NHANES 2017-2018: The Comorbidity Between Osteoporosis and Diabetes

BIOS 6102: Biostatistical Methods II
Spring 2021
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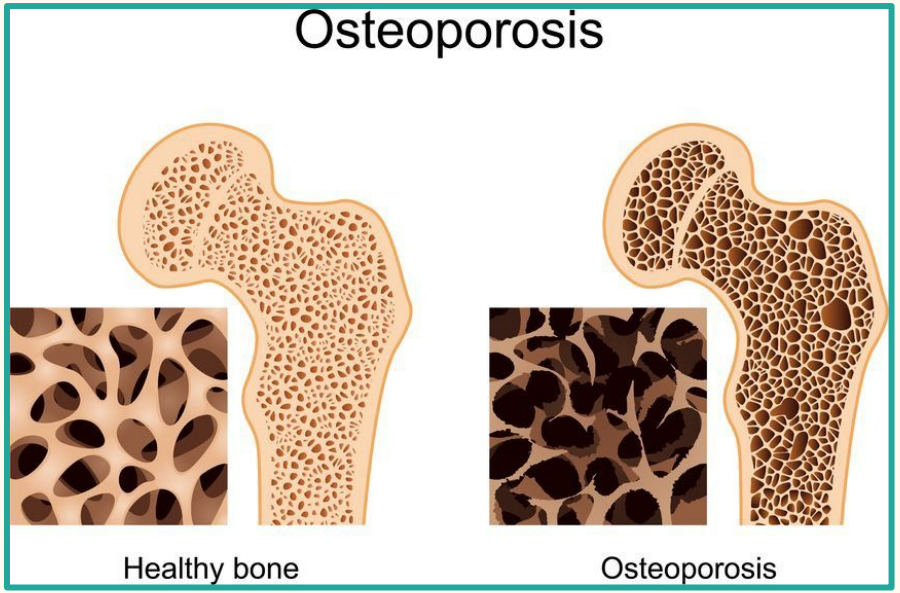
BACKGROUND: OSTEOPOROSIS

- **Osteoporosis** means "**porous bone,**" and is a chronic disease.
- The National Osteoporosis Foundation defines osteoporosis as "**a bone disease that occurs when the body loses too much bone, makes too little bone, or both.**"
- As a result, **bones become weak and may break** from a fall or, in serious cases, from sneezing or minor bumps.
- Viewed under a microscope, healthy bone looks like a **honeycomb**.



https://www.spineuniverse.com/conditions/osteoporosis/osteoporosis-silent-thief

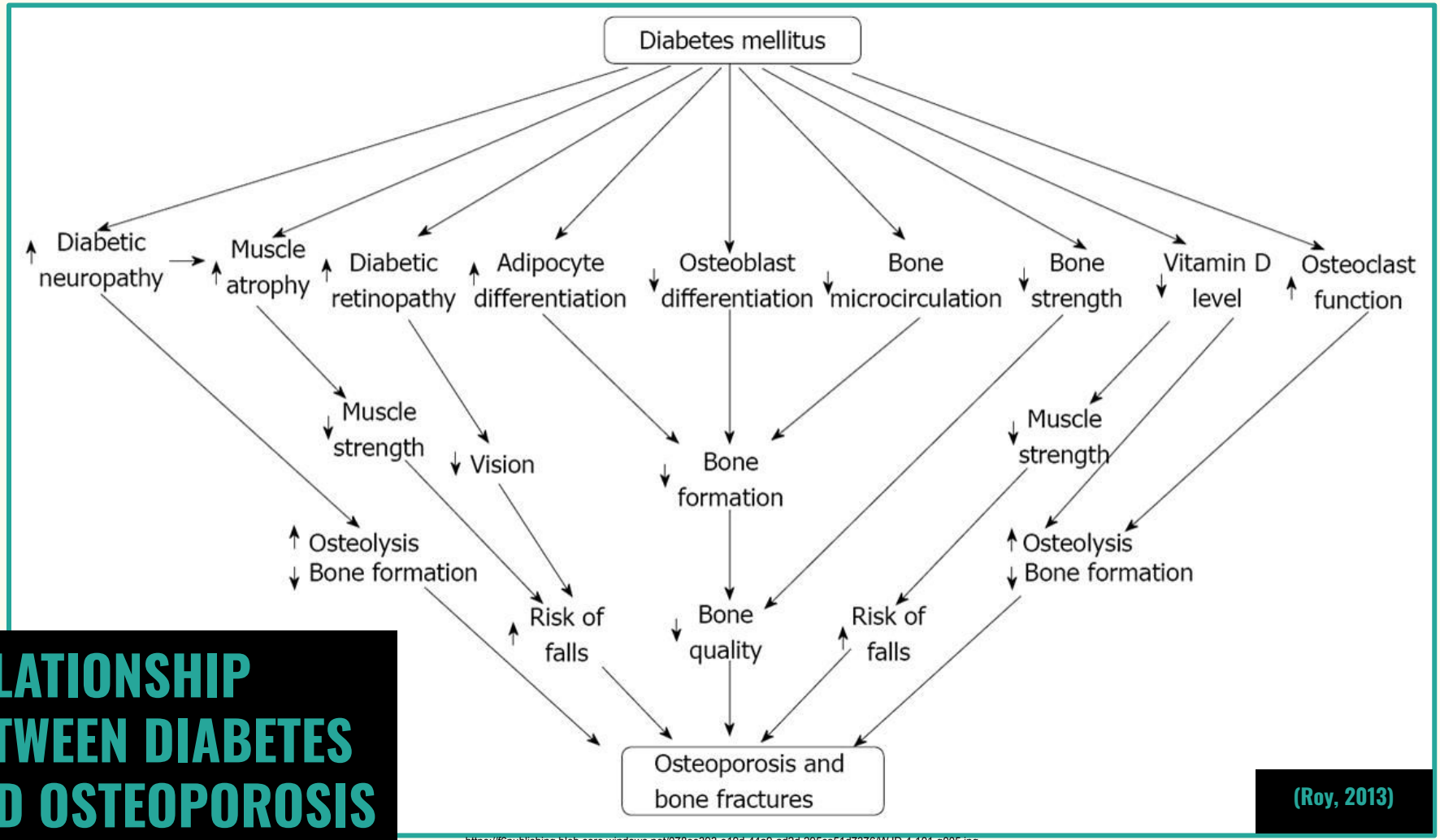
- **Possible risk factors:**
  1. Age 50 and above
  2. Female
  3. Smoking / tobacco exposure
  4. Drinking / alcohol consumption
  5. Race (Non-Hispanic White and Asian)

BACKGROUND: DIABETES

- Diabetes mellitus (diabetes) is a chronic health condition that occurs when the **body creates too much sugar while trying to turn food into energy.**
- There are 3 main types:
  - **Type 1** -- Immune system destroys the cells that release insulin.
  - **Type 2** -- Body isn't able to use insulin properly.
  - **Gestational** -- Diabetes diagnosed during pregnancy (often temporary)
- According to Health Central (Barros):
  - Type 1 diabetes is the most common chronic disease in children.
  - 95% of diabetes patients have type 2.
  - 7 million people live with undiagnosed diabetes
  - **30 million Americans live with diabetes.**
  - **80 million American adults have prediabetes.**
- **Possible risk factors:**
  1. Age 45 and above (Type II)
  2. Overweight / physical inactivity
  3. Smoking / tobacco exposure
  4. High blood pressure
  5. Race (African-American, Hispanic, Native American, Asian-American race, or Pacific Islander)

https://healthcise.com/researchers-claim-type-2-diabetes-is-reversible/

RELATIONSHIP BETWEEN DIABETES AND OSTEOPOROSIS



(Roy, 2013)

https://f6publishing.blob.core.windows.net/078ee393-e19d-44a9-ad2d-295ca51d7376/WJD-4-101-g005.jpg

