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Changes in persistent organic pollutant levels from adolescence to young adulthood

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Abstract

Elimination rates and their corresponding half-lives are conceptually important and intuitively accessible pharmacokinetic measures of toxicant elimination, but regression-based estimates are biased proportional to the degree of continuing (background) exposure. We propose an alternative estimator, the censored normal regression model, which uses all observations, but treats individuals whose initial level failed to exceed their follow-up level as censored observations to weight the regression estimates from those that declined between blood draws. In this manner, we derive the intrinsic elimination rate, the elimination rate free from ongoing exposure, as a parameter in a regression with an unobserved, latent dependent variable. We utilize sequential measurements of persistent organic pollutants (POPs) levels from adolescence to adulthood, a period of intense change in size and body composition, to quantify individual-level change within a community exposed to significant quantities of contaminants over an extended period of time. Although much research has been conducted on effects of POPs, far less attention has been given to vectors of intake and changes in toxicant levels during the life course. We apply exploratory factor analysis (EFA) to types and timing of consumption, along with physical behavioral

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characteristics, to identify a structure of seven underlying factors. Although several variables show factorial complexity, the latent constructs included an age/maturation and period-related factor, a nutritional composite, consumption prior to pregnancy, fish and fowl consumed during pregnancy, factors distinguishing body mass and weight from height, and bottom-feeding fish consumption. Unadjusted and adjusted half-lives using the censored normal regression estimator, as well as estimated half-lives from conventional log concentration regressions, are reported for PCB groupings, specific congeners, *p,p′*-DDE, and HCB.

Keywords

Polychlorinated biphenyls; PCBs; persistent organic pollutants; POPs; hexachlorobenzene; HCB; *p,p′*-dichlorophenyldichloroethylene; DDT; Mohawk; Native American

1. Introduction

Persistent organic pollutants (POPs) are resistant to degradation, become widely distributed geographically, biomagnify in food chains, and bioaccumulate in the fatty tissue of non-humans and humans. Adverse effects to health, including the alteration of growth (Burns et al. 2011; Mendez et al. 2011), maturation and development (Denham et al. 2005; Dhooge et al. 2011; Dickerson et al. 2011; Ottinger et al. 2009), and cognitive function (Grandjean and Landrigan 2006; Newman et al. 2006; Newman et al. 2009; Stewart et al. 2000), have been reported. Polychlorinated biphenyls (PCBs) dichlorodiphenyldichloroethane (*p,p′*-DDE, a metabolite of DDT), and hexachlorobenzene (HCB), are widely recognized as persistent environmental pollutants. Although the use and emissions of these chemicals were severely restricted in the US in the mid-1970s, these toxicants are extremely difficult to destroy by either chemical, thermal, or biochemical processes due to their high thermodynamic stability, and destruction presents the risk of generating extremely toxic dibenzodioxins and dibenzofurans through partial oxidation (Hansen 1999; Shibamoto et al. 2007).

Humans continue to be exposed to different mixtures of POPs, especially PCBs, at background levels and via direct routes of intake (ingestion, inhalation, intrauterine transmission, etc.) (Grandjean et al. 2008; Knobeloch et al. 2009; Lignell et al. 2009; Matsumoto et al. 2009; World Health Organization 2003). Exposure beyond background levels continues primarily through the dietary intake of contaminated animal, fish, or fowl fats. Bottom feeding and long-lived predatory fish can accumulate high levels in their body fat and these residues can be passed on to humans and wildlife that consume them (Startin and Rose 2003). Exposures to PCBs, *p,p′*-DDE, and HCB have been linked to diabetes (Lee et al. 2010; Turyk et al. 2009), high blood pressure/hypertension (Goncharov et al. 2008; Langer 2010), thyroid hormone disruption (Chevrier et al. 2007; Langer et al. 2009; Schell et al. 2009; Schell and Gallo 2010), effects on sexual maturation and differentiation (Denham et al. 2005; Dhooge et al. 2011; Dickerson et al. 2011; Ottinger et al. 2009), and reproduction (Cohn et al. 2010; Cohn et al. 2011; Needham et al. 2011; Wigle et al. 2008). These endocrine disruption effects of POPs continue to be of concern, especially during critical times of growth and development such as adolescence and young adulthood, primarily due to their long half-lives (Stehr-Green 1989) and potentially adverse long-term health consequences.

