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ASSOCIATION BETWEEN BISPHENOL A EXPOSURE AND BONE MINERAL DENSITY IN POST-MENOPAUSAL WOMEN, NHANES 2005-2008

By

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Degree to be awarded: MPH

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Committee Chair

ASSOCIATION BETWEEN BISPHENOL A EXPOSURE AND BONE MINERAL DENSITY IN POST-MENOPAUSAL WOMEN, NHANES 2005-2008

By

Juan Li

Bachelor of Preventive Medicine, Fudan University, 1988

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An abstract of
A thesis submitted to the Faculty of the
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Abstract

ASSOCIATION BETWEEN BISPHENOL A EXPOSURE AND BONE MINERAL DENSITY IN POST-MENOPAUSAL WOMEN, NHANES 2005-2008

By Juan Li

BACKGROUD: Humans are widely exposed to the estrogenic/anti-androgen compound bisphenol A (BPA) through food and drinks packaging. Numerous studies report that BPA alters endocrine function in animals, yet data from human studies is limited.
OBJECTIVES: The primary aim of this study was to explore the association between BPA exposure and bone mineral density (BMD) in post-menopausal women.
METHODS: We used data from the National Health and Nutrition Examination Survey (2005-2008), a population sample of noninstitutionalized U.S. residents. Post-menopausal women 50 years of age and older who completed the adult household questionnaire and participated in the mobile examination component were included. The primary outcome variable was BMD of the total hip. BMD was measured using dual-energy X-ray absorptiometry (DEXA). BPA concentration, the exposure, was measured by liquid chromatography mass spectrometry (LC-MS) in urine samples. We fit a logistic model with BMD, dichotomized based on the definition of the osteoporosis, as the outcome and quartiles of BPA as the exposure. **RESULTS:** The adjusted odds ratios comparing the upper quartiles of BPA (in ascending order) to the lowest quartile were 1.17 (0.32-4.23), 0.88 (0.22-3.57), and 0.50 (0.12-1.99).
CONCLUSION: We found no association between urine BPA and BMD in this cross-sectional study.

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INTRODUCTION

Bisphenol A (BPA), an endocrine disruptor, is found in products used daily because it is a constituent of epoxy resin and polycarbonate plastic. It alters endocrine function by mimicking estrogen, a natural hormone, and may fool the body by stimulating reactions that are unnecessary and potential harmful[1]. Therefore, it has received attention due to public awareness of its presence in consumer products and in the environment.

The relationship between osteoporosis and estrogen is well established. Higher estrogen levels are associated with increased bone mineral density (BMD) and protect women from BMD loss[2]. Further, poor bone density has been associated with a higher probability of fractures. Fractures are a significant public health problem in elderly women. Fractures lead to high medical costs, an inability to live independently, and even risk of death[3]. Therefore, if BPA alters estrogen levels in the body and influences a woman's risk for osteoporosis and bone fractures, it would have important public health consequences.

To date, few studies have examined the association between BPA exposures and human osteoporosis among women. We used the National Health and Nutrition Examination Survey (NHANES) 2005-2008 data to investigate the association between BPA exposure and BMD among post-menopausal women age 50 years age and older who participated in the mobile examination component of NHANES.

BACKGROUND

Sources of BPA Exposure:

Bisphenol-A (BPA) is used to manufacture polycarbonate plastic epoxy resins, which are used in plastic bottles, as protective coating on food containers, and as sealants in dentistry[5].

Recently, the Centers for Disease Control and Prevention reported that 95% of Americans have detectable levels of BPA in their urine of about 1.33 microg/L (1.36 microg/g creatinine) [5]. These levels could be due to leaching of BPA into food and water stored in containers made of materials containing BPA including plastic bottles made of polycarbonate plastic and metal cans lined with resins that contain BPA. Another way in which humans can be exposed to BPA is through the environment because BPA is commonly detected at low concentrations in both indoor and outdoor air, and even in house dust[8]. For these reasons, exposure of humans to BPA is high and wide spread.

BPA and Endocrine disruption:

Bisphenol-A is a man-made chemical that may interfere with the production or activity of hormones of the endocrine system that can be harmful to human health. BPA has been linked with developmental, reproductive, neural, immune, and other problems in wildlife and laboratory animals[1, 4, 9, 10].

