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RESEARCH ARTICLE

Associations between Thyroid Hormones and Blood and Urine Lead

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Abstract

Data from National Health and Nutrition Examination Survey for 2007-2012 were used to evaluate associations between urine and blood lead and Thyroid Stimulating Hormone (TSH), Free and Total Triiodothyronine (FT3, TT3), and Free and Total Thyroxine (FT4, TT4). Among iodine deficient as well as iodine replete males, blood lead was found to be positively associated ($p <= 0.04$) with TSH and urine lead was observed to have a negative association ($p <= 0.01$) with FT4. Among iodine deficient females, a negative association between blood lead and TT3 ($p < 0.01$) and a negative association between urine lead and FT3 ($p = 0.01$) was observed.

Keywords

Smoking, Race/Ethnicity, Thyroid, Blood/Urine lead, NHANES

Introduction

There have been quite a few studies that have investigated the association between exposure to lead and thyroid function in both occupationally exposed as well as general population.

In a study of 211 freshwater fish consumers from two communities in Canada, Abdelouahab, et al. [1] reported negative correlation between serum Thyroid Stimulating Hormone (TSH) and blood lead for females but this association was not observed among males. Zheng, et al. [2] suggested that lead exposures likely related to diminished transthyretin levels in cerebrospinal fluid. Meeker, et al. [3] reported that lead was associated with non-monotonic decrease with the levels of TSH. Yorita Christensen, et al. [4] used 2007-2008 data from National Health and Nutrition Examination Survey (NHANES) to analyze associations between thyroid hormones and 11 metals including lead, mercury, and cadmium but did not report any association between lead and thyroid hormones. Chen, et al. [5] also used NHANES 2007-2008 data and did not find any associations of blood and urine lead with any of the thyroid hormones. Kahn, et al. [6] reported lead exposure to contribute to maternal thyroid dysfunction by stimulating autoimmunity to the thyroid gland.

In a study of male adolescents who were exposed to low levels of lead for a long time as auto repairers with mean blood lead levels of 7.3 ± 2.92 µmol/L or 151.1 µg/dL, Dundar, et al. [7] reported a negative association between blood lead and Free Thyroxine (FT4) levels but without significant changes in TSH and Free Triiodothyronine (FT3) levels. Tuppurainen, et al. [8] reported a weak but statistically significant negative association between duration of exposure to lead and Total Thyroxine (TT4) and FT4 among male workers occupationally exposed to lead with mean blood lead levels of 2.7 ± 1.15 µmol/L (or 55.9 µg/dL) but the association was reported to be stronger among workers with more intense exposure to lead. In a study of 77 male secondary lead workers with moderate exposure to lead, Erfurth, et al. [9] reported minor changes in the endocrine function affecting hypothalamic-pituitary axis. In this study [9], median plasma lead levels were 0.14 µg/dL among active workers and 0.08 µg/dL among retired workers. In a study of 58 males who were exposed to lead as petrol pump workers or automobile mechanics [10] with mean blood levels of 2.49 ± 0.45 µmol/L (or 51.6 µg/dL) were not found to differ in T3 and T4 levels when compared with controls but they did have higher TSH levels as compared to controls. These authors concluded that mean blood lead level of 2.4 µmol/L or 49.7 µg/dL may increase the pituitary release of TSH without changes in circulating levels of T3 and T4. In a study of 75 subjects

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exposed to lead at work in Argentina, Lopez, et al. [11] reported positive association between TSH and blood lead when blood lead was in the range of 8 and 26 µg/dL and negative correlations were reported with T3 and T4 when blood lead was in the range of 50 and 98 µg/dL. Krieg, Jr. [12]), in a meta-analysis of published articles, did not find evidence for an effect of occupational lead exposure on thyroid function in males.

From the studies described above, it can be concluded that among those who are occupationally exposed, lead does affect thyroid hormones levels depending up on the length of lead exposure and observed levels of lead at a given point in time. On the other hand, the studies done on general US population using NHANES data for 2007-2008, lead levels among general population may not be high enough to result in observed associations between lead and thyroid hormones. However, in a preliminary analysis using expanded NHANES data for 2007-2012, associations between the levels of blood as well as urine lead were observed with FT3 and TT3 depending up on gender and urine iodine levels. Consequently, this study was undertaken to study associations between blood and urine lead levels and thyroid hormones among US population aged >= 12 years.

Materials and Methods

Data source and data description

Data for those aged >= 12 years from NHANES for the period 2007-2012 on demographics, serum cotinine, serum albumin, fasting, body measures, urinary creatinine, medical questionnaire, prescription drug use, and blood and urine lead were downloaded and match merged. Sampling weights are created in NHANES to account for the probabilities of selection and response as well as total population of US for certain combinations of age, race/ethnicities, and gender. All analyses completed for this study incorporated sampling weights as well as sampling design information in order to develop appropriate statistical estimates.

Data on thyroid were available for FT3, FT4, TT3, TT4, Thyroglobulin (TGN), and TSH as well as Thyroglobulin Antibodies (TgAb) and Thyroid Peroxidase Antibodies (TPOAb). All those females who were pregnant at the time of participation in NHANES, all those who self-reported having thyroid problems at the time of participation in NHANES, all those for whom TgAb > 20 IU/mL and/or TPO > 35 IU/mL, all those for whom the values of blood lead and/or urine lead were missing, and all those for whom values of any independent variables were missing were deleted from the analyses databases. Details for sample selection for blood lead are shown in Figure 1. For blood lead, a total of 7960 NHANES participants and a total of 4856 for urine lead were available for analysis. Sample size details are given in Table 1.

While data on blood lead were available for full NHANES samples, data for urine lead were available for only 1/3 of NHANES samples, and data for thyroid variables were available for the full NHANES sample for 2007-2008, and 1/3 NHANES sample for 2009-2010 and 2011-2012. Thus, for the purpose of the analysis for this study, data to analyze association between blood lead and thyroid variables included full NHANES sample for 2007-2008 and only 1/3 NHANES sample for 2009-2012. Data to analyze association between urine lead and thyroid variables included only 1/3 NHANES samples for 2007-2012.

Derived variables and variable selection

Associations between thyroid variables and age, race/ethnicity, gender, smoking, and Iodine Sufficiency Status (IOS) have previously been reported (Jain, 2013) and as such were selected for the analysis for this study also. Io-

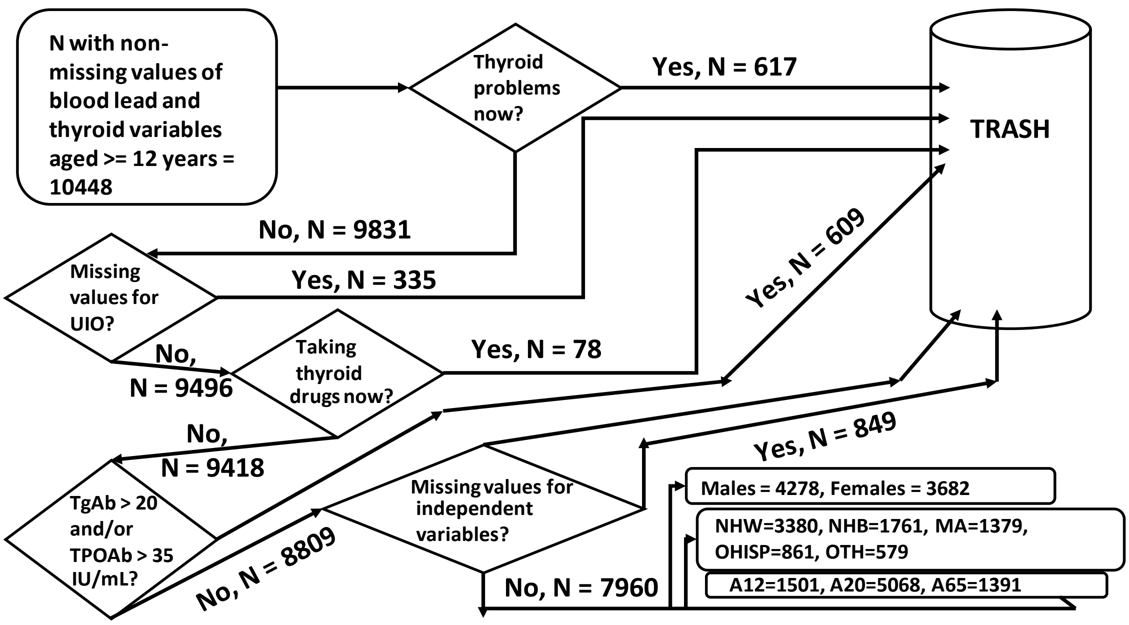

Figure 1: Sample selection process for blood lead.

Table 1: Actual sample sizes used in analyses by urine iodine status, gender, race/ethnicity, age, and smoking status. Data from National Health and Nutrition Examination Survey 2007-2012.

		For blood lead				For urine lead			
		Males		Females		Males		Females	
Urine iodine status	Demographic group	N	%	N	%	N	%	N	%
Iodine deficient	Total	1181	100.0	1329	100.0	777	100.0	856	100.0
	Age: 12-19 years	205	17.4	231	17.4	125	16.1	156	18.2
	Age: 20-64 years	816	69.1	921	69.3	550	70.8	507	59.2
	Age: >= 65 years	160	13.5	177	13.3	102	13.1	103	12.0
	Non-Hispanic White	482	40.8	557	41.9	311	40.0	346	40.4
	Non-Hispanic Black	295	25.0	336	25.3	202	26.0	211	24.6
	Mexican American	191	16.2	188	14.1	120	15.4	113	13.2
	Other Hispanics	106	9.0	139	10.5	64	8.2	99	11.6
	Other Race/ethnicities	107	9.1	109	8.2	80	10.3	87	10.2
	Nonsmoker	807	68.3	1041	78.3	544	70.0	690	80.6
	Smoker	374	31.7	288	21.7	233	30.0	166	19.4
Iodine replete	Total	3097	100.0	2353	100.0	1820	100.0	1403	100.0
	Age: 12-19 years	615	19.9	450	19.1	371	20.4	270	19.2
	Age: 20-64 years	1859	60.0	1472	62.6	1092	60.0	880	62.7
	Age: >= 65 years	623	20.1	431	18.3	357	19.6	253	18.0
	Non-Hispanic White	1398	45.1	943	40.1	778	42.7	557	39.7
	Non-Hispanic Black	615	19.9	515	21.9	385	21.2	319	22.7
	Mexican American	552	17.8	448	19.0	318	17.5	245	17.5
	Other Hispanics	324	10.5	292	12.4	160	8.8	163	11.6
	Other Race/ethnicities	208	6.7	155	6.6	80	4.4	119	8.5
	Nonsmoker	2208	71.3	1925	81.8	1351	74.2	1154	82.3
	Smoker	829	26.8	428	18.2	469	25.8	249	17.7

dine Sufficiency (IOS) was defined as Iodine Deficient (IOD) if urine iodine was < 100 µg/L and Iodine Replete (IOR) if urine iodine was >= 100 µg/L. Four separate databases, namely, IOD males, IOR males, IOD females, and IOR females were generated. Nonsmokers were defined as those who had serum cotinine < 10 ng/mL and smokers were defined as those who had serum cotinine >= 10 ng/mL. Use of drugs other than thyroid treatment that may affect thyroid hormone levels were selected for analysis. In addition, fasting time, Body Mass Index (BMI), and NHANES survey year to account for any changes over time were also selected for analysis. For females, status on menarche and menopause as well as number of live births as a measure of parity was selected.

Indicator variables were created for the use of drugs other than thyroid treatment drugs (0 = not used, 1 = used), menarche (0 = in menarche, 1 = premenarche), and menopause (0 = not in menopause, 1 = in menopause). NHANES survey was used as an ordinal variable. Because of positively skewed distributions, log10 transformed variables were created for FT3, FT4, TT3, TT4, TGN, TSH, BMI, urine creatinine, urine albumin, blood lead, and urine lead.