Although much research has been conducted on health effects of POPs, far less attention has been given to vectors of intake and changes in toxicant levels during the life course. To the best of our knowledge, no other study has utilized sequential measurements of POP levels from adolescence to adulthood, a period of intense change in size and body composition to quantify individual-level change within a community exposed to significant quantities of contaminants over an extended period of time.

We begin by reporting serum levels of persistent organochlorines (PCBs, *p*,*p*′-DDE, HCB) within Akwesasne Mohawk adolescents (collected between 1995–2000) and again in young adulthood (collected between 2000–2005), with an average interval of four years between measurements. The Mohawk of Akwesasne have had significant changes in lifestyle following the discovery of contamination of the St. Lawrence River on which they depended for fish, hence reducing their reliance on the traditional fish-based diet to a less healthy one containing more fat and calories (Ravenscroft and Schell 2007). However, a substantial proportion of our sample evidence an absolute increase in POP levels at follow-up (young adulthood) over their baseline measure (adolescence).

Elimination half-life, the amount of time required to reduce a toxicant to one-half its level at initial measurement, is a conceptually important, and intuitively accessible, pharmacokinetic measure of toxicant elimination, but its conceptual utility is predicated on the assumption that differences in rates of elimination from the body depend primarily on compound-related pharmacokinetics and host-related factors that affect individuals' metabolism rates (Lotti 2003; Matthews and Dedrick 1984). Continuing exposure between initial and follow-up measurement violates this assumption and confounds estimation of elimination kinetics. Most of the literature on elimination half-lives is now dismissed as having reported "apparent" elimination half-lives (Shirai and Kissel 1996; Milbrath et al., 2009; see discussion of apparent versus intrinsic half-lives in Ritter, 2011). The concern over bias introduced by ongoing exposure is so severe that it has led some to conclude that it is impossible to offer reliable half-life figures from longitudinal data with ongoing environmental exposure (Lotti 2003; Yakushiji et al. 1984). At a minimum, the concern has produced a preference for the development of methods for half-life estimation from cross-sectional data (Ritter et al. 2011; Wong et al. 2013) or regression of log serum concentrations on time after primary exposure ceases for longitudinal data (cf. Bartell 2012). Neither of these approaches is likely to have strong causal inference after extrapolation to the real world (Manski 1995) or adequately respond to bias introduced by ongoing exposure and host-related factors on elimination (Milbrath et al. 2009).

Accordingly, this analysis has two objectives. First, we determine the factor structure underlying fifteen items representing dietary intake, measures of body burden/storage reservoirs, and other known correlates of toxicant exposure. Second, we estimate intrinsic elimination rates using an exponential decay model and a regression method ideally suited to a population under continuing exposure, with and without adjustment for within-individual effects of the (seven) identified constructs and other host-related covariates. We report the corresponding intrinsic elimination half-lives for PCBs, *p*,*p*′-DDE, and HCB.

2. Materials and Methods

2.1 Sample and site characteristics

The Akwesasne Mohawk Nation (AMN) is a sovereign nation situated on the St. Lawrence River with territory bordering New York State, Ontario and Quebec, Canada. The Akwesasne community is one of several communities comprising the Kahniakehaka/ Mohawk nation, and is traditionally known as the keeper of the Eastern Door of the Iroquois Confederacy (the Haudenosaunee Confederacy) with a population approximating 12,000 – 13,000 people (Akwesasne Task Force On The Environment 1997; Fitzgerald et al. 1998; George-Kanentiio 1995).