Bisphenol A affects endocrine functions in several different ways. It can over stimulate effects of estrogen and androgen in the body by mimicking them through binding to their receptors. This can alter normal cell signaling and thereby change

physiological response to these hormones[1]. Besides mimicking these hormones, research suggests that BPA can also cause alterations in endogenous hormone synthesis, hormone metabolism, and hormone concentrations in blood [4, 9, 10, 12].

Summary of experimental animal's studies:

BPA was first shown to be estrogenic in 1938, in ovariectomized rats[25]. BPA was stimulated the reproductive system in female rats, and thus, it acts as an environmental estrogen. More recent evidence has suggested that BPA also exhibits other modes of endocrine disruption in addition to binding to estrogen receptors, such as alterations in the endogenous hormone synthesis, metabolism, and concentrations in blood[12]. Actions mediated by membrane associated receptor signaling may underlie most reported effects of the low dose BPA (effects have been reported at doses as low as 1 pM or 0.23 ppt). Since this level is within the range of human environmental exposure, hazardous effects of BPA on human health are within the realm of possibility [15].

Summary of BPA measured in humans:

Very little information is available about the long-term effects of BPA on the human body. A study by Bushnik, et al. reported urinary BPA was detected in 91% of Canadians 6-79 years of age (2007-2009 Health Measure Survey), with a geometrics mean concentration of 1.16 microg/L (1.4 microg/g creatinine)[69]. A study by Galloway, et al. in an Italian population ages 20-74, reported a geometric mean of urinary BPA concentration as 3.59 ng/ml (95% CI 3.42-3.77)[70]. Nepomnaschy studied urine samples from 60 premenopausal women using NHANES. The urine samples were collected daily for 2 or 4 weeks and were stored for 20 years. Their results showed that BPA in urine

samples taken from an individual were stable without any daily variation across 2 to 4 weeks, and BPA was stable after 20 year storage[6]. BPA levels from this study had an inter-quartile range from 1.1 to 3.1 ng/mg creatinine[6].

Osteoporosis and bone fractures:

According to the National Institutes of Health Osteoporosis and Related Bone Diseases National Resource Center, osteoporosis is "a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and increased susceptibility to fracture in the hip, spine, and wrist"[36]. The World Health Organization (WHO) diagnostic criteria, defines osteoporosis as a BMD value >2.5 standard deviations below the mean of a young adult reference group[37].

Women have higher risk of osteoporosis, and in fact, 80% of osteoporotic people are women. Even though, 10 million people in the US are diagnosed with osteoporosis, 18 million more are pre-osteoporotic due to low mineral density of their bones[38].

Osteoporosis is responsible for1.5 million fractures in the United States each year[39, 40, 41]. The medical care expenses and costs are high[42]. The estimated costs of hospital and nursing home care related to osteoporosis are more than $17 billion each year[42]. In addition, an increased risk of osteoporosis-related fractures can cause a lot of pain and disability, reducing the ability of work and participate in life activities[42].

As life expectancy of people increases, the elderly population increases and more people are at risk of getting osteoporosis.

Osteoporosis is caused either by inadequate bone accumulation during the normal cycle of bone growth and maturation or by excessive bone loss. Even though knowledge of the causes of osteoporosis is unclear, genetic, other behavior factors, and medical conditions are most likely to contribute[40].

Osteoporosis can be classified into primary and secondary osteoporosis[44]. Primary osteoporosis occurs more in post-menopausal women. Secondary osteoporosis occurs more in men[36].

The gold-standard method for diagnosis osteoporosis is by Dual-energy X-ray absorptiometry (DEXA), which is the most accurate way to measure BMD.

There are many known and suspected risk factors for osteoporosis and bone fractures. These risk factors include biologic and behavioral factors, such as family history of fractures, gender (female), age (age > 70 years), early onset of menopause, longer time since menopause, race/ ethnicity, insufficient calcium intake, vitamin D deficiency, smoking, excessive alcohol consumption, and inactivity especially lack of weight bearing exercise.

Race/ Ethnicity

Bone mineral densities are difference between race groups. A study by Kleerekoper et al. reported that older black women had higher BMD than white women[73].

Menopause

Menopausal status is strongly associated with bone density[45]. Several studies have suggested that estrogen deficiency due to menopause is associated with rapid BMD

loss[51]. Many of these studies found that this rapid BMD loss begins to level off after 5 to 10 years. One prospective cohort study found that BMD decreased by 0.3% per year in premenopausal women, 2.3% per year women less than 5 years post menopause, and 0.65% per year in women more than 5 years postmenopause[53]. Luisetto et al. reported women with late menopause showed a significantly faster bone loss than those with early menopause. In addition, they reported menopause-related BMD loss of 8.1% for the spine and 3.4% for the forearm in the first year postmenopause. Ten years later, BMD loss was below 1% per year for the spine and 0.4% per year for the foream[52].

