FACTORS THAT PREDICT SERUM DIOXIN CONCENTRATIONS IN MICHIGAN, USA

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Abstract

Linear regression models were performed to identify factors that explain variation in serum TEQ and 2,3,7,8-TCDD concentrations measured from the 946 participants in the University of Michigan Dioxin Exposure Study (UMDES). The regression analyses accounted for sampling weights, stratification, and clustering to insure the inferences from the regression models were applicable to the population from which participants were selected. We found that demographic factors were by far the most important contributors to the population variation in both serum TEQ and TCDD. Residing in Midland/Saginaw and living with contaminated soil and household dust contributed little to the variation in serum TEQ, but explained small percentages of the serum TCDD. Food consumption was a small contribution to the variation in serum TEQ, but was slightly larger for TCDD.

Introduction

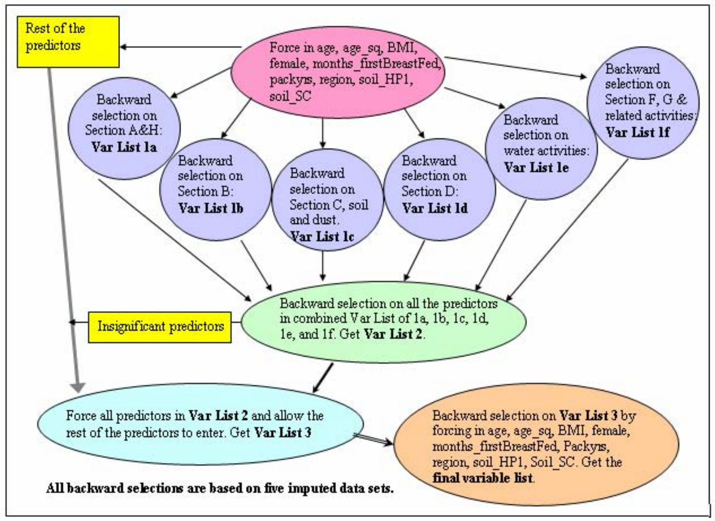
The University of Michigan Dioxin Exposure Study (UMDES) was undertaken in response to concerns among the population of Midland and Saginaw Counties (Michigan, USA) that the discharge of dioxin-like compounds from the Dow Chemical Company facilities in Midland, Michigan (USA) has resulted in contamination of soils in the Tittabawassee River flood plain and areas of the City of Midland, leading to an increase in residents' body burdens of PCDDs, PCDFs and PCBs[1]. To understand the factors that predict residents' body burdens, 946 people, sampled from five geographically-defined populations by using a two-stage area probability household sample design, participated in an interview and gave blood samples for analysis of the WHO 29 dioxin-like compounds[3]. Soil and household dust samples were analyzed for the same set of congeners. The objective of this presentation is to discuss the factors that explain variation in the blood serum dioxin concentrations in this population.

Materials and Methods

The entire protocol for the University of Michigan Dioxin Exposure Study can be found on our study website.[2] Briefly, adults age 18 and over who had lived in their current residence for five or more years were eligible to participate. Eligible subjects were randomly selected from the populations of five counties in Michigan, USA and invited to complete an interview, donate an 80 milliliter whole blood sample, have their household dust collected, and have their soil sampled. Three counties (Midland, Saginaw, and part of Bay Counties, MI) were chosen because of their proximity to the Dow Chemical Company and two counties (Jackson and Calhoun Counties, MI) were chosen as a reference population. Serum, household dust, and soil were analyzed for the 29 congeners recognized by the World Health Organization as having dioxin-like activity, including TCDD. Samples that fell below the limit of detection were estimated using LOD/$\sqrt{2}$. All serum results are lipid adjusted and survey weighted to reflect the entire referent population region. Multiple imputation procedures were used (five imputations) to impute missing values in explanatory variables.

A multi-stage backwards selection was applied to identify factors that predict the serum dioxin levels (Figure 1). In each step of backwards selection:
(1) The point estimates from the 5 imputed datasets were averaged to get a combined estimate.
(2) The combined p-values were calculated across the 5 imputed dataset in a manner that accounted for variation between datasets and variation within datasets.
(3) The backwards selection then eliminated from the pool of covariates the least significant variable (the variable having the largest combined p-value). This procedure was repeated until all variables with p-values greater than the significance level were eliminated from the model. For the initial backwards selection step, variables were kept in the model if the p-value was ≤ 0.1. For all subsequent steps, variables were kept in the model if the p-value was ≤ 0.05. Results (Table 2) are presented for TEQ (based on WHO 2005 TEFs) and for 2,3,7,8-TCDD. All regression analyses were performed using SAS version 9.1.