For each of the four databases, for each of the six thyroid variables, namely, FT3, FT4, TT3, TT4, TGN, and TSH, a regression model each fitted for blood lead and a regression model each for urine lead for a total of 48 models. Details of dependent and independent variables used in each of the four sets of models are given in Table 2. Dependent variables were always the log10 transformed values of one of the thyroid variables, namely, FT3, FT4, TT3, TT4, TGN, and TSH. Categorical independent variables were used for race/ethnicity (non-Hispanic white or NHW, non-Hispanic black or NHB, Mexican American or MA, Other Hispanics (OHISP), other unclassified race/ethnicities or OTH), smoking (nonsmoker, smoker) and age (12-19 years old or A12, 20-64 years old or A20, and >= 65-years-old or A65).

Laboratory methods

Laboratory methods to measure blood lead are available at https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/PbCd_G.htm#Description_of_Laboratory_Methodology, for urine lead at https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/UHM_G.htm#Description_of_Laboratory_Methodology , for serum albumin at https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/BIOPRO_G.htm#Description_of_Laboratory_Methodology, for urinary iodine at https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/UIO_G.htm#Description_of_Laboratory_Methodology, for urinary creatinine at https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/ALB_CR_G.htm#Description_of_Laboratory_Methodology, and for all thyroid variables at https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/THYROD_G.htm#Description_of_Laboratory_Methodology. There was no change in laboratory methodology used to measure any of the thyroid variables over 2007-2012 but there was a change in the laboratory used to measure TT3 from University of Washington Medical Center, De-

Table 2: Independent variables used^ in regression models.

Hg variable of interest	Independent variable	Type	Models fitted for			
			Male: Iodine deficient	**Male: Iodine replete**	**Female: Iodine deficient**	**Female: Iodine replete**
Blood lead	Race/ethnicity	Categorical	X	X	X	X
	Age	Categorical	X	X	X	X
	Smoking status	Categorical	X	X	X	X
	Use of drugs other than thyroid treatment drugs	Indicator	X	X	X	X
	Poverty income ratio	Continuous	X	X	X	X
	Log10 of Body Mass Index	Continuous	X	X	X	X
	Log10 of Blood Lead	Continuous	X	X	X	X
	Log10 of Serum Albumin	Continuous	X	X	X	X
	NHANES** survey year	Ordinal	X	X	X	X
	Number of live births	Continuous			X	X
	Menopause	Indicator			X	X
	Premenarche	Indicator			X	X
	Hormone use	Indicator			X	X
Urine lead	Race/ethnicity	Categorical	X	X	X	X
	Age	Categorical	X	X	X	X
	Smoking status	Categorical	X	X	X	X
	Use of drugs other than thyroid treatment drugs	Indicator	X	X	X	X
	Poverty income ratio	Continuous	X	X	X	X
	Log10 of Body Mass Index	Continuous	X	X	X	X
	Log10 of UIHG***	Continuous	X	X	X	X
	Log10 of Serum Albumin	Continuous	X	X	X	X
	NHANES** survey year	Ordinal	X	X	X	X
	Number of live births	Continuous			X	X
	Menopause	Indicator			X	X
	Premenarche	Indicator			X	X
	Hormone use	Indicator			X	X
	Log10 of Urine Creatinine	Continuous	X	X	X	X

**National Health and Nutrition Examination Survey; ^Independent variables used in the models are shown with an X.

partment of Laboratory Medicine in 2009 to Collaborative Laboratory Services in 2010 and while data for 2010 was corrected to account for this change in laboratories before being released in the public domain, a correction to post-2010 data as given below was recommended (https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/THYROD_G.htm#Analytic_Notes).

TT4 (modified) = 4.067036 + 5.492497*((TT4/10.0)**3) - 5.673583*((TT4/10.0)**3)*log(TT4/10.0)

In order to make pre-2010 and post-2010 data compatible for the purpose of analysis, the above-mentioned correction was applied o 2011-2012 TT4 data for the purpose of this study.

Software and statistical analysis

SAS University Edition (www.sas.com) was used to analyze all data for this study. Specifically, SAS Proc FREQ was used to analyze frequency distributions and SAS Proc SURVEYREG was used to fit regression models, estimate regression slopes, compute Adjusted Geometric Means (AGM) and do the pairwise comparisons.

Results

In the process of fitting 48 regression models - 4 models each for each of the six thyroid variables, two sets of Adjusted Geometric Means (AGM), one for blood lead and one for urine lead were generated. Or, for each combination of gender and IOS, an AGM each for TSH, FT3, FT4, TT3, TT4, and TGN by race/ethnicity, age, and smoking status was generated. There were minimal differences, if any, between the AGMs generated for blood and urine lead respectively. Consequently, while AGMs generated for blood lead are presented as Table 3, AGMs generated for urine lead are presented as Supplementary Table S1. Similarly, regression coefficients while fitting regression models for blood lead are presented as Table 4, regression coefficients generated while fitting model's urine lead are presented as Supplementary Table S2. However, data on regression coefficients estimated for the associations between urine lead, NHANES survey year, and urine creatinine and the six thyroid variables are also presented as Table 5.

Table 3: Adjusted geometric means with 95% confidence intervals by gender, race/ethnicity, smoking status, and Iodine Sufficiency Status (IOS) for Thyroid Stimulating Hormone (TSH), Free Triiodothyronine (FT3), Free Thyroxin (FT4), Total Triiodothyronine (TT3), Total Thyroxin (TT4), and Thyroglobulin (TGN) when association with blood lead was investigated. Data from National Health and Nutrition Examination Survey 2007-2012.

Gender: IOS	Category	TSH in µIU/mL	FT3 in pg/mL	FT4 in ng/dL	TT3 in ng/dL	TT4 in µg/mL	TGN in ng/mL
Male: IOD*	12-19 years (A12)	1.43 (1.26-1.63)	3.68 (3.6-3.76)	0.804 (0.772-0.837)	132.81 (128.7-137.05)	7.48 (7.2-7.78)	10.96 (9.17-13.11)
	20-64 years (A20)	1.41 (1.32-1.5)	3.37 (3.33-3.4)	0.803 (0.788-0.819)	116.86 (114.23-119.54)	7.59 (7.46-7.73)	10.44 (9.34-11.67)
	>= 65 years (A65)	1.44 (1.13-1.83)	3.09 (2.98-3.21)	0.778 (0.735-0.825)	111.07 (106.1-116.28)	7.53 (7.17-7.91)	14.62 (10.95-19.51)
	Non-Hispanic White (NHW)	1.48 (1.33-1.64)	3.32 (3.25-3.39)	0.782 (0.765-0.799)	118.59 (115.6-121.65)	7.31 (7.13-7.5)	10.32 (9.14-11.66)
	Non-Hispanic Black (NHB)	1.32 (1.19-1.45)	3.3 (3.23-3.36)	0.762 (0.735-0.79)	115.13 (112.05-118.3)	7.2 (7.02-7.38)	13.35 (11.75-15.18)
	Mexican American (MA)	1.37 (1.19-1.57)	3.43 (3.35-3.52)	0.821 (0.782-0.862)	123.2 (118-128.62)	7.71 (7.47-7.96)	9.76 (8.3-11.46)
	Other Hispanics (OHISP)	1.47 (1.25-1.72)	3.41 (3.32-3.51)	0.794 (0.751-0.84)	122.64 (115.41-130.32)	7.58 (7.25-7.93)	10.66 (8.64-13.14)
	Others (OTH)	1.51 (1.26-1.8)	3.4 (3.33-3.48)	0.818 (0.782-0.855)	120.14 (116.03-124.39)	7.89 (7.63-8.17)	16.46 (10.82-25.03)
	Nonsmokers (NSM)	1.5 (1.36-1.66)	3.4 (3.36-3.44)	0.788 (0.769-0.807)	120.78 (118.63-122.97)	7.54 (7.37-7.7)	10.33 (9.21-11.57)
	Smokers (SM)	1.35 (1.22-1.51)	3.35 (3.25-3.45)	0.802 (0.773-0.833)	119.03 (114.95-123.26)	7.53 (7.32-7.75)	13.65 (11.23-16.58)
	SSD**		A12 > A20 > A65 (p < 0.01), NHW < MA (p = 0.02), NHB < MA (p < 0.01), NHB < OHISP (p = 0.01), NHB < OTH (p = 0.02)	NHW < OTH (p = 0.03), NHB < MA (p = 0.01), NHB < OTH (p < 0.01)	A12 > A20 (p < 0.01), A12 > A65 (p < 0.01), NHB < MA (p < 0.01), NHB < OHISP (p = 0.04), NHB < OTH (p = 0.03)	NHW < MA (p < 0.01), NHW < OTH (p < 0.01), NHB < MA (p < 0.01), NHB < OHISP (p = 0.04), NHB < OTH (p < 0.01)	A20 < A65 (p < 0.01), NHW < NHB (p = 0.01), NHW < OTH (p = 0.02), NHB > MA (p < 0.01), NHB < OTH (p = 0.03), MA < OTH (p < 0.01), OHISP < OTH (p = 0.03), NSM < SM (p < 0.01)
Male: IOR*	12-19 years (A12)	1.43 (1.33-1.53)	3.68 (3.62-3.74)	0.799 (0.772-0.827)	134.6 (130.72-138.59)	7.51 (7.29-7.74)	9.21 (8.27-10.26)
	20-64 years (A20)	1.34 (1.28-1.41)	3.34 (3.31-3.38)	0.79 (0.776-0.805)	116.41 (114.57-118.28)	7.57 (7.46-7.69)	9.1 (8.64-9.59)
	>= 65 years (A65)	1.45 (1.32-1.6)	3.06 (3.01-3.11)	0.803 (0.781-0.825)	103.81 (100.91-106.8)	7.91 (7.67-8.15)	9.7 (8.3-11.33)
	Non-Hispanic White (NHW)	1.64 (1.58-1.71)	3.32 (3.29-3.35)	0.788 (0.771-0.805)	116.52 (114.15-118.93)	7.33 (7.21-7.45)	9.48 (9-9.98)
	Non-Hispanic Black (NHB)	1.24 (1.17-1.32)	3.31 (3.27-3.36)	0.783 (0.765-0.802)	115.94 (112.5-119.49)	7.52 (7.31-7.73)	12.64 (11.48-13.92)
	Mexican American (MA)	1.35 (1.24-1.46)	3.38 (3.33-3.43)	0.787 (0.759-0.816)	118.82 (115.97-121.74)	7.79 (7.58-7.99)	7.82 (6.82-8.97)
	Other Hispanics (OHISP)	1.38 (1.27-1.49)	3.43 (3.35-3.51)	0.796 (0.768-0.825)	120.52 (116.91-124.25)	7.79 (7.53-8.06)	8.89 (7.72-10.24)
	Others (OTH)	1.45 (1.29-1.62)	3.31 (3.21-3.42)	0.834 (0.809-0.859)	116.3 (111.69-121.1)	7.9 (7.62-8.19)	8.5 (7.21-10.01)
	Nonsmokers (NSM)	1.52 (1.44-1.61)	3.35 (3.32-3.38)	0.793 (0.78-0.807)	116.45 (114.73-118.19)	7.63 (7.52-7.75)	8.48 (7.95-9.04)