Age

Age has also been correlated with osteoporosis and bone fractures. Data from NHANES III, suggest that women aged 65 years and older are 6 times more likely to have osteoporosis than women younger than 65 years[55]. A cross-sectional study of 55 to 70-year-old women found a negative correlation between age and BMD (R^2=0.057, p=0.003)[56]. Many studies that have found an association between fracture risk and age have not separated the effects of menopausal status and age. Luisetto et al, however, examined the effects of menopausal status and age on BMD loss and found that both factors were associated with BMD loss but had different effects[52]. The Luisetto study reported that age was responsible for 66% of the bone loss and menopause was responsible for 33%[52].

Body Mass Index

Higher weight is associated with a decreased risk of osteoporosis[55, 60]. Low body weight has consistently been associated with risk of osteoporosis-related bone fracture[49].

In a cross-sectional study of the characteristics of women with high BMD, Ito et al. found that the body weight of women with high BMD was significantly higher than that of women with low BMD[57]. Lloyd et al. also noted a positive association between weight and BMD (R^2=0.023, P=0.06)[56]. The prevalence of osteoporosis in another study was 33% among women who had a BMI of 25 or lower but only 8% among women who had a BMI above 25[42]. Ross et al. suggests that the correlation between BMI and BMD may be explained by poor health or insufficient padding of the bones[46].

Exercise

Renchen et al. found that amenorrheric athletes had significantly lower BMD (<0.01) at several different bone sites[62]. In contrast, studies of exercise that did not lead to amenorrhea showed a positive effect of exercise on the BMD of the leg bones[63]. Etherring et al. found that athletes with a lifetime history of strenuous, weight-bearing exercise had markedly higher BMD than matched controls[64]. Ross et al. report that several studies have found exercise not only maintains BMD but also increase it[46].

Smoking

Felson et al. found no association between smoking and risk of bone fracture[58]. Many other studies, however, have reported a positive and significant association between smoking and fracture[58]. Both Hollenbach et al. and Cooper et al. reported a statistically significant dose-response relationship between current smoking and BMD at the hip[59]. One mechanism by which smoking may affect BMD is through the effect of smoking on estrogen levels. Smokers are known to have an earlier menopause, lower circulating levels of estrogen metabolites, and lower body weight than nonsmokers[59].

Alcohol consumption

Alcohol consumption has been associated with an increased risk of osteoporosis[60]. The odds ratio for osteoporosis, was increased among those who drank alcoholic beverages (OR = 2.4; p = 0.02) as assessed by a multiple logistic model.

Summary:

The relation between BMD and estrogen is well established in the literature. Since humans are widely exposed to BPA, which may alter the estrogen levels, we explore the association between BPA exposure and BMD. This study may provide insight into the relation between exogenous estrogens and BMD.

Association between Bisphenol A exposure and bone mineral density in post-menopausal women, NHANES 2005-2008

BACKGROUND: Osteoporosis is a disease where bone mineral density is decreased that result in fragile bones and increases the risk of bone fracture. Higher estrogen levels increase bone mineral density (BMD) and protect women from BMD loss. Animal studies suggest exposure to Bisphenol A (BPA), an endocrine disruptor, may alter estrogen levels, however, data from human studies are limited.
OBJECTIVES: The primary aim of this study was to explore the association between BPA exposure and BMD in post-menopausal women.
METHODS: We used data from The National Health and Nutrition Examination Survey (NHANES 2005-2008) to evaluate the association between BPA and BMD in post-menopausal women age 50 and older. The primary outcome, osteoporosis, was based on BMD of the total hip. Osteoporosis was defined as BMD>2.5 standard deviations below the mean of a young adults reference group. BMD was measured using Dual-energy X-ray absorptiometry (DEXA). The exposure, BPA, was measured by liquid chromatography mass spectrometry in urine samples. We conducted logistic regression to evaluate the association between BPA and BMD, and adjusted for race and smoking in the final model.
RESULTS: The adjusted OR comparing the upper quartiles of BPA (in ascending order) to the lowest quartile were 1.17 (0.32-4.23), 0.88 (0.22-3.57), 0.50 (0.12-1.99).
CONCLUSION: We found no association between urine BPA and BMD.
KEY WORDS: Bisphenol-A, bone mineral density, osteoporosis.