RATIONALE: OSTEOPOROSIS & DIABETES

- In 2010, osteoporosis and low bone mass were estimated to be a **major public health threat for almost 54 million U.S.** women and men aged 50 and older, and that number has only grown.
  - Among the 54 million, 10.2 million adults are estimated to have osteoporosis, of which more than 80% were women (Wright, 2014).
- Economic burden was estimated at **17 billion USD** in 2005 (Burge, 2007).
- In a study based on almost 380,000 fractures in female Medicare beneficiaries, 10% had **another fracture** within 1 year, 18% within 2 years, and **31% within 5 years** (Balasubramanian, 2019).
- "Although bone health is primarily associated with age, recent studies have shown that individuals with **diabetes mellitus (DM)** have up to **6 times higher incidence** of **osteoporotic fractures** compared to the general population." (Dumic-Cule, et al., 2018)

To reduce this alarming public health burden,
additional research regarding the risk factors for and
causal pathway associated with both diabetes and osteoporosis is needed.

ALL VARIABLES* OF INTEREST

NHANES VARIABLE NAME	SAS LABEL	ENGLISH TEXT	TARGET	TYPE	CODED VALUES
OSQ060	**Ever told had osteoporosis/brittle bones**	**Has a doctor ever told {you/SP} that {you/s/he} had osteoporosis, sometimes called thin or brittle bones?**	**Both males and females 50 YEARS - 150 YEARS**	**Categorical**	**1: Osteoporosis** **2: No Osteoporosis**
DIQ010SAS	**Doctor told you have diabetes**	**The next questions are about specific medical conditions. {Other than during pregnancy, {have you/has SP}/{Have you/Has SP}} ever been told by a doctor or health professional that {you have/{he/she/SP} has} diabetes or sugar diabetes?**	**Both males and females 1 YEARS - 150 YEARS**	**Categorical**	**1: Diabetes (Including Borderline)** **2: No Diabetes**
RIAGENDR	Gender	Gender of the participant	Both males and females 0 YEARS - 150 YEARS	Categorical	1: Male 2: Female
RIDAGEYR	Age in years at screening	Age in years of the participant at the time of screening. Individuals 80 and over are topcoded at 80 years of age.	Both males and females 0 YEARS - 150 YEARS	Categorical	1: 1-9 years old 2: 10-19 years old 3: 20-29 years old 4: 30-39 years old 5: 40-49 years old 6: 50-59 years old 7: 60-69 years old 8: 70-79 years old 9: 80 years old and above
RIDRETH3	Race/Hispanic origin w/ NH Asian	Recode of reported race and Hispanic origin information, with Non-Hispanic Asian Category	Both males and females 0 YEARS - 150 YEARS	Categorical	1: Mexican American 2: Other Hispanic 3: Non-Hispanic White 4: Non-Hispanic Black 5: Non-Hispanic Asian 6: Other Race - Including multiracial
ALQ111 & ALQ121	Ever had a drink of any kind of alcohol = “No” & Past 12 mo how often have alcohol drink	The next questions are about drinking alcoholic beverages. Included are liquor (such as whiskey or gin), beer, wine, wine coolers, and any other type of alcoholic beverage. In {your/SP's} entire life, {have you/has he/has she} had at least 1 drink of any kind of alcohol, not counting small tastes or sips? By a drink, I mean a 12 oz. beer, a 5 oz. glass of wine, or one and a half ounces of liquor. & During the past 12 months, about how often did {yo/SP} drink any type of alcoholic beverage? PROBE: How many days per week, per month, or per year did {you/SP} drink?	Both males and females 18 YEARS - 150 YEARS	Categorical	0: Never Drinker 1: Former Drinker 2: Occasional Drinker 3: Frequent Drinker
SMDANY	Used any tobacco product last 5 days?	Used any tobacco product last 5 days?	Both males and females 12 YEARS - 150 YEARS	Categorical	1: Tobacco 2: No Tobacco

From 2017-2018 NHANES - National Health and Nutrition Examination Survey

METHODS

- **TARGET POPULATION:** The NHANES target population is the noninstitutionalized civilian resident population of the United States.
- **SAMPLE POPULATION:** Noninstitutionalized U.S. civilian population of all ages residing in all 50 states and Washington D.C.
- **ANALYTICAL SAMPLE SIZE:** All 2017-2018 NHANES participants who completed the interview (n = 9,254)
  - Eligibility criteria for both outcomes:
    - Above age 50 (minimum target for osteoporosis variable): n = 3,069
    - Responded yes/no to osteoporosis/brittle bone question (variable OSQ060): n = 3,053
      - Because diabetes typically onests after the age of 45, these parameters also fit well with the second outcome (diabetes).
  - Exclusion criteria for both outcomes:
    - Osteoporosis response = refused, don't know, missing: n = 16
  - **Final Analytical Sample Size: n = 3,053**

https://www.cdc.gov/nchs/nhanes/participant.htm

STATISTICAL ANALYSES PERFORMED

All variables are coded as **categorical** (2 outcomes each with 6 predictors). Therefore, **logistic regression** methods were utilized.

1. **Osteoporosis** with predictor variables age (primary), diabetes, gender, race, alcohol consumption, and tobacco use
2. **Diabetes** with predictor variables age (primary), osteoporosis, gender, race, alcohol consumption, and tobacco use

Stepwise regression analysis was not necessary as the chosen predictors are known to have an association with the outcomes.

METHODS UTILIZED FOR BOTH OUTCOMES:

1. **Descriptive statistics**
2. Bivariate analyses: Wald **chi-square**
3. Logistic regression modeling: Wald **95% confidence intervals** and **chi-square**
    - Univariate model
    - Multivariable model

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OUTCOME #1: OSTEOPOROSIS

OUTCOME #1: STUDY OBJECTIVES

PRIMARY PREDICTOR VARIABLE:

1. Examine the association of **age** and being told by a physician that you have **osteoporosis/brittle bones**.

SECONDARY PREDICTOR VARIABLES:

2. Examine the association of **diabetes** and being told by a physician that you have **osteoporosis/brittle bones**.
3. Examine the association of **gender** and being told by a physician that you have **osteoporosis/brittle bones**.
4. Examine the association of **race** and being told by a physician that you have **osteoporosis/brittle bones**.
5. Examine the association of **alcohol consumption** and being told by a physician that you have **osteoporosis/brittle bones**.
6. Examine the association of **tobacco use** and being told by a physician that you have **osteoporosis/brittle bones**.

OSTEOPOROSIS: DESCRIPTIVE STATISTICS & BIVARIATE ANALYSIS

Table 1. Descriptive Statistics & Bivariates Analysis of NHANES 2017-2018 Participants Regarding "Has a doctor ever told {you/SP} that {you/s/he} had osteoporosis, sometimes called thin or brittle bones?"

