C serology

People with Hepatitis B e antigen (HBeAg) positive or HCV antibody positive were excluded.

(2) Elevated alcohol consumption

People reported the number of days that they drank alcohol in the past 12 months and average drinks they consumed on drinking days. By multiplying these two variables and divided by 365, I estimated the number of drinks per day over the last year. If men drink more than 2 drinks per day or women drink more than 1 drink per day, they are thought to be consuming excessive alcohol, and were excluded.

(3) Decreased renal function

People with estimated glomerular filtration rate (eGFR) less than 30 ($ml/min/1.73m^2$) were assumed to have decreased renal function, and they were excluded. To calculate eGFR, I used the Modification of Diet in Renal Disease (MDRD) study equation. The equation requires serum creatinine level (33), for which the original value in NHANES III needs to be calibrated (34).

MDRD equation: $eGFR = 175 \times (\text{standardized serum creatinine})^{-1.154} \times (age)^{-0.203} \times 0.742$ or $\times 1.212$ (if the subject is black)

Calibration for serum creatinine (mg/dl): Standardized Serum Creatinine

= 0.960*NHANES Creatinine – 0.184

(4) People with abnormal thyroid hormone levels

People suspected of hyperthyroidism accelerate bone mineral density decrease and are protected against metabolic syndrome were excluded. People with thyroid stimulating hormone (TSH) lower than 0.1 mU/L were excluded.

(5) Pregnant women

Women who reported they were pregnant were excluded.

As a result, a total of 3297 males and 3843 females remained. Among these people, ultrasonography results were unavailable for 265 males and 272 females, and bone mineral density results were unavailable for 196 males and 281 females. As a result, 2836 males and 3290 females remained, and they were used for analysis.

Obtaining Dataset

All the dataset used in this study was downloaded from CDC website in Jan. 2016 (32). The dataset was provided, divided into some parts, such as an interview part,

a laboratory part, and an ultrasonography part. After downloading all the dataset, they were combined by using the sequential numbers assigned to each observation.

Bone Mineral Density

Bone mineral density (BMD) at the femoral neck was used as outcome. Bone mineral density can be measured at various parts of the body, but femoral neck is reported to have the highest predictive value for hip fracture (10, 35).

Bone mineral density was measured using dual-energy X-ray absorptiometry (DEXA) instruments (QDR-1000, Hologic, Waltham, MA). A quality control program was used to ensure data quality (36). Examinees excluded from this exam were women who have positive or uncertain pregnancy test, women who have possibility of pregnancy, people whose both hips had been fractured or broken previously, and people who had hip pins or artificial hips.

NAFLD Status

NAFLD status was used as a main exposure in our models. NAFLD is identified by

the diagnosis of liver steatosis and the lack of excessive alcohol intake. Liver steatosis was identified by abdominal ultrasonography, and alcohol intake was assessed by interview. In NHANES III, liver steatosis was graded as four groups, severe, moderate, mild steatosis, and normal liver, using the following parameters. "1) the presence of liver-to-kidney contrast (yes, no, or not assessed); 2) the degree of brightness of the liver parenchyma (none, intermediate, moderate, or severe); 3) the presence of posterior deep beam attenuation (yes, no, or not assessed); 4) the presence of echogenic walls in the small intrahepatic vessels (yes, no, or not assessed); and 5) the definition of the gallbladder walls (clear, intermediate, obliterated, or not assessed)." (37)

Two different NAFLD status categorizations were used as a main exposure in my models. In the primary analysis, steatosis was treated as a dichotomous variable (i.e., present (moderate or severe) or absent (normal-mild)), following the previous article assessing the prevalence of NAFLD (37). People with present liver steatosis was categorized into NAFLD group, and people with absent liver steatosis was categorized into non-NAFLD group. In the secondary analysis, another NAFLD categorization that also takes into account alanine aminotransferase (ALT) level was used, to represent the severity within the NAFLD group. People with present

liver steatosis and high ALT were categorized into high ALT NAFLD (HA NAFLD) group. People with present liver steatosis but with normal ALT level were categorized into normal ALT NAFLD (NA NAFLD) group. People with mild steatosis or normal liver were categorized into non-NAFLD group. There is no consensus about the ALT cut point for NAFLD, though higher ALT among NAFLD is related to nonalcoholic steatohepatitis (NASH), the most extreme form of NAFLD. 20 to 40 U/L have been used to predict NASH, and higher cut point improves specificity and lower cut point improves sensitivity of NASH (37-40). In this study 30 U/L was used as a cut point.

Gender, age, race and body mass index

Gender, age, race and body mass index (BMI) were controlled for in this study. Effect modifications of these variables with the main exposure variable, NAFLD status, were also considered.

Menopausal status

Menopausal status was not defined by a single variable in NHANES III dataset, so I divided women into premenopausal and postmenopausal by using the following criteria. The criteria were based on the previous coding scheme (41, 42). The following criteria were "applied sequentially so that the successive rules were applied only to women not already categorized: a) age ≥ 60 years, postmenopausal; b) bilateral oophorectomy, postmenopausal; c) a period or pregnancy within the previous 12 months, premenopausal; d) follicle-stimulating hormone level > 40 IU/L, postmenopausal; e) current use of oral contraceptive pill, premenopausal;" f) People who did not experience a menstrual period last year, postmenopausal. After this categorization 39 females were still not decided about their menopausal status. I categorized 11 females who are over 50 years old into postmenopausal, and 28 females who are under 50 into premenopausal.

Statistical Analysis

Analysis was done taking account for the survey design and sampling weights, because NHANES III was conducted based on a complex, multi-stage sampling. Subpopulation was specified by using SUBPOPN or SUBPOPX statement to

prevent losing design effect information. In descriptive analysis, statistics such as mean and proportion were calculated using PROC DESCRIPT. Multiple linear regression analysis was done using PROC REGRESS. All the analysis was done by using SAS-Callable SUDAAN Ver. 11.0.1 accounting for stratification, sample weight, and clustering.

Variable selection for the final model

Based on the literature review, variables to be controlled for were decided (Fig 1). Based on the stratification and assessment of the changes in the effect of NAFLD on BMD, interaction terms to be included were decided (Table 3, S1 Table). The full model including the exposure variable, confounders, and all the interaction terms were first fitted to the dataset. Starting from the full model, the most statistically insignificant interaction term was iteratively removed using backward elimination, until there are no insignificant interaction terms or there are no interaction terms. In this way, the reduced model was obtained.

Survey Design & Sampling Weights in NHANES III

NHANES is a national survey program to assess the national health and nutritional status of adults and children in the United States. NHANES surveys include demographic, socioeconomic status, and health-related interview, as well as laboratory tests. This survey program began early in 1960s, and NHANES III (from 1988 to 1994) was the seventh in a series of these surveys.

NHANES III was planned to represent the civilian, no institutionalized, two months or older population in the 50 states and the District of Columbia of the United States, using a complex, multi-stage sampling (43). The first stage was selecting 81 primary sampling units (PSUs) that were mostly counties. PSUs were stratified into 47 strata, including 13 strata each of which has only one county. From each of 34 stratum that have multiple counties, two PSUs were selected with probability of proportional to size (PPS). From each of 13 strata that have one county, one PSU was selected with certainty. For the operational reason, these 13 PSUs were divided into 21 survey locations. Therefore, the NHANES III consists of 81 PSUs and 89 survey locations. The second stage of the design was area segments, mainly consisted of city or suburban blocks or combinations of them. The third stage of sample selection consisted of households and certain types of group quarters such as dormitories. The fourth stage of sampling was selecting persons

within households or quarters. The total number of designated sample persons was 39,695. Among them, 30,818 were examined at the mobile examination centers (MEC) (43).

Sampling weights were calculated through three stages (44). The first stage comes from the complex survey design that is non-equal probability of selection. The second stage is the adjustment for nonresponse. The third stage comes from poststratification weights to Census Bureau estimates of the U.S. population. The poststratification enables us to estimate parameters in target population more accurately. Sampling weight variables are provided with the dataset for the convenience of researchers. In this study, I used the sampling weight variable named WTPFEX6, which is appropriate to analyze the data collected for samples interviewed and examined at MEC (44).

Results

Characteristics of NAFLD-specified groups

A total of 6126 people were included in this study. 24.9% of participants have moderate to severe NAFLD. The demographic data are described in Table 1a. Male proportion is larger and premenopausal female proportion is smaller in NAFLD group, compared with non-NAFLD group. NAFLD group has higher age, weight and BMI than non-NAFLD group.

Liver enzymes, AST and ALT, are higher in NAFLD group. Femoral neck bone mineral density is higher in NAFLD group, and osteopenia, and osteoporosis proportions are lower in NAFLD group, which are affected by the larger BMI and weight.

BMDs were also compared between NAFLD group and non-NAFLD group within each stratum by gender/menopausal status, races, age or BMI (Table 1b). When the dataset was stratified by gender/menopausal status, race, or age, NAFLD group had higher BMD than non-NAFLD group. When the dataset was stratified by BMI level, NAFLD group had lower BMD than non-NAFLD group, though there was no statistical significance observed.

Unadjusted effect of NAFLD on BMD

Crude analysis of the NAFLD effect showed statistically significant protective effect on BMD (Table 2). Effects of NAFLD on BMD were assessed also for groups stratified by confounder variables, gender/menopausal status, races, age, and BMI (Table 3). When the dataset was stratified by gender/menopausal status, races and age levels, NAFLD showed protective effects on BMD. In contrast, when the group is stratified by BMI levels, NAFLD showed negative effects on BMD, though they were not statistically significant (Table 3). Effect modifications for the NAFLD effects on BMD were assessed by the statistical significance of interaction term. There were no statistical significance observed for the interactions between the exposure variable and the stratification variables, but all the variables showed 10% differences in the effect of NAFLD on BMD (Table 3). Thus, all the interaction terms of these variables with the exposure variable were introduced into the full model (model1 in Table 1).

Adjusted NAFLD effect on bone mineral density

The full model (model1 in Table 4) did not show any statistical significance in the interaction terms related to NAFLD (Table 4). Backward elimination based on the statistical significance in each interaction term was conducted repeatedly, and the reduced model (model2 in Table 1) did not have any interaction terms. Though the point estimate showed a small negative effect (beta coefficient: -0.007, 95%CI: -0.016, 0.003), there was no statistical significance in the effect of NAFLD on BMD (Table 4). This does not support the hypothesis that NAFLD has a negative association with BMD.

Other variables such as gender/menopausal status, races, age and BMI showed the statistically significant effects consistent with previous biological and epidemiological explanations. Females have lower BMD than males, and menopause accelerates the decrease in BMD (3). Black people have higher BMD than white people (45, 46). As people age, BMD decreases. BMI or body size has a protective effect for BMI (3). Thus this model is appropriate to test the effect of NAFLD.

High ALT NAFLD and normal ALT NAFLD effects on bone mineral density

As a secondary analysis, I used another categorization for NAFLD, taking into account ALT level (mentioned in methods section). People were categorized into three groups, people with NAFLD and high ALT (HA NAFLD) group, people with NAFLD but normal ALT (NA NAFLD) group, and the group without NAFLD (non-NAFLD). In the same way as the primary analysis, stratification analysis was conducted, and interaction terms to be included for the full model were decided. (S2 Table).

The full model showed a statistical significance in the interaction term between HA NAFLD and BMI (beta coefficient: 0.004, 95% CI: 0.001, 0.007) (model3 in Table 5). After statistical significance based backward elimination was conducted for each interaction term iteratively, there was one statistically significant interaction term between HA NAFLD and BMD remained, and the coefficient was a positive value (model4 in Table 5). The main effect of HA NAFLD showed a statistically significant negative effect on BMD in this model (beta coefficient: -0.051, 95% CI: -0.081, -0.020). In this analysis, BMI variable is centered around 27 kg/m^2, so the result means that HA NAFLD has a statistically significant negative effect on BMD at the BMI of 27 kg/m^2. The interaction term means that

the negative effect of HA NAFLD is diminished for higher BMI people than 27 kg/m^2, and strengthened for lower BMI people.

Discussion

In this study, there was no statistical significance observed in the association between nonalcoholic fatty liver disease (NAFLD) and bone mineral density (BMD). The primary hypothesis that there is a negative association between NAFLD and BMD was not supported. In the secondary analysis, another NAFLD categorization using ALT level showed that high ALT NAFLD has statistically significant negative effect on BMD at the overall average BMI level, 27 kg/m^2. The statistically significant positive beta coefficient of interaction term between high ALT NAFLD and BMI means the negative effect of high ALT NAFLD is diminished for higher BMI people, and is strengthened for lower BMI people (Table 5; Fig 3).