According to the National Institutes of Health Osteoporosis and Related Bones Diseases National Resource Center, osteoporosis is "a disease characterized by low bone mass and structural deterioration of bone tissue, leading to increased risk of bone fracture" [36]. The relationship between osteoporosis and estrogen is well established[2, 55]. Higher estrogen levels increase bone mineral density (BMD) and protected women from BMD loss[2]. BPA is an endocrine disruptor that has been shown to mimic estrogen activity in animal studies.[1] If BPA exposure alters estrogen levels in the body; it may also affect a woman's risk for osteoporosis and bone fractures.

Since BPA is commonly used, in food and drink packaging, most people are exposed to it, but there are no published human studies of the effect of BPA on BMD. A study by Bushnik, et al reported urinary BPA was detected in 91% of the study population in Canadians 6-79 years of age (2007-2009 Health Measure Survey) with a geometric mean concentration of 1.16 microg/L (1.4 microg/g creatinine). Nepomnaschy studied urine samples from 60 premenopausal women using NHANES. Urine samples from the same individual were collected 2 or 4 weeks apart and then stored for 20 years. The study results suggest that BPA in urine samples were stable across the 2 to 4 week timeframe. Further, BPA was stable after 20 years of storage[6]. The BPA levels in this study had an inter-quartile range from 1.1 to 3.1 ng/mg creatinine[6].

We use National Health and Nutrition Examination Survey (NHANES) data to look at the relation between BPA levels and BMD.

Materials and Methods

Data source: NHANES is a cross-sectional, national survey conducted by the Center for Diseases Control & Prevention (CDC) that assesses the health and nutrition of children and adults in the United States. The study population is a stratified, multistage probability sample of the civilian, non-institutionalized U.S. population. The samples are weighted to be representative of the U.S. population. Personal household interviews and mobile examinations of about 20,696 people were performed for NHANES from January 2005 and December 2008.

The household adult questionnaire, administered to participants 20 years of age and older, includes an extensive series of questions about the participants' health. A wide range of tests are performed at the mobile examination center including blood draws and dual energy x-ray absorptiometry (DEXA) scans. More detailed information on the NHANES questionnaires, datasets, and related documentation, can be finding through the website: http://www.cdc.gov/nchs/nhanes.htm.

This secondary data analysis was determined to be exempt from review by the Emory University Institutional Review Board (IRB).

Study population. Menopausal status is strongly associated with bone density[2]. Therefore, the study population was limited to post-menopausal women 50 years of age and older who participated in the mobile examination component of NHANES (n=1705). Menopausal status was defined according to the following criteria: had a hysterectomy, had both ovaries removed, and current age one year older than the age at last menstrual period. We excluded pre-menopausal women and women whose menopausal status was

unknown as well as women under the age of 50. The study population was further limited to women who had BPA measured (n=677).

Measurement of BPA A urine sample was collected from each participant and analyzed for BPA levels by the CDC using liquid chromatography mass spectrometry[72]. Detailed BPA analysis methods have been published elsewhere, including the quality control system that was used to prevent contamination during collection, handling, and analysis of samples[72]. The lower limit of detection for BPA was 0.4 ng/ml. BPA levels below the detection limit were assigned a value of 0.28 ng/ml (http://www.cdc.gov/nchs/nhanes.htm).

Measurement of BMD The primary outcome was the mean BMD of the total hip. BMD measurements were obtained using dual-energy X-ray absorptiometry (DEXA). We limited our analyses to the total hip because the BMD of the hip subregions are highly correlated with the BMD of the total hip (r=0.76-0.98)[61]. Osteoporosis status was based on the World Health Organization (WHO) diagnostic criteria, which defines osteoporosis as a BMD value >2.5 standard deviations (SD) below the mean of a young adult reference group[37]. The reference group in this analysis was the mean for young adults, ages 20-30 years old, in the NHANES data.