Characteristic (n = 3,069***)	Total (n = 3,051)	Osteoporosis (n = 396)	Not Osteoporosis (n = 2,655)	Wald Chi-Square P-value
Age**				**<.0001***
50 to 59 Years Old, n (%)	915 (29.97)	57 (6.23)	858 (93.77)	
60 to 69 Years Old, n (%)	1,100 (36.03)	120 (10.91)	980 (89.09)	
70 to 79 Years Old, n (%)	617 (20.21)	119 (19.29)	498 (80.71)	
80+ Years Old, n (%)	421 (13.79)	100 (23.75)	321 (76.25)	
Diabetes Status				0.4344
Diabetes & Borderline, n (%)	874 (28.65)	120 (13.73)	754 (86.27)	
No Diabetes, n (%)	2,177 (71.35)	276 (12.68)	1,901 (87.32)	
Gender				**<.0001***
Male, n (%)	1,513 (49.56)	54 (3.57)	1,459 (96.43)	
Female, n (%)	1,540 (50.44)	342 (22.21)	1,198 (77.79)	
Race/Ethnicity				**0.0010***
Mexican American, n (%)	347 (11.37)	34 (9.80)	313 (90.20)	
Other Hispanic, n (%)	290 (9.50)	40 (13.79)	250 (86.21)	
Non-Hispanic White, n (%)	1,172 (38.39)	188 (16.04)	984 (83.96)	
Non-Hispanic Black, n (%)	725 (23.75)	72 (9.93)	653 (90.07)	
Non-Hispanic Asian, n (%)	391 (12.81)	50 (12.79)	341 (87.21)	
Other Race - Including Multi-Racial, n (%)	128 (4.19)	12 (9.38)	116 (90.63)	
Alcohol Consumption				**0.0005***
Never Drinker, n (%)	291 (10.89)	47 (16.15)	244 (83.85)	
Former Drinker, n (%)	787 (29.46)	114 (14.49)	673 (85.51)	
Occasional Drinker, n (%)	456 (17.07)	33 (7.24)	423 (92.76)	
Frequent Drinker, n (%)	1,137 (42.57)	153 (13.46)	984 (86.54)	
Tobacco Use				**0.0225***
Tobacco, n (%)	495 (18.51)	49 (9.90)	446 (90.10)	
No Tobacco, n (%)	2,179 (81.49)	299 (13.72)	1,880 (86.28)	

*Statistically significant ($p < 0.05$).

** NHANES Target: Both males and females 50 YEARS - 150 YEARS

*** Responses of "refused", "don't know," and missing were excluded from analyses (n = 16).

RESULTS

According to the variables selected to measure the predictors for **osteoporosis** utilizing Wald chi-square p-values at alpha = 0.05, the results were:

1. AGE (PRIMARY PREDICTOR):

- **p = <0.0001, statistically significant**

2. DIABETES STATUS:

- p = 0.4344, not statistically significant

3. GENDER:

- **p = <0.0001, statistically significant**

4. RACE/ETHNICITY:

- **p = 0.0010, statistically significant**

5. ALCOHOL CONSUMPTION:

- **p = 0.0005, statistically significant**

6. TOBACCO USE:

- **p = 0.0225, statistically significant**

OSTEOPOROSIS: UNIVARIATE & MULTIVARIATE LOGISTIC ANALYSES

Table 2. Univariate & Multivariate Logistic Analyses of NHANES 2017-2018 Participants Regarding Factors Associated with Osteoporosis

Characteristic (n = 3,069***)	Univariate Crude Odds Ratio (95% Wald CI)	Univariate Wald P-Value	Multivariate Crude Odds Ratio (95% Wald CI)	Multivariate Wald P-Value
Age**				
50 to 59 Years Old	**0.213 (0.150-0.303)***	**<.0001***	**0.195 (0.127-0.301)***	**<.0001***
60 to 69 Years Old	**0.393 (0.293-0.527)***	**<.0001***	**0.401 (0.275-0.583)***	**<.0001***
70 to 79 Years Old	0.767 (0.568-1.036)	0.0838	0.871 (0.598-1.267)	0.4694
80+ Years Old	1.0		1.0	
Diabetes Status				
Diabetes & Borderline	1.096 (0.871-1.380)	0.4345	1.193 (0.910-1.565)	0.2024
No Diabetes	1.0		1.0	
Gender				
Male	**0.130 (0.096-0.174)***	**<.0001***	**0.110 (0.079-0.153)***	**<.0001***
Female	1.0		1.0	
Race/Ethnicity				
Mexican American	**0.569 (0.386-0.837)***	**0.0042***	0.724 (0.461-1.137)	0.1611
Other Hispanic	0.837 (0.579-1.210)	0.3453	1.086 (0.704-1.678)	0.7087
Non-Hispanic White	1.0		1.0	
Non-Hispanic Black	**0.577 (0.432-0.771)***	**0.0002***	0.719 (0.514-1.007)	0.0549
Non-Hispanic Asian	0.767 (0.549-1.073)	0.1218	1.041 (0.681-1.593)	0.8515
Other Race - Including Multi-Racial	0.541 (0.293-1.001)	0.0504	0.892 (0.458-1.738)	0.737
Alcohol Consumption				
Never Drinker	1.239 (0.868-1.768)	0.2379	0.763 (0.514-1.133)	0.18
Former Drinker	1.089 (0.839-1.415)	0.5211	0.919 (0.689-1.227)	0.5671
Occasional Drinker	**0.502 (0.339-0.743)***	**0.0006***	0.725 (0.474-1.111)	0.1397
Frequent Drinker	1.0		1.0	
Tobacco Use				
Tobacco	**0.691 (0.502-0.951)***	**0.0233***	1.263 (0.878-1.816)	0.2086
No Tobacco	1.0		1.0	

**Statistically significant.*

*** NHANES Target: Both males and females 50 YEARS - 150 YEARS*

*** Responses of "refused", "don't know," and missing were excluded from analyses (n = 16).

Univariate and multivariate logistic analyses for each predictor versus outcome was utilized to obtain the odds ratios (OR), 95% Wald confidence intervals (CI), and Wald p-values (alpha = 0.05).

STATISTICALLY SIGNIFICANT RESULTS

1. AGE (PRIMARY PREDICTOR):
- 50 to 59 Years Old **(protective)**
  - UNIVARIATE: OR = 0.213 (0.150-0.303) and p = <.0001
  - MULTIVARIATE: OR = 0.195 (0.127-0.301) and p = <.0001
- 60 to 69 Years Old **(protective)**
  - UNIVARIATE: OR = 0.393 (0.293-0.527) and p = <.0001
  - MULTIVARIATE: OR = 0.401 (0.275-0.583) and p = <.0001

2. DIABETES STATUS: *No statistically significant results*

3. GENDER:
- Male **(protective)**
  - UNIVARIATE: OR = 0.130 (0.096-0.174) and p = <.0001
  - MULTIVARIATE: OR = 0.110 (0.079-0.153) and p = <.0001

4. RACE/ETHNICITY:
- Mexican American
  - UNIVARIATE: OR = 0.569 (0.386-0.837) and p = 0.0042
  - *MULTIVARIATE: not statistically significant*
- Non-Hispanic Black (almost **protective**)
  - UNIVARIATE: OR = 0.577 (0.432-0.771) and p = 0.0002
  - *(close)* MULTIVARIATE: OR = 0.719 (0.514-1.007) and p = 0.0549

5. ALCOHOL CONSUMPTION:
- Occasional Drinker
  - UNIVARIATE: OR = 0.502 (0.339-0.743) and p = 0.0006
  - *MULTIVARIATE: not statistically significant*