	Smokers (SM)	1.3 (1.22-1.38)	3.35 (3.3-3.4)	0.801 (0.781-0.822)	118.77 (115.05-122.62)	7.69 (7.48-7.91)	10.28 (9.21-11.47)
	SSD**	NHW > NHB (p < 0.01), NHW > MA (p < 0.01), NHW > OHISP (p < 0.01), NHW > OTH (p = 0.02), NHB < OHISP (p = 0.04), NHB < OTH (p = 0.02), NSM > SM (p < 0.01)	A12 > A20 > A65 (p < 0.01), NHW < MA (p = 0.04), NHW < OTH (p = 0.01), NHB < MA (p = 0.03), NHB < OHISP (p = 0.01)	NHW < OTH (p < 0.01), NHB < OTH (p < 0.01), MA < OTH (p < 0.01), OHISP < OTH (p = 0.02)	A12 > A20 > A65 (p < 0.01), NHB < MA (p = 0.03)	A12 < A65 (p = 0.01), A20 < A65 (p < 0.01), NHW < MA (p < 0.01), NHW < OHISP (p < 0.01), NHW < OTH (p < 0.01), NHB < MA (p = 0.01), NHB < OTH (p = 0.02)	NHW < NHB (p < 0.01), NHW > MA (p = 0.01), NHB > MA (p < 0.01), NHB > OHISP (p < 0.01), NHB > OTH (p < 0.01), NSM < SM (p < 0.01)
Female: IOD*	12-19 years (A12)	1.44 (1.25-1.66)	3.45 (3.37-3.54)	0.796 (0.768-0.824)	122.7 (117.49-128.13)	7.72 (7.45-7.99)	10.27 (8.66-12.19)
	20-64 years (A20)	1.33 (1.23-1.43)	3.15 (3.09-3.2)	0.785 (0.766-0.804)	114.07 (111.44-116.76)	7.8 (7.65-7.95)	12.8 (11.63-14.09)
	>= 65 years (A65)	1.33 (1.15-1.54)	3.03 (2.93-3.14)	0.806 (0.778-0.836)	110.08 (104.1-116.41)	7.72 (7.34-8.13)	16.15 (12.18-21.41)
	Non-Hispanic White (NHW)	1.54 (1.42-1.68)	3.2 (3.16-3.24)	0.783 (0.767-0.799)	116.29 (113.65-118.98)	7.71 (7.51-7.91)	12.62 (11.47-13.89)
	Non-Hispanic Black (NHB)	1.17 (1.03-1.33)	3.18 (3.12-3.24)	0.793 (0.772-0.814)	114.05 (110.51-117.71)	7.64 (7.43-7.86)	17.86 (15.68-20.34)
	Mexican American (MA)	1.46 (1.28-1.66)	3.25 (3.16-3.34)	0.793 (0.764-0.824)	118.22 (113.66-122.97)	7.86 (7.57-8.17)	10.37 (8.23-13.06)
	Other Hispanics (OHISP)	1.32 (1.12-1.57)	3.22 (3.11-3.33)	0.789 (0.759-0.821)	117.37 (110.39-124.8)	7.64 (7.04-8.28)	11.23 (9.25-13.64)
	Others (OTH)	1.36 (1.12-1.66)	3.18 (3.06-3.31)	0.821 (0.775-0.87)	111.66 (106.62-116.94)	7.88 (7.51-8.28)	13.36 (10.45-17.07)
	Nonsmokers (NSM)	1.42 (1.31-1.54)	3.2 (3.14-3.25)	0.799 (0.782-0.815)	116.21 (113.28-119.21)	7.97 (7.81-8.14)	11.01 (9.88-12.26)
	Smokers (SM)	1.31 (1.16-1.48)	3.22 (3.13-3.3)	0.792 (0.768-0.818)	114.79 (110.53-119.21)	7.53 (7.19-7.87)	15.01 (12.67-17.79)
	SSD**	NHW > NHB (p < 0.01), NHB < MA (p = 0.01)	A12 > A20 > A65 (p <= 0.03)		A12 > A20 (p < 0.01), A12 > A65 (p < 0.01)		A12 < A20 (p = 0.02), A12 < A65 (p = 0.01), NHW < NHB (p < 0.01), NHB > MA (p < 0.01), NHB > OHISP (p < 0.01), NHB < OTH (p = 0.03), NSM < SM (p < 0.01)
Female: IOR*	12-19 years (A12)	1.39 (1.27-1.52)	3.3 (3.23-3.37)	0.799 (0.773-0.826)	125.84 (120.55-131.36)	7.82 (7.62-8.04)	11.34 (9.57-13.44)
	20-64 years (A20)	1.28 (1.21-1.35)	3.15 (3.11-3.18)	0.775 (0.76-0.79)	111.53 (108.87-114.27)	7.88 (7.74-8.03)	11.62 (10.67-12.65)
	>= 65 years (A65)	1.48 (1.32-1.66)	3.02 (2.96-3.08)	0.762 (0.733-0.792)	104.66 (101.45-107.97)	8.26 (7.97-8.56)	12.04 (10.55-13.74)
	Non-Hispanic White (NHW)	1.57 (1.49-1.66)	3.2 (3.17-3.23)	0.771 (0.754-0.789)	116.57 (114.43-118.75)	7.79 (7.66-7.92)	11.9 (11.12-12.73)
	Non-Hispanic Black (NHB)	1.19 (1.11-1.27)	3.09 (3.05-3.14)	0.781 (0.758-0.804)	110.98 (106.96-115.14)	7.8 (7.58-8.02)	16.74 (15.15-18.5)

	Mexican American (MA)	1.41 (1.3-1.53)	3.19 (3.14-3.24)	0.798 (0.775-0.822)	113.94 (109.04-119.06)	8.21 (7.95-8.48)	8.2 (7.01-9.59)
	Other Hispanics (OHISP)	1.39 (1.27-1.53)	3.15 (3.09-3.21)	0.771 (0.741-0.803)	114.69 (111.03-118.46)	8 (7.67-8.33)	11.88 (9.98-14.14)
	Others (OTH)	1.37 (1.19-1.58)	3.14 (3.06-3.22)	0.771 (0.743-0.8)	112.29 (106.65-118.23)	8.15 (7.87-8.44)	11.13 (9.09-13.63)
	Nonsmokers (NSM)	1.48 (1.39-1.57)	3.16 (3.13-3.18)	0.793 (0.78-0.807)	113.06 (110.99-115.16)	8.03 (7.91-8.14)	10.01 (9.36-10.71)
	Smokers (SM)	1.29 (1.19-1.4)	3.15 (3.11-3.2)	0.764 (0.739-0.79)	114.3 (110.65-118.07)	7.95 (7.74-8.16)	13.59 (11.68-15.82)
	SSD**	A20 < A65 (p = 0.02), NHW > NHB (p < 0.01), NHW > MA (p = 0.02), NHW > OHISP (p = 0.03), NHW > OTH (p = 0.03), NHB < MA (p < 0.01), NHB < OHISP (p < 0.01), NSM > SM (p < 0.01)	A12 > A20 > A65 (p < 0.01), NHW > NHB (p < 0.01), NHB < MA (p < 0.01)		A12 > A20 > A65 (p < 0.01), NHW > NHB (p = 0.01)	A12 < A65 (p = 0.02), A20 < A65 (p = 0.01), NHW < MA (p < 0.01), NHW < OTH (p = 0.03), NHB < MA (p = 0.01), NHB < OTH (p = 0.03),	NHW < NHB (p < 0.01), NHW < MA (p < 0.01), NHB > MA (p < 0.01), NHB > OHISP (p < 0.01), NHB > OTH (p < 0.01), MA < OHISP (p < 0.01), MA < OTH (p < 0.01), NSM < SM (p < 0.01)

*IOD = Iodine Deficient or urine iodine < 100 ng/mL; IOR = Iodine Replete or urine iodine >= 100 ng/mL; **SSD = Statistically Significant Differences.

Blood lead

Statistics for Iodine Deficient (IOD) males: A12 had the highest AGMs for FT3 (3.68 vs. 3.09 pg/mL) and TT3 (132.81 vs. 111.07 ng/dL) and A65 had the lowest AGMs and pairwise differences were almost always statistically significant ($p < 0.01$, Table 3). For FT3, FT4, TT3, and TT4, NHW and/or NHB had lower AGMs than MA, OHISP, and/or OTH (Table 3). For example, for TT4, NHW < MA (7.31 vs. 7.71 µg/mL, $p < 0.01$, Table 3), NHW < OTH (7.31 vs. 7.89 µg/mL, $p < 0.01$, Table 3), NHB < MA (7.20 vs. 7.71 µg/mL, $p < 0.01$, Table 3), NHB < OHISP (7.20 vs. 7.58 µg/mL, $p = 0.04$, Table 3), and NHB < OTH (7.31 vs. 7.89 µg/mL, $p < 0.01$, Table 3). For TGN, NSM < SM (10.33 vs. 13.65 ng/mL, $p < 0.01$, Table 3). For TGN, OTH > NHB > OHISP > NHW > MA.

Interactions between age and smoking were found to be statistically significant ($p < 0.05$) for FT3 (Figure 2, Panel A) and TT3 (Figure 3, Panel A). For FT3, A12-A20 differences were found to be 0.47 and 0.15 pg/mL among nonsmokers and smokers respectively, A12-A65 differences were found to be 0.69 and 0.08 pg/mL among nonsmokers and smokers respectively, and A20-A65 differences were found to be 0.21 and 0.48 pg/mL among nonsmokers and smokers respectively (Figure 2, Panel A). For TT3, A12-A20 differences were found to be 26.2 and 6.0 ng/dL among nonsmokers and smokers respectively, A12-A65 differences were found to be 29.7 and 14.2 ng/dL among nonsmokers and smokers respectively, and A20-A65 differences were found to be 3.5 and 8.2 ng/dL among nonsmokers and smokers respectively (Figure 3, Panel A). Thus, A12-A20 and A12-A65 differences are primarily determined by nonsmokers and A20-A65 differences are primarily contributed to by smokers. Interaction between race/ethnicity and smoking was observed to be statistically significant for FT4 (Figure 2, Panel B). There were substantial differences in the observed racial/ethnic variability contributed to by smokers and nonsmokers respectively. For example, MA > NHW by 0.006 ng/dL among nonsmokers but by 0.073 ng/dL among smokers and MA-OTH differences were -0.042 ng/dL among nonsmokers and 0.049 ng/dL among smokers (Figure 2, Panel B).

Finally, for IOD males, there was a statistically significant interaction between age and race/ethnicity for TGN (Figure 2, Panel C). AGMs for TGN were higher for NHB when compared to NHW, MA, OHSP, and OTH by 1.48, 2.59, 1.19, and 2.82 ng/mL respectively for A12, by 4.20, 5.94, 6.54, and 6.30 ng/mL for A20, and by 3.44, 2.43, 0.22, and -38.30 (this data point not shown in Figure 2, Panel C) for A65. Thus, contribution to racial/ethnic differences was higher for A20 than for A12 and A65.

A positive association between fasting time and FT3, FT4, and TT3 was observed ($p <= 0.02$, Table 4). BMI was positively associated with the levels of FT3 and TT3 ($p = 0.03$, Table 4). Increase in the levels of blood lead was associated with the increase in the levels of TSH (β =