Measurement of confounders In the adjusted analysis, we considered several confounders based on interview data including age, race, body mass index (BMI), height, tobacco use, alcohol use, and hormone therapy. Race/ethnicity was categorized into five categories: Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black and other race-including multi-racial. BMI was categorized according to World Health

Organization criteria (<18.5, 18.5-25, >25-29, ≥30 kg/m^2). Height was dichotomized as <64 inches or ≥64 inches. Smoking tobacco is associated with an increases risk of osteoporosis[59]. Participants were classified into those who never smoked, smoked some days, or smoked every day. Alcohol consumption is also associated with an increased risk of osteoporosis[60]. Participants reported the average number of alcohol beverages consumed per day in past the 12 months. We categorized alcohol as ≤1 drink/day vs. ≥2 drinks/day. Hormone therapy was assessed based on answers to a serial of questions about post-menopausal hormone use. We dichotomized hormone therapy use as yes vs. no.

Statistical Analysis Geometric means of BPA and BMD were compared across categories of demographic, lifestyle, and reproductive health factors using the Kruskal-Wallis test. We performed logistic regression using BMD dichotomized as ≥2.5 SD vs. <2.5 SD based on the reference group of young adults ages 20-30 in the NHANES data. NHANES samples weights were applied to the model. BPA was divided into quartiles with the lowest quartile as the reference group. We evaluated confounding based on subject matter knowledge and by comparing the ORs for the BPA variables in the unadjusted model to the ORs adjusted for different combinations of the covariates. Covariates were retained if the ORs for any BPA level changed by greater than 10%. The final model included race and smoking as confounders. We also evaluated BMD as a continuous variable using linear regression. We evaluated confounding by comparing the predicted means of BMD in the unadjusted model to the predicted means to BMD adjusted for each covariate. The final model included race and smoking as confounders.

All analyses were conducted using SAS statistical software (Version 9.1, SAS Institute Inc. Cary, NC USA).

Results

Among eligible women, 677 post-menopausal women age 50 years and older, the geometric mean of BPA was 2.87 ng/ml [95 % confidence interval (CI), 2.4-3.34 ng/ml]. BPA levels differed by race and ethnic groups (Kruskal-Wallis test p=0.1987) (Table 1). BPA seemed to decrease with age, but the confidence intervals were wide and the Kruskal-Wallis test was not significant (p=0.7293) (Table 1). The Kruskal-Wallis test was significant for BMI, but the BPA levels did not have a dose response relation with BMI. BPA levels were higher in women who experienced premature menopause (menopause at less than 40 years) than women who did not experience menopause prematurely, but the confidence interval of those with premature menopause contained that of women who experienced normal menopause. BPA was also higher for women who were not on hormone therapy.

Among eligible women, 1,705 women age 50 years and older, the geometric mean for BMD for the overall population was 0.84 gm/cm^2 (95% CI 0.83-0.85 gm/cm^2). The p-value for the Kruskal-Wallis test was statistically significant for the race/ethnicity variable although the BMD levels did not differ meaningfully (Table 2). BMD decreased with age. BMD increased with increasing BMI (P<0.0001) and was higher among those ≥ 64 inches compared to those <64 inches tall. BMD was lower for those who smoked every day compared to non-smokers (P<0.0001). BMD was lower for women with history of hip fracture. BMD was higher for women who used hormone therapy

compared to those who did not although the difference was small. The BMD levels did not change substantially across quartile of BPA.

The results for the subset of post-menopausal women who had both BPA and BMD data were similar (table3).

Based on preliminary analyses, we considered race, smoking, and hormone therapy as potential confounders, but only race and smoking were retained in the final models. The OR for the lower middle quartile of BPA was 1.17 (CI: 0.32-4.26) compared with the lowest quartile of BPA, the OR for upper middle quartile was 0.88 (CI: 0.22-3.57) compared with the lowest quartile, and the OR for the upper quartile was 0.50 (CI: 0.12-1.99) compared with the lowest quartile (Table 4).

BMD was treated as a continuous variable in the linear regression model, and the exposure was quartiles of BPA exposure. The final model adjusted for race, smoking, and hormone therapy. The predicted mean levels of BMD were 0.85 (0.81-0.88), 0.85(0.80-0.89), 0.89(0.84-0.94), and 0.83 (0.78-0.89) for the quartiles of BPA in ascending order (Table 5).

Conclusions and discussion

Information on the effect of BPA on the human body in general is limited. However, previous studies in animals have suggested that BPA has estrogenic properties[1]. Endogenous estrogen levels have been associated with a protective effect against osteoporosis[51]. Nevertheless, in post-menopausal women, we found no association between urine BPA levels and BMD.