6. TOBACCO USE:
- Tobacco (Yes)
  - UNIVARIATE: OR = 0.691 (0.502-0.951) and p = 0.0233
  - *MULTIVARIATE: not statistically significant*

OUTCOME #1: RESULTS

According to the variables selected as predictors with respect to the outcome of **osteoporosis:**

1. **PRIMARY PREDICTOR:** Compared to individuals 80 years old and above, people age **50 to 59** and **60 to 69 years old had lower odds** (OR = 0.195, p = <.0001 and OR = 0.401, p = <.0001) of being told by a physician that they have **osteoporosis/brittle bones** after adjusting for other selected factors.
2. There was **no statistically significant association between diabetes** status (compared to no diabetes status) and being told by a physician that you have osteoporosis/brittle bones.
3. Compared to females, **males had lower odds** of being told by a physician that they have **osteoporosis/brittle bones** (OR = 0.110, p = <.0001) after adjusting for other selected factors.
4. Compared to non-Hispanic whites, **non-Hispanic blacks** were the only race that came *close* to having statistically significant results.
    - This group had **reduced odds** (OR = 0.719, 95% CI = 0.514-1.007, p = 0.0549) of being told by a physician that they have **osteoporosis/brittle bones** after adjusting for other selected factors.
5. After adjusting for other selected factors, there was **no statistically significant association between amount of alcohol consumption** (compared to frequent drinking) and being told by a physician that you have osteoporosis/brittle bones.
6. After adjusting for other selected factors, there was **no statistically significant association between tobacco (yes) use** (compared to no tobacco use) and being told by a physician that you have osteoporosis/brittle bones.

OUTCOME #2: DIABETES

(Bonus for Midterm)

OUTCOME #2: STUDY OBJECTIVES

PRIMARY PREDICTOR VARIABLE:

1. Examine the association of **age** and being told by a physician that you have **diabetes (including borderline).**

SECONDARY PREDICTOR VARIABLES:

2. Examine the association of **osteoporosis** and being told by a physician that you have **diabetes (including borderline).**
3. Examine the association of **gender** and being told by a physician that you have **diabetes (including borderline).**
4. Examine the association of **race** and being told by a physician that you have **diabetes (including borderline).**
5. Examine the association of **alcohol consumption** and being told by a physician that you have **diabetes (including borderline).**
6. Examine the association of **tobacco use** and being told by a physician that you have **diabetes (including borderline).**

DIABETES: DESCRIPTIVE STATISTICS & BIVARIATE ANALYSIS

Table 3. Descriptive Statistics and Bivariate Analysis of NHANES 2017-2018 Participants Regarding "Other than during pregnancy, {have you/has SP}/{Have you/Has SP}} ever been told by a doctor or health professional that {you have/{he/she/SP} has} diabetes or sugar diabetes?"

Characteristic (n = 3,069***)	Total (n = 3,051)	Diabetes & Borderline (n = 874)	Not Diabetes (n = 2,177)	Wald Chi-Square P-value
Age				**<.0001***
50 to 59 Years Old, n (%)	918 (10.32)	175 (19.06)	743 (80.94)	
60 to 69 Years Old, n (%)	1,104 (12.41)	355 (32.16)	749 (67.84)	
70 to 79 Years Old, n (%)	619 (6.96)	226 (36.51)	393 (63.49)	
80+ Years Old, n (%)	426 (4.79)	127 (29.81)	299 (70.19)	
Osteoporosis Status**				0.4344
Osteoporosis, n (%)	396 (12.98)	120 (30.30)	276 (69.70)	
No Osteoporosis, n (%)	2,655 (87.02)	754 (28.40)	1,901 (71.60)	
Gender				**0.0002***
Male, n (%)	1,520 (49.56)	485 (31.91)	1,035 (68.09)	
Female, n (%)	1,547 (50.44)	398 (25.73)	1,149 (74.27)	
Race/Ethnicity				**0.0141***
Mexican American, n (%)	347 (11.31)	118 (34.01)	229 (65.99)	
Other Hispanic, n (%)	294 (9.59)	75 (25.51)	219 (74.49)	
Non-Hispanic White, n (%)	1,177 (38.38)	308 (26.17)	869 (73.83)	
Non-Hispanic Black, n (%)	726 (23.67)	211 (29.06)	515 (70.94)	
Non-Hispanic Asian, n (%)	395 (12.88)	127 (32.15)	268 (67.85)	
Other Race - Including Multi-Racial, n (%)	128 (4.17)	44 (34.38)	84 (65.63)	
Alcohol Consumption				**<.0001***
Never Drinker, n (%)	292 (10.89)	83 (28.42)	209 (71.58)	
Former Drinker, n (%)	790 (29.47)	285 (36.08)	505 (63.92)	
Occasional Drinker, n (%)	458 (17.08)	91 (19.87)	367 (80.13)	
Frequent Drinker, n (%)	1,141 (42.56)	315 (27.61)	826 (72.39)	
Tobacco Use				**0.0258***
Tobacco, n (%)	497 (18.52)	123 (24.75)	374 (75.25)	
No Tobacco, n (%)	2,187 (81.48)	651 (29.77)	1,536 (70.23)	

*Statistically significant ($p < 0.05$).

** NHANES Target: Both males and females 50 YEARS - 150 YEARS

*** Responses of "refused", "don't know," and missing were excluded from analyses (n = 16).

RESULTS

According to the variables selected to measure the predictors for **diabetes** utilizing Wald chi-square p-values at alpha = 0.05, the results were:

1. AGE (PRIMARY PREDICTOR):

- **p = <0.0001, statistically significant**

2. OSTEOPOROSIS STATUS:

- p = 0.4344, not statistically significant

3. GENDER:

- **p = 0.0002, statistically significant**

4. RACE/ETHNICITY:

- **p = 0.0141, statistically significant**

5. ALCOHOL CONSUMPTION:

- **p = <0.0001, statistically significant**

6. TOBACCO USE:

- **p = 0.0258, statistically significant**

DIABETES: UNIVARIATE & MULTIVARIATE LOGISTIC ANALYSES

Table 4. Univariate & Multivariate Logistic Analyses of NHANES 2017-2018 Participants Regarding Factors Associated with Diabetes

Characteristic (n = 3,069)	Univariate Crude Odds Ratio (95% Wald CI)	Univariate Wald P-Value	Multivariate Crude Odds Ratio (95% Wald CI)	Multivariate Wald P-Value
Age				
50 to 59 Years Old	**0.555 (0.425-0.723)***	**<.0001***	**0.515 (0.373-0.709)***	**<.0001***
60 to 69 Years Old	1.116 (0.875-1.423)	0.3765	1.026 (0.766-1.374)	0.8644
70 to 79 Years Old	**1.354 (1.039-1.764)***	**0.0247***	1.256 (0.928-1.700)	0.1404
80+ Years Old	1.0		1.0	
Osteoporosis Status**				
Osteoporosis	1.096 (0.871-1.380)	0.4345	1.157 (0.885-1.514)	0.2858
No Osteoporosis	1.0		1.0	
Gender				
Male	**1.353 (1.156-1.583)***	**0.0002***	**1.622 (1.344-1.958)***	**<.0001***
Female	1.0		1.0	
Race/Ethnicity				
Mexican American	**1.454 (1.124-1.881)***	**0.0044***	**1.516 (1.129-2.036)***	**0.0057***
Other Hispanic	0.966 (0.721-1.295)	0.8181	1.021 (0.736-1.416)	0.8994
Non-Hispanic White	1.0		1.0	
Non-Hispanic Black	1.156 (0.940-1.421)	0.1685	**1.270 (1.007-1.602)***	**0.0433***
Non-Hispanic Asian	**1.337 (1.043-1.713)***	**0.0217***	**1.551 (1.154-2.084)***	**0.0036***
Other Race - Including Multi-Racial	**1.478 (1.003-2.177)***	**0.048***	**1.591 (1.033-2.449)***	**0.035***
Alcohol Consumption				
Never Drinker	1.041 (0.783-1.385)	0.7808	1.045 (0.772-1.415)	0.7767
Former Drinker	**1.480 (1.218-1.798)***	**<.0001***	**1.380 (1.127-1.689)***	**0.0018***
Occasional Drinker	**0.650 (0.499-0.846)***	**0.0014***	**0.633 (0.482-0.833)***	**0.0011***
Frequent Drinker	1.0		1.0	
Tobacco Use				
Tobacco	**0.776 (0.621-0.970)***	**0.0261***	0.833 (0.654-1.063)	0.1418
No Tobacco	1.0		1.0	