Industrial development along the St. Lawrence River began in the 1950s, and major industrial facilities located around Cornwall, Ontario, and Massena, New York, discharged significant quantities of contaminants, including PCBs, *p,p′*-DDE, HCB and mirex, into the St. Lawrence River and its three tributaries (Sloan and Jock 1990). Contamination of the local waters entered the local food chain, and some local species of fish, birds, amphibians and mammals were found to have levels exceeding the US Food and Drug administration's tolerance limits for human consumption (Forti et al. 1995; Sloan and Jock 1990), leading to the issuance of fish and game advisories in the late 1980s and early 1990s (Fitzgerald et al. 1995; Fitzgerald et al. 1998).

2.2 Data collection

The University at Albany, State University of New York's Institutional Review Board approved all study protocols and informed consent procedures. Additionally, assent from minors was obtained from all participants. For both projects, all data collection was performed by project staff, all members of the Akwesasne community, and data were collected without prior knowledge of participants' exposure status. Study protocols and methods have previously been described in detail (Gallo et al. 2011; Newman et al. 2006; Newman et al. 2009; Schell et al. 2003), and are briefly reviewed here.

Data were collected for the Mohawk Adolescent Well-Being Study (MAWBs) between 1995 and 2000. In brief, 294 mother/youth pairs were recruited, and due to attrition resulted in a final sample size of 271 participants (131 males and 140 females) between 10 and 16.99 years of age (for more detail on recruitment and sampling see Schell et al. 2002, 2003; Gallo et al. 2005, 2007).

In MAWBs, the youth's mother completed interviews and questionnaires to obtain information about the youth's family background including sociodemographic status and sources of exposure such as diet (from Food Frequency Questionnaire (FFQ)), breastfeeding history and duration, as well as the mother's consumption of locally caught fish, fowl and game before and during the pregnancy with the child participant (from a modified dietary questionnaire). Two overall questions were asked about locally-caught fish consumption: 1) whether the mother consumed any locally caught fish (yes/no); and 2) how many meals she consumed before (12 mos) and during her pregnancy (9 mos). This information was then characterized further into types of fish consumed (bass, trout, sturgeon, etc.) and number of meals eaten of each type of fish. Since consumption of bottom-feeding fish would result in

higher toxicant levels given the toxicants' predilection to bind to sediment (Startin and Rose 2003), chemical viscosity and density (Kuzyk et al. 2005a; Kuzyk et al. 2005b; Wirgin et al. 2011), fish consumption-based measures were also differentiated between bottom-feeding (catfish, bullhead, eel and sturgeon) and top-feeding fish (bass, perch, walleye/pickerel, pike, and trout).

The Young Adult Well-Being study (YAWBs) was conducted from 2000 to 2005. Young adults were eligible if they had participated in MAWBs, and were now between 17 and 20 years of age (Gallo et al. 2011). The YAWBs sample consisted of 154 participants; however two persons were omitted because reported organochlorine levels from our earlier study, MAWBs, were not available and one person was excluded because serum POP levels were not available from the follow-up study, leaving a final sample size of 151 individuals.

In YAWBs, each participant completed interviews and sociodemographic questionnaires providing information about life style factors, recreational and traditional activities, current cigarette and alcohol use, breastfeeding history and duration (in consultation with their mother and checked against MAWBs data), prescription and over-the-counter medicine use, diet, sex (males =0, females =1), age (when blood was drawn), educational status (as the highest year of education completed), body mass index (calculated), weight (kg; self-report), height (cm; self-report), and, as a proxy for socioeconomic status, education, current and past employment and living environment. (For more detail see Gallo et al. 2011).

2.3 Laboratory analysis of toxicants and lipid measurements

For both MAWBs and YAWBs, blood specimens were collected by trained Mohawk staff. The sample was collected within a five-hour window to minimize the effects of diurnal variation (particularly with regard to endocrine assessment). Approximately 95% of the participants had their blood drawn at first rising. Participants were asked to not eat any locally caught, trapped, or grown food for three days prior to the collection and to not eat or drink anything after 10 p.m. the previous evening.