Because of the cross-sectional design of NHANES, the outcome and exposure were measured at the same time. However, BPA levels prior to development of osteoporosis are the true exposure of interest. If BPA levels change overtime differentially by outcome status then we may not have observed an association between BPA and BMD where one truly existed. Nepomnaschy, et al. reported measurements for the BPA level in human are stable across a 2 to 4 week period, but this stability may not persist across the longer timeframe during which osteoporosis develops. Despite the limitations of the study design, this study provided the opportunity to examine whether BPA showed evidence of an estrogenic effect in humans, specifically in relation to osteoporosis. The results of this study do not suggest an effect of BPA on BMD.

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TABLES AND FIGURES

Table 1. Geometric mean BPA (unweighted) by population characteristics of post-menopausal women 50 year of age and older who participated in NHANES 2005-2008 (n=677).

Variable	N	Geometric Mean (ng /ml)	95% CI	Kruskal-Wallis test
Race/Ethnicity				p=0.20
Mexican American	110	3.30	1.78-4.82	
Other Hispanic	43	2.38	1.46-3.30	
Non-Hispanic White	358	2.68	2.00-3.36	
Non-Hispanic Black	151	3.10	2.43-3.77	
Other Race-Including Multi-Racial	15	3.90	0.00-9.05	
Age				p=0.73
50-54	82	4.06	1.50-6.70	
55-59	108	3.12	2.31-3.89	
60-64	133	2.58	1.87-3.33	
65-69	105	2.60	1.68-3.52	
70-74	85	3.47	1.54-5.46	
≥75	150	2.22	1.77-2.63	
BMI (kg/m2)				p=0.00
Underweight	10	2.87	1.22-4.52	
Normal	177	2.20	1.73-2.67	
Over	216	3.38	2.06-4.70	
Obesity	267	2.87	2.43-3.31	
Height				p=0.46

<64 inches	411	3.03	2.32-3.74	
≥64 inches	260	2.57	2.05-3.09	
BMD				p=0.43
≥2.5 SD	479	2.85	2.29-3.41	
< 2.5 SD	62	4.03	1.44-6.62	
Alcohol(Average number of alcoholic/days- in the past 12 months)				p=0.95
≤1	194	2.90	1.71-4.09	
≥2	132	2.77	2.01-3.53	
Smoke				p=0.96
Not at all	177	2.38	1.76-3.00	
Some days	12	1.95	1.04-2.86	
Every day	86	2.35	1.74-2.96	
Status of menopause				p=0.30
Premature-menopause (<40 years)	140	3.71	2.08-5.34	
Normal-menopause (>=40 years)	537	2.65	2.23-3.07	
Fracture				P=0.17
No	573	2.96	2.42-3.50	
Yes	104	2.39	1.53-3.25	
Hormone therapy				p=0.13
No	404	3.3	2.5-4.0	
Yes	273	2.3	1.9-2.7	

Table 2. Geometric mean bone mineral density by population characteristics of post-menopausal women 50 year of age and older who participated in NHANES 2005-2008 (n=1705).

Variable	N	Geometric Mean (gm /cm^2)	95% CI	Kruskal-Wallis test
Race/Ethnicity				p<0.00
Mexican American	253	0.85	0.83-0.87	
Other Hispanic	122	0.84	0.82-0.86	
Non-Hispanic White	943	0.82	0.81-0.83	
Non-Hispanic Black	333	0.89	0.87-0.91	
Other Race-Including Multi-Racial	54	0.82	0.79-0.85	
Age				p<0.00
50-54	216	0.90	0.88-0.92	
55-59	279	0.88	0.86-0.90	
60-64	335	0.87	0.85-0.89	
65-69	254	0.85	0.83-0.87	
70-74	213	0.82	0.80-0.84	
≥75	371	0.75	0.74-0.76	
BMI (kg/m2)				p<0.00
Underweight	24	0.64	0.59-0.69	
Normal	509	0.77	0.76-0.78	
Over	582	0.84	0.83-0.85	
Obesity	585	0.91	0.90-0.92	
Height				p<0.00
<64 inches	997	0.82	0.81-0.83	
≥64 inches	703	0.87	0.86-0.88	