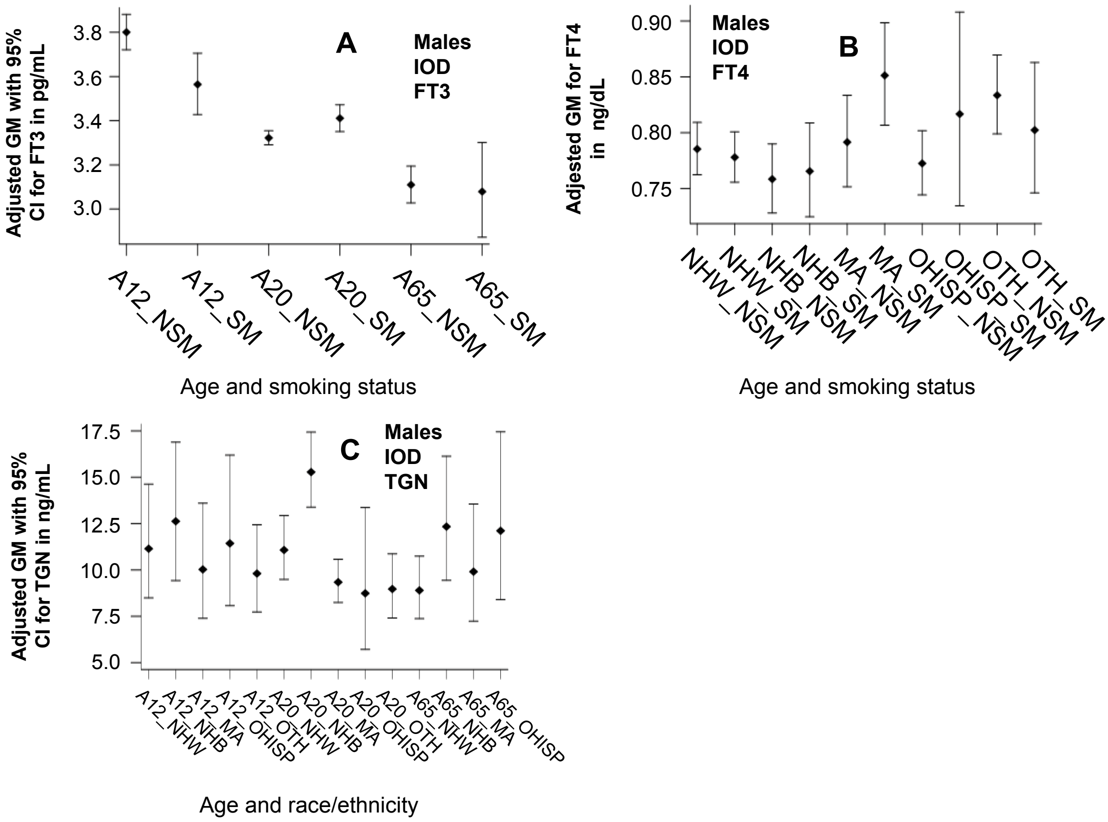

Figure 2: Adjusted geometric means with 95% Confidence Intervals (CI) for (A) for Free Triiodothyronine (FT3) in pg/mL for Iodine Deficient (IOD) males by age and smoking status (A12 = Aged 12-19 years, A20 = Aged 20-64 years, A65 = Aged >= 65 years, NSM = Nonsmokers, SM = Smokers), (B) for Free Thyroxine (FT4) in ng/dL for IOD males by race/ethnicity and smoking status (NHW = Non-Hispanic White, NHB = Non-Hispanic Black, MA = Mexican American, OHISP = Other Hispanics, OTH = other unclassified race/ethnicities), and (C) for Thyroglobulin (TGN) in ng/mL for IOD males by age and race/ethnicity.

0.11057, $p = 0.04$). A 10% increase in the untransformed value of blood lead was associated with a 1.1% increase in the untransformed values of TSH. Levels of FT4 ($\beta = 0.122$, $p < 0.01$) increased but that of TT4 decreased ($\beta = -0.0108$, $p = 0.01$) over 2007-2012.

Statistics for Iodine Replete (IOR) males: For FT3 and TT3, A12 > A20 > A65 ($p < 0.01$). For TT4, A12 < A65 (7.51 vs. 7.91 µg/mL, $p < 0.01$, Table 3) and A20 < A65 (7.57 vs. 7.91 µg/mL, $p < 0.01$, Table 3). For FT3, FT4, TT3, and TT4, as it was observed for IOD males, NHW and/or NHB had lower AGMs than MA, OHISP, and/or OTH (Table 3). And, as for IOD males, for IOR males also, for TGN, NSM < SM (8.48 vs. 10.28 ng/mL, $p < 0.01$, Table 3) and NHB > NHW > OHISP > OTH > MA. For TSH, NSM > SM (1.52 vs. 1.30 µIU/mL, $p < 0.01$) and NHW had the highest AGM and NHB the lowest AGM (1.64 vs. 1.24 µIU/mL, $p < 0.01$).

Statistically significant interactions between age and smoking for FT3 (Figure 3, Panel B) and between age and race/ethnicity for FT4 (Figure 3, Panel C) were observed. For FT3, while for A12, nonsmokers had higher AGM than smokers (3.73 vs. 3.63 pg/mL), for A20 (3.32 vs. 3.37 pg/mL) and A65 (3.05 vs. 3.07 pg/mL), nonsmokers had lower AGMs than smokers (Figure 2, Panel B). For FT4, the difference in AGMs between OTH and NHW, NHB, MA, and OHISP was 0.057, 0.036, 0.027, and 0.024 ng/dL respectively for A12, 0.065, 0.072, 0.032, and 0.049 respectively for A20, and 0.014, 0.042, 0.081, and 0.040 ng/dL respectively for A65 (Figure 2, Panel C).

Use of drugs other than thyroid treatment drugs was observed to decrease the levels of FT3 ($\beta = -0.0171$, $p < 0.01$, Table 4) and TT3 ($\beta = -0.024$, $p < 0.01$, Table 4). A positive association between fasting time and FT3 and TT3 was observed ($p <= 0.01$, Table 4). BMI was positively associated with the levels of FT3, TT3, TT4, and TGN (< 0.01) but negatively associated with the levels of FT4 ($p = 0.01$). Increase in the levels of blood lead was associated with the increase in the levels of TSH ($\beta = 0.0618$, $p = 0.04$). A 10% increase in the untransformed value of blood lead was associated with a 0.6% increase in the untransformed values of TSH. Levels of FT4 ($\beta = 0.1183$, $p < 0.01$) increased over 2007-2012.

Statistics for Iodine Deficient (IOD) females: For FT3 and TT3, AGMs were in the order A12 > A20 > A65 and almost all pairwise differences were statistically significant ($p < 0.01$, Table 3). For TGN, A12 had lower AGM than both A20 and A65 (10.27 vs. 12.80 and 16.15 ng/mL, $p < 0.01$, Table 3). For TGN, the order in which AGMs by race/ethnicity were observed was NHB (17.86 ng/mL) > OTH (13.36 ng/mL) > NHW (12.62 ng/mL) > OHISP (11.23 ng/mL) > MA (10.37 ng/mL) and some of these differences were statistically significant. For TGN,

Table 4: Regression slopes with p-values by age and gender for the models fitted for log10 transformed values of Thyroid Stimulating Hormone (TSH in nIU/mL), Free Triiodothyronine (FT3 in fg/mL), Free Thyroxin (FT4 in pg/dL), Total Triiodothyronine (TT3 in pg/dL), Total Thyroxin (TT4 in ng/mL), and Thyroglobulin (TGN in fg/mL) when association with blood lead was investigated. Data from National Health and Nutrition Examination Survey 2007-2012. Statistically significant associations are shown in bold letters.

Gender: IOS	Independent variable	TSH	FT3	FT4	TT3	TT4	TGN
Male: IOD*	Use other drugs	-0.037065779 (0.28)	-0.008215337 (0.09)	0.0103028727 (0.26)	-0.012609734 (0.17)	0.014032962 (0.11)	0.0065196708 (0.87)
	Fasting in hours	-0.000612081 (0.73)	**0.0016496535 (0)**	**0.0007985239 (0.02)**	**0.0016788756 (0.02)**	0.0003806791 (0.45)	0.0026515297 (0.53)
	Poverty income ratio	0.0015097725 (0.8)	-0.002249327 (0.07)	-0.000979113 (0.56)	-0.002983687 (0.18)	-0.001726884 (0.25)	-0.001890045 (0.87)
	Log10 of Body Mass Index	0.1353845906 (0.32)	**0.0406589662 (0.03)**	-0.001868129 (0.96)	**0.099276504 (0.03)**	0.0627047093 (0.13)	0.0712478469 (0.71)
	Log10 of Serum Albumin	0.6647769285 (0.1)	**0.223483551 (0)**	-0.097939711 (0.29)	**0.3531044459 (0)**	-0.076536462 (0.41)	-0.673733775 (0.22)
	Lg10 of Blood Lead	**0.1105665567 (0.04)**	-0.008447674 (0.13)	-0.01377589 (0.2)	-0.012574298 (0.23)	-0.008348064 (0.34)	0.0302216627 (0.64)
	NHANES survey cycle	0.0019232639 (0.92)	-0.003236359 (0.29)	**0.0121946118 (0)**	-0.000720082 (0.89)	**-0.010788304 (0.01)**	0.0139275255 (0.44)
	R^2 in percent	2.8	30.9	6.2	18.3	5.0	8.0
Male: IOR*	Use other drugs	0.023149433 (0.36)	**-0.017148042 (0)**	0.0060513245 (0.35)	**-0.024017872 (0)**	0.009344698 (0.32)	-0.060085942 (0.03)
	Fasting in hours	0.0007070414 (0.59)	**0.0009779981 (0)**	0.0004500466 (0.23)	**0.0011716019 (0.01)**	0.0003204781 (0.36)	-0.003363325 (0.06)
	Poverty Income Ratio	-0.002118725 (0.69)	**-0.003268413 (0)**	-0.000279512 (0.8)	**-0.00551787 (0)**	-0.00111354 (0.43)	-0.003278765 (0.61)
	Log10 of Body Mass Index	0.2108936607 (0.05)	**0.0491633032 (0)**	**-0.073973343 (0.01)**	**0.101456823 (0)**	**0.0675861483 (0)**	**0.3308218629 (0)**
	Log10 of Serum Albumin	0.3565304989 (0.09)	**0.2541341853 (0)**	-0.088252294 (0.2)	**0.2911937567 (0)**	-0.058409572 (0.47)	-0.533308716 (0.14)
	Lg10 of Blood Lead	**0.0617500552 (0.02)**	-0.008514174 (0.08)	-0.015141522 (0.13)	-0.006632611 (0.31)	-0.010870387 (0.22)	0.0346090971 (0.35)
	NHANES survey cycle	-0.005324027 (0.51)	-0.003272757 (0.21)	**0.0118291574 (0)**	0.0015936298 (0.64)	-0.006303805 (0.06)	0.000885978 (0.95)
	R^2 in percent	6.0	30.1	6.3	20.8	4.2	5.3
Female: IOD*	Use other drugs	-0.019199135 (0.55)	-0.002866774 (0.63)	0.0082121054 (0.25)	-0.000557795 (0.97)	**0.0236065558 (0.02)**	0.0578299402 (0.18)
	Fasting in hours	0.0075027757 (0.03)	**0.001333764 (0)**	0.0002278611 (0.65)	0.0004716519 (0.47)	0.0007126796 (0.27)	0.0002878735 (0.88)
	Poverty Income Ratio	-0.002890589 (0.68)	-0.002455487 (0.09)	-0.001547872 (0.32)	**-0.006217204 (0)**	**-0.004619988 (0.01)**	-0.007612611 (0.31)
	Log10 of Body Mass Index	**0.2399973248 (0.03)**	**0.0517147882 (0.01)**	-0.024946026 (0.34)	**0.0909759416 (0.03)**	**0.096691019 (0.01)**	0.0306783316 (0.84)
	Log10 of Serum Albumin	0.0455124368 (0.88)	**0.1736607624 (0.02)**	-0.06170066 (0.45)	-0.065987868 (0.6)	**-0.378424338 (0)**	-0.12641695 (0.81)
	Lg10 of Blood Lead	0.0611458809 (0.21)	-0.005627128 (0.57)	0.0029226235 (0.81)	**-0.033757165 (0.01)**	-0.003164823 (0.81)	0.0526994513 (0.43)
	NHANES survey cycle	-0.009394394 (0.56)	-0.002042453 (0.33)	**0.0146301173 (0)**	-0.001900373 (0.55)	**-0.008318777 (0.04)**	0.0067406461 (0.72)
	Premenarche	**0.1650352097 (0.02)**	**0.0388657006 (0.01)**	-0.022047273 (0.26)	**0.076279679 (0)**	**-0.046544845 (0.01)**	0.0958813162 (0.33)
	Menopause	0.0567437982 (0.1)	-0.011683835 (0.05)	0.0091105501 (0.28)	0.0005254126 (0.96)	0.003380469 (0.76)	0.0252302102 (0.56)
	No of live births	-0.011717488 (0.15)	0.0000479555 (0.97)	-0.002352227 (0.14)	-0.002429194 (0.31)	0.0000927245 (0.96)	-0.008791034 (0.43)
	R^2 in percent	9.1	16.6	5.1	9.2	13.3	8.5
Female: IOR*	Use other drugs	0.0121621155 (0.46)	**-0.021035976 (0)**	0.002202594 (0.67)	**-0.031848284 (0)**	-0.000337082 (0.96)	0.0063424389 (0.86)
	Fasting in hours	0.0060879619 (0)	**0.0012754254 (0)**	0.0004620015 (0.24)	**0.0014080414 (0)**	0.0001018241 (0.82)	0.0005962346 (0.82)
	Poverty Income Ratio	0.0030432476 (0.51)	**-0.00368989 (0)**	-0.000011409 (0.99)	**-0.005365296 (0.02)**	-0.000443187 (0.77)	-0.008612939 (0.26)
	Log10 of Body Mass Index	**0.377353859 (0)**	**0.0705398018 (0)**	**-0.04174673 (0.04)**	**0.0879106429 (0)**	**0.0490881087 (0.01)**	0.1122607097 (0.4)