Figure1. Linear regression modeling strategy



Results

- The overall model explained 73% of the variance in the serum TEQ and 67% of the variance in TCDD. Demographic factors (age, age^2, BMI, BMI loss in the past 12 months, gender, months a woman breast fed, pack-years of smoking, and the interaction term for gender*age) were the most important predictors of both TEQ and TCDD (explaining 40% and 30% of the variance in the serum TEQ and TCDD, respectively) (see Table 1). The region variable, representing the population from which each participant was selected (floodplain, near flood plain, out of flood plain, or Midland plume), was forced into the model as a 0,1 variable to examine whether there was a difference in the mean serum TEQ in comparison to the Jackson/Calhoun (J/C) population, after adjustment for all other factors. The results showed no significant differences. However, living in any area of Midland and Saginaw counties in 1960-1979 was associated with increased serum TEQ (the parameter estimate of 0.0029 indicates that the $\log_{10}$ serum TEQ increased by 0.0029 pg/g for each year of residence). Similar results were seen for TCDD.

Table 1: Adjusted R^2

Contribution to Adjusted R^2 (%)	TEQ-2005	2,3,7,8-TCDD
Overall model	72.56	67.17
Demographic factors	40.32	29.55
Residence factors	0.22	2.85
Soil and household dust	0.15	0.53
Property use factors	2.21	1.25
Food consumption, fishing, and hunting	1.83	2.64

- A principal goal of this study was to determine whether soil or household dust contamination was associated with increased serum TEQ. The top 1” house perimeter soil showed no significant relationship to the serum TEQ or TCDD. The garden soil TCDD was significantly related to serum TCDD. The highest TEQ level found in any soil sample on each property (referred to as the maximum soil concentration) was significantly associated with the increased serum TEQ but the magnitude of this association was small (parameter estimate of 0.0000099).

- Water activities on the Tittabawassee River were positively associated with serum TEQ and TCDD. Consumption of fish from the contaminated area (Tittabawassee River, Saginaw River, Saginaw Bay) showed little relationship to the serum TEQ but showed a clear association with serum TCDD. Fishing in 1980-2005 around the Saginaw River and Bay was positively associated with serum TEQ and TCDD.

Table 2: Results of important predictors from the linear regression model with the outcome variable of $\log_{10}$ Serum dioxin concentration. Blue-shaded values indicate significant positive estimates and yellow shaded values indicate significant negative estimates ($p \leq 0.05$).