**Statistically significant.*

*** NHANES Target: Both males and females 50 YEARS - 150 YEARS*

*** Responses of "refused", "don't know," and missing were excluded from analyses (n = 16).

Univariate and multivariate logistic analyses for each predictor versus outcome was utilized to obtain the odds ratios (OR), 95% Wald confidence intervals (CI), and Wald p-values (alpha = 0.05).

STATISTICALLY SIGNIFICANT RESULTS

1. **AGE (PRIMARY PREDICTOR):**
   - 50 to 59 Years Old **(protective)**
     - UNIVARIATE: OR = 0.555 (0.425-0.723) and p = <.0001
     - MULTIVARIATE: OR = 0.515 (0.373-0.709) and p = <.0001
   - 70 to 79 Years Old
     - UNIVARIATE: OR = 1.354 (1.039-1.764) and p = 0.0247
     - *MULTIVARIATE: not statistically significant*
2. **DIABETES STATUS:** *No statistically significant results*
3. **GENDER:**
   - Male **(harmful)**
     - UNIVARIATE: OR = 1.353 (1.156-1.583) and p = 0.0002
     - MULTIVARIATE: OR = 1.622 (1.344-1.958) and p = <.0001
4. **RACE/ETHNICITY:**
   - Mexican American **(harmful)**
     - UNIVARIATE: OR = 1.454 (1.124-1.881) and p = 0.0044
     - MULTIVARIATE: OR = 1.516 (1.129-2.036) and p = 0.0057
   - Non-Hispanic Black **(harmful)**
     - *UNIVARIATE: not statistically significant*
     - MULTIVARIATE: OR = 1.270 (1.007-1.602) and p = 0.0433
   - Non-Hispanic Asian **(harmful)**
     - UNIVARIATE: OR = 1.337 (1.043-1.713) and p = 0.0217
     - MULTIVARIATE: OR = 1.551 (1.154-2.084) and p = 0.0036
   - Other Race - Including Multi-Racial **(harmful)**
     - UNIVARIATE: OR = 1.478 (1.003-2.177) and p = 0.048
     - MULTIVARIATE: OR = 1.591 (1.033-2.449) and p = 0.035

DIABETES: UNIVARIATE & MULTIVARIATE LOGISTIC ANALYSES

Table 4. Univariate & Multivariate Logistic Analyses of NHANES 2017-2018 Participants Regarding Factors Associated with Diabetes

Characteristic (n = 3,069)	Univariate Crude Odds Ratio (95% Wald CI)	Univariate Wald P-Value	Multivariate Crude Odds Ratio (95% Wald CI)	Multivariate Wald P-Value
Age				
50 to 59 Years Old	**0.555 (0.425-0.723)***	**<.0001***	**0.515 (0.373-0.709)***	**<.0001***
60 to 69 Years Old	1.116 (0.875-1.423)	0.3765	1.026 (0.766-1.374)	0.8644
70 to 79 Years Old	**1.354 (1.039-1.764)***	**0.0247***	1.256 (0.928-1.700)	0.1404
80+ Years Old	1.0		1.0	
Osteoporosis Status**				
Osteoporosis	1.096 (0.871-1.380)	0.4345	1.157 (0.885-1.514)	0.2858
No Osteoporosis	1.0		1.0	
Gender				
Male	**1.353 (1.156-1.583)***	**0.0002***	**1.622 (1.344-1.958)***	**<.0001***
Female	1.0		1.0	
Race/Ethnicity				
Mexican American	**1.454 (1.124-1.881)***	**0.0044***	**1.516 (1.129-2.036)***	**0.0057***
Other Hispanic	0.966 (0.721-1.295)	0.8181	1.021 (0.736-1.416)	0.8994
Non-Hispanic White	1.0		1.0	
Non-Hispanic Black	1.156 (0.940-1.421)	0.1685	**1.270 (1.007-1.602)***	**0.0433***
Non-Hispanic Asian	**1.337 (1.043-1.713)***	**0.0217***	**1.551 (1.154-2.084)***	**0.0036***
Other Race - Including Multi-Racial	**1.478 (1.003-2.177)***	**0.048***	**1.591 (1.033-2.449)***	**0.035***
Alcohol Consumption				
Never Drinker	1.041 (0.783-1.385)	0.7808	1.045 (0.772-1.415)	0.7767
Former Drinker	**1.480 (1.218-1.798)***	**<.0001***	**1.380 (1.127-1.689)***	**0.0018***
Occasional Drinker	**0.650 (0.499-0.846)***	**0.0014***	**0.633 (0.482-0.833)***	**0.0011***
Frequent Drinker	1.0		1.0	
Tobacco Use				
Tobacco	**0.776 (0.621-0.970)***	**0.0261***	0.833 (0.654-1.063)	0.1418
No Tobacco	1.0		1.0	

**Statistically significant.*

*** NHANES Target: Both males and females 50 YEARS - 150 YEARS*

*** Responses of "refused", "don't know," and missing were excluded from analyses (n = 16).

Univariate and multivariate logistic analyses for each predictor versus outcome was utilized to obtain the odds ratios (OR), 95% Wald confidence intervals (CI), and Wald p-values (alpha = 0.05).

STATISTICALLY SIGNIFICANT RESULTS

5. ALCOHOL CONSUMPTION:

- Former Drinker **(harmful)**
  - UNIVARIATE: OR = 1.480 (1.218-1.798) and p = <.0001
  - MULTIVARIATE: OR = 1.380 (1.127-1.689) and p = 0.0018
- Occasional Drinker **(protective)**
  - UNIVARIATE: OR = 0.650 (0.499-0.846) and p = 0.0014
  - MULTIVARIATE: OR = 0.633 (0.482-0.833) and p = 0.0011

6. TOBACCO USE:

- Tobacco (yes)
  - UNIVARIATE: OR = 0.776 (0.621-0.970) and p = 0.0261
  - *MULTIVARIATE: not statistically significant*

OUTCOME #2: RESULTS

According to the variables selected as predictors with respect to the outcome of **diabetes:**