	Log10 of Serum Albumin	0.2849512363 (0.39)	**0.1792830379 (0)**	-0.08458671 (0.21)	-0.039605998 (0.69)	**-0.411087258 (0)**	-0.365461581 (0.33)
	Lg10 of Blood Lead	0.0239281375 (0.49)	-0.009003318 (0.17)	0.0091433572 (0.23)	-0.022773137 (0.08)	0.003635171 (0.76)	-0.037406285 (0.67)
	NHANES survey cycle	0.0043626117 (0.62)	-0.003190543 (0.13)	**0.0130269123 (0)**	0.0055692255 (0.2)	-0.00359465 (0.36)	0.0006056034 (0.98)
	Premenarche	**0.2020825192 (0)**	**0.051894233 (0)**	-0.014187607 (0.4)	**0.0717723245 (0)**	-0.033760292 (0.06)	-0.021924191 (0.85)
	Menopause	0.0414536832 (0.11)	-0.001923664 (0.67)	0.004842686 (0.46)	-0.002008668 (0.81)	-0.002995773 (0.72)	0.0468999028 (0.28)
	No of live births	-0.001967319 (0.67)	**-0.00334126 (0)**	-0.000483147 (0.65)	-0.002535476 (0.07)	-0.000195662 (0.89)	0.0105347204 (0.22)
	R^2 in percent	9.8	22.6	5.7	14.1	5.9	6.8

*IOD = Iodine Deficient or urine iodine < 100 ng/mL; IOR = Iodine Replete or urine iodine >= 100 ng/mL.

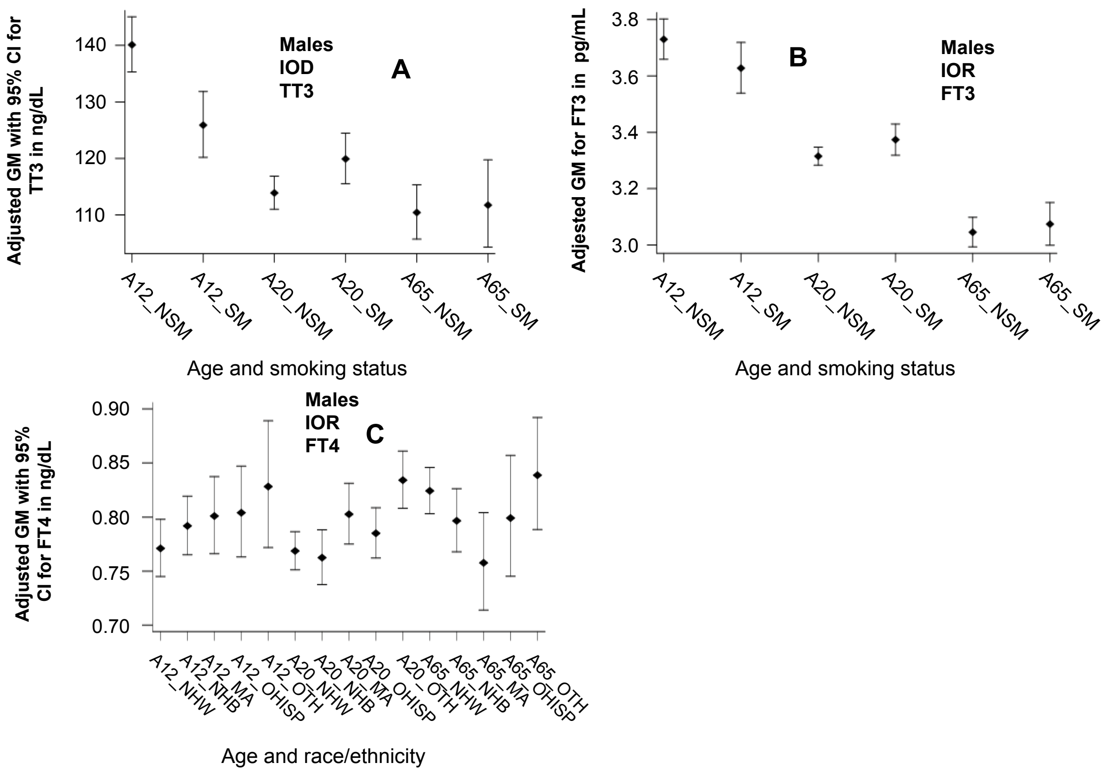

Figure 3: Adjusted geometric means with 95% Confidence Intervals (CI) for (A) for total triiodothyronine (TT3) in ng/dL for iodine deficient males by age and smoking status (A12 = Aged 12-19 years, A20 = Aged 20-64 years, A65 = Aged >= 65 years, NSM = No-smokers, SS = Smokers), (B) for Free Triiodothyronine (FT3) in pg/mL for iodine replete males by age and smoking status, and (C) for Free Thyroxine (FT4) in ng/dL for iodine replete males by age and race/ethnicity (NHW = Non-Hispanic White, NHB = Non-Hispanic Black, MA = Mexican American, OHISP = Other Hispanics, OTH = other unclassified race/ethnicities).

NSM < SM (11.01 vs. 15.01 ng/mL, p0.01, Table 3). For TSH, NHW > NHB (1.54 vs. 1.17 µIU/mL, p < 0.01) and MA > NHB (1.46 vs. 1.17 µIU/mL, p < 0.01).

For IOD females, there were statistically significant interactions between race/ethnicity and smoking for TT4 (Figure 4, Panel A) and between age and smoking for TSH (Figure 4, Panel B). For TT4, the difference for AGMs between NHB and NHW, MA, OHISP, and OTH was 0.32, -0.31, 0.30, and 0.25 µg/mL respectively among nonsmokers, and -0.42, -0.14, -0.26, and -0.71 µg/mL among smokers (Figure 4, Panel A). Thus, NHB smokers had the lowest AGM for TT4, NHW had the lowest AGM for TT4 among nonsmokers. For TSH, overall nonsmokers had higher AGM than smokers (1.52 vs. 1.30 µIU/mL), nonsmoker-smoker differences were -0.21, 0.25, and 0.26 µIU/mL for A12, A20, and A65 respectively (Figure 4, Panel B).

Use of drugs other than thyroid treatment drugs was observed to increase the levels of TT4 (β = 0.0336, p = 0.02, Table 4). A positive association between fasting time and FT3 was observed (p < 0.01, Table 4). BMI was positively associated with the levels of TSH, FT3, TT3, and TT4 (p <= 0.03). Increase in the levels of blood lead was associated with the decrease in the levels of TT3 (β = -0.0338, p = 0.01). A 10% increase in the untransformed value of blood lead was associated with a 0.3% decrease in the untransformed values of TT3. Levels of FT4 (β = 0.0146, p < 0.01) increased but that of TT4 de-

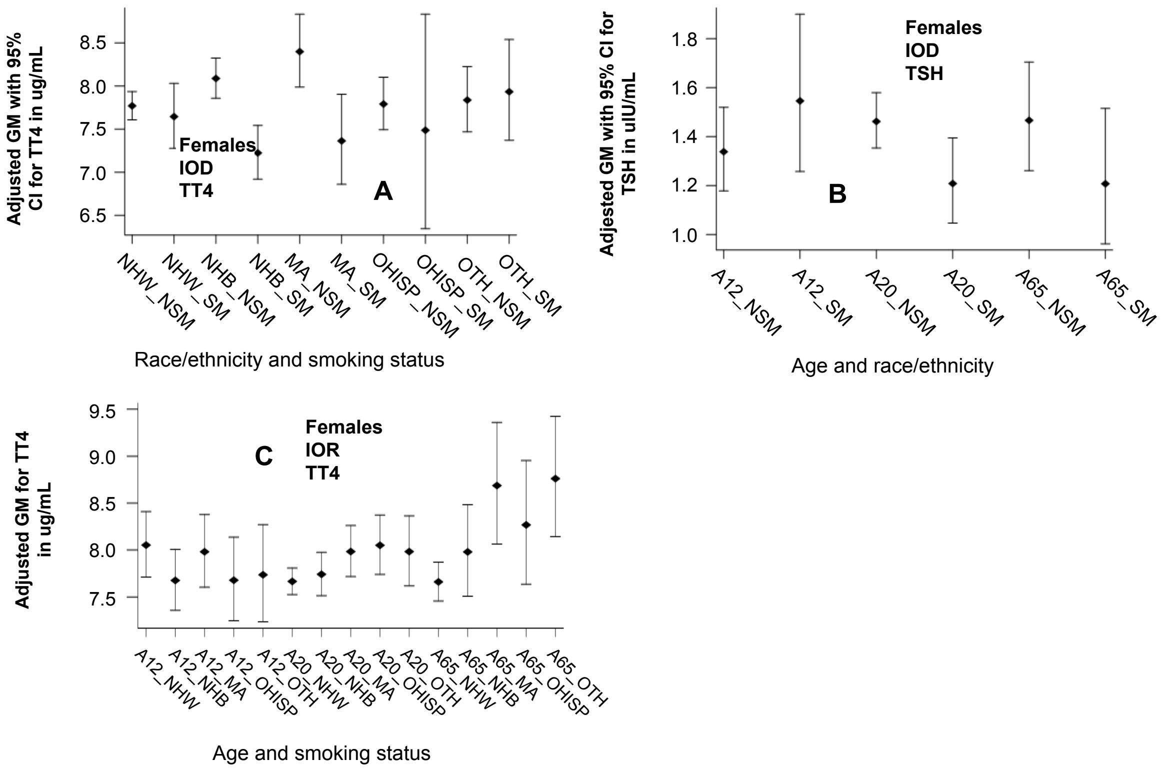

Figure 4: Adjusted geometric means with 95% Confidence Intervals (CI) for (A) for Total Thyroxine (TT4) in µg/mL for iodine deficient females by race/ethnicity and smoking status (NHW = Non-Hispanic White, NHB = Non-Hispanic Black, MA = Mexican American, OHISP = Other Hispanics, OTH = other unclassified race/ethnicities, NSM = Nonsmokers, SM = Smokers), (B) for Thyroid Stimulating Hormone (TSH) in µIU/mL for Iodine Deficient (IOD) females by age and smoking status (A12 = Aged 12-19 years, A20 = Aged 20-64 years, A65 = Aged >= 65 years), and (C) for Total Thyroxine (TT4) in µg/mL for Iodine Replete (IOR) females by age and smoking status.

creased (β = -0.0083, p = 0.04) over 2007-2012. Being in premenarche was associated with higher levels of TSH (β = 0.165, p = 0.02), FT3 (β = 0.0389, p = 0.01), and TT3 (β = 0.0763, p < 0.01) but lower levels of TT4 (β = -0.0465, p = 0.01). Menopausal status did not affect the levels of any of the six thyroid variables.

Statistics for Iodine Replete (IOR) females: For FT3 and TT3, AGMs were in the order A12 > A20 > A65 and all pairwise differences were statistically significant (p < 0.01, Table 3). For TT4, A12 < A65 (7.82 vs. 8.26 µg/mL, p = 0.02) and A20 < A65 (7.88 vs. 8.26 µg/mL, p < 0.01). AGMs for NHW > NHB for TSH (1.57 vs. 1.19 µIU/mL, p < 0.01), FT3 (3.20 vs. 3.09 pg/mL, p < 0.01), and TT3 (116.57 vs. 110.58 ng/dL, P < 0.01). For TGN, AGMs were observed in the order NHB (16.74 ng/mL) > NHW (11.9 ng/mL) > OHISP (11.88 ng/mL) > OTH (11.13 ng/mL) > MA (8.2 ng/mL) and the pairwise differences between NHW and NHB, NHW and MA, NHB and MA, NHB and OHISP, NHB and OTH, MA and OHISP, and MA and OTH were statistically significantly different (p <= 0.01, Table 3). For TSH, NSM > SM (1.48 vs. 1.29 µIU/mL, p < 0.01, Table 3) but for TGN, NSM < SM (10.01 vs. 13.59 ng/mL, p < 0.01).