Previous reports from Asia showed negative effects of NAFLD on BMD (15, 16). A possible explanation to this difference from these articles may be racial or ethnical difference. In NHANES III, Asian people are categorized into the other race-ethnicity group, which also include other Hispanics, and Native American. The proportion categorized into this other race-ethnicity group is too small to analyze, so they are not recommended to be included in analysis (44). In this

study, they were not included in multivariate linear regression analysis. Another explanation is that the effect observed in this study may be attenuated. Around 7-9 % people were excluded at the last step of selecting participants respectively because their bone mineral density result or fatty liver result was unavailable (Fig 2). These excluded people include people who already had had hip fractures and/or have hip pins or artificial hips, who were not eligible for the measurement of bone mineral density. Excluding these people may have resulted in the attenuation of the association.

The result of secondary analysis says the possible negative effect of high ALT NAFLD on BMD. Previous reports showed there are more nonalcoholic steatohepatitis (NASH) cases included among NAFLD people with high ALT than NAFLD people with normal ALT (39). Thus, this study can link the severity of NAFLD or NASH with lower BMD. However, we also need to carefully interpret the result, because some researchers reported that ALT level and histological NAFLD severity are not correlated (38, 47).

As mentioned in the introduction, there is a possibility that insulin resistance may explain this relationship. I compared insulin resistance between different

NAFLD groups, and the result showed that high ALT NAFLD group has stronger insulin resistance than normal ALT NAFLD group and non-NAFLD group (S3 Table, S1 Fig). This means insulin resistance could explain the negative effect of high ALT NAFLD. However, as BMI increases, the intensity of insulin resistance in high ALT NAFLD group becomes stronger, compared with other groups (S1 Fig). This result is not consistent with the effect modification by BMI in model4 in Table 5. Therefore, insulin resistance could partially support the relationship between high ALT NAFLD and BMD, but it cannot fully explain the relationship.

In the introduction, vitamin D was also suggested as another possible factor to intervene NAFLD-BMD relationship. I compared 25 hydroxyvitamin D levels (25 OH D) among different NAFLD groups and BMI groups (S4 Table, S2 Fig). High ALT NAFLD group had lower 25(OH)D than normal ALT NAFLD and non-NAFLD groups among people with BMI of 20-25. However, among people with BMI of more than 25, high ALT NAFLD had higher 25(OH)D, which is contrary to the mechanism proposed in the introduction. The difference in 25(OH)D of high ALT NAFLD group from the other groups became larger as BMI increases. Therefore, high ALT NAFLD group with higher BMI may gain protective effect on

BMD through higher level of 25(OH)D. This trend of 25(OH)D change may support the effect modification by BMI observed in model4 in Table5.

Therefore, these observations about insulin resistance and vitamin D may support the relationship observed in model4 in table 5. Insulin resistance may intervene the negative association between high ALT NAFLD and BMD to some extent. Also, the vitamin D level may strengthen this relationship among low BMI people, and attenuate it among higher BMI people. However, these inferences are based on a descriptive analysis. Further researches are required to show the importance of these factors.

The strength of this study is that the study population and the design represent the U.S. population. Most of the reports about the relationship between NAFLD and BMD came from Asia before (48, 49). The weakness is that I cannot say anything about the causality, because this study is a cross sectional study. Another weakness is a bias introduced when selecting participants. As mentioned, some participants did not have an available bone mineral density result or an available ultrasonography result. They were not included in this study.

Obesity becomes prevalent, and the prevalence of NAFLD is increasing. Also, as the population ages, osteoporosis and bone fractures are more prevalent. The result of this study will be beneficial for the future researches in these areas.

Future Directions

This study showed a possible effect of NAFLD with high ALT on bone mineral density among lower BMI people. One future direction is to explore the way to use this finding for prevention of bone fractures. In this study, I assessed the effect on bone mineral density, but the more important outcome is bone fractures from the view of public health and individual health. Bone fractures are not only caused by low bone mineral density, but also other factors, such as bone quality and bone size. Thus, the result can be different, and needs to be revealed.

Another direction is to assess this relationship in a longitudinal way. If a longitudinal study confirms the same effect of high ALT NAFLD on bone mineral density, ALT level among NAFLD may be used as a marker to predict bone mineral density change. Previously, ALT level among NAFLD people was studied to predict NASH cases, but there may be another possibility.

These future studies and this study will be beneficial not only for the future epidemiological and biological researches, but also for the future public health and individual health.

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Tables

Table1a. Characteristics of subjects with NAFLD and without NAFLD (n=6126)

	NAFLD N=1702	Non-NAFLD N=4424	P value
Sum of Weight (%)	24.9	75.1	
Demographic variables			
Gender (%)			< 0.01
Males	52.4	44.6	
Premenopausal females	11.9	20.0	
Postmenopausal females	35.7	35.4	
Race (%)			< 0.01
White	80.5	80.1	
Black	7.4	9.6	
Mexican-American	5.8	3.0	
Others	6.3	7.3	
Age (years)	55.6	54.0	< 0.01
Weight (kg)	87.6	74.2	< 0.01
BMI (kg/m2)	30.7	26.4	< 0.01
Clinical variables			
AST (U/L)	23.5	20.0	< 0.01
ALT (U/L)	22.2	15.2	< 0.01
Bone mineral density			
Femoral neck (g/cm2)	0.80	0.77	< 0.01
Osteoporosis (%)	3.6	5.7	0.01
Osteopenia (%)	33.5	42.8	< 0.01

Abbreviations: AST, Aspartate Aminotransferase; ALT, Alanine Aminotransferase.

Values are shown as weighted mean or weighted percentage.

Table 1b. Femoral neck BMD for persons with NAFLD and without NAFLD by gender/menopausal status, races, age, and BMI.

	NAFLD	Non-NAFLD	P value
Gender/Menopausal status			
Males	0.839 (0.007)	0.813 (0.004)	< 0.01
Postmenopausal Females	0.741 (0.007)	0.701 (0.005)	< 0.01
Premenopausal Females	0.827 (0.011)	0.804 (0.007)	0.06
Race			
White	0.792 (0.005)	0.760 (0.004)	< 0.01
Black	0.900 (0.009)	0.868 (0.006)	< 0.01
Mexican American	0.832 (0.006)	0.812 (0.005)	0.01
Age			
40 – 50 years	0.863 (0.008)	0.818 (0.005)	< 0.01
50 – 60 years	0.800 (0.009)	0.772 (0.006)	< 0.01
60 – 75 years	0.753 (0.007)	0.712 (0.004)	< 0.01
BMI			
- 25 kg/cm2	0.712 (0.012)	0.725 (0.005)	0.35
25 - 30 kg/cm2	0.780 (0.008)	0.788 (0.004)	0.35
30 - 35 kg/cm2	0.821 (0.008)	0.828 (0.009)	0.52
35 - kg /cm2	0.874 (0.010)	0.876 (0.013)	0.90

Data are expressed as an estimate (standard error). Moderate to severe steatosis people are categorized into NAFLD group, and mild steatosis or normal liver people are categorized into non-NAFLD group.

Table 2. Unadjusted association of NAFLD with femoral neck BMD.

	Beta coefficient of NAFLD	P value
All participants	0.031 (0.005)	< 0.01

Data are expressed as a beta estimate (standard error). Moderate to severe steatosis people are categorized into NAFLD group, and mild steatosis or normal liver people are categorized into non-NAFLD group.

Beta coefficient of NAFLD describes the difference of mean BMD among NAFLD group from mean BMD among non-NAFLD group.

Table 3. NAFLD effect on BMD for each gender/menopausal status, race, age, and BMI group is described as the slope of NAFLD in each linear regression model. Slope of NAFLD means the difference of BMD among NAFLD group from BMD among non-NAFLD group within each group.

	Slope of NAFLD	P value for Interaction term
Gender/Menopausal status		0.47
Males	0.026 (0.008)	
Postmenopausal Females	0.040 (0.009)	
Premenopausal Females	0.023 (0.012)	
Race		0.36
White	0.032 (0.006)	
Black	0.032 (0.010)	
Mexican American	0.019 (0.007)	
Age		0.47
40 – 50 years	0.045 (0.008)	
50 – 60 years	0.028 (0.010)	
60 – 75 years	0.042 (0.007)	
BMI		0.97
- 25 kg/cm2	-0.013 (0.013)	
25 - 30 kg/cm2	-0.008 (0.008)	
30 - 35 kg/cm2	-0.007 (0.010)	
35 - kg /cm2	-0.002 (0.016)	

Data are expressed as an estimate (standard error). Moderate to severe steatosis people are categorized into NAFLD group, and mild steatosis or normal liver people are categorized into non-NAFLD group.

Linear regression models have BMD as outcome, NAFLD status as exposure, one stratification variable, and the interaction term between the exposure and the stratification variable. P value describes the statistical significance in the interaction term.

Table 4. Multiple liner regression analysis for the NAFLD effect on bone mineral density controlling for other covariates.

	Model1	P value	Model2	P value
Intercept	0.733 (0.023)	< 0.01	0.738 (0.018)	< 0.01
NAFLD	0.009 (0.042)	0.83	-0.007 (0.005)	0.17
Non-NAFLD	Ref.		Ref.	
Postmenopausal Female	-0.098 (0.005)	< 0.01	-0.100 (0.005)	< 0.01
Premenopausal Female	-0.037 (0.007)	< 0.01	-0.039 (0.006)	< 0.01
Male	Ref.		Ref.	
Black	0.088 (0.005)	< 0.01	0.089 (0.005)	< 0.01
Mexican-American	0.027 (0.005)	< 0.01	0.025 (0.004)	< 0.01
White	Ref.		Ref.	
Age	-0.0034 (0.0002)	< 0.01	-0.0034 (0.0002)	< 0.01
BMI	0.0097 (0.0007)	< 0.01	0.0095 (0.0005)	< 0.01
Interaction terms				
NAFLD*Gender/Menopausal		0.74		
NAFLD*Postmenopausal	-0.006 (0.012)	0.62		
NAFLD*Premenopausal	-0.011 (0.016)	0.47		
NAFLD*Male	Ref.			
NAFLD*Races		0.57		
NAFLD*Black	0.006 (0.010)	0.53		
NAFLD*Mexican-American	-0.004 (0.008)	0.63		
NAFLD*White	Ref.			
NAFLD*Age	0.0001 (0.0005)	0.82		
NAFLD*BMI	-0.0006 (0.0010)	0.52		

Data are expressed as a beta estimate (standard error). Moderate to severe steatosis people are categorized into NAFLD group, and mild steatosis or normal liver people are categorized into non-NAFLD group. Age and BMI are dealt as continuous variables. Age variable and BMI variable are centered in these models around overall means, 54 and 27 respectively.

Model1 is a full model, controlling for gender/menopausal status, races, age, BMI, and their interactions with NAFLD status. (N=5860)

Model2 is a reduced model. Interaction terms were assessed, and insignificant terms were removed iteratively using backward elimination. All the interaction terms were not statistically significant, and removed. (N=5860)

Table 5. Multiple linear regression analysis for the NAFLD effects with high ALT or with normal ALT on bone mineral density controlling for covariates.

	Model3	P value	Model4	P value
Intercept	0.811 (0.004)	< 0.01	0.812 (0.004)	< 0.01
High ALT (HA) NAFLD	-0.0518 (0.0181)	< 0.01	-0.0505 (0.0150)	< 0.01
Normal ALT (NA) NAFLD	0.0067 (0.0085)	0.43	0.0003 (0.0054)	0.96
Non-NAFLD	Ref.		Ref.	
Postmenopausal	-0.098 (0.005)	< 0.01	-0.101 (0.004)	< 0.01
Premenopausal	-0.037 (0.007)	< 0.01	-0.040 (0.006)	< 0.01
Male	Ref.		Ref.	
Black	0.088 (0.005)	< 0.01	0.089 (0.005)	< 0.01
Mexican-American	0.027 (0.005)	< 0.01	0.027 (0.005)	< 0.01
White	Ref.		Ref.	
Age	-0.0034 (0.0003)	< 0.01	-0.0034 (0.0002)	< 0.01
BMI	0.0097 (0.0009)	< 0.01	0.0097 (0.0007)	< 0.01
Interaction terms				
HA/NA NAFLD * gender/menopausal		0.48		
HA NAFLD * Postmenopausal	-0.015 (0.025)	0.55		
HA NAFLD * Premenopausal	0.021 (0.032)	0.52		
NA NAFLD * Postmenopausal	-0.009 (0.012)	0.49		
NA NAFLD * Premenopausal	-0.021 (0.016)	0.19		
HA/NA NAFLD * races		0.65		
HA NAFLD * Black	0.011 (0.035)	0.76		
HA NAFLD * Mexican-American	0.024 (0.021)	0.25		
NA NAFLD * Black	0.005 (0.010)	0.63		
NA NAFLD * Mexican-American	-0.008 (0.010)	0.45		
HA/NA NAFLD * age		0.27		
HA NAFLD * Age	0.0020 (0.0012)	0.11		
NA NAFLD * Age	-0.0003 (0.0006)	0.65		
HA/NA NAFLD * BMI		< 0.01		< 0.01
HA NAFLD * BMI	0.005 (0.002)	< 0.01	0.004 (0.002)	< 0.01

NA NAFLD * BMI	-0.001 (0.001)	0.27	-0.001 (0.001)	0.27

Data are expressed as beta estimate (standard error). Moderate to severe steatosis with high ALT people are categorized into HA NAFLD group, moderate to severe steatosis with normal ALT people are categorized into NA NAFLD group, and mild steatosis or normal liver people are categorized into non-NAFLD group. Age and BMI are dealt as continuous variables. Age variable and BMI variable are centered in these models around overall means, 54 and 27 respectively.