1. **PRIMARY PREDICTOR:** Compared to individuals 80 years old and above, people age **50 to 59 years old had lower odds** (OR = 0.515, p = <.0001) of being told by a physician that they have **diabetes (including borderline)** after adjusting for other selected factors.
2. There was **no statistically significant association between osteoporosis status** (compared to no osteoporosis status) and being told by a physician that they have diabetes (including borderline) after adjusting for other selected factors.
3. Compared to females, **males had increased odds** of being told by a physician that they have **diabetes (including borderline)** (OR = 1.622, p = <.0001) after adjusting for other selected factors.
4. Compared to non-Hispanic whites, four racial groups had **increased odds** of being told by a physician that they have **diabetes (including borderline)** after adjusting for other selected factors: **Mexican Americans** (OR = 1.516, p = 0.0057), **non-Hispanic blacks** (OR = 1.270, p = 0.0433), **Non-Hispanic Asians** (OR = 1.551, p = 0.0036), and **other races - including multi-racial** (OR = 1.591, p = 0.035).
5. Compared to frequent drinkers, **former drinkers** had **increased odds** (OR = 1.380, p = 0.0018) while **occasional drinkers** had **reduced odds** (OR = 0.633, p = 0.0011) of being told by a physician that they have **diabetes (including borderline)** after adjusting for other selected factors.
6. After adjusting for other selected factors, there was **no statistically significant association between tobacco (yes) use** (compared to no tobacco use) and being told by a physician that you have diabetes (including borderline).

DISCUSSION & RECOMMENDATIONS

- The primary predictor of age did show an overall relationship with both osteoporosis and diabetes, which was expected.
- According to the variables selected for this study, neither osteoporosis nor diabetes were predictors for each other.
- Because the osteoporosis question was only asked to individuals over 50 years old, the multivariate analysis for diabetes had to be coded to exclude ages 1-49. For consistency, the univariate analysis for diabetes was also coded this way.
- Some results were very unexpected:
  - This may be because many variables selected from the NHANES study were from the questionnaire data, which could have resulted in bias and/or error.
  - A better measure could have been to use DEXA bone density scans (for osteoporosis) and fasting glucose levels (for diabetes) from the **laboratory data**, for example, which are "gold standards."
  - This would have been **more objective**, but it would further reduce the sample size.
- Crude odds ratios were used, and many confidence intervals contained 1.0. **Age adjusted odds ratios** would likely have provided results closer to what is typically expected for these variables.
- As with all cross-sectional studies, causation (risk ratio) cannot be determined.
- Many other potential predictors for osteoporosis and diabetes could potentially be studied in the future.
  - These include blood iron levels, physical activity, marital status, education, triglycerides, blood pressure, etc.

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- Wright, N.C., et al., *The recent prevalence of osteoporosis and low bone mass in the United States based on bone mineral density at the femoral neck or lumbar spine.* J Bone Miner Res, 2014. 29(11): p. 2520-6.