For TT4, statistically significant interaction between age and race/ethnicity was observed (Figure 4, Panel C). AGMs for NHW as compared to NHB, MA, OHISP, and OTH differed by 0.38, 0.07, 0.37, and 0.32 µg/mL respectively for A12, by -0.08, -0.32, -0.38, and -0.32 µg/mL for A20, and by -0.32, -1.03, -0.61, and -1.10 µg/mL respectively for A20 (Figure 4, Panel C). Statistically significant interaction between age and smoking for FT3 (Figure 5, Panel A), between race/ethnicity and smoking for FT4 (Figure 5, Panel B), and between age and race/ethnicity for FT3 was also observed (Figure 5, Panel C) were observed. Nonsmoker-smoker differences for FT3 were 0.14, -0.05, and -0.63 pg/mL respectively for A12, A20, and A65 respectively (Figure 5, Panel A). Nonsmoker-smoker differences in AGMs for FT4 for NHW, NHB, MA, OHSP, and OTH were 0.008, 0.006, -0.071, 0.018, and 0.116 ng/dL respectively (Figure 5, Panel B). Thus, for MA, smokers had higher AGM for FT4 than nonsmokers. For FT3, the differences in AGMs for NHW as compared to NHB, MA, OHISP, and OTH were 0.23, 0.11, 0.16, and 0.16 pg/mL respectively for A12, -0.002, -0.09, -0.05, and 0.01 pg/mL respectively for A20, and 0.09, 0.01, 0.04, and 0.007 pg/mL respectively for A65 (Figure 5, Panel C). Thus, racial/ethnic differences for FT3 were largest for A12.

Use of drugs other than thyroid treatment drugs was observed to decrease the levels of FT3 (β = -0.021, p < 0.01, Table 4) and TT3 (β = -0.03184, p < 0.01, Table 4). A positive association between fasting time and FT3 and TT3 was observed (p < 0.01, Table 4). BMI was positively associated with the levels of TSH, FT3, TT3, and TT4 (p < 0.01) but negatively associated with the levels of FT4 (p = 0.04). Levels of blood lead were not found to be associated with the levels of any of the six thyroid

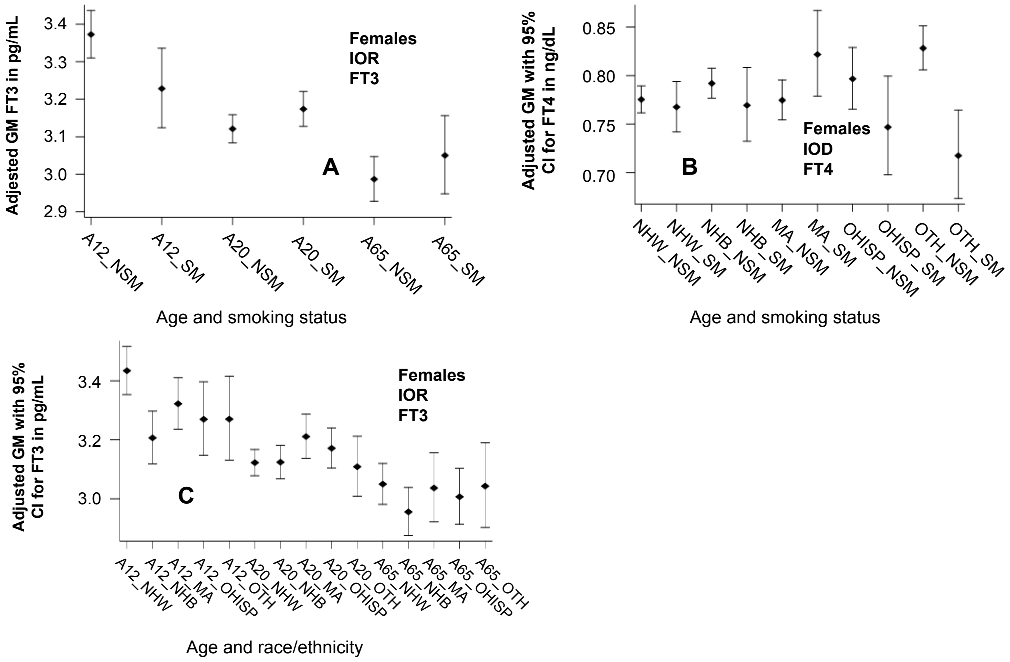

Figure 5: Adjusted geometric means with 95% Confidence Intervals (CI) for (A) for Free Triiodothyronine (FT3) in pg/mL for Iodine Replete (IOR) females by age and smoking status (A12 = Aged 12-19 years, A20 = Aged 20-64 years, A65 = Aged >= 65 years, NSM = Nonsmokers, SM = Smokers), (B) for Free Thyroxine (FT4) in ng/dL for IOR females by race/ethnicity and smoking status (NHW = Non-Hispanic White, NHB = Non-Hispanic Black, MA = Mexican American, OHISP = other Hispanics, OTH = other unclassified race/ethnicities), and (C) for Free Triiodothyronine (FT3) in pg/mL for IOR females by age and race/ethnicity for IOR females by age and race/ethnicity.

Table 5: Regression slopes with p-values by age and gender for the models fitted for log10 transformed values of Thyroid Stimulating Hormone (TSH in nIU/mL), Free Triiodothyronine (FT3 in fg/mL), Free Thyroxin (FT4 in pg/dL), Total Triiodothyronine (TT3 in pg/dL), Total Thyroxin (TT4 in ng/mL), and Thyroglobulin (TGN in fg/mL) when association with urine lead was investigated. Data from National Health and Nutrition Examination Survey 2007-2012. Statistically significant slopes are displayed in bold letters.

Gender: IOS	**Independent variable**	**TSH**	**FT3**	**FT4**	**TT3**	**TT4**	**TGN**
Male: IOD*	Log10 of Urine Lead	0.0953369519 (0.11)	0.001840619 (0.72)	**-0.023835145 (0.02)**	0.0025197556 (0.81)	-0.008671475 (0.35)	0.0153603499 (0.78)
	NHANES survey cycle	0.00778842 (0.71)	-0.004064014 (0.19)	**0.013635186 (0)**	-0.002955405 (0.56)	-0.00896487 (0.06)	0.0133139461 (0.5)
	Log10 of Urine Creatinine	-0.086948445 (0.16)	0.0160065483 (0.07)	0.0174653237 (0.14)	0.0164875274 (0.22)	0.0080016924 (0.49)	0.1291737626 (0.08)
	R^2 in percent	2.2	30.6	7.0	17.2	5.1	10.5
Male: IOR*	Log10 of Urine Lead	0.0410074728 (0.1)	-0.004712712 (0.33)	**-0.024040038 (0.01)**	0.0039154333 (0.56)	-0.015953964 (0.05)	0.0517085591 (0.16)
	NHANES survey cycle	-0.001768468 (0.87)	-0.003666564 (0.19)	0.0085708044 (0.05)	0.0002098628 (0.96)	**-0.011986282 (0)**	0.0012280675 (0.93)
	Log10 of Urine Creatinine	-0.044428942 (0.4)	0.0146126729 (0.06)	0.0183813787 (0.13)	0.0075758394 (0.46)	0.0064332484 (0.7)	-0.087538719 (0.16)
	R^2 in percent	6.1	30.8	6.1	20.5	5.7	6.0
Female: IOD*	Log10 of Urine Lead	0.0001457806 (1)	**-0.023101706 (0.01)**	0.0107963267 (0.36)	**-0.02725571 (0.02)**	-0.009828297 (0.42)	0.023556915 (0.7)
	NHANES survey cycle	0.0013230706 (0.94)	-0.002343581 (0.25)	**0.0157923713 (0)**	0.0006743429 (0.85)	-0.008096723 (0.09)	-0.004495262 (0.82)
	Log10 of Urine Creatinine	-0.012920841 (0.78)	**0.0219270083 (0.01)**	-0.006418433 (0.67)	**0.0289782561 (0.04)**	-0.000072435 (1)	-0.05737875 (0.37)
	R^2 in percent	9.5	20.0	6.0	8.6	12.4	8.8
Female: IOR*	Log10 of Urine Lead	-0.022938005 (0.59)	-0.007028532 (0.27)	0.0011231727 (0.88)	**-0.021506431 (0.04)**	-0.017114036 (0.16)	-0.038422486 (0.56)
	NHANES survey cycle	0.0042268246 (0.69)	-0.001479838 (0.58)	**0.0140811206 (0)**	0.0050989341 (0.34)	-0.006420846 (0.18)	-0.00008967 (1)
	Log10 of Urine Creatinine	-0.078257244 (0.09)	**0.0256713699 (0.01)**	0.0044048337 (0.7)	0.0267121505 (0.13)	0.0074417583 (0.67)	0.0430685262 (0.63)
	R^2 in percent	10.2	23.3	7.6	13.7	6.5	7.1

*IOD = Iodine Deficient or urine iodine < 100 ng/mL; IOR = Iodine Replete or urine iodine >= 100 ng/mL.

variables for IOR females. Levels of FT4 (β = 0.013, $p < 0.01$) increased over 2007-2012. Being in premenarche was associated with higher levels of TSH (β = 0.2021, $p < 0.01$), FT3 (β = 0.0519, $p < 0.01$), and TT3 (β = 0.0718, $p < 0.01$). Menopausal status did not affect the levels of any of the six thyroid variables. Number of live births was associated with lower levels of FT3 (β = -0.0033, $p < 0.01$, Table 4).

Urine lead

Since there was very little, if any, differences in AGMs for the six thyroid variables when blood lead as compared to urine lead as one of the independent variables, the results about variabilities in AGMs by age, gender, IOS, race/ethnicity, and smoking status, these results are not presented but are presented in Table S2.

For IOD males, there was a negative association between the levels of urine lead and FT4 (β = -0.02384, p = 0.02, Table 5). A 10% increase in the untransformed values of urine lead as associated with a 0.23% decrease in the untransformed values of FT4. For IOR males, there was a negative association between the levels of urine lead and FT4 (β = -0.02404, p = 0.01, Table 5). A 10% increase in the untransformed values of urine lead as associated with a 0.23% decrease in the untransformed values of FT4. For IOD females, there was a negative association between the levels of urine lead and FT3 (β = -0.0231, p = 0.01, Table 5) and TT3 (β = -0.0273, p = 0.01, Table 5). A 10% increase in the untransformed values of urine lead as associated with a 0.22% decrease in the untransformed values of FT3 and 0.26% decrease in the untransformed values of TT3. For IOR females, there was a negative association between the levels of urine lead and TT3 (β = -0.0215, p = 0.04, Table 5). A 10% increase in the untransformed values of urine lead as associated with a 0.21% decrease in the untransformed values of TT3. For IOD males, levels of FT4 increased over 2007-2012 (β = 0.0136, $p < 0.01$, Table 5). For IOR males, levels of TT4 decreased over 2007-2012 (β = -0.012, $p < 0.01$, Table 5). For IOD females, levels of FT3 (β = -0.0231, p = 0.01, Table 5) and TT3 (β = -0.0273, p = 0.02, Table 5) decreased over 2007-2012 (β = 0.0136, $p < 0.01$, Table 5). For IOR females, levels of TT3 decreased over 2007-2012 (β = -0.0215, p = 0.04, Table 5).