Abbreviations: HA NAFLD, NAFLD with high ALT; NA NAFLD, NAFLD with normal ALT.

Model3 is a full model, controlling for gender/menopausal status, races, age, BMI, and their interactions with NAFLD status. (N=5788)

Model4 is a reduced model. Interaction terms were assessed, and insignificant terms were removed iteratively using backward elimination. Only the interaction term between NAFLD status and BMI was statistically significant, and remained (N=5788)

Figures and Figure Legends

Figure 1. The association assessed in this study is confounded by gender/menopausal status, age, BMI, and races.

Figure 2. Participants selected after applying the inclusion and exclusion criteria.

At the last step, 265 males and 272 females did not have available ultrasonography results. 196 males and 281 females did not have available bone mineral density results.

Figure 3. Femoral neck BMD predicted by the final model for different NAFLD groups at different BMI levels

Abbreviations: HA NAFLD, NAFLD with high ALT; NA NAFLD, NAFLD with normal ALT.

Moderate to severe steatosis with high ALT people are categorized into HA NAFLD group, moderate to severe steatosis with normal ALT people are

categorized into NA NAFLD group, and mild steatosis or normal liver people are categorized into non-NAFLD group.

The final model has NAFLD group variable as exposure, and controls for gender/menopausal status, races, age, and BMI. The interaction term between NAFLD group and BMI is included.

The BMD values were predicted for each NAFLD group at different BMI levels. The population was stratified by BMI into 15-20, 20-25, 25-30, 30-35, and 35-40 kg/m2 groups. For each group, average value of age was used. For BMI, not mean but the middle value of each range was used (e.g. for 20-25 BMI group, 22.5 was used). For categorical variables, gender/menopausal status and races, the proportion of each group was used. For each NAFLD and BMI group, these values are plugged into the final model, and predicted BMDs were obtained.

Fig 1. The association assessed in this study is confounded by gender/menopausal status, age, BMI, and races.

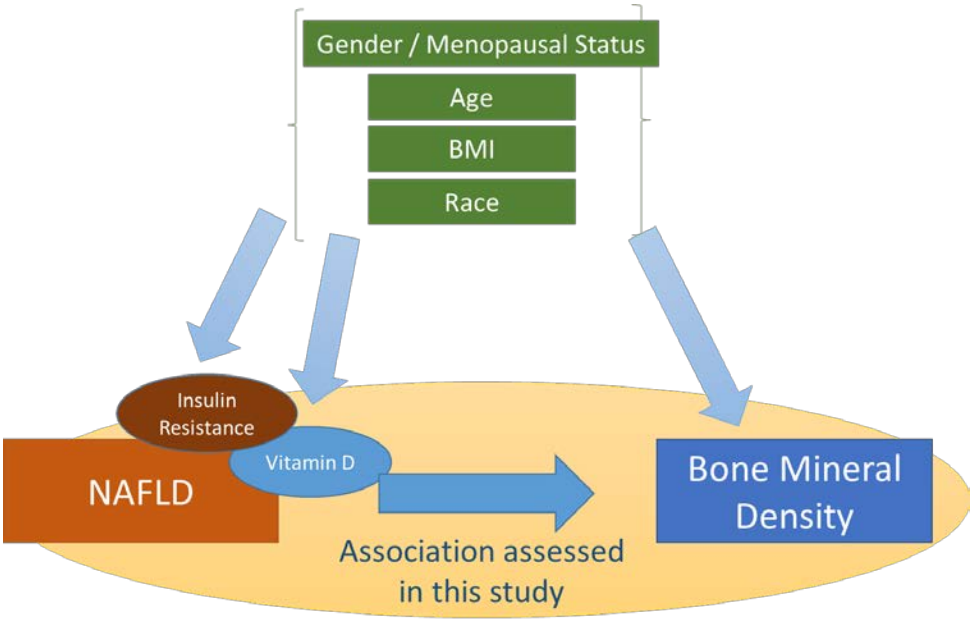


Fig 2. Participants selected after applying the inclusion and exclusion criteria.

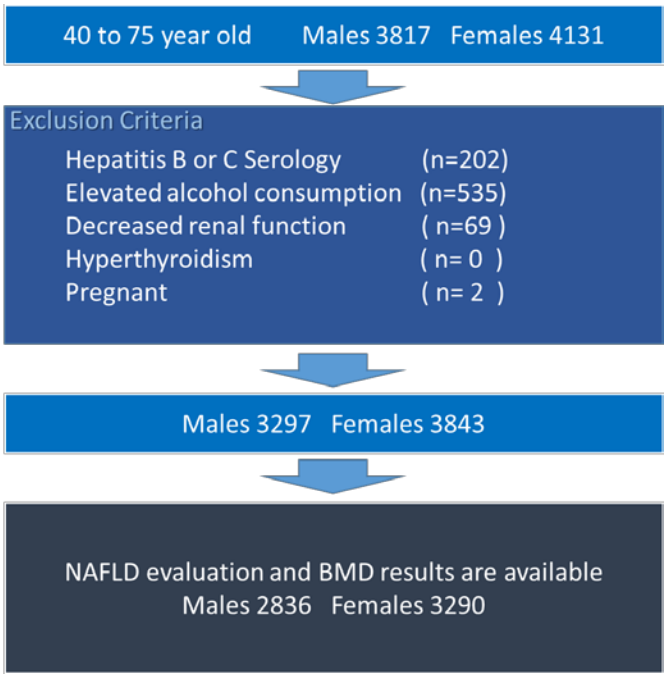
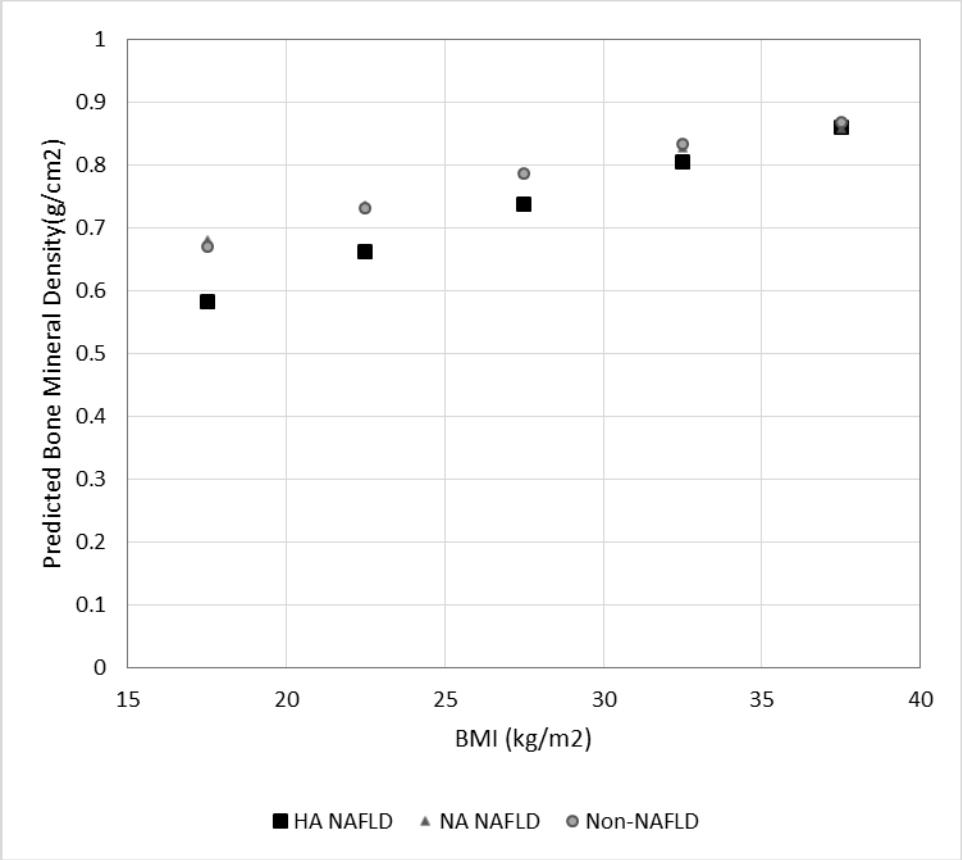


Fig 3. Femoral neck BMD predicted by the final model for different NAFLD groups at different BMI levels



Appendices

Supporting Information

S1 Table. Unadjusted association of high ALT NAFLD and normal ALT NAFLD with bone mineral density.

	Beta coefficients of NAFLD	P value
All participants		
HA NAFLD	0.055 (0.014)	< 0.01
NA NAFLD	0.026 (0.005)	< 0.01
Non-NAFLD	Ref.	

Data are expressed as beta estimate (standard error). Moderate to severe steatosis with high ALT people are categorized into HA NAFLD group, moderate to severe steatosis with normal ALT people are categorized into NA NAFLD group, and mild steatosis or normal liver people are categorized into non-NAFLD group.

Beta coefficients of NAFLD describes the difference of mean BMD of each NAFLD status from mean BMD among non-NAFLD group.

S2 Table. HA NAFLD and NA NAFLD effects on BMD for each gender/menopausal status, race, age, and BMI group are described as the slopes of HA NAFLD and NA NAFLD in each linear regression model.

	Effects of NAFLD		Interaction term
	Slope of HA NAFLD	Slope of NA NAFLD	P value
Gender/Menopausal status			0.39
Males	0.0318 (0.0165)	0.0255 (0.0079)	
Postmenopausal Females	0.0826 (0.0290)	0.0326 (0.0091)	
Premenopausal Females	0.0002 (0.0367)	0.0249 (0.0116)	
Race			0.25
White	0.058 (0.016)	0.027 (0.006)	
Black	0.028 (0.030)	0.030 (0.011)	
Mexican American	0.050 (0.013)	0.008 (0.008)	
Age			0.26
40 – 50 years	0.031 (0.021)	0.050 (0.010)	
50 – 60 years	0.041 (0.024)	0.025 (0.011)	
60 – 75 years	0.092 (0.027)	0.037 (0.008)	
BMI			0.76
25 kg/cm2	-0.014 (0.048)	-0.014 (0.016)	
25 - 30 kg/cm2	-0.020 (0.023)	-0.007 (0.009)	
30 - 35 kg/cm2	0.002 (0.019)	-0.010 (0.011)	
35 - kg /cm2	0.035 (0.030)	-0.010 (0.015)	

Data are expressed as an estimate (standard error). Moderate to severe steatosis with high ALT people are categorized into HA NAFLD group, moderate to severe steatosis with normal ALT people are categorized into NA NAFLD group, and mild steatosis or normal liver people are categorized into non-NAFLD group.

Linear regression models have BMD as outcome, NAFLD status as exposure, one stratification variable, and the interaction term between the exposure and the stratification variable. P value describes the statistical significance in the interaction term.

S3 Table. Median value of HOMA-IR was calculated for each level of BMI and NAFLD status.

	HA NAFLD	NA NAFLD	Non-NAFLD
BMI			
15-20	No observations	1.17 (0.24)	1.17 (0.04)
20-25	2.13 (0.36)	1.98 (0.07)	1.56 (0.04)
25-30	4.04 (0.30)	3.28 (0.14)	2.25 (0.06)
30-35	6.03 (0.57)	4.30 (0.17)	3.11 (0.06)
35-40	9.17 (1.42)	5.84 (0.43)	4.77 (0.39)

Abbreviation: HOMA, homeostatic model assessment; IR, insulin resistance; HA NAFLD, NAFLD with high ALT; NA NAFLD, NAFLD with normal ALT.

Data are expressed as a median estimate (standard error). Median HOMA-IR was calculated because the HOMA-IR distribution was right skewed.

HOMA-IR quantifies the strength of insulin resistance. HOMA-IR was calculated by serum insulin (uU/mL) * serum glucose (mmol/L) / 22.5. Serum insulin and serum glucose should be measured at fasting state. I only included people who ate or drank last more than 6 hours before. To exclude extremely low or high blood glucose people, only the people with glucose level of 50mg/dl to 250mg/dl were included. The total number of people included in this table was 4674.