SAS CODE

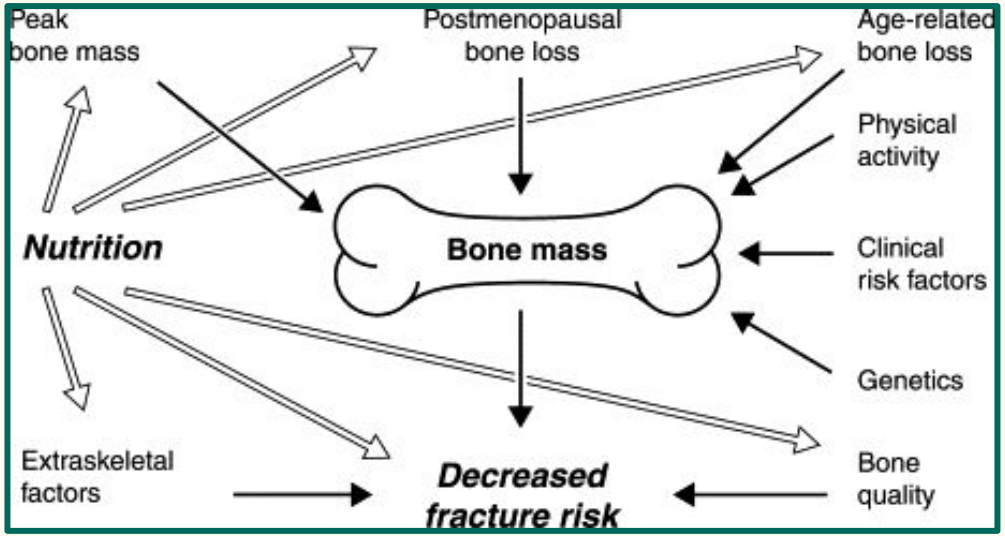
```
/* Sarah Grunblatt
SPRING 2021
BIOS 6102 Final Project – SAS Code */

/* Import data sets */

LIBNAME R XPORT 'C:\Users\sarah\Desktop\BIOS 2 – Final Project\DEMO_J.XPT';
LIBNAME D 'C:\Users\sarah\Desktop\BIOS 2 – Final Project\';
PROC COPY IN = R OUT = D;
RUN;
PROC CONTENTS DATA = D.DEMO_J ;
RUN;

LIBNAME R XPORT 'C:\Users\sarah\Desktop\BIOS 2 – Final Project\OSQ_J.XPT';
LIBNAME D 'C:\Users\sarah\Desktop\BIOS 2 – Final Project\';
PROC COPY IN = R OUT = D;
RUN;
PROC CONTENTS DATA = D.OSQ_J;
RUN;

LIBNAME R XPORT 'C:\Users\sarah\Desktop\BIOS 2 – Final Project\ALQ_J.XPT';
LIBNAME D 'C:\Users\sarah\Desktop\BIOS 2 – Final Project\';
PROC COPY IN = R OUT = D;
RUN;
PROC CONTENTS DATA = D.ALQ_J;
RUN;

LIBNAME R XPORT 'C:\Users\sarah\Desktop\BIOS 2 – Final
Project\SMQRTU_J.XPT';
LIBNAME D 'C:\Users\sarah\Desktop\BIOS 2 – Final Project\';
PROC COPY IN = R OUT = D;
RUN;
PROC CONTENTS DATA = D.SMQRTU_J ;
RUN;

LIBNAME R XPORT 'C:\Users\sarah\Desktop\BIOS 2 – Final Project\DIQ_J.XPT';
LIBNAME D 'C:\Users\sarah\Desktop\BIOS 2 – Final Project\';
PROC COPY IN = R OUT = D;
RUN;
PROC CONTENTS DATA = D.DIQ_J;
RUN;

/* Check for duplicates. */
PROC SORT DATA = D.DEMO_J ;
        BY SEQN;
        RUN;
PROC SORT DATA = D.OSQ_J;
        BY SEQN;
        RUN;
PROC SORT DATA = D.ALQ_J;
        BY SEQN;
        RUN;
PROC SORT DATA = D.SMQRTU_J ;
        BY SEQN;
        RUN;
PROC SORT DATA = D.DIQ_J;
        BY SEQN;
        RUN;

DATA DUPLICATE;
SET D.DEMO_J ;
BY SEQN;
IF NOT (FIRST.SEQN AND LAST.SEQN) THEN OUTPUT DUPLICATE ;
RUN;

DATA DUPLICATE;
SET D.OSQ_J;
BY SEQN;
IF NOT (FIRST.SEQN AND LAST.SEQN) THEN OUTPUT DUPLICATE ;
RUN;

DATA DUPLICATE;
SET D.ALQ_J;
BY SEQN;
IF NOT (FIRST.SEQN AND LAST.SEQN) THEN OUTPUT DUPLICATE ;
RUN;

DATA DUPLICATE;
SET D.SMQRTU_J ;
BY SEQN;
IF NOT (FIRST.SEQN AND LAST.SEQN) THEN OUTPUT DUPLICATE ;
RUN;

DATA DUPLICATE;
SET D.DIQ_J;
BY SEQN;
IF NOT (FIRST.SEQN AND LAST.SEQN) THEN OUTPUT DUPLICATE ;
RUN;

/* Horizontally combine datasets to add columns. */
DATA COMBINED_NHANES_1718;
MERGE D.DEMO_J(in=ina) D.OSQ_J(in=inb) D.ALQ_J(in=inc)
D.SMQRTU_J(in=ind) D.DIQ_J(in=ine);
BY SEQN;
RUN;

/* Keep the variables of interest according to how coded in NHANES for OSTEO
outcome. */
data d.select;
set COMBINED_NHANES_1718 (keep= seqn OSQ060 RIAGENDR RIDAGEYR
RIDRETH3 DMDEDUC2 ALQ111 ALQ121 SMDANY DIQ010);
where RIDAGEYR >= 40;

/* Changing age to categorical */
if RIDAGEYR=. then Age="";
else if RIDAGEYR<40 then Age="1";
else if RIDAGEYR>=40 and RIDAGEYR<50 then Age ="2";
else if RIDAGEYR>=50 and RIDAGEYR<60 then Age ="3";
else if RIDAGEYR>=60 and RIDAGEYR<70 then Age ="4";
else if RIDAGEYR>=70 and RIDAGEYR<80 then Age ="5";
else if RIDAGEYR>=80 and RIDAGEYR<90 then Age ="6";
else if RIDAGEYR>=90 then Age ="7";
else Age= "9";

/* Numeric to text Osteoporosis. */
if OSQ060 in (., 7, 9) then OsteoStatus="";
else if OSQ060=1 then OsteoStatus="Osteoporosis";
else OsteoStatus="No Osteoporosis";

/* Numeric to text Race */
if RIDRETH3=. then Race="";
else if RIDRETH3=1 then Race="1";
else if RIDRETH3=2 then Race="2";
else if RIDRETH3=3 then Race="3";
else if RIDRETH3=4 then Race="4";
else if RIDRETH3=6 then Race="6";
else Race= "7";

/* Changing Diabetes to categorical */
if DIQ010 in (.,7,9) then DiabetesStatus="";
else if DIQ010 in (1,3) then DiabetesStatus="1";
else if DIQ010=2 then DiabetesStatus="2";

/* Numeric to text gender. */
if RIAGENDR=. then Gender="";
else if RIAGENDR=1 then Gender="Male";
else if RIAGENDR=2 then Gender="Female";

/* Numeric to text Tobacco. */
if SMDANY in (., 7, 9) then Tobacco="";
else if SMDANY=1 then Tobacco="Tobacco";
else Tobacco="No Tobacco";

/* integrate two variables
                create drinking status:
                        1. never, ever
                        2. never, former, occasional, frequent <someone: ever&dok>*/
if ALQ111 in (., 7, 9) then everdok="";
else if ALQ111=1 then everdok="1";
else everdok="2";

if ALQ121 in (., 77, 99) then curdok="";
else if ALQ121 in (1,2,3,4) then curdok="1";
else if ALQ121 in (5,6,7,8,9,10) then curdok="2";
else curdok="3";

if everdok="" then dok="";
else if everdok="0" then dok="3";
else do;
if curdok="" then dok="";
else if curdok="0" then dok="3";
else if curdok="1" then dok="2";
else dok="1";
end;

label
RIDAGEYR='Age in years at screening'
Age='Age, 1:(1-9), 2:(10-19), 3:(20-29), 4:(30-39), 5:(40-49), 6:(50-59), 7:(60-69), 8:(70-79), 9:>80'

RIAGENDR='Gender, 1: male, 2:female'
Gender='Gender, 1:Male, 2:Female'

RIDRETH3='Race: 1: Mexican American, 2:Other Hispanic, 3:Non-Hispanic White, 4:Non-Hispanic Black, 6: Non-Hispanic Asian, 7: Other Race & Multi-Racial'
Race='Race: 1: Mexican American, 2:Other Hispanic, 3:Non-Hispanic White, 4:Non-Hispanic Black, 6: Non-Hispanic Asian, 7: Other Race & Multi-Racial'

OSQ060='Ever told had osteoporosis/brittle bones: 1:yes, 2:no, 7: Refused, 9: Do not know'
OsteoStatus='Osteoporosis Status: 1:Osteoporosis, 2: No Osteoporosis'

DIQ010SAS='Doctor told you have diabetes: 1:yes, 2:no, 3:borderline, 7: Refused, 9: Do not know'
DiabetesStatus='Diabetes Status: 1:(Diabetes,borderline), 2: No Diabetes'

SMDANY='Used any tobacco product last 5 days?: 1:yes, 2:no, 7: Refused, 9: Do not know'
Tobacco='Tobacco: 1:yes, 2:no, 7: Refused, 9: Do not know'

/* Integrate two variables alcohol */
ALQ111='Ever had a drink of any kind of alcohol: 1:yes, 2:no, 7: Refused, 9: Do not know'
ALQ121='Past 12 mo how often have alcohol drink, 0: Never in the last year,
                1: Every day, 2: Nearly every day, 3: 3 to 4 times a week,
                4: 2 times a week, 5: Once a week, 6: 2 to 3 times a month,
                7: Once a month, 8: 7 to 11 times in the last year,
                9: 3 to 6 times in the last year, 10: 1 to 2 times in the last year,
                77: Refused, 99: Do not know'
everdok='Ever drinker, 1:yes, 0:no'
curdok='current drinker, 1:yes, 0:no'
dok='drinking status, 0:Never Drinker, 1:Former Drinker, 2:Occasional Drinker, 3:Frequent Drinker';
run;

/* Chi Squared Des. Stat. / Gu, Grady, for OSTEO*/
proc freq data = d.select;
                tables Age*OsteoStatus / chisq;
                run;
proc freq data = d.select;
                tables Gender*OsteoStatus / chisq;
                run;
proc freq data = d.select;
                tables RIDRETH3*OsteoStatus / chisq;
                run;
proc freq data = d.select;
                tables DiabetesStatus*OsteoStatus / chisq;
                run;
proc freq data = d.select;
                tables Tobacco*OsteoStatus / chisq;
                run;
proc freq data = d.select;
                tables Dok*OsteoStatus / chisq;
                run;

/* Chi Squared Des. Stat. / Gu, Grady, for DIABETES*/
proc freq data = d.select;
                tables Age*DiabetesStatus / chisq;
                run;
proc freq data = d.select;
                tables Gender*DiabetesStatus / chisq;
                run;
proc freq data = d.select;
                tables RIDRETH3*DiabetesStatus / chisq;
                run;
proc freq data = d.select;
                tables OsteoStatus*DiabetesStatus / chisq;
                run;
proc freq data = d.select;
                tables Tobacco*DiabetesStatus / chisq;
                run;
proc freq data = d.select;
                tables Dok*DiabetesStatus / chisq;
                run;

/* REFERENCES
no diabetes  = REF = 2: no diabetes  (highest frequency)
NO OSTEO  = REF = 2: no osteo  (highest frequency)
female  = REF = 2: female  (highest frequency)
80+ years  = REF = 9  (oldest age b/c outcome increases with age)
non-hispanic white  = REF = 3  (highest frequency)
frequent drinker  = REF = 3:Frequent Drinker  (highest frequency?)
no tobacco  = REF = 2: no  (highest frequency) */

/* Logistic Regression is used to predict the CATEGORICAL dependent variable
using a given set of independent variables. */

/* Univariate Analysis for Osteo */
                proc logistic data=d.select;
                                class Age (ref='9') param = ref;
                                model OsteoStatus(event='0') = Age ; run;
                proc logistic data=d.select;
                                class Gender (ref='F') param = ref;
                                model OsteoStatus(event='0') = Gender ; run;
                proc logistic data=d.select;
                                class Race (ref='3') param = ref;
                                model OsteoStatus(event='0') = Race  ; run;
                proc logistic data=d.select;
                                class DiabetesStatus (ref='2') param = ref;
                                model OsteoStatus(event='0') = DiabetesStatus ;
run;
                proc logistic data=d.select;
                                class Tobacco (ref='N') param = ref;
                                model OsteoStatus(event='0') = Tobacco ; run;
                proc logistic data=d.select;
                                class Dok (ref='3') param = ref;
                                model OsteoStatus(event='0') = Dok ; run;

/* Univariate Analysis for Diabetes */
                proc logistic data=d.select;
                                class Age (ref='9') param = ref;
                                model DiabetesStatus(event='1') = Age ; run;
                proc logistic data=d.select;
                                class Gender (ref='F') param = ref;
                                model DiabetesStatus(event='1') = Gender ; run;

                proc logistic data=d.select;
                                class Race (ref='3') param = ref;
                                model DiabetesStatus(event='1') = Race ; run;
                proc logistic data=d.select;
                                class OsteoStatus (ref='N') param = ref;
                                model DiabetesStatus(event='1') = OsteoStatus ;
run;
                proc logistic data=d.select;
                                class Tobacco (ref='N') param = ref;
                                model DiabetesStatus(event='1') = Tobacco  ; run;

                proc logistic data=d.select;
                                class Dok (ref='3') param = ref;
                                model DiabetesStatus(event='1') = Dok  ; run;

/* Multivariate Analysis for Osteo */
                proc logistic data=d.select;
                                class Age (ref='9') Gender (ref='F') Race (ref='3')
DiabetesStatus (ref='2') Tobacco (ref='N') Dok (ref='3') param = ref;
                                model OsteoStatus(event='0') = Age Gender Race
DiabetesStatus Tobacco Dok ; run;

/* Multivariate Analysis for Diabetes */
/* Cannot use youngest age as reference when using OsteoStatus SMDANY Dok as
covariates.
                All these three variables do not have values at the
youngest age. For example, OsteoStatus only have values for age over 50.
                Must either delete those three covariates or use
Age=6 as reference. Elected to use Age=6 as reference. */
                proc logistic data=d.select;
                                class Age (ref='6') Gender (ref='F') Race (ref='3')
OsteoStatus (ref='N') Tobacco (ref='N') Dok (ref='3') param = ref;
                                model DiabetesStatus(event='1') = Age Gender
Race OsteoStatus Tobacco Dok  ; run;

/* Save SAS output as Word file??? */
```

