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Estimation of age- and sex-specific background human serum concentrations of PCDDs, PCDFs, and PCBs in the UMDES and NHANES populations

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HIGHLIGHTS

- First use of quantile regression to estimate distribution of serum dioxin levels.
- Combining NHANES with UMDES referent data provides better percentile estimates.
- Provide formulas to allow calculation of percentile estimates for all ages by sex.
- Estimate where individuals fall in general population distribution of serum dioxins.
- Allow congener specific estimates of population distribution of serum dioxins.

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ABSTRACT

Age- and sex-specific estimates of serum dioxin concentrations are important for comparisons among populations. However, such comparisons are problematic because populations have different age and sex structures and values are typically reported only in broad age ranges that are not comparable across studies. There are few studies that report congener-specific serum concentrations, and none that provide these by sex for age as a continuous function. We combined the NHANES 2003–2004 data with the University of Michigan Dioxin Exposure Study (UMDES) referent population 2005 data to achieve stable and accurate estimates of mean and quantiles of serum dioxins by sex over ages 18–85. Survey-weighted linear and quantile regression models were fitted on the combined data with the log-transformed congener concentration as outcome and age, sex, and data source as covariates. Formulas are provided to allow calculations of age- and sex-specific mean and quantile estimates over ages 18–85. For instance, the geometric mean, median, 75th percentile, and 95th percentile of serum TEQ for men aged 50 can be estimated, respectively, from the formulas as 18.33, 19.02, 22.60, and 30.37 pg g^{-1} lipids among the Michigan general population, and as 15.71, 15.89, 22.60, and 29.90 pg g^{-1} lipids among US non-Hispanic whites. These methods and results are useful for comparing the congener-specific human serum dioxin concentrations in any individual to the general population mean, median, 75th percentile, and 95th percentile, and for comparing the serum dioxin concentration in any group of interest to the US and the Michigan general populations.

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1. Introduction

The University of Michigan Dioxin Exposure Study (UMDES) was undertaken in response to concerns that dioxin-like compounds from the Dow Chemical Company facilities in Midland, Michigan resulted in contaminated soils in the nearby region, leading to an increase in residents' body burden of polychlorinated-*p*-dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs). In order to study this issue, as part of the study we characterized the serum dioxin concentrations in a referent population from an area in Michigan (Jackson and Calhoun counties) approximately 200 km away that had no known point source of PCDDs, PCDFs, or polychlorinated biphenyls (PCBs), so that we could estimate the background serum concentrations in the general population of Michigan. The background serum concentrations provide important comparisons for assessing whether the population of interest has elevated serum levels. There is limited literature on background serum levels, which makes it difficult to determine whether any individual or any group has elevated serum dioxin levels. One of the most important sources of information on background serum concentrations in the US is the National Health and Nutrition Examination Survey (NHANES) 2003–2004 data (Patterson et al., 2009).

PCDDs, PCDFs, and PCBs are highly persistent in the environment and they bioaccumulate up the food chain. Exposure in the general population is principally through eating animal-derived fats in meats, fish, poultry, and dairy products. Serum samples are routinely used for the measurement of body burdens of these compounds, since it has been demonstrated that for 2,3,7,8-tetrachloro-*p*-dibenzodioxin (TCDD) there is a 1:1 partitioning of TCDD between serum and adipose tissue when a correction for their lipid content is made (Patterson et al., 1988). As a result, several large-scale epidemiologic studies of the general population of the United States have provided estimates of the mean and quantiles of the distribution of serum PCDDs, PCDFs, and PCBs (Patterson et al., 2008, 2009; Wong et al., 2008). These studies demonstrate that age and sex are important predictors of serum PCDDs, PCDFs, and PCBs. However, these studies estimate the mean and quantiles (median, 75th percentile, 95th percentile) of the serum distribution either in the entire study population or only in broad age and sex strata. Comparisons of the overall mean and quantiles of serum concentrations between populations should be made cautiously if there are differences in the age and sex structures.