S4 Table. Median value of serum vitamin D (25 OH D) for each level of BMI and NAFLD status

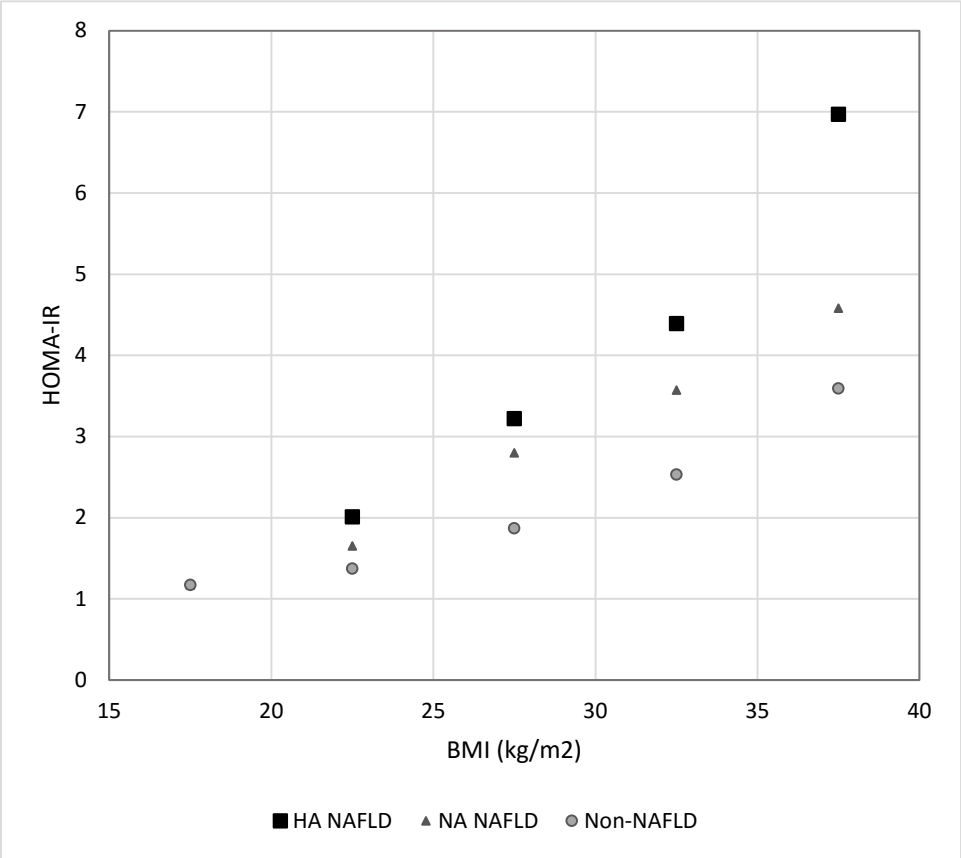
	HA NAFLD	NA NAFLD	Non-NAFLD
BMI			
15-20	No observations	64.50 (8.59)	65.55 (3.53)
20-25	66.00 (4.14)	72.38 (4.99)	74.67 (1.41)
25-30	76.50 (3.54)	69.00 (2.09)	70.66 (1.12)
30-35	74.74 (5.44)	65.66 (3.08)	67.97 (2.95)
35-40	69.89 (7.39)	55.16 (1.73)	56.52 (3.05)

Data are expressed as a median estimate (standard error). Serum vitamin D level (nmol/L) was used.

Data are expressed as a median estimate (standard error). Median vitamin D was calculated because the vitamin D distribution was right skewed.

The total number of people included in this table was 5702.

S1 Figure. Median HOMA-IR for different NAFLD groups at different BMI levels



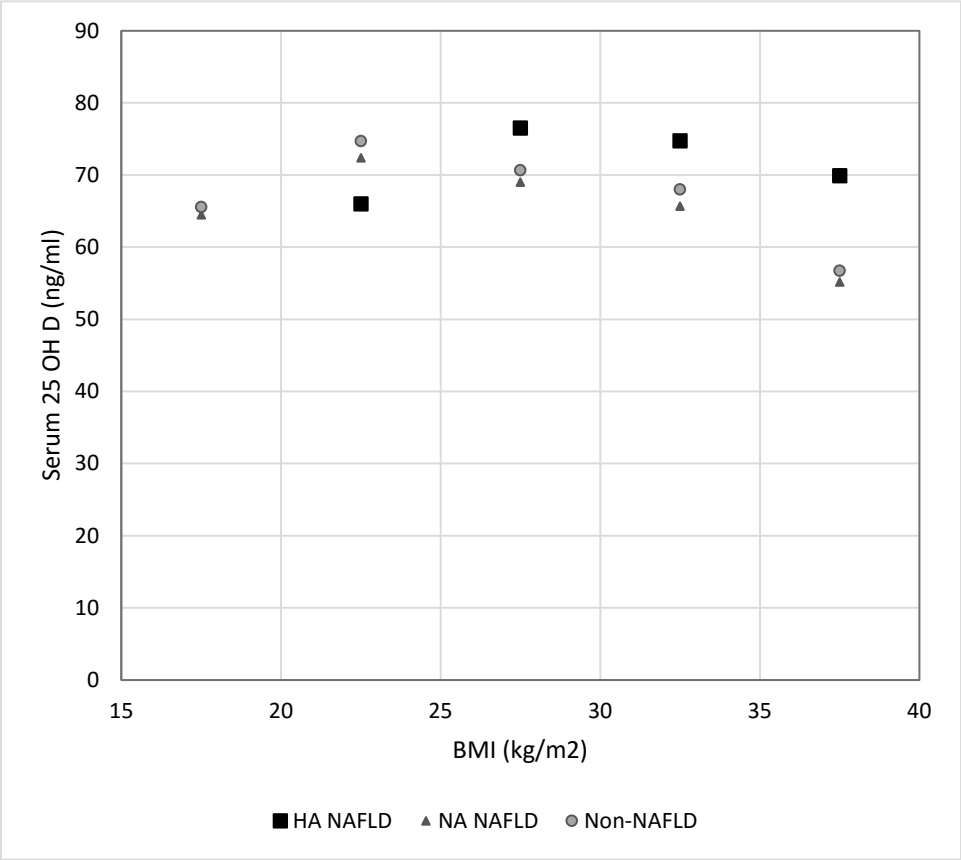
HA NAFLD does not have a plot in the BMI group of 15-20, because there are no observations with BMI of 15-20 among HA NAFLD group.

Abbreviations: HOMA-IR, homeostatic model assessment of insulin resistance; HA NAFLD, NAFLD with high ALT; NA NAFLD, NAFLD with normal ALT.

Moderate to severe steatosis with high ALT people are categorized into HA NAFLD group, moderate to severe steatosis with normal ALT people are categorized into NA NAFLD group, and mild steatosis or normal liver people are categorized into non-NAFLD group.

The median HOMA-IR was obtained for each NAFLD group at different BMI levels. The population was stratified by BMI into 15-20, 20-25, 25-30, 30-35, and 35-40 kg/m2 groups.

S2 Figure. Median 25 OH(D) for different NAFLD groups at different BMI levels



HA NAFLD does not have a plot in the BMI group of 15-20, because there are no observations with BMI of 15-20 among HA NAFLD group.

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; HA NAFLD, NAFLD with high ALT; NA NAFLD, NAFLD with normal ALT.

Moderate to severe steatosis with high ALT people are categorized into HA NAFLD group, moderate to severe steatosis with normal ALT people are categorized into NA NAFLD group, and mild steatosis or normal liver people are categorized into non-NAFLD group.

The median 25(OH)D was obtained for each NAFLD group at different BMI levels. The population was stratified by BMI into 15-20, 20-25, 25-30, 30-35, and 35-40 kg/m2 groups.

SAS Source Codes

There are three source code files attached.

- data_combine_code.sas
- final_analysis_thesis.sas
- final_analysis_thesis_discussion.sas

The first code, data_combin_code.sas, combines datasets obtained from NHANE III website, and extract variables necessary for this study. Finally it outputs nhanes3final.sas7bdat dataset file in the same directory.

The second code, final_analysis_thesis.sas, includes descriptive analysis, simple linear regression, and multiple linear regression. The first analysis comparing NAFLD and BMD, and the second analysis comparing HA NAFLD and NA NAFLD with BMD are included.

The third code, final_analysis_thesis_discussion.sas, includes descriptive analysis about insulin resistance and vitamin D that was mentioned in discussion part.