	TEQ-2005		**2,3,7,8-TCDD**	
Important Predictors	**Estimate**	**P-value**	**Estimate**	**P-value**
Demographics				
Age at interview	0.0203	0.000	0.0135	0.001
Age^2	-0.0001	0.000	0.0000	0.316
BMI (Unit: kg/m^2)	0.0073	0.003	0.0051	0.015
BMI loss in the past 12 months	0.0106	0.000	0.0182	0.003
Gender (1 for female; 0 for male)	0.1033	0.229	-0.3760	0.000
Num. of months the first child was breast-fed	-0.0051	0.001	-0.0104	0.002
Num. of months for all children except first one were breast-fed	-0.0018	0.009		
Pack-years of smoking	-0.0021	0.000	-0.0038	0.000
At least High school graduate (Y vs. N)			-0.1142	0.001
The participant is white in addition to being Hispanic (Y vs. N)			-0.1113	0.010
Interaction term: Gender x Age	0.0033	0.000	0.0097	0.000
Interaction term: BMI x Gender	-0.0083	0.004		
Residence				
M/S Floodplain vs. Jackson/Calhoun	-0.0337	0.223	-0.0235	0.634
M/S Near Floodplain vs. Jackson/Calhoun	-0.0051	0.851	0.0851	0.087
M/S Out Floodplain vs. Jackson/Calhoun	-0.0251	0.244	-0.0059	0.884
M/S Plume vs. Jackson/Calhoun	-0.0374	0.183	-0.0012	0.988
Num. of yrs lived in Midland/Saginaw in 1940-59			0.0059	0.012
Num. of yrs lived in Midland/Saginaw in 1960-79	0.0029	0.036	0.0084	0.005
Soil and household dust				
Soil dioxin concentrations for house perimeter 0-1"	-1.7E-04	0.190	-9.8E-04	0.653
Soil dioxin concentrations for soil contact 0-6"	5.3E-04	0.163	7.1E-03	0.001
Maximum soil concentration	9.9E-06	0.009		
Household dust dioxin loading pg/m^2	-2.3E-05	0.041		
Property Use				
Num. of yrs in 40-59 lived in a farm or property where crops, livestock or poultry were raised	0.0064	0.001		
Num. of yrs in 40-59 lived in a property ever damaged by a fire	-0.0788	0.041	-0.1321	0.024
Num. of yrs in 60-79 lived in a property ever damaged by a fire	0.0306	0.000	0.0289	0.001
Num. of yrs in 40-59 lived in a property where trash or yard waste was burned			0.0073	0.007
Num. of yrs in 60-79 used weed killers on the property	-0.0054	0.001		
Personally did work in the flower or other garden (Y vs. N)	-0.0293	0.036		
Flood waters from the Tittabawassee R. entered into the home (Y vs. N)			0.1131	0.018
Water Activities				
Did water activities near the Tittabawassee R. in 60-79 (⩾1 per month vs. never)	0.2516	0.012	0.2992	0.045
Did water activities near the Tittabawassee R. after 80 (⩾1 per month vs. never)			0.2404	0.024
Did water activities near the Tittabawassee R. after 80 (<1 per month but ever did vs. never)			0.1169	0.001
Did water activities near the Saginaw R. or Bay after 80 (⩾1 per month vs. never)			-0.3186	0.000
Food consumption, Fishing and Hunting Activities				
Num. of yrs ate fish after 80			0.0056	0.000
Num. of yrs ate fish caught from the Tittabawassee R., Saginaw R. or Bay after 80			0.0083	0.001
Ate walleye or perch that were caught from the Saginaw R. or Bay during the last 5 years (⩾1 per month vs. never)			-0.2583	0.001
Ate walleye or perch that were caught from the Saginaw R. or Bay during the last 5 years (<1 per month but ever ate vs. never)			-0.1583	0.019

Important Predictors	TEQ-2005		2,3,7,8-TCDD	
	Estimate	P-value	Estimate	P-value
Ate walleye or perch that were caught from the Kalamazoo R., somewhere else, store-bought or bought in a restaurant during the last 5 yrs (⩾1 per month vs. never)	0.0622	0.001		
Ate walleye or perch that were caught from the Kalamazoo R., somewhere else, store-bought or bought in a restaurant during the last 5 yrs (<1 per month but ever ate vs. never)	0.0528	0.023		
Ate any fish other than walleye and perch that were caught from the Saginaw R. or Bay during the last 5 years (⩾1 per month vs. never)	-0.2873	0.000		
Ate the skin of the Wild Turkey, Pheasant, Grouse, Quail, or Woodcock during the last 5 yrs (Y vs. N)	0.0608	0.032		
Did fishing activities in the Saginaw R. or Bay after 80 (⩾1 per month vs. never)	0.0959	0.001	0.1845	0.002
Did hunting activities near the Saginaw R. or Bay in 60-79 (Y vs. N)	0.1200	0.012		
Did hunting activities in the surrounding areas of the Saginaw R. or Bay after 80 (⩾1 per month vs. never)	-0.2244	0.001	-0.2604	0.109
Did hunting activities in the surrounding areas of the Saginaw R. or Bay after 80 (< 1 per month but ever did vs. never)	-0.0894	0.043	-0.1549	0.042
Ate eggs, milk or other dairy products from cows that were home-raised in the Tittabawassee R. during the last 5 yrs (⩾1 per month vs. never)			0.2109	0.016

Discussion

This study was large and was capable of finding small associations that are statistically significant. Inferences regarding these associations should include consideration not only of the statistical significance of the parameter estimate, but also the magnitude of the effect, and the amount of variance in serum TEQ explained by the factor. A number of the significant findings above are both small in magnitude and explain little variation in serum TEQ. We found that demographic factors were by far the most important contributors to the population variation in both serum TEQ and TCDD. Residing in Midland/Saginaw and living with contaminated soil and household dust contributed very little to the variation in serum TEQ, but explained small percentages of the serum TCDD. Food consumption was a small contribution to the variation in serum TEQ, but was slightly larger for TCDD.

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