In this article we provide sex-specific estimates for the mean, median, 75th, and 95th percentiles of the serum TEQ and PCDD, PCDF, and PCB congeners as a function of age in the Michigan general population. In addition, we provide the equations that allow calculations of predicted serum levels for any specific age between 18 and 85 years. We also compare these estimates to the US general population, based on the NHANES 2003–2004 samples (Patterson et al., 2009), and provide prediction equations for the US general population, as well.

2. Materials and methods

2.1. Referent population of the UMDES

A total of 251 residents in Jackson and Calhoun counties (J/C), Michigan, who were 18 years or older, had lived in their current residence for at least 5 years, and met Red Cross criteria for blood donation, provided an 80 ml sample of blood in 2005. These residents were selected using a two-stage area probability selection of housing units and a third stage of selection of an eligible person within each sampled housing unit (Garabrant et al., 2009). Participants provided written, informed consent that had been approved by the University of Michigan Health Sciences Institutional Review Board. All serum analyses were performed by Vista Analytical Laboratory of El Dorado Hills, CA, using high resolution gas chromatography-mass spectrometry. Analyses were performed for the 29 PCDDs, PCDFs, and PCBs for which consensus toxic equivalency factors (TEF) have been published (Van den Berg et al., 2006), using modified US EPA protocols 8290 (US Environmental Protection Agency, 1994) and 1668 (US Environmental Protection Agency, 1999) for sample extraction and quantitation. The serum PCDD, PCDF, and PCB concentrations were lipid adjusted and are reported in parts per trillion (ppt) or picograms/gram (pg g^{-1}) lipids.

2.2. NHANES 2003–2004

As part of the NHANES 2003–2004, the serum samples were collected in a statistically representative sample of the US population (Centers for Disease Control and Prevention, 2005). After the samples were collected, they were shipped to the CDC's National Center for Environmental Health (NCEH) (Patterson et al., 2008, 2009; Wong et al., 2008). The serum concentrations of PCDDs, PCDFs, and PCBs were analyzed by using high resolution gas chromatography-mass spectrometry. The PCDDs, PCDFs, and PCBs concentrations were also lipid adjusted and are reported in ppt or pg g^{-1} lipids. In contrast to the UMDES, the NHANES 2003–2004 did not include measurements of three PCB congeners: PCB-77, PCB-114, and PCB-123. Consequently, our analyses of the NHANES data include 7 PCDDs, 10 PCDFs, and 9 PCBs. Since the population in the J/C was predominantly non-Hispanic whites (91%), we restricted the analysis of the NHANES data to non-Hispanic whites. In addition, we excluded pregnant women and study participants who were younger than 18 years. These restrictions resulted in a sample size ranging from 699 to 727 for different congeners.

2.3. Combining the UMDES with the NHANES data sets

Compared to the J/C data, the NHANES has a larger data set, which allows more stable estimates in small age strata such as among people older than 75 years. On the other hand, compared to the NHANES, the J/C data have lower limits of detection (LOD) and thus lower proportions of data below the LODs, which allows more accurate estimates of serum dioxin levels at the low end of the distribution, and consequently, in the lower population percentiles. Since the methods for serum and lipid quantification are comparable between the Vista Analytical Laboratories and the NCEH laboratory and the results were verified via blind sample introduction (Chen et al., 2010), we concatenated the two data sources, with an indicator for data source (1 for NHANES, 0 for UMDES), to achieve better estimates of the mean and quantiles of PCDDs, PCDFs, and PCBs in the two populations for all age groups. We standardized the survey weights within each data source by dividing by their respective mean sampling weights to prevent the UMDES results from being overwhelmed by the NHANES data due to its much larger sampling weights.

2.4. Limits of detection (LOD)

Conventional approaches to handle LODs include replacing the value below the LOD with 0, LOD/2, LOD/$\sqrt{2}$, and LOD. However, these approaches may lead to biased estimates of mean and quantiles for serum concentrations of PCDDs, PCDFs, and PCBS, especially in the NHANES population, in which a high proportion of data are measured near the LODs. A better approach to handle the LOD problem is to use multiple imputation technique based on a statistical model. Here, we used the method described by Chen et al. (2010). Specifically, we repeated the following steps 5 times to generate 5 imputed data sets for each congener: