



Predictors of serum 2378-TCDD and 23478-PeCDF concentration in a background population in Michigan, USA and in a representative USA sample

Brenda Gillespie¹, Chiung-Wen Chang¹, Elizabeth Hedgeman¹, Heidi Reichert¹, Billing Hong¹, Qixuan Chen¹, Olivier Jolliet¹, Kristine Knutson¹, Shih-Yuan Lee¹, James Lepkowski¹, Kristen Olson¹, Peter Adriaens¹, Avery Demond¹, Timothy Towey¹, Lynn Zwica¹, Kathy LaDronka¹, Barbara Ward¹, William Luksemburg², Martha Maier², Alfred Franzblau¹, David Garabrant¹

¹University of Michigan, Ann Arbor, Michigan, USA; ²Vista Analytical Laboratory, El Dorado Hills, California, USA

Introduction and Objectives

Serum dioxin concentrations were measured in two U.S. samples thought only to be exposed to background dioxin levels. Both samples were population-based: one of a 2-county area of Michigan, U.S. (the University of Michigan Dioxin Exposure Study, UMDES), and the other of the entire U.S. (the National Health and Nutrition Examination Survey, NHANES).

Here we examined predictors of serum 2378-TCDD and 23478-PeCDF within both populations using regression models, accounting for the complex sample designs and values below the limit of detection (LOD). In addition to age and gender, the effects of body mass index (BMI), weight loss or gain, smoking, breastfeeding, race and dietary intake were also investigated.

Methods

UMDES Sample

- Data collected in Jackson and Calhoun Counties of Michigan, USA, using a two-stage probability household sampling design.
- Eligible subjects were at least 18 years of age, lived in their current residence for at least 5 years, and provided written informed consent.
- An exposure questionnaire collected demographics, smoking and pregnancy history, occupational exposure, and food consumption.
- Serum samples were collected from subjects medically eligible to give blood as defined by the American Red Cross.
- Chemical analyses, reporting lipid-adjusted concentrations, were performed by Vista Analytical Laboratory, Inc. (El Dorado Hills, California, USA).

NHANES Sample

- The NHANES database of national health and vitality information for a sample of the U.S. population is publicly available through the U.S. National Center for Health Statistics. The NHANES data were taken from the 2001-2002 sample release.
- Serum samples were collected from medically eligible persons; a sub-sample aged ≥ 20 was selected for analysis of serum dioxins and furans.
- Chemical analyses, reporting lipid-adjusted concentrations, were performed by the Centers for Disease Control and Prevention laboratories.

Statistical Methods

- For both samples, interval-censored regression methods were used to handle left censoring in cases where dioxin levels fell below the LOD. In addition, the analyses incorporated the complex sample design weights within the model specification.
- Covariates considered included age, gender, race, BMI, BMI gain or loss in the previous year, smoking (pack-years), duration of breastfeeding, and selected interactions. In addition, food indicators and quantities were explored for beef, pork, poultry, game, fish, and dairy. Past 5-year meals per year were available in UMDES, and past 24-hour servings (gm) were available in NHANES.
- Backward elimination was used to arrive at the final models. All analyses were performed using STATA 9.2; regression analyses used the intreg procedure.

Results

Subjects from UMDES (n=251) were slightly older than those from NHANES (n=1228) (mean (s.d.) age: UMDES 52.3 (15.2), NHANES 49.1 (18.7) years). UMDES was 96% Caucasian while NHANES was 44% Caucasian, 29% Hispanic, 23% African American and 4% Other/Multi-racial. Other characteristics were similar between UMDES and NHANES.

2378-TCDD

Figure 1 shows TCDD values with model estimates (lines) by age and gender for (a) UMDES and (b) NHANES. UMDES had larger serum volumes, and thus smaller LOD values (below LOD: UMDES 21%, NHANES 87%).

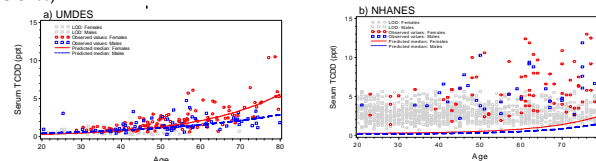


Figure 1. Plots of TCDD data and model predicted medians by age and gender for both (a) UMDES and (b) NHANES. For values below the LOD, the LOD itself is plotted (grey circles/squares). One value of 42.7 ppt for a 65-year-old male (BMI=39.9, BMI loss in past year=-1.1) was omitted from the NHANES plot to show more detail for the other values.

- UMDES: higher TCDD was associated with increasing age, female gender (at older ages), BMI, and BMI loss (especially at older ages), whereas breastfeeding and smoking were associated with lower TCDD.
- NHANES: higher TCDD was associated with increasing age, female gender, BMI loss (especially among males), African American and Other/Multi-racial versus Caucasian & Hispanic, whereas smoking was associated with lower TCDD at older ages.

Table 1. Regression results predicting serum TCDD concentration

	UMDES	NHANES
Age	.0117 (.0023)	-.0026 (.0104)
Age ²	-----	.0002 (.0001)
Sex (female)	-.3091 (.1732)	.2533 (.0791)
BMI	.0071 (.0034)	-----
BMI loss (past yr)	-.0575 (.0302)	.0314 (.0134)
Breastfeeding (month)	-.0133 (.0043)	-----
Pack Years	-.0029 (.0011)	.0178 (.0045)
Race (African American) †	-----	-.2584 (.0857)
Race (Other or Multi-racial) †	-----	.2947 (.1209)
Age*Sex	.0077 (.0030)	-----
Sex*BMI loss	-----	-.0562 (.0209)
Age*BMI loss	.0017 (.0006)	-----
Age*Pack Years	-----	-.0003 (.0001)

†Reference group for race is Caucasian & Hispanic combined

23478-PeCDF

Figure 2 shows PeCDF values with model estimates (lines) by age and gender for (a) UMDES and (b) NHANES. Similar overall effects can be seen. The UMDES had larger serum volumes, resulting in smaller LOD values (below LOD: UMDES 1%, NHANES 35%).

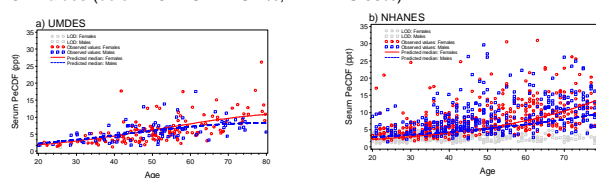


Figure 2. Plots of PeCDF data and model predicted medians by age and gender for (a) UMDES and (b) NHANES. For values below the LOD, the LOD itself is plotted (grey circles/squares).

Results, cont.

- UMDES: Higher PeCDF was associated with older age, female gender (at older ages), and BMI loss. Lower PeCDF was associated with BMI gain, breastfeeding and smoking (until older ages).
- NHANES: Higher PeCDF was associated with older age and female gender (at older ages). Lower PeCDF was associated with BMI gain.
- Dietary intake was not significantly related to PeCDF in either model.

Table 2. Regression results predicting serum PeCDF concentration

	UMDES	NHANES
	Estimate (s.e.)	Estimate (s.e.)
Age	.0255 (.0037)	.0089 (.0014)
Age ²	-.0002 (<.0001)	-----
Sex (female)	-.1528 (.1148)	-.2098 (.1096)
BMI	.0103 (.0038)	-----
BMI loss (past yr)	.0150 (.0039)	-----
BMI gain (past yr)	-.0218 (.0063)	-.0190 (.0062)
Breastfeeding (month)	-.0096 (.0023)	-----
Pack-years	-.0097 (.0035)	-----
Race (Hispanic) †	-----	-.1734 (.0844)
Race (African American) †	-----	-.1490 (.0627)
Age*Sex	.0033 (.0013)	.0047 (.0021)
Age*Pack-years	.0001 (<.0001)	-----
BMI*Sex	-.0107 (.0046)	-----
Age*Race (Hispanic) †	-----	.0014 (.0017)
Age*Race (African American) †	-----	.0031 (.0011)

† Reference group for race is Caucasian

Conclusions

Serum dioxin concentrations in exposed populations are often compared to background populations. Modeling dioxin as a function of demographic and lifestyle variables in a background population can allow background prediction in new populations.

2378-TCDD

These results showed generally low levels of serum TCDD in background U.S. populations, but higher concentrations with older age particularly among women. Breastfeeding was associated with lower TCDD levels in UMDES. Both samples showed higher TCDD with BMI loss, particularly at older ages in UMDES, suggesting that TCDD is concentrated as body fat is lost. Smoking was associated with lower TCDD in both samples. Race effects could only be investigated in NHANES data: African American and Other/Multi-racial had higher TCDD levels than Caucasians or Hispanics. There was no evidence that specific foods consumed had an impact on serum TCDD levels.

23478-PeCDF

These results showed generally low levels of serum PeCDF in background U.S. populations, but higher concentrations with older age. For age > 60, females had higher levels than males in both UMDES and NHANES. Both samples showed lower PeCDF with BMI gain, suggesting a dilution effect. UMDES showed higher PeCDF with BMI loss. Breastfeeding was associated with lower PeCDF in UMDES. Smoking showed an interesting interaction with age: smoking was linked with lower PeCDF in middle age, but higher PeCDF at ages > 65, possibly due to liver damage from long-term tobacco use. Race effects could only be investigated in NHANES data: Hispanics showed the lowest levels of PeCDF.

Financial support for this study comes from the Dow Chemical Company through an unrestricted grant to the University of Michigan.