data_combine_code.sas

```
libname combine ".\";

/* First run the following programs to obtain each dataset.
*/

/* After downloading each dataset from NHANES III website, */
/* the following codes attached with each dataset were run, and I
obtained SAS format datasets. */
/*
".\adult.sas";
".\exam.sas";
".\lab.sas";
".\lab2.sas";
".\nhanes17A.sas";
".\nhanes34A.sas";
*/
/*
I stored these SAS datasets created in the current dicretory. The names
are as follows,
adult.sas7bdat, exam.sas7bdat, lab.sas7bdat, lab2.sas7bdat,
nhanes17A.sas7bdat, and nhanes34A.sas7bdat
*/



/*********************************/
/* Extracting variables used in this study */
/*********************************/

libname combine ".\";

DATA fltrd_adult ;
  length SEQN 8;
  set combine.adult;
```

```
  keep SEQN SDPSTRA6 SDPPSU6 WTPFEX6
       MXPSESSR HXPSESSR
       HAR1 HAR3 HAR5
       DMPPIR
       HFA8R
  ;
RUN;

DATA fltrd_exam ;
  length SEQN 8;
  set combine.exam;
  keep SEQN SDPSTRA6 SDPPSU6 WTPFEX6
          HSAGEIR
       HSSEX  DMARACER DMAETHNR DMARETHN
       BMPBMI BMPWT BMPHT
       MYPF3S MYPF4
          BDPEXFLR  BDPFNBMD  BDPTOBMD
          MAPE3S MAPE4
          MAPF12 MAPF15 MAPF21 MAPF22 MAPF32S
       MAPF25 MAPF26 MAPF27 MAPF28 MAPF29
          PEP6G1 PEP6G3 PEP6H1 PEP6H3 PEP6I1 PEP6I3
  ;

RUN;


DATA fltrd_lab ;
  length SEQN 8;
  set combine.lab;
  keep SEQN SDPSTRA6 SDPPSU6 WTPFEX6
       G1P G1PSI SGP SGPSI TGP TGPSI LCP LCPSI
       HDP HDPSI CEP CRP ASPSI ATPSI SSP SAP HCP I1P I1PSI
          FHPSI
          PHPFAST
  ;
RUN;
```

```
/* PHPFAST : Computed number of hours since last ate or drank. 88888
should be converted into . */


DATA fltrd_lab2 ;
  length SEQN 8;
  set combine.lab2;
  keep SEQN SDPSTRA6 SDPPSU6 WTPFEX6
  T4P T4PSI THP THPSI VDP VDPSI ;
RUN;

DATA fltrd_17a ;
  length SEQN 8;
  set combine.nhanes17a;
  keep SEQN
  BDPSCAN BGPNNBMD BGPITBMD  BGPFSBMD ;
RUN;


DATA fltrd_34a ;
  length SEQN 8;
  set combine.nhanes34a;
  keep SEQN
       GUPHSPF GUPHSPFR
       GUPHSLKC /* Liver to kidney contrast */
       GUPHSPB /* Parenchymal brightness */
       GUPHSDBA /* Deep beam attenuation */
       GUPHSVW /* Vessel walls  */
       GUPHSDGB /* GB waLL*/
       GUPHSPF /* HS primary finding */
  ;
RUN;

DATA combine.nhanes3cmbd;
  merge fltrd_adult fltrd_exam fltrd_lab fltrd_lab2 fltrd_17a fltrd_34a
;
```

```
  by SEQN;
RUN;


DATA nhanes3;
  set combine.nhanes3cmbd;
  /* Weights and sampling design */
  ststr = SDPSTRA6;
  psu = SDPPSU6;
  sweight = WTPFEX6;

  /* People who took exam at MEC */
  mec_exam = 2;
  if MXPSESSR in (1, 2, 3) then mec_exam = 1;
  /* People who took exam at HOME */
  home_exam = 2;
  if HXPSESSR in (1, 2, 3, 8) then home_exam = 1;

  /* AGE, GENDER, RACE-ETHNICITY. These variables have no missing
values from 40 <= age <= 75. */
  /* Guideline: http://www.cdc.gov/nchs/data/nhanes/nhanes3/nh3gui.pdf
*/
  age = HSAGEIR ; /* HSAGEIR comes from adult interview. So 1888
younter people seems to be coded as missing. */
  if 20 <= age <= 29 then age_cat = 1;
  else if 30 <= age <= 39 then age_cat = 2 ;
  else if 40 <= age <= 49 then age_cat = 3 ;
  else if 50 <= age <= 59 then age_cat = 4 ;
  else if 60 <= age <= 74 then age_cat = 5 ;

  if HSSEX = 1 then female = 2 ; /* When male */
  else if HSSEX = 2 then female = 1;
  race = DMARACER ;  /* 1: White 2: Black 3: Others.  I WON'T USE THIS
VARIABLE. */
  raceeth = DMARETHN ; /* 1: NH white 2: NH black 3: Mexican-American
4: Others */
```

```
                    /* Others group includes other Hispanics,
Asians, and Native American. Sample size is small to analyze. */

  bodyweight = BMPWT;  /* Weight: BMPWT (kg) */
  if bodyweight = 888888 then bodyweight = . ;
  height = BMPHT ;    /* Standing height:  BMPHT (cm) */
  if height = 88888 then bodyweight = . ;
  BMI = BMPBMI ;      /* BMI */
  if (bmi = 8888) then bmi = .;
  calc_bmi = bodyweight / (height/100) / (height/100) ; /* I confirmed
that BMI and CALC_BMI correlate completely */

  /* alcohol consumption */
  excess_alc = . ;
  days_of_drk = MAPE3S;
  if days_of_drk in (888, 999) then days_of_drk = . ;
  num_of_drk = MAPE4;
  if num_of_drk in (888, 999) then num_of_drk = . ;
  if num_of_drk = 90 then num_of_drk = 9;
  avrg_num_drk = num_of_drk * days_of_drk / 365;
  if (female = 1) and (avrg_num_drk > 1 ) then  excess_alc = 1;
  if (female = 2) and (avrg_num_drk > 2 ) then  excess_alc = 1;

  /* LAB data */
  tsh = THP;
  if (tsh = 888888) then tsh = .;
  hbv = SAP; /* Hepatitis B surface antigen (HBsAg) */
  hcv = HCP; /* Hepatitis C antibody (HCV-antibody) */

  cre = CEP; /* mg/dl
https://en.wikipedia.org/wiki/Renal_function#Estimated_GFR_.28eGFR.29_u
sing_Modification_of_Diet_in_Renal_Disease_.28MDRD.29_formula*/
  if (cre = 8888) then cre = . ;

  std_cre = 0.960 * cre - 0.184 ;
  egfr = 175 * (std_cre ** (-1.154)) * (age ** (-0.203)) * 0.742 ;
```

```
  if (race = 2) then egfr = egfr * 1.212 ;

  /* Hyperthyroidism */
  hyper_thy = .;
  if 0 <= tsh < 0.1 then hyper_thy = 1;
  else if 0.1 <= tsh then hyper_thy = 2;

  /* Hepatitis */
  hepatitis = 2;
  if hbv = 1 then  hepatitis = 1;
  if hcv = 1 then hepatitis = 1;

  /* Renal dysfunction */
  renal_dys = .;
  if 0 < egfr < 30 then renal_dys = 1;
  else if 30 <= egfr  then renal_dys = 2;

  /* HOMA-IR*/
  insulin = I1P;  /* uU/mL */
  if insulin = 888888 then insulin = .;
  glucose = SGPSI;  /* mmol/L */
  if glucose = 88888 then glucose = .;
  homa_ir = (insulin * glucose)/22.5 ;
  /* This formula is confirmed by the article,
http://care.diabetesjournals.org/content/27/6/1487.long */

  /* Hours after the person ate or drank last. */
  hrs_last_eat  =  PHPFAST ;
  if hrs_last_eat = 88888 then hrs_last_eat = . ;

  /* ALT */
  alt = ATPSI ; /* Alanine aminotransferase: SI (U/L) (U/L) */
  if alt = 888 then alt = . ;

  /* Vitamin D*/
  vitamin_d = VDPSI ;
```

```
  /* Bone mineral density */
  /* Explanation:
ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/nhanes/nhanes3/17A/readme.
txt */

  /* CRP */
  if crp = 88888 then crp = . ;   /* NOT USED */

  bmd_fn = BDPFNBMD ;
  if bmd_fn = 88888 then bmd_fn = . ;

  bmd_tr = BDPTOBMD ;  /* NOT USED */
  if bmd_tr = 88888 then bmd_tr = . ;

  bmd_nn = BGPNNBMD ;  /* NOT USED */
  if bmd_nn = 88888 then bmd_nn = . ;

  bmd_it = BGPITBMD ;  /* NOT USED */
  if bmd_it = 88888 then bmd_it = . ;

  bmd_fs = BGPFSBMD ;  /* NOT USED */
  if bmd_fs = 88888 then bmd_fs = . ;

  bmd_exam = BDPEXFLR ;
  bmd_fn_exam = 2;
  if 0 <= BGPNNBMD <= 5 then bmd_fn_exam = 1;

  /* fatty liver */
  /* Explanation: http://www.cdc.gov/nchs/nhanes/nhanes3/HGUHS.htm */
  fld_status = GUPHSPF ;

  if fld_status in (7,8) then fld = . ;
  else if fld_status in (1, 2) then fld = 2; /*Normal (or mild) */
  else if fld_status in (3, 4) then fld = 1; /*Moderate-severe */
```

```
  /* Four categories in fattyliver   */
  fld_cat = fld_status;
  if fld_cat in (7,8) then fld_cat = . ; /* 1: Normal, 2: Mild, 3:
Moderate, 4: Severe */

  /* New two categories in fattyliver */
  if fld_status in (7,8)          then fld2 = . ;
  else if fld_status in (1 )      then fld2 = 2; /*Normal */
  else if fld_status in (2, 3, 4) then fld2 = 1; /*Mild-Moderate-severe
*/


  /* Fattyliver with ALT severity. I feel this variable is hard to use.
Because the number of fld_alt =3 people is not so large.  */
  fld_alt3 = .;
  if (female in ( 1, 2 )) then do;
    if GUPHSPF in (1, 2) then fld_alt3 = 3;
    else if (GUPHSPF in (3,4) and (0 < alt < 30 ))   then fld_alt3 = 2;
    else if (GUPHSPF in (3,4) and 880 >= alt >= 30 ) then fld_alt3 = 1;
  end;

  /* Menopausal status */
  postmenop = . ;
  premenop = .; /* I won't use this variable. */
  gendermenop = . ;

  bilat_ovrmv = .;
  if MAPF28 = 2 then bilat_ormv = 1; /* 1: Both removed */

  preg_lasty = .;
  period_lasty = .;

  if (MAPF12 = 1) then preg_lasty = 1; /* Current pregnant: MYPC17 =
1*/
  if (MAPF15 in (1,2,3,4) ) then preg_lasty = 1; /* Pregnant last less
than 12 months.  It's wired, but all of them from 13 to 16 y.o.  */
```

```
  if (MAPF21 = 1) or (MAPF22 in (1,2,3,4,5,6) ) then period_lasty = 1;
/* last menstrual period: MYPC3. It's wired, but all of them from 13 to
16 y.o. */

  fsh_level = FHPSI ; /* Unit is (IU/L) */

  contraceptrx = . ; /* MYPC7S asks how many months ago, stop taking
contraceptive pills.*/
  if (MAPF32S = 0) or (MAPF32S = 777) then contraceptrx = 1;

  if (female=1) and (age>=60) then postmenop = 1;
  else if (female=1) and (bilat_ovrmv = 1) then postmenop = 1;
  else if (female=1) and (preg_lasty = 1) then premenop = 1 ;
  else if (female=1) and (period_lasty = 1) then premenop =1 ;  /*
Experienced menopause last year. */
  else if (female=1) and (fsh_level > 40) then postmenop =1 ;
  else if (female=1) and (contraceptrx = 1) then premenop = 1;

  /* Additional coding for menopausal status. */
  else if (female=1) and (MAPF21 in (2, 9) ) then do ; postmenop = 1;
mapf21_cat = 1 ; end;  /* No Menopause last year */
  /* 39 females could not be coded. So I devide them into two, by 50
years old.  */
  else if (female=1) and (age > 50 ) then do; postmenop = 1 ;
special_post = 1; end; /* 11 females are into post*/
  else if (female=1) and (40 <= age <= 50 ) then do; premenop = 1;
special_pre = 1; end;  /* 28 females are into pre */

  /* Coding based on gender and menopausal status */
  if (female = 2) then gendermenop = 1;
  else if (female = 1 )and ( premenop = 1 )then  gendermenop = 2 ;
  else if (female = 1 )and ( postmenop = 1 )then  gendermenop = 3 ;

  /* lab values */
  /* SBP */
```

```
  sbp = PEP6G1;
  if sbp = 888 then sbp = .;

  /* DBP */
  dbp = PEP6G3;
  if dbp = 888 then dbp = .;

  /* FPG: We already have this variable. glucose. */

  /* TG */
  tg = tgp;
  if tg = 888 then tg = .;
  if tg = 8888 then tg = .;

  /* HDL */
  hdl = hdp;
  if hdl = 888 then hdl = . ;

  /* LDL */
  ldl = lcp;
  if ldl = 888 then ldl =.;

  /* AST */
  ast = ASPSI ;
  if ast = 888 then ast = .;
RUN;
DATA nhanes3;
  set nhanes3;
  bmi_flag = . ;
  hepat_flag = . ;
  alc_flag = .;
  renal_flag = .;
  thyro_flag = .;
  preg_flag = .;

  if bmi = . then bmi_flag = 1;
```

```
  if hepatitis = 1 then hepat_flag = 1;
  if excess_alc = 1 then alc_flag = 1;
  if renal_dys = 1 then renal_flag = 1;
  if MAPF12 = 1  then preg_flag = 1;
RUN;

DATA combine.nhanes3final;
  set nhanes3;
RUN;
```