Discussion

This author has previously evaluated the association between thyroid function and organochlorine pesticides [13], polycyclic aromatic hydrocarbons [14], and arsenic [15] using the same approach, namely, fitting separate models for IOD males, IOD females, IOR males, and IOR females and has generated AGMs for all six thyroid hormones. The results generated by these publications and this communication with respect to the variability in the AGMs by age, gender, race/ethnicity, and smoking status have been similar, if not exactly the same. For example, nonsmokers almost always had higher AGMs for TSH than smokers and smokers always had higher TGN than nonsmokers. Similarly, NHB always had highest levels of TGN when compared with other race/ethnicities. However, while these three publications used MA and OHISP as one racial/ethnic group, namely, all Hispanics, this communication used MA and OHISP as separate racial/ethnic groups. IOS and smoking status were defined the same way as in this article. Consequently, rest of the discussion will exclusively focus on the associations of thyroid variables with blood and urine lead.

Mean levels of blood lead over 50 µg/dL among occupationally exposed populations as reported by Dundar, et al., Tuppurainen, et al., and Singh, et al. [7,8,10] are manifold higher than those that are observed in general populations. For NHANES 2007-2012 data analyzed for this study, for general US population, unadjusted geometric mean blood lead levels were observed to be 1.36 (1.29 - 1.43), 1.32 (1.27 - 1.37), 0.94 (0.88 - 1.01), an 0.95 (0.92 - 0.99) µg/dL for IOD males, IOR males, IOD females, and IOR females respectively. And, unadjusted geometric mean urine lead levels were observed to be 0.31 (0.29 - 0.34), 0.61 (0.57 - 0.64), 0.23 (0.21 - 0.26), and 0.51 (0.48 - 0.53) µg/L for IOD males, IOR males, IOD females, and IOR females respectively. As can be seen, lead levels in general populations are many times lower in magnitude and this may be why Yorita Christensen, et al. [4] and Chen, et al. [5] who used NHANES 2007-2008 data could not find any associations between the levels of lead and any thyroid hormone. However, using expanded NHANES data for 2007-2012 than the NHANES 2007-2008 data used by Yorita Christensen, et al. [4] and Chen, et al. [5], TSH levels were observed to increase with increase in the levels of blood lead for IOD and IOR males ($p \le 0.04$, Table 4) and for IOD females, blood lead levels had a negative association with the levels of TT3 (p = 0.01, Table 4). Even when the associations between blood levels and TSH, FT3, and TT3 were not observed to be statistically significant, irrespective of gender and IOS, there was always a positive association between TSH and blood lead and always a negative association between blood lead and FT3 and TT3. For urine lead also, there was a statistically insignificant positive association with TSH (Table 5) for IOD males, IOR males, and IOD females. In addition, there was a statistically significant association between urine lead and FT4 (p = 0.01, Table 5) for both IOD and IOR males. Thus, IOS and gender affects the association between blood as well as urine lead levels and TSH, FT3, TT3, and FT4. However, a 10% change in the levels of blood and urine lead, even when statistically significant, was accompanied by less than 1% change in the levels of TSH, FT3, TT3, or FT4. This raises two issues. First, is the larger sample size for NHANES 2007-2012 as compared to NHANES 2007-2008 solely responsible for the statistically significant association seen for this study but not for the studies by Yorita Christensen, et al. [4] and Chen, et al. [5]? This probably is true because there certainly is a better chance to observe differences to be statistically significant when sample sizes are large, if, in fact, true differences and/or correlations do exist. The second and more important issue is whether or not small changes of less than 1%, even if statistically significant, associated with a 10% change in the levels of blood and/or urine lead clinically significant? This question cannot be answered in a definitive manner and need additional real-life data among patients under treatment for thyroid conditions and need further clinical work. If these small changes upward for TSH and downwards for FT3 and/or TT3 or FT4 lead to change from being euthyroid to hypothyroid, then they are clinically significant. Otherwise, they are not.

Factors affecting thyroid function by two other toxic metals, namely, mercury and cadmium have also been studied and mechanism involved in how they affect thyroid hormones have been proposed by [16-18] and by [19,20] for cadmium) but mechanism of how lead interferes in peripheral metabolism of thyroid hormones has not been proposed as described by McGregor [21] in a review article. However, as per rodent models, lead may interfere with thyroid hormone metabolism via direct reduction in thyroid hormone production from thyroid tissues [22].

Large sample size provided by NHANES adds strength to the data analyses and results generated but cross-sectional nature of data dents the comfort levels that can be placed in these results. On the other hand, a longitudinal follow-up study of the size of NHANES may never be possible because of financial and practical reasons like possible conflicts in treatment and research goals.

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Table S1: Adjusted geometric means with 95% confidence intervals by gender, race/ethnicity, smoking status, and Iodine Sufficiency Status (IOS) for Thyroid Stimulating Hormone (TSH), Free Triiodothyronine (FT3), Free Thyroxin (FT4), Total Triiodothyronine (TT3), Total Thyroxin (TT4), and Thyroglobulin (TGN) when association with urine lead was investigated. Data from National Health and Nutrition Examination Survey 2007-2012.

Gender: IOS	Category	TSH in µIU/mL	FT3 in pg/mL	FT4 in ng/dL	TT3 in ng/dL	TT4 in µg/mL	TGN in ng/mL
Male: IOD*	12-19 years (A12)	1.34 (1.14-1.59)	3.81 (3.73-3.89)	0.819 (0.781-0.858)	132.87 (128.09-137.82)	7.43 (7.12-7.76)	10.49 (8.74-12.6)
	20-64 years (A20)	1.41 (1.33-1.51)	3.35 (3.32-3.39)	0.813 (0.797-0.829)	117.75 (115.42-120.13)	7.52 (7.36-7.68)	10.25 (9.04-11.64)
	>= 65 years (A65)	1.42 (1.09-1.84)	3.07 (2.99-3.15)	0.806 (0.759-0.857)	109.08 (103.66-114.79)	7.52 (7.16-7.9)	15.1 (11.36-20.08)
	Non-Hispanic White (NHW)	1.44 (1.27-1.63)	3.37 (3.31-3.44)	0.792 (0.77-0.814)	118.15 (114.9-121.49)	7.23 (7.05-7.42)	10.75 (9.38-12.32)
	Non-Hispanic Black (NHB)	1.36 (1.23-1.51)	3.33 (3.27-3.38)	0.773 (0.74-0.807)	114.89 (111.58-118.3)	7.2 (6.95-7.46)	13.12 (11.22-15.34)
	Mexican American (MA)	1.29 (1.1-1.52)	3.46 (3.37-3.55)	0.839 (0.795-0.885)	122.46 (117.39-127.76)	7.61 (7.32-7.92)	9.88 (8.32-11.72)
	Other Hispanics (OHISP)	1.41 (1.15-1.72)	3.44 (3.35-3.54)	0.83 (0.788-0.875)	122.51 (115.1-130.39)	7.58 (7.24-7.93)	10.53 (8.26-13.43)
	Others (OTH)	1.46 (1.17-1.83)	3.4 (3.32-3.48)	0.832 (0.793-0.872)	119.67 (115.45-124.04)	7.84 (7.55-8.15)	15.31 (10.09-23.24)
	Nonsmokers (NSM)	1.45 (1.3-1.62)	3.38 (3.34-3.42)	0.797 (0.778-0.816)	121.64 (119.32-124.01)	7.49 (7.33-7.66)	10.27 (9.09-11.6)
	Smokers (SM) SSD**	1.34 (1.17-1.52)	3.42 (3.35-3.48)	0.829 (0.795-0.864)	117.4 (113.22-121.73)	7.49 (7.24-7.75)	13.45 (11.09-16.32)
Male: IOR*	12-19 years (A12)	1.4 (1.29-1.52)	3.69 (3.61-3.78)	0.804 (0.777-0.832)	136.42 (132.01-140.98)	7.51 (7.25-7.78)	9.49 (8.23-10.95)
	20-64 years (A20)	1.31 (1.24-1.39)	3.35 (3.3-3.4)	0.805 (0.789-0.821)	117.14 (115.01-119.3)	7.6 (7.47-7.73)	9.09 (8.63-9.57)
	>= 65 years (A65)	1.48 (1.34-1.64)	3.05 (2.99-3.11)	0.816 (0.789-0.844)	105.03 (101.43-108.75)	7.88 (7.6-8.17)	9.5 (8.04-11.23)
	Non-Hispanic White (NHW)	1.64 (1.57-1.72)	3.32 (3.28-3.37)	0.8 (0.782-0.818)	117.66 (114.68-120.72)	7.33 (7.19-7.48)	9.4 (8.74-10.1)
	Non-Hispanic Black (NHB)	1.27 (1.19-1.36)	3.3 (3.25-3.35)	0.793 (0.774-0.812)	116.95 (113.15-120.88)	7.52 (7.29-7.76)	13.11 (11.71-14.69)
	Mexican American (MA)	1.32 (1.21-1.44)	3.36 (3.3-3.41)	0.801 (0.773-0.83)	118.83 (115.68-122.07)	7.82 (7.59-8.05)	7.69 (6.58-9)
	Other Hispanics (OHISP)	1.32 (1.22-1.43)	3.43 (3.35-3.52)	0.81 (0.776-0.845)	122.11 (117.98-126.4)	7.76 (7.46-8.08)	8.93 (7.74-10.31)
	Others (OTH)	1.47 (1.25-1.72)	3.36 (3.25-3.47)	0.839 (0.806-0.873)	118.71 (112.94-124.77)	7.89 (7.58-8.22)	8.48 (7.18-10.02)
	Nonsmokers (NSM)	1.49 (1.4-1.59)	3.35 (3.32-3.39)	0.804 (0.79-0.819)	117.72 (115.82-119.65)	7.62 (7.49-7.75)	8.55 (8-9.15)
	Smokers (SM) SSD**	1.31 (1.22-1.4)	3.35 (3.28-3.42)	0.812 (0.788-0.838)	119.97 (115.45-124.67)	7.71 (7.44-7.98)	10.24 (9.1-11.54)
Female: IOD*	12-19 years (A12)	1.5 (1.27-1.79)	3.45 (3.37-3.53)	0.808 (0.775-0.842)	123.04 (117.75-128.58)	7.71 (7.37-8.06)	10.62 (8.77-12.86)
	20-64 years (A20)	1.29 (1.17-1.42)	3.13 (3.08-3.19)	0.794 (0.777-0.812)	113.66 (110.76-116.63)	7.78 (7.63-7.94)	12.89 (11.67-14.23)
	>= 65 years (A65)	1.38 (1.17-1.62)	3.04 (2.92-3.17)	0.815 (0.772-0.86)	110.86 (104.56-117.54)	7.78 (7.33-8.26)	15.58 (11.4-21.29)
	Non-Hispanic White (NHW)	1.57 (1.42-1.74)	3.2 (3.15-3.25)	0.791 (0.773-0.809)	115.57 (112.67-118.54)	7.6 (7.35-7.85)	12.79 (11.31-14.46)
	Non-Hispanic Black (NHB)	1.22 (1.07-1.39)	3.15 (3.09-3.21)	0.797 (0.775-0.82)	113.78 (109.5-118.23)	7.68 (7.37-8.02)	17.91 (15.59-20.59)
	Mexican American (MA)	1.52 (1.32-1.75)	3.26 (3.16-3.37)	0.798 (0.758-0.839)	118.49 (113.64-123.55)	7.91 (7.55-8.29)	10.55 (8.24-13.52)
	Other Hispanics (OHISP)	1.34 (1.13-1.58)	3.21 (3.1-3.33)	0.806 (0.773-0.84)	117.95 (111.33-124.96)	7.65 (7.18-8.16)	10.86 (8.58-13.75)
	Others (OTH)	1.32 (1.07-1.63)	3.19 (3.06-3.33)	0.837 (0.785-0.892)	113 (107.79-118.46)	7.94 (7.53-8.38)	13.46 (10.35-17.5)
	Nonsmokers (NSM)	1.38 (1.27-1.5)	3.2 (3.14-3.26)	0.808 (0.789-0.828)	117.25 (114.27-120.31)	7.94 (7.74-8.14)	11 (9.8-12.35)
	Smokers (SM) SSD**	1.39 (1.21-1.59)	3.2 (3.12-3.29)	0.803 (0.772-0.834)	114.24 (109.61-119.07)	7.58 (7.24-7.94)	15.06 (12.15-18.67)