BPA				p=0.36
BPA<0.9 ng/ml	187	0.85	0.83-0.87	
BPA 0.9-1.9 ng/ml	138	0.84	0.81-0.87	
BPA 1.9-3.7 ng/ml	107	0.87	0.84-0.90	
BPA 3.7-383.0 ng/ml	109	0.83	0.80-0.86	
Missing	136			
Alcohol(Average number of # alcoholic drink/days-in the past 12 months)				p=0.77
≤1	514	0.86	0.85-0.87	
≥2	321	0.86	0.84-0.88	
Smoke				p=0.00
Not at all	455	0.85	0.84-0.86	
Some days	33	0.89	0.82-0.96	
Every day	214	0.79	0.77-0.81	
Menopause status				
Premature-menopause (<40 years)	332	0.84	0.82-0.86	p=0.89
Normal-menopause (>=40 years)	1370	0.84	0.83-0.85	
Fracture				p<0.00
No	1460	0.85	0.84-0.86	
Yes	245	0.80	0.78-0.82	
Hormone therapy				p=0.00
No	943	0.83	0.82-0.84	
Yes	762	0.85	0.84-0.86	

Table 3. Geometric mean bone mineral density (BMD) by population characteristics of post-menopausal women 50 year of age and older who participated in NHANES 2005-2008. (Subset to women who had both BPA and BMD data) (n=541).

Variable	N	Geometric Mean (gm /cm^2)	95% CI	Kruskal-Wallis test
Race/Ethnicity				P=0.00
Mexican American	87	0.87	0.83-0.91	
Other Hispanic	37	0.84	0.79-0.89	
Non-Hispanic White	296	0.83	0.81-0.85	
Non-Hispanic Black	108	0.89	0.86-0.92	
Other Race-Including Multi-Racial	13	0.78	0.73-0.83	
Age				P<0.00
50-54	69	0.90	0.87-0.93	
55-59	90	0.89	0.86-0.92	
60-64	109	0.86	0.83-0.89	
65-69	82	0.84	0.81-0.87	
70-74	67	0.83	0.80-0.86	
≥75	113	0.75	0.73-0.77	
BMI (kg/m2)				P<0.00
Underweight	10	0.65	0.57-0.73	
Normal	159	0.77	0.75-0.79	
Over	194	0.86	0.84-0.88	
Obesity	177	0.91	0.89-0.93	
Height				P<0.00
<64 inches	321	0.82	0.80-0.84	

≥64 inches	219	0.88	0.86-0.90	
BPA				P=0.36
<0.9 ng/ml	187	0.85	0.83-0.87	
0.9-1.9 ng/ml	138	0.84	0.81-0.87	
1.9-3.7 ng/ml	107	0.87	0.84-0.90	
3.7-383.0 ng/ml	109	0.83	0.80-0.86	
Alcohol(Average number of # alcoholic drink/days-in the past 12 months)				P=0.89
≤1	166	0.87	0.85-0.89	
≥2	122	0.87	0.84-0.90	
Smoke				P<0.00
Not at all	143	0.87	0.84-0.90	
Some days	12	0.99	0.82-1.16	
Every day	71	0.79	0.76-0.82	
Menopause status				
Premature-menopause (<40 years)	119	0.84	0.81-0.87	P=0.83
Normal-menopause (>=40 years)	422	0.85	0.84-0.86	
Fracture				P=0.04
No	461	0.85	0.84-0.86	
Yes	80	0.81	0.78-0.84	

Hormone therapy				P=0.11
No	305	0.84	0.82-0.86	
Yes	236	0.86	0.84-0.88	

Table 4. Adjusted odds ratios (OR) and 95% confidence intervals (CI) for a weighted logistic regression model of bone mineral density (BMD) and quartiles of bisphenol A (BPA), among post-menopausal women 50 year of age and older who participated in NHANES 2005-2008.

BPA	Osteoporosis	Not osteoporosis	OR*	95% CI
<0.9 ng/ml	18	169	1.00	
0.9-1.9 ng/ml	20	118	1.17	0.32-4.26
1.9-3.7 ng/ml	6	101	0.88	0.22-3.57
3.7-383.0 ng/ml	18	91	0.49	0.12-1.99

*Adjusted for race and smoking

Table 5. Predicted mean bone mineral density (BMD) by quartile of bisphenol A (BPA) based on a linear regression model adjusted for race and smoking, among post-menopausal women 50 year of age and older who participated in NHANES 2005-2008.

BPA	N	Predicted Mean BMD	95% CI
<0.9 ng/ml	187	0.85	0.81-0.88
0.9-1.9 ng/ml	138	0.85	0.80-0.89
1.9-3.7 ng/ml	107	0.89	0.84-0.94
3.7-383.0 ng/ml	109	0.83	0.78-0.89