NHANES 2017-2018: The Comorbidity Between Osteoporosis and Diabetes

BIOS 6102: Biostatistical Methods II
Spring 2021
Sarah Grunblatt, MS, MS, MEd, MEd, MA

BONE MASS

- Many factors affect bone mass.
- Examples include:
  - Nutrition (Macronutrients in addition to micronutrients such as Vitamin D, Iron, etc.)
  - Age
  - Hormones
  - Body Composition
  - Physical Activity



- Appropriate nutrition is one important strategy for maximizing bone growth (achieving peak bone mass) and achieving bone maintenance (forestalling postmenopausal and age-related bone loss).
- Nutrition improves bone mass as well as reducing falls through extraskeletal actions, thus reducing the risk of osteoporosis.

(Image modified from Rizzoli 2008.)

BACKGROUND: BLOOD IRON LEVELS

- **COLLECTION:** A blood sample is drawn to perform a serum iron test, which measures how much iron is in the blood.

- **Normal value range is:**
  - Iron: 60 to 170 micrograms per deciliter (mcg/dL), or 10.74 to 30.43 micromoles per liter (micromol/L)
  - Total iron binding capacity (TIBC): 240 to 450 mcg/dL, or 42.96 to 80.55 micromol/L
  - Transferrin saturation: 20% to 50%

WHAT ABNORMAL RESULTS MEAN:

Higher-than-normal iron level may be a sign of:

- Too much iron in the body (hemochromatosis)
- Anemia due to red blood cells being destroyed too quickly (hemolytic anemia)
- Liver tissue death
- Inflammation of the liver (hepatitis)
- Iron poisoning
- Frequent blood transfusions

Lower-than-normal level may be a sign of:

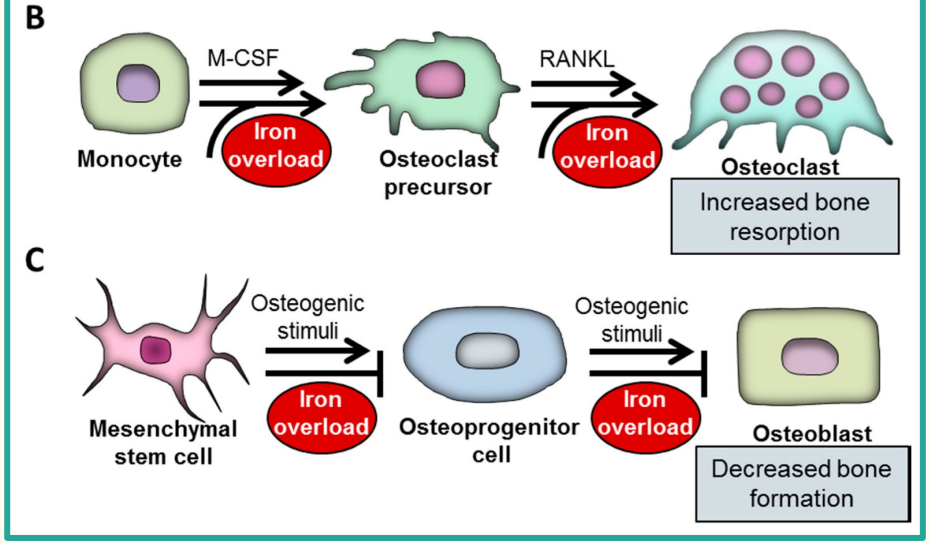
- Long-term digestive tract bleeding
- Heavy menstrual bleeding
- Intestinal conditions that cause poor absorption of iron
- Not enough iron in the diet
- Pregnancy

ASSOCIATIONS OF IRON METABOLISM AND BONE HOMEOSTASIS

- **(A) Association between iron metabolism and bone homeostasis.**
- (B) The effect of iron overload on differentiation and function of osteoclasts.
- (C) Osteoblasts differentiate from multipotent mesenchymal stem cells (MSCs).

A

Iron Metabolism	Bone homeostasis
Iron uptake > iron excretion Iron overload	Bone resorption > Bone formation Bone loss
Iron uptake = iron excretion Iron sufficiency	Bone resorption = Bone formation Balanced bone homeostasis
Iron uptake < iron excretion Iron deficiency	Bone resorption > Bone formation Bone loss



https://www.mdpi.com/1424-8247/11/4/107