Female: IOR*	12-19 years (A12)	1.34 (1.15-1.56)	3.28 (3.21-3.37)	0.814 (0.782-0.848)	126.37 (120.44-132.59)	7.65 (7.37-7.94)	11.38 (9.63-13.44)
	20-64 years (A20)	1.3 (1.21-1.39)	3.13 (3.09-3.17)	0.781 (0.767-0.795)	111.69 (109.1-114.33)	7.88 (7.69-8.07)	11.98 (10.97-13.09)
	>= 65 years (A65)	1.5 (1.31-1.72)	2.99 (2.91-3.07)	0.78 (0.745-0.817)	104.08 (100.68-107.6)	8.2 (7.82-8.6)	12.6 (10.89-14.56)
	Non-Hispanic White (NHW)	1.57 (1.46-1.68)	3.17 (3.14-3.21)	0.778 (0.76-0.796)	116.89 (114.68-119.14)	7.76 (7.6-7.93)	11.68 (10.72-12.73)
	Non-Hispanic Black (NHB)	1.19 (1.09-1.3)	3.07 (3.02-3.13)	0.796 (0.772-0.822)	111.62 (107.02-116.42)	7.78 (7.5-8.07)	17.43 (15.37-19.77)
	Mexican American (MA)	1.38 (1.24-1.55)	3.17 (3.1-3.24)	0.813 (0.788-0.838)	113.36 (108.92-117.97)	8.1 (7.77-8.44)	8.79 (7.29-10.6)
	Other Hispanics (OHISP)	1.39 (1.25-1.55)	3.12 (3.05-3.18)	0.79 (0.751-0.83)	115.08 (111.4-118.88)	7.88 (7.55-8.22)	12.23 (10.18-14.69)
	Others (OTH)	1.39 (1.21-1.59)	3.13 (3.04-3.22)	0.783 (0.75-0.817)	111.54 (104.73-118.78)	8.02 (7.67-8.38)	11.24 (9.32-13.56)
	Nonsmokers (NSM)	1.45 (1.36-1.54)	3.15 (3.12-3.18)	0.8 (0.789-0.811)	114.02 (111.76-116.32)	7.97 (7.84-8.11)	10.13 (9.4-10.92)
	Smokers (SM) SSD**	1.31 (1.18-1.46)	3.11 (3.05-3.17)	0.784 (0.75-0.819)	113.34 (109.58-117.23)	7.84 (7.6-8.09)	14.15 (12.25-16.35)

*IOD = Iodine Deficient or urine iodine < 100 ng/mL; IOR = Iodine Replete or urine iodine >= 100 ng/mL; **SSD = Statistically Significant Differences.

Table S2: Regression slopes with p-values by age and gender for the models fitted for log10 transformed values of Thyroid Stimulating Hormone (TSH in nIU/mL), Free Triiodothyronine (FT3 in fg/mL), Free Thyroxin (FT4 in pg/dL), Total Triiodothyronine (TT3 in pg/dL), Total Thyroxin (TT4 in ng/mL), and Thyroglobulin (TGN in fg/mL) when association with urine lead was investigated. Data from National Health and Nutrition Examination Survey 2007-2012.

Gender: IOS	Independent variable	TSH	FT3	FT4	TT3	TT4	TGN
Male: IOD*	Use other drugs	-0.041729571 (0.23)	-0.004998617 (0.28)	0.0058692827 (0.57)	-0.008826299 (0.35)	0.0127114681 (0.25)	-0.012511563 (0.78)
	Fasting in hours	0.001053229 (0.59)	0.0013697767 (0)	0.0005277099 (0.22)	0.0014467365 (0.07)	0.0004071162 (0.54)	0.0004843149 (0.9)
	Poverty income ratio	0.0029208698 (0.68)	-0.002606113 (0.05)	-0.000306579 (0.88)	-0.003209813 (0.18)	-0.00151061 (0.36)	-0.003193748 (0.79)
	Log10 of Body Mass Index	0.1291103684 (0.4)	0.0149201116 (0.53)	0.0307936898 (0.45)	0.0792441774 (0.13)	0.092007564 (0.07)	0.0031531602 (0.99)
	Log10 of Serum Albumin	0.4129115234 (0.32)	0.1883106832 (0.01)	-0.109531337 (0.28)	0.3333803522 (0.01)	-0.08160535 (0.39)	-0.794363062 (0.14)
	Lg10 of Urine Lead	0.0953369519 (0.11)	0.001840619 (0.72)	-0.023835145 (0.02)	0.0025197556 (0.81)	-0.008671475 (0.35)	0.0153603499 (0.78)
	NHANES survey cycle	0.00778842 (0.71)	-0.004064014 (0.19)	0.013635186 (0)	-0.002955405 (0.56)	-0.00896487 (0.06)	0.0133139461 (0.5)
	Log10 of Urine Creatinine	-0.086948445 (0.16)	0.0160065483 (0.07)	0.0174653237 (0.14)	0.0164875274 (0.22)	0.0080016924 (0.49)	0.1291737626 (0.08)
	R^2 in percent	2.2	30.6	7.0	17.2	5.1	10.5
Male: IOR*	Use other drugs	0.0158209176 (0.58)	-0.015118854 (0)	0.005516323 (0.43)	-0.021867024 (0)	0.0091927245 (0.35)	-0.060404399 (0.08)
	Fasting in hours	0.0002345584 (0.87)	0.0009736951 (0)	0.0005191691 (0.2)	0.0013028445 (0.01)	0.0008275148 (0.01)	-0.002903823 (0.2)
	Poverty income ratio	-0.004671608 (0.39)	-0.003101883 (0.01)	-0.000113954 (0.94)	-0.005812839 (0)	-0.00054396 (0.74)	-0.001325143 (0.86)
	Log10 of Body Mass Index	0.2604719205 (0.03)	0.0457424671 (0.01)	-0.093562406 (0)	0.1095715878 (0)	0.0889042563 (0)	0.3685867642 (0)
	Log10 of Serum Albumin	0.4786779581 (0.06)	0.2440321318 (0)	-0.128463955 (0.07)	0.3102244212 (0.01)	-0.043956356 (0.65)	-0.67335109 (0.12)
	Lg10 of Urine Lead	0.0410074728 (0.1)	-0.004712712 (0.33)	-0.024040038 (0.01)	0.0039154333 (0.56)	-0.015953964 (0.05)	0.0517085591 (0.16)
	NHANES survey cycle	-0.001768468 (0.87)	-0.003666564 (0.19)	0.0085708044 (0.05)	0.0002098628 (0.96)	-0.011986282 (0)	0.0012280675 (0.93)
	Log10 of Urine Creatinine	-0.044428942 (0.4)	0.0146126729 (0.06)	0.0183813787 (0.13)	0.0075758394 (0.46)	0.0064332484 (0.7)	-0.087538719 (0.16)
	R^2 in percent	6.1	30.8	6.1	20.5	5.7	6.0
Female: IOD*	Use other drugs	-0.030970781 (0.3)	-0.005814891 (0.36)	0.0092684511 (0.32)	-0.009887018 (0.46)	0.0177998781 (0.1)	0.0441167345 (0.4)

	Fasting in hours	0.0093415716 (0.01)	0.000975207 (0.01)	0.0002025127 (0.72)	0.0001525891 (0.83)	0.0003948886 (0.54)	-0.000721781 (0.76)
	Poverty income ratio	-0.002437874 (0.75)	-0.002929346 (0.09)	-0.001634487 (0.43)	-0.004732598 (0.03)	-0.004180829 (0.03)	-0.011892319 (0.17)
	Log10 of Body Mass Index	0.1432673728 (0.28)	0.0745862222 (0)	-0.006438141 (0.86)	0.1046194589 (0.03)	0.1279341042 (0)	-0.103299472 (0.58)
	Log10 of Serum Albumin	-0.275062447 (0.35)	0.2467554083 (0)	0.0397201057 (0.68)	-0.018621729 (0.88)	-0.273818575 (0.01)	-0.242771295 (0.65)
	Lg10 of Urine Lead	0.0001457806 (1)	-0.023101706 (0.01)	0.0107963267 (0.36)	-0.02725571 (0.02)	-0.009828297 (0.42)	0.023556915 (0.7)
	NHANES survey cycle	0.0013230706 (0.94)	-0.002343581 (0.25)	0.0157923713 (0)	0.0006743429 (0.85)	-0.008096723 (0.09)	-0.004495262 (0.82)
	Premenarche	0.1949854466 (0.01)	0.0396472053 (0.01)	-0.017500274 (0.32)	0.1023391137 (0)	-0.03661465 (0.03)	0.1073157638 (0.35)
	Menopause	0.0589830325 (0.16)	-0.004784154 (0.43)	0.0084306603 (0.41)	0.0022860747 (0.86)	0.0021618108 (0.85)	0.0886920045 (0.09)
	No of live births	-0.008815085 (0.29)	0.0000857385 (0.95)	-0.001533925 (0.38)	0.0002667178 (0.92)	0.0017312153 (0.42)	-0.012177621 (0.33)
	Log10 of Urine Creatinine	-0.012920841 (0.78)	0.0219270083 (0.01)	-0.006418433 (0.67)	0.0289782561 (0.04)	-0.000072435 (1)	-0.05737875 (0.37)
	R^2 in percent	9.5	20.0	6.0	8.6	12.4	8.8
Female: IOR*	Use other drugs	-0.000835102 (0.97)	-0.018293566 (0)	0.0001061241 (0.99)	-0.035970654 (0)	-0.003528111 (0.67)	0.0247968783 (0.5)
	Fasting in hours	0.0049804044 (0.01)	0.0012219425 (0)	0.000563582 (0.26)	0.00132801 (0.02)	0.0002487644 (0.67)	0.0019567428 (0.46)
	Poverty income ratio	0.0013969862 (0.8)	-0.003622742 (0)	0.0012522923 (0.44)	-0.006915019 (0.01)	-0.000863236 (0.61)	-0.002982205 (0.75)
	Log10 of Body Mass Index	0.3711518293 (0)	0.0591197244 (0)	-0.045367546 (0.02)	0.0777061983 (0)	0.0530403314 (0.02)	0.1063789949 (0.44)
	Log10 of Serum Albumin	0.1484132393 (0.66)	0.2109729765 (0)	-0.092892315 (0.21)	0.020716145 (0.87)	-0.370987992 (0)	-0.229754537 (0.55)
	Lg10 of Urine Lead	-0.022938005 (0.59)	-0.007028532 (0.27)	0.0011231727 (0.88)	-0.021506431 (0.04)	-0.017114036 (0.16)	-0.038422486 (0.56)
	NHANES survey cycle	0.0042268246 (0.69)	-0.001479838 (0.58)	0.0140811206 (0)	0.0050989341 (0.34)	-0.006420846 (0.18)	-0.00008967 (1)
	Premenarche	0.2041473346 (0.02)	0.0460675003 (0)	-0.012450181 (0.52)	0.0492137682 (0.01)	-0.03785661 (0.08)	0.0268229674 (0.87)
	Menopause	0.0466849563 (0.12)	0.0011550495 (0.81)	0.0072606064 (0.29)	0.0058881765 (0.52)	0.0034871102 (0.68)	0.0381946363 (0.4)
	No of live births	-0.003275855 (0.53)	-0.002910525 (0.01)	-0.000984332 (0.42)	-0.002921732 (0.06)	-0.000265694 (0.88)	0.0133847812 (0.2)
	Log10 of Urine Creatinine	-0.078257244 (0.09)	0.0256713699 (0.01)	0.0044048337 (0.7)	0.0267121505 (0.13)	0.0074417583 (0.67)	0.0430685262 (0.63)
	R^2 in percent	10.2	23.3	7.6	13.7	6.5	7.1

*IOD = Iodine Deficient or urine iodine < 100 ng/mL; IOR = Iodine Replete or urine iodine >= 100 ng/mL.