final_analysis_thesis.sas

```
/*
Software versions used for this analysis.

SAS (r) Proprietary Software 9.4 (TS1M1)

SUDAAN Release 11.0.1, Build 326
SAS-Callable, 32 bit version
*/

libname thesis "./";
DATA nh3;   set thesis.nhanes3final;  RUN;
PROC SORT data = nh3;   by ststr psu ; RUN;
options ls=132;

DATA nh3;
  set nh3;
  bmd_fn2 = 10 * bmd_fn ; /* To obtain more number of decimal places in
SUDAAN output. The meaning is the same as bmd_fn, but the scale is 10
times. */
  bmd_fn3 = 100 * bmd_fn ;  /* To obtain more number of decimal places
in SUDAAN output. The meaning is the same as bmd_fn, but the scale is
100 times. */

  c_bmi = bmi - 27 ;
  c_age = age - 54 ;

  glucose_mg = glucose * 18 ;

  bmi_cat = . ;
  if 0 < bmi < 25 then bmi_cat = 1;
  else if 25 <= bmi < 30 then bmi_cat = 2;
  else if 30 <= bmi < 35 then bmi_cat = 3;
  else if 35 <= bmi < 90 then bmi_cat = 4;
```

```
  else bmi_cat = .;

  /* Reverse order coding */

  rgendermenop = . ;
  if gendermenop = 1 then rgendermenop = 3; /* Males (reference) */
  else if gendermenop = 2 then rgendermenop = 2; /* Premenop */
  else if gendermenop = 3 then rgendermenop = 1; /* Postmenop */
  else rgendermenop = . ;

  rraceeth3 = . ;
  if raceeth = 1 then rraceeth3 = 3; /* White (reference) */
  else if raceeth = 2 then rraceeth3 = 1;  /* Black */
  else if raceeth = 3 then rraceeth3 = 2;  /* Mexican-American */
  else if raceeth = 4 then rraceeth3 = . ;
  else rraceeth3 = . ;

  wb_race = .;
  if raceeth = . then wb_race = . ;
  else if raceeth = 3 then wb_race = . ;
  else if raceeth = 1 then wb_race = 2 ; /* White (reference) */
  else if raceeth = 2 then wb_race = 1 ; /* Black (reference) */

RUN;


/*************************/
/* Descriptive analysis  */
/*************************/

/* Run to obtain numbers of people. */
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup fld ;
```

```
  level    2   ;

  table fld  ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Gender */
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup fld gendermenop ;
  level    2   3       ;

  table fld * gendermenop ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup fld gendermenop ;
  level    2   3       ;

  TEST CHISQ;
  table fld * gendermenop ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Race */
```

```
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup fld raceeth ;
  level    2   4       ;

  table fld * raceeth ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup fld raceeth ;
  level    2   4       ;

  TEST CHISQ;
  table fld * raceeth ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Age */
PROC DESCRIPT data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup fld ;
  level    2   ;

  var age  ;
```

```
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup fld ;
  level    2   ;

  var age  ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Weigtht */
PROC DESCRIPT data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup  fld ;
  level     2    ;

  var bodyweight ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
```

```
  subgroup fld ;
  level    2   ;

  var bodyweight ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* BMI */
PROC DESCRIPT data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup  fld ;
  level     2    ;

  var bmi ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup fld ;
  level    2   ;

  var bmi ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
```

```
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Smoking Status */
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup fld smk ;
  level    2   3       ;

  table fld * smk ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup fld smk ;
  level    2   3       ;

  table fld * smk ;
  test chisq;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* systolic blood pressure */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
```

```
  subgroup  fld ;
  level     2    ;
  var sbp ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* diastolic blood pressure */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup  fld ;
  level     2    ;
  var dbp ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;


/* Blood glucose */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup  fld ;
  level     2    ;
  var glucose_mg;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
```

```
/* Triglyceride */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup  fld ;
  level     2    ;
  var tg;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* HDL-chol */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup  fld ;
  level     2    ;
  var hdl;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* LDL-chol */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup  fld ;
  level     2    ;
  var ldl;
```

```
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* AST */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup  fld ;
  level     2    ;
  var ast ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup fld ;
  level    2   ;

  var ast ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* ALT */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
```

```
  subgroup  fld ;
  level     2    ;
  var alt ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup fld ;
  level    2   ;

  var alt ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Femur neck BMD  */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup  fld ;
  level     2    ;
  var bmd_fn ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT data = nh3 filetype=SAS design=wr;
```

```
  nest ststr psu;
  weight sweight ;

  subgroup fld ;
  level    2   ;

  var bmd_fn ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Osteoporosis */
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  NEWVAR osteoporo_two : if osteoporosis in (0) then osteoporo_two = 2
else osteoporo_two = osteoporosis;

  subgroup fld raceeth osteoporo_two ;
  level    2   4       2 ;

  table fld * osteoporo_two ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  NEWVAR osteoporo_two : if osteoporosis in (0) then osteoporo_two = 2
else osteoporo_two = osteoporosis;

  subgroup fld raceeth osteoporo_two ;
```

```
  level    2   4       2 ;

  table fld * osteoporo_two ;
  test chisq;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Osteopenia */
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  NEWVAR osteopenia_two : if osteopenia in (0) then osteopenia_two = 2
else osteopenia_two = osteopenia ;

  subgroup fld raceeth osteopenia_two;
  level    2   4       2;

  table fld * osteopenia_two ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  NEWVAR osteopenia_two : if osteopenia in (0) then osteopenia_two = 2
else osteopenia_two = osteopenia ;

  subgroup fld raceeth osteopenia_two;
  level    2   4       2;

  table fld * osteopenia_two ;
  test chisq;
```

```
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;


/* Education */
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup gendermenop fld educ_cat ;
  level    3           2   4       ;

  table fld * educ_cat ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;


/* Categories by PIR */
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup gendermenop fld pir_cat ;
  level    3           2   3       ;

  table fld * pir_cat ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/************/
```

```
/* Table 1b */
/************/
/* gender menop */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  subpopx (gendermenop = 1) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (gendermenop = 1) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  subpopx (gendermenop = 3) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
```

```
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (gendermenop = 3) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  subpopx (gendermenop = 2) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (gendermenop = 2) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
```

```
/* race */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  subpopx (raceeth = 1) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (raceeth = 1) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  subpopx (raceeth = 2) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
```

```
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (raceeth = 2) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  subpopx (raceeth = 3) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (raceeth = 3) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* age_cat */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
```

```
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  subpopx (age_cat = 3) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (age_cat = 3) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  subpopx (age_cat = 4) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
```

```
  level     2    ;
  var bmd_fn3 ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (age_cat = 4) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  subpopx (age_cat = 5) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (age_cat = 5) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* BMI category */

PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
```

```
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  subpopx (bmi_cat = 1) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (bmi_cat = 1) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  subpopx (bmi_cat = 2) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
```

```
  var bmd_fn3 ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (bmi_cat = 2) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  subpopx (bmi_cat = 3) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (bmi_cat = 3) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
```

```
  var bmd_fn3 ;
  subpopx (bmi_cat = 4) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup  fld ;
  level     2    ;
  var bmd_fn3 ;
  contrast fld = ( 1 -1 )/name = "NAFLD vs Non-NAFLD" ;
  print p_mean ;
  subpopx (bmi_cat = 4) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;



/******************/
/* Crude analysis */
/******************/
/* No stratification */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld ;
  PRINT / WSUMFMT=Fw.3;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
```

```
RUN;

/* Having interaction term between gendermenop * nafld */
PROC REGRESS  data = nh3 filetype=SAS design=wr;   /* ref: gendermenop
=1 */
  nest ststr psu;
  weight sweight ;
  NEWVAR gendermenop1 : if gendermenop in (1) then gendermenop1 = 3
else if gendermenop in (3) then gendermenop1 = 1 else if gendermenop in
(2) then gendermenop1 = 2;;
  subgroup fld     female gendermenop1 bmi_cat age_cat  raceeth
wb_race ;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld gendermenop1 fld * gendermenop1 ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;  /* ref: gendermenop
=3 */
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld gendermenop fld * gendermenop ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;   /* ref: gendermenop
=2 */
  nest ststr psu;
  weight sweight ;
```

```
  NEWVAR gendermenop2 : if gendermenop in (2) then gendermenop2 = 3
else if gendermenop in (3) then gendermenop2 = 2 else if gendermenop in
(1) then gendermenop2 = 1;;
  subgroup fld     female gendermenop2 bmi_cat age_cat  raceeth
wb_race ;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld gendermenop2 fld * gendermenop2 ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;


/* Stratify by gender */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld ;
  PRINT / WSUMFMT=Fw.3;
  subpopx (gendermenop = 1 ) and (0 < bmd_fn < 5 ) and ( fld != .  )
and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag !=
1) and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld ;
```

```
  subpopx (gendermenop = 3 ) and (0 < bmd_fn < 5 ) and ( fld != .  )
and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag !=
1) and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld ;

  subpopx (gendermenop = 2 ) and (0 < bmd_fn < 5 ) and ( fld != .  )
and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag !=
1) and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Having interaction term between races * nafld */
PROC REGRESS  data = nh3 filetype=SAS design=wr;   /* ref: raceeth =1
*/
  nest ststr psu;
  weight sweight ;
  NEWVAR raceeth1 : if raceeth in (1) then raceeth1 = 3 else if raceeth
in (3) then raceeth1 = 1 else raceeth1 = raceeth ;
  subgroup fld     female raceeth1 bmi_cat age_cat  raceeth  wb_race ;
  level    2       2      3           3       5         4        2
;

  model bmd_fn2 = fld raceeth1 fld * raceeth1 ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
```

```
PROC REGRESS  data = nh3 filetype=SAS design=wr;   /* ref: raceeth =2
*/
  nest ststr psu;
  weight sweight ;
  NEWVAR raceeth2 : if raceeth in (2) then raceeth2 = 3 else if raceeth
in (3) then raceeth2 = 2 else raceeth2 = raceeth ;
  subgroup fld     female raceeth2 bmi_cat age_cat  raceeth  wb_race ;
  level    2       2      3           3       5         4        2
;

  model bmd_fn2 = fld raceeth2 fld * raceeth2 ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female raceeth bmi_cat age_cat  raceeth  wb_race ;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld raceeth fld * raceeth;

  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Stratify by races */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5         4        2
;
```

```
  model bmd_fn2 = fld ;

  subpopx (raceeth = 1 ) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld ;

  subpopx (raceeth = 2 ) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld ;

  subpopx (raceeth = 3 ) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Having interaction term between age_group * nafld */
```

```
PROC REGRESS  data = nh3 filetype=SAS design=wr;   /* ref: age_cat =3
*/
  nest ststr psu;
  weight sweight ;
  NEWVAR age_cat3 : if age_cat in (3) then age_cat3 = 5 else if age_cat
in (5) then age_cat3 = 3 else if age_cat in (4) then age_cat3 = 4 else
age_cat3 = .  ;
  subgroup fld     female raceeth  bmi_cat age_cat3  raceeth  wb_race ;
  level    2       2      3           3       5         4        2
;

  model bmd_fn2 = fld age_cat3 fld * age_cat3 ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;   /* ref: age_cat =4
*/
  nest ststr psu;
  weight sweight ;
  NEWVAR age_cat4 : if age_cat in (4) then age_cat4 = 5 else if age_cat
in (5) then age_cat4 = 4 else if age_cat in (3) then age_cat4 = 3 else
age_cat4 = .  ;
  subgroup fld     female raceeth  bmi_cat age_cat4  raceeth  wb_race ;
  level    2       2      3           3       5         4        2
;

  model bmd_fn2 = fld age_cat4 fld * age_cat4 ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;   /* ref: age_cat =5
*/
  nest ststr psu;
  weight sweight ;
```

```
  subgroup fld     female raceeth  bmi_cat age_cat  raceeth  wb_race ;
  level    2       2      3           3       5        4        2
;

  model bmd_fn2 = fld age_cat fld * age_cat ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Stratify by age_group */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5        4        2
;
  model bmd_fn2 = fld ;

  subpopx (age_cat = 3 ) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5        4        2
;
  model bmd_fn2 = fld ;
```

```
  subpopx (age_cat = 4 ) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld ;

  subpopx (age_cat = 5 ) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;


/* Having interaction term between bmi_cat * nafld */
PROC REGRESS  data = nh3 filetype=SAS design=wr;   /* ref: bmi_cat = 1
*/
  nest ststr psu;
  weight sweight ;
  NEWVAR bmi_cat1 : if bmi_cat in (1) then bmi_cat1 = 4 else if bmi_cat
in (4) then bmi_cat1 = 1 else bmi_cat1 = bmi_cat  ;
  subgroup fld     female raceeth  bmi_cat1 age_cat  raceeth  wb_race ;
  level    2       2      3           4       5         4        2
;

  model bmd_fn3 = fld bmi_cat1 fld * bmi_cat1 ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
```

```
PROC REGRESS  data = nh3 filetype=SAS design=wr;   /* ref: bmi_cat = 2
*/
  nest ststr psu;
  weight sweight ;
  NEWVAR bmi_cat2 : if bmi_cat in (2) then bmi_cat2 = 4 else if bmi_cat
in (4) then bmi_cat2 = 2 else bmi_cat2 = bmi_cat  ;
  subgroup fld     female raceeth  bmi_cat2 age_cat  raceeth  wb_race ;
  level    2       2      3           4       5         4        2
;