In MAWBs, assessment of cholesterol, triglycerides, and glucose was performed at the Clinical Chemistry and Hematology Laboratory, Wadsworth Center for Laboratories and Research, New York State Department of Health, a CLIA-approved member of the CDC reference laboratory network for lipid measurements (Myers et al. 2000). In YAWBs, clinical chemistries were performed at the clinical laboratories of the Albany Medical Center in Albany, NY, a New York State and CLIA accredited laboratory meeting all proficiency requirements.

Organochlorine pesticide and PCB analyses for both studies were conducted at the University at Albany's Exposure Assessment Laboratory. The laboratory is accredited by the NYSDOH Clinical Laboratory Evaluation Program and participated in the Arctic Monitoring and Assessment Programme (AMAP) Ring Test for Persistent Organic Pollutants in Human Serum. The same laboratory analysis protocol was used for both studies (for more detail see Schell et al. 2003 and Gallo et al. 2011). Analysis of low and high level QC performance samples indicated accuracy and precision of ±15% of nominal and ≤15% RSD, respectively. Complete details of the laboratory protocol for PCB analysis

have been published (DeCaprio et al. 2000, 2005). In brief, high resolution, ultratrace, congener-specific analysis was performed by parallel dual-column (splitless injection) gas chromatography (GC) with electron capture detection (ECD) (Agilent Technologies, Inc., Santa Clara, CA). This method quantitates up to 83 individual PCB congeners and 18 PCB congeners as pairs or triplets, as well as *p*,*p*′-DDE, HCB, and mirex (a total of 94 analytical peaks). An instrument change (i.e., from an Agilent model 5890 GC with standard ECDs to a model 6890 with micro-ECDs) allowed for a lowering of detection limits for most individual congeners in YAWBs as compared to MAWBS. LODs (MDLs) for detected congeners ranged from 2 to 24 ppt (pg/g serum) for a 2.5 g serum specimen and are listed in a previous publication (Gallo et al. 2011). The analytes include all of the major Aroclor-derived congeners typically present in human samples plus a number of sporadic or rare congeners. Individual chlorinated biphenyl (CB) congeners are identified according to the IUPAC numbering system (Ballschmiter and Zell 1980; Guitart et al. 1993). Data were expressed on a whole-weight basis without lipid adjustment to maintain consistency with the earlier data analyses.

2.4 Congener Groupings

Due to improvements in technology, limits of detection (LOD) for PCBs were marginally lower in the second project. Of the 16 PCB congeners detected in 50% or more of the sample, the LOD of nine PCB congeners and *p*,*p*′-DDE decreased by less than 0.01 ppb and by less than 0.02 ppb for the remaining seven PCB congeners and HCB. According to most common practice and to maintain consistency with previous study data, results below the LOD were imputed as ½ the LOD prior to log transformation. Analysis of the data with an input of zero for data below the LOD resulted in no significant differences in geometric mean levels from that using ½ LOD imputation. To insure comparability of our data with the majority of previous work, we chose to use mass-based concentrations (*i.e.*, ng/g serum; ppb) for statistical analyses. However, some workers have also employed MW-based concentration data (*i.e.*, pmol/g serum or lipid) for such analyses (*e.g.*, Fängström et al. 2005). Repeat analyses in the present study using the pmol/g metric demonstrated only minimal differences in the results compared to those using the ng/g metric (data not shown).

Both the degree of chlorination and chlorination pattern of individual PCB congeners were considered in the composition of the PCB groupings. Environmental persistence, bioaccumulation in food chains, distribution in human tissue, and the toxicologic action (*i.e.*, dioxin-like vs. Ah receptor-independent effects) of PCBs depend on the chemical structure of individual congeners (Laden et al. 1999; McFarland and Clarke 1989). Therefore, we grouped individual PCB congeners with >50% detection rate according to structure and mechanism in both studies.

To compare levels between the follow-up study (YAWBs) and those in the previous one (MAWBs), we constructed three groups of PCB congeners using the same commonly detected PCBs congeners groupings that were used in MAWBs (for more detail see Schell et