  model bmd_fn3 = fld bmi_cat2 fld * bmi_cat2 ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;   /* ref: bmi_cat = 3
*/
  nest ststr psu;
  weight sweight ;
  NEWVAR bmi_cat3 : if bmi_cat in (3) then bmi_cat3 = 4 else if bmi_cat
in (4) then bmi_cat3 = 3 else bmi_cat3 = bmi_cat  ;
  subgroup fld     female raceeth  bmi_cat3 age_cat  raceeth  wb_race ;
  level    2       2      3           4       5         4        2
;

  model bmd_fn3 = fld bmi_cat3 fld * bmi_cat3 ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;   /* ref: bmi_cat = 4
*/
  nest ststr psu;
  weight sweight ;
  subgroup fld     female raceeth  bmi_cat age_cat  raceeth  wb_race ;
```

```
  level    2       2      3           4       5         4        2
;

  model bmd_fn3 = fld bmi_cat fld * bmi_cat ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Stratify by bmi_group */

PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld ;

  subpopx (bmi_cat = 1) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5         4        2
;
  model bmd_fn3 = fld ;

  subpopx (bmi_cat = 2) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
```

```
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld ;

  subpopx (bmi_cat = 3) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
;
  level    2       2      3           3       5         4        2
;
  model bmd_fn2 = fld ;

  subpopx (bmi_cat = 4) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;



/*******************/
/* Table 4         */
/*******************/
/*************************************************************/
/* Model analysis  */
/*************************************************************/
```

```
/* Model analysis */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
rgendermenop rraceeth3  ;
  level    2       2      3           3       5         4        2
3            3          ;
  model bmd_fn3 = fld rgendermenop rraceeth3 age bmi fld*rgendermenop
fld*rraceeth3 fld*age fld*bmi ;

  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Do backward elimination !! */
/* Drop AGE * FLD, because p = 0.8239  */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
rgendermenop rraceeth3  ;
  level    2       2      3           3       5         4        2
3            3          ;
  model bmd_fn3 = fld rgendermenop rraceeth3 age bmi fld*rgendermenop
fld*rraceeth3 fld*bmi ;

  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;


/* Drop FLD * RGENDERMENOP, because p = 0.7165 */
```

```
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
rgendermenop rraceeth3  ;
  level    2       2      3           3       5         4        2
3           3          ;
  model bmd_fn3 = fld rgendermenop rraceeth3 age bmi fld*rraceeth3
fld*bmi ;

  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Drop FLD * RRACEETH3 , because p  = 0.5556  */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
rgendermenop rraceeth3   ;
  level    2       2      3           3       5         4        2
3           3          ;
  model bmd_fn3 = fld rgendermenop rraceeth3 age bmi fld*bmi ;

  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Drop BMI * FLD , p = 0.5001  */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
rgendermenop rraceeth3  ;
```

```
  level    2       2      3           3       5         4        2
3            3          ;
  model bmd_fn3 = fld rgendermenop rraceeth3 age bmi ;

  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
/* This is the final model. No interaction terms. */


/*********************************************************/
/*********************************************************/
/* FROM HERE, Different NAFLD categorization is used. */
/* ALT level is taken into account. */
/*********************************************************/
/*********************************************************/

/*********************************************************/
/*  FLD_ALT3 analysis                                    */
/*********************************************************/
PROC FREQ data = nh3;
  tables fld * fld_alt3 ;
RUN;

/* Stratification analysis */
/* No stratification */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  model bmd_fn3 = fld_alt3 ;
```

```
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Having interaction term btw nafld * gender */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  reflevel gendermenop = 1;
  model bmd_fn3 = fld_alt3 gendermenop fld_alt3 * gendermenop ;
  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  reflevel gendermenop = 2;
  model bmd_fn3 = fld_alt3 gendermenop fld_alt3 * gendermenop ;
  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
```

```
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  reflevel gendermenop = 3;
  model bmd_fn3 = fld_alt3 gendermenop fld_alt3 * gendermenop ;
  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Stratify by gender */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  model bmd_fn3 = fld_alt3 ;
  subpopx (gendermenop = 1 ) and (0 < bmd_fn < 5 ) and ( fld != .  )
and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag !=
1) and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  model bmd_fn3 = fld_alt3 ;
  subpopx (gendermenop = 3 ) and (0 < bmd_fn < 5 ) and ( fld != .  )
and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag !=
1) and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
```

```
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  model bmd_fn3 = fld_alt3 ;
  subpopx (gendermenop = 2 ) and (0 < bmd_fn < 5 ) and ( fld != .  )
and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag !=
1) and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Having interaction term btw nafld * raceeth */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         3        2
3 ;
  reflevel raceeth = 1;
  model bmd_fn3 = fld_alt3 raceeth fld_alt3 * raceeth ;
  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         3        2
3 ;
  reflevel raceeth = 2;
  model bmd_fn3 = fld_alt3 raceeth fld_alt3 * raceeth ;
```

```
  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         3        2
3 ;
  reflevel raceeth = 3;
  model bmd_fn3 = fld_alt3 raceeth fld_alt3 * raceeth ;
  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Stratify by raceeth */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  model bmd_fn3 = fld_alt3 ;
  subpopx (raceeth = 1 ) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
```

```
  level    2       2      3           3       5         4        2
3 ;
  model bmd_fn3 = fld_alt3 ;
  subpopx (raceeth = 2 ) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  model bmd_fn3 = fld_alt3 ;
  subpopx (raceeth = 3 ) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Having interaction term btw nafld * age_cat */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         3        2
3 ;
  reflevel age_cat = 3;
  model bmd_fn3 = fld_alt3 age_cat fld_alt3 * age_cat ;
  subpopx  (age_cat in (3,4,5)) and (0 < bmd_fn < 5 ) and ( fld != .  )
and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag !=
1) and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
```

```
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         3        2
3 ;
  reflevel age_cat = 4;
  model bmd_fn3 = fld_alt3 age_cat fld_alt3 * age_cat ;
  subpopx  (age_cat in (3,4,5)) and (0 < bmd_fn < 5 ) and ( fld != .  )
and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag !=
1) and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         3        2
3 ;
  reflevel age_cat = 5;
  model bmd_fn3 = fld_alt3 age_cat fld_alt3 * age_cat ;
  subpopx  (age_cat in (3,4,5)) and (0 < bmd_fn < 5 ) and ( fld != .  )
and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag !=
1) and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Stratify by age_cat */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  model bmd_fn3 = fld_alt3 ;
```

```
  subpopx (age_cat = 3 ) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  model bmd_fn3 = fld_alt3 ;
  subpopx (age_cat = 4 ) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  model bmd_fn3 = fld_alt3 ;
  subpopx (age_cat = 5 ) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Having interaction term btw nafld and bmi_cat*/
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
```

```
  level    2       2      3           4       5         4        2
3 ;
  reflevel bmi_cat = 1;
  model bmd_fn3 = fld_alt3 bmi_cat fld_alt3 * bmi_cat ;
  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           4       5         4        2
3 ;
  reflevel bmi_cat = 2;
  model bmd_fn3 = fld_alt3 bmi_cat fld_alt3 * bmi_cat ;
  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           4       5         4        2
3 ;
  reflevel bmi_cat = 3;
  model bmd_fn3 = fld_alt3 bmi_cat fld_alt3 * bmi_cat ;
  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
```

```
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           4       5         4        2
3 ;
  reflevel bmi_cat = 4;
  model bmd_fn3 = fld_alt3 bmi_cat fld_alt3 * bmi_cat ;
  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;


/* Stratify by bmi_cat */

PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  model bmd_fn3 = fld_alt3 ;
  subpopx (bmi_cat = 2) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
fld_alt3 ;
  level    2       2      3           3       5         4        2
3 ;
  model bmd_fn3 = fld_alt3 ;
```

```
  subpopx (bmi_cat = 3) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;



/**************/
/* Table 5    */
/**************/
/* Full model */
PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
rgendermenop rraceeth3    fld_alt3 ;
  level    2       2      3           3       5         4        2
3           3           3;
  model bmd_fn3 = fld_alt3 rgendermenop rraceeth3 c_age c_bmi
fld_alt3 * rgendermenop fld_alt3 * rraceeth3 fld_alt3 * c_age fld_alt3
* c_bmi ;

  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Drop FLD_ALT3 * RRACEETH3, because p = 0.6546 */

PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
rgendermenop rraceeth3   fld_alt3 ;
  level    2       2      3           3       5         4        2
3           3          3;
```

```
  model bmd_fn3 = fld_alt3 rgendermenop rraceeth3 c_age c_bmi
fld_alt3 * rgendermenop  fld_alt3 * c_age fld_alt3 * c_bmi ;

  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Drop FLD_ALT3 *   RGENDERMENOP , p = 0.4661  */

PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
rgendermenop rraceeth3   fld_alt3 ;
  level    2       2      3           3       5         4        2
3           3          3;
  model bmd_fn3 = fld_alt3 rgendermenop rraceeth3 c_age c_bmi
fld_alt3 * c_age fld_alt3 * c_bmi ;

  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* Drop C_AGE * FLD_ALT3, p = 0.4043  */

PROC REGRESS  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup fld     female gendermenop bmi_cat age_cat  raceeth  wb_race
rgendermenop rraceeth3   fld_alt3 ;
  level    2       2      3           3       5         4        2
3           3          3;
  model bmd_fn3 = fld_alt3 rgendermenop rraceeth3 c_age c_bmi
fld_alt3 * c_bmi ;
```

```
  subpopx  (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* stop here, because C_BMI * FLD_ALT3 has p =  0.0014 */



/**************************/
/*** Calculate quintiles ***/
/**************************/
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var age ;
  print mean nsum;
  subpopx  (15 <= bmi < 20 ) and (raceeth in (1,2,3)) and (0 < bmd_fn <
5 ) and ( fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag !=
1 ) and (alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 )
and (preg_flag != 1) ;
RUN; /* age = 54.19 , nsum = 202 */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var age ;
  print mean nsum;
  subpopx  (20 <= bmi < 25 ) and (raceeth in (1,2,3)) and (0 < bmd_fn <
5 ) and ( fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag !=
1 ) and (alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 )
and (preg_flag != 1) ;
RUN; /* age = 54.03 , nsum = 1531 */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
```

```
  var age ;
  print mean nsum;
  subpopx  (25 <= bmi < 30 ) and (raceeth in (1,2,3)) and (0 < bmd_fn <
5 ) and ( fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag !=
1 ) and (alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 )
and (preg_flag != 1) ;
RUN; /* age = 54.93 , nsum = 2280 */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var age ;
  print mean nsum;
  subpopx  (30 <= bmi < 35 ) and (raceeth in (1,2,3)) and (0 < bmd_fn <
5 ) and ( fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag !=
1 ) and (alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 )
and (preg_flag != 1) ;
RUN; /* age = 54.96 ,  nsum = 1206 */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var age ;
  print mean nsum;
  subpopx  ( 35 <= bmi < 40 ) and (raceeth in (1,2,3)) and (0 < bmd_fn
< 5 ) and ( fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag
!= 1 ) and (alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 )
and (preg_flag != 1) ;
RUN; /* age = 54.51 , nsum = 431 */
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var age ;
  print mean nsum;
  subpopx  ( 40 <= bmi < 45 ) and (raceeth in (1,2,3)) and (0 < bmd_fn
< 5 ) and ( fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag
!= 1 ) and (alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 )
and (preg_flag != 1) ;
```

```
RUN; /* age = 53.26 , nsum = 132 */



PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup rgendermenop rraceeth3 ;
  level    3            3         ;
  tables rgendermenop rraceeth3;
  print colper;
  subpopx  (15 <= bmi < 20 ) and (raceeth in (1,2,3)) and (0 < bmd_fn <
5 ) and ( fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag !=
1 ) and (alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 )
and (preg_flag != 1) ;
RUN;
/*  rgendermenop  1: 48.99 2: 22.79 3: 28.22    */
/*  rraceeth3     1: 11.24  2: 1.23 3: 87.52    */
PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup rgendermenop rraceeth3 ;
  level    3            3         ;
  tables rgendermenop rraceeth3;
  print colper;
  subpopx  (20 <= bmi < 25 ) and (raceeth in (1,2,3)) and (0 < bmd_fn <
5 ) and ( fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag !=
1 ) and (alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 )
and (preg_flag != 1) ;
RUN;
/*  rgendermenop  1: 35.00  2: 23.32  3: 41.69   */
/*  rraceeth3     1: 6.82   2: 2.61   3: 90.57   */

PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
```

```
  subgroup rgendermenop rraceeth3 ;
  level    3            3         ;
  tables rgendermenop rraceeth3;
  print colper;
  subpopx  (25 <= bmi < 30 ) and (raceeth in (1,2,3)) and (0 < bmd_fn <
5 ) and ( fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag !=
1 ) and (alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 )
and (preg_flag != 1) ;
RUN;
/* rgendermenop  1:31.00   2:12.50    3: 56.50 */
/* rraceeth3     1:9.35    2:4.36     3: 86.30 */

PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup rgendermenop rraceeth3 ;
  level    3            3         ;
  tables rgendermenop rraceeth3;
  print colper;
  subpopx  (30 <= bmi < 35 ) and (raceeth in (1,2,3)) and (0 < bmd_fn <
5 ) and ( fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag !=
1 ) and (alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 )
and (preg_flag != 1) ;
RUN;
/* rgendermenop  1: 35.94   2: 13.50   3: 50.56 */
/* rraceeth3     1: 11.99   2: 5.53    3: 82.48 */

PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup rgendermenop rraceeth3 ;
  level    3            3         ;
  tables rgendermenop rraceeth3;
  print colper;
  subpopx  (35 <= bmi < 40 ) and (raceeth in (1,2,3)) and (0 < bmd_fn <
5 ) and ( fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag !=
```

```
1 ) and (alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 )
and (preg_flag != 1) ;
RUN;
/*  rgendermenop  1: 49.37 2: 21.22  3: 29.41 */
/*  rraceeth3     1:  13.67 2: 5.21  3: 81.13 */

PROC CROSSTAB data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  subgroup rgendermenop rraceeth3 ;
  level    3            3         ;
  tables rgendermenop rraceeth3;
  print colper;
  subpopx  (40 <= bmi < 45 ) and (raceeth in (1,2,3)) and (0 < bmd_fn <
5 ) and ( fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag !=
1 ) and (alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 )
and (preg_flag != 1) ;
RUN;
/*  rgendermenop  1: 53.03  2: 18.87  3: 28.1  */
/*  rraceeth3     1: 15.49  2: 4.10   3: 80.41  */

/* I used these values to create the last figure. */
```

final_analysis_thesis_discussion.sas

```
/* This code is used for discussion part. */
/* Insulin resistance and vitamin D were assessed.  */

libname thesis "./";
DATA nh3;   set thesis.nhanes3final;  RUN;
PROC SORT data = nh3;   by ststr psu ; RUN;
options ls=132;

/*
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var age;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN; */  /* Mean is 54*/
/*
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var bmi;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;  */ /* Mean is 27 */

DATA nh3;
  set nh3;
  glucose_mg = glucose * 18 ;
RUN;
```

```
/************************/
/* HOMA-IR Analysis */
/************************/

/* HOMA-IR */
PROC DESCRIPT data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;

  subgroup fld ;
  level    2   ;

  var homa_ir ;
  subpopx (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3, 4,
5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag != 1)
and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/*
PROC UNIVARIATE data = nh3;
  var  homa_ir ;
  histogram homa_ir ;
  class fld ;
  where ( 50 < glucose_mg < 250 ) and ( 6 <= hrs_last_eat < 24 ) and (0
< bmd_fn < 5 ) and ( fld ^= .  ) and (age_cat in ( 3, 4, 5) ) and
(hepat_flag ^= 1 ) and (alc_flag ^= 1) and (renal_flag ^= 1) and
(thyro_flag ^= 1 ) and (preg_flag ^= 1) ;
RUN;
PROC UNIVARIATE data = nh3;
  var  homa_ir ;
  histogram homa_ir ;
  class fld ;
  where (15 <= bmi < 20 ) and ( 50 < glucose_mg < 250 ) and ( 6 <=
hrs_last_eat < 24 ) and (0 < bmd_fn < 5 ) and ( fld ^= .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag ^= 1 ) and (alc_flag ^= 1)
and (renal_flag ^= 1) and (thyro_flag ^= 1 ) and (preg_flag ^= 1) ;
```

```
RUN;
PROC UNIVARIATE data = nh3;
  var  homa_ir ;
  histogram homa_ir ;
  class fld ;
  where (20 <= bmi < 25 ) and ( 50 < glucose_mg < 250 ) and ( 6 <=
hrs_last_eat < 24 ) and (0 < bmd_fn < 5 ) and ( fld ^= .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag ^= 1 ) and (alc_flag ^= 1)
and (renal_flag ^= 1) and (thyro_flag ^= 1 ) and (preg_flag ^= 1) ;
RUN;
PROC UNIVARIATE data = nh3;
  var  homa_ir ;
  histogram homa_ir ;
  class fld ;
  where (25 <= bmi < 30 ) and ( 50 < glucose_mg < 250 ) and ( 6 <=
hrs_last_eat < 24 ) and (0 < bmd_fn < 5 ) and ( fld ^= .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag ^= 1 ) and (alc_flag ^= 1)
and (renal_flag ^= 1) and (thyro_flag ^= 1 ) and (preg_flag ^= 1) ;
RUN;
PROC UNIVARIATE data = nh3;
  var  homa_ir ;
  histogram homa_ir ;
  class fld ;
  where (30 <= bmi < 35 ) and ( 50 < glucose_mg < 250 ) and ( 6 <=
hrs_last_eat < 24 ) and (0 < bmd_fn < 5 ) and ( fld ^= .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag ^= 1 ) and (alc_flag ^= 1)
and (renal_flag ^= 1) and (thyro_flag ^= 1 ) and (preg_flag ^= 1) ;
RUN;
PROC UNIVARIATE data = nh3;
  var  homa_ir ;
  histogram homa_ir ;
  class fld ;
  where (35 <= bmi < 40 ) and ( 50 < glucose_mg < 250 ) and ( 6 <=
hrs_last_eat < 24 ) and (0 < bmd_fn < 5 ) and ( fld ^= .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag ^= 1 ) and (alc_flag ^= 1)
and (renal_flag ^= 1) and (thyro_flag ^= 1 ) and (preg_flag ^= 1) ;
```

```
RUN;



PROC UNIVARIATE data = nh3;
  var insulin ;
  histogram insulin ;
  class fld ;
  where ( 50 < glucose_mg < 250 ) and ( 6 <= hrs_last_eat < 24 ) and (0
< bmd_fn < 5 ) and ( fld ^= .  ) and (age_cat in ( 3, 4, 5) ) and
(hepat_flag ^= 1 ) and (alc_flag ^= 1) and (renal_flag ^= 1) and
(thyro_flag ^= 1 ) and (preg_flag ^= 1) ;
RUN;

PROC UNIVARIATE data = nh3;
  var vitamin_d ;
  histogram vitamin_d ;
  class fld ;
  where  (0 < bmd_fn < 5 ) and ( fld ^= .  ) and (age_cat in ( 3, 4, 5)
) and  (hepat_flag ^= 1 ) and (alc_flag ^= 1) and (renal_flag ^= 1) and
(thyro_flag ^= 1 ) and (preg_flag ^= 1) ;
RUN;
*/

/* Calculate */
DATA nh3_valid_ins;
   set nh3;
   valid_ins = . ;
   if ( 50 < glucose_mg < 250 ) and ( 6 <= hrs_last_eat < 24 ) then
valid_ins = 1;
RUN;

PROC DESCRIPT  data = nh3_valid_ins filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var homa_ir ;
```

```
  percentile 25 50 75 ;
  print ;
  subpopx  (15 <= bmi < 40 ) and (valid_ins = 1) and (raceeth in
(1,2,3)) and (0 < bmd_fn < 5 ) and ( fld != .  ) and (age_cat in ( 3,
4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1) and (renal_flag !=
1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN;

/* S3 Table and S1 Figure. */

%macro show_homair( bmi_lower , bmi_upper);
PROC DESCRIPT  data = nh3_valid_ins filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var homa_ir ;
  percentile 25 50 75 ;
  print ;
  subpopx  (fld_alt3 = 1) and ( &bmi_lower <= bmi < &bmi_upper ) and
(valid_ins = 1) and (raceeth in (1,2,3)) and (0 < bmd_fn < 5 ) and (
fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and
(alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 ) and
(preg_flag != 1) ;
RUN; /* HA NAFLD */

PROC DESCRIPT  data = nh3_valid_ins filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var homa_ir ;
  percentile 25 50 75 ;
  print ;
  subpopx  (fld_alt3 = 2) and ( &bmi_lower <= bmi < &bmi_upper ) and
(valid_ins = 1)   and (raceeth in (1,2,3)) and (0 < bmd_fn < 5 ) and (
fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and
(alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 ) and
(preg_flag != 1) ;
RUN; /* NA NAFLD */
```

```
PROC DESCRIPT  data = nh3_valid_ins filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var homa_ir ;
  percentile 25 50 75 ;
  print ;
  subpopx  (fld_alt3 = 3) and ( &bmi_lower <= bmi < &bmi_upper ) and
(valid_ins = 1) and (raceeth in (1,2,3)) and (0 < bmd_fn < 5 ) and (
fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and
(alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 ) and
(preg_flag != 1) ;
RUN; /* Normal */
%mend;


%show_homair (15 , 40) ; /* Number of total people in table. 4674 */
%show_homair (15 , 20) ;
%show_homair (20 , 25) ;
%show_homair (25 , 30) ;
%show_homair (30 , 35) ;
%show_homair (35 , 40) ;


DATA nh3_valid_ins;
   set nh3;
   valid_ins = . ;
   if ( 50 < glucose_mg < 250 ) and ( 6 <= hrs_last_eat < 24 ) then
valid_ins = 1;
RUN;

/* Mean HOMA-IR is not approprite, because the distribution is right-
skewed. */
/* However, just in case, confirmed that the result is consistent with
the medican analysis. => Consistent */
/* Not written in manuscript. */
```

```
%macro show_homair_mean( bmi_lower , bmi_upper);
PROC DESCRIPT  data = nh3_valid_ins filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var homa_ir ;
  print mean lowmean upmean ;
  subpopx  (fld_alt3 = 1) and ( &bmi_lower <= bmi < &bmi_upper ) and
(valid_ins = 1) and (raceeth in (1,2,3)) and (0 < bmd_fn < 5 ) and (
fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and
(alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 ) and
(preg_flag != 1) ;
RUN; /* HA NAFLD */

PROC DESCRIPT  data = nh3_valid_ins filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var homa_ir ;
  print mean lowmean upmean ;
  subpopx  (fld_alt3 = 2) and ( &bmi_lower <= bmi < &bmi_upper ) and
(valid_ins = 1)   and (raceeth in (1,2,3)) and (0 < bmd_fn < 5 ) and (
fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and
(alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 ) and
(preg_flag != 1) ;
RUN; /* NA NAFLD */

PROC DESCRIPT  data = nh3_valid_ins filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var homa_ir ;
  print mean lowmean upmean ;
  subpopx  (fld_alt3 = 3) and ( &bmi_lower <= bmi < &bmi_upper ) and
(valid_ins = 1) and (raceeth in (1,2,3)) and (0 < bmd_fn < 5 ) and (
fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and
(alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 ) and
(preg_flag != 1) ;
```

```
RUN; /* Normal */
%mend;


%show_homair_mean (15 , 20) ;
%show_homair_mean (20 , 25) ;
%show_homair_mean (25 , 30) ;
%show_homair_mean (30 , 35) ;
%show_homair_mean (35 , 40) ;

/* Fasting insulin value is another way to show insulin resistance.
This result was also conssitent with median HOMA-IR. */
/* Not written in manuscript. */

%macro show_insulin( bmi_lower , bmi_upper);
PROC DESCRIPT  data = nh3_valid_ins filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var insulin ;
  percentile 25 50 75 ;
  print ;
  subpopx  (fld_alt3 = 1) and ( &bmi_lower <= bmi < &bmi_upper ) and
(valid_ins = 1) and (raceeth in (1,2,3)) and (0 < bmd_fn < 5 ) and (
fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and
(alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 ) and
(preg_flag != 1) ;
RUN; /* HA NAFLD */

PROC DESCRIPT  data = nh3_valid_ins filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var insulin ;
  percentile 25 50 75 ;
  print ;
  subpopx  (fld_alt3 = 2) and ( &bmi_lower <= bmi < &bmi_upper ) and
(valid_ins = 1)   and (raceeth in (1,2,3)) and (0 < bmd_fn < 5 ) and (
```

```
fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and
(alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 ) and
(preg_flag != 1) ;
RUN; /* NA NAFLD */

PROC DESCRIPT  data = nh3_valid_ins filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var insulin ;
  percentile 25 50 75 ;
  print ;
  subpopx  (fld_alt3 = 3) and ( &bmi_lower <= bmi < &bmi_upper ) and
(valid_ins = 1) and (raceeth in (1,2,3)) and (0 < bmd_fn < 5 ) and (
fld != .  ) and (age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and
(alc_flag != 1) and (renal_flag != 1) and (thyro_flag != 1 ) and
(preg_flag != 1) ;
RUN; /* Normal */
%mend;

%show_insulin (15 , 20) ;
%show_insulin (20 , 25) ;
%show_insulin (25 , 30) ;
%show_insulin (30 , 35) ;
%show_insulin (35 , 40) ;



/************************/
/* VITAMIN D Analysis */
/************************/

/*
PROC UNIVARIATE data=nh3;
  var vitamin_d;
  histogram vitamin_d;
  class fld ;
```

```
  where (15 <= bmi < 20 ) and  (0 < bmd_fn < 5 ) and ( fld ^= .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag ^= 1 ) and (alc_flag ^= 1)
and (renal_flag ^= 1) and (thyro_flag ^= 1 ) and (preg_flag ^= 1) ;
RUN;
PROC UNIVARIATE data=nh3;
  var vitamin_d;
  histogram vitamin_d;
  class fld ;
  where (20 <= bmi < 25 ) and  (0 < bmd_fn < 5 ) and ( fld ^= .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag ^= 1 ) and (alc_flag ^= 1)
and (renal_flag ^= 1) and (thyro_flag ^= 1 ) and (preg_flag ^= 1) ;
RUN;
PROC UNIVARIATE data=nh3;
  var vitamin_d;
  histogram vitamin_d;
  class fld ;
  where (25 <= bmi < 30 ) and  (0 < bmd_fn < 5 ) and ( fld ^= .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag ^= 1 ) and (alc_flag ^= 1)
and (renal_flag ^= 1) and (thyro_flag ^= 1 ) and (preg_flag ^= 1) ;
RUN;
*/


/* S4 Table and S2 Figure. */

%macro show_vit_d( bmi_lower , bmi_upper);
PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var vitamin_d ;
  percentile 25 50 75 ;
  print ;
  subpopx  (fld_alt3 = 1) and ( &bmi_lower <= bmi < &bmi_upper ) and
(raceeth in (1,2,3)) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
```

```
RUN; /* HA NAFLD */

PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var vitamin_d ;
  percentile 25 50 75 ;
  print ;
  subpopx  (fld_alt3 = 2) and ( &bmi_lower <= bmi < &bmi_upper )  and
(raceeth in (1,2,3)) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN; /* NA NAFLD */

PROC DESCRIPT  data = nh3 filetype=SAS design=wr;
  nest ststr psu;
  weight sweight ;
  var vitamin_d ;
  percentile 25 50 75 ;
  print ;
  subpopx  (fld_alt3 = 3) and ( &bmi_lower <= bmi < &bmi_upper )  and
(raceeth in (1,2,3)) and (0 < bmd_fn < 5 ) and ( fld != .  ) and
(age_cat in ( 3, 4, 5) ) and  (hepat_flag != 1 ) and (alc_flag != 1)
and (renal_flag != 1) and (thyro_flag != 1 ) and (preg_flag != 1) ;
RUN; /* Normal */
%mend;

%show_vit_d (15 , 40) ; /* Number of people in the table => 5465 */
%show_vit_d (15 , 20) ;
%show_vit_d (20 , 25) ;
%show_vit_d (25 , 30) ;
%show_vit_d (30 , 35) ;
%show_vit_d (35 , 40) ;

PROC UNIVARIATE data=nh3;
  var bmi;
```

```
  where  (raceeth in (1,2,3)) and (0 < bmd_fn < 5 ) and ( fld ^= .  )
and (age_cat in ( 3, 4, 5) ) and  (hepat_flag ^= 1 ) and (alc_flag ^=
1) and (renal_flag ^= 1) and (thyro_flag ^= 1 ) and (preg_flag ^= 1) ;
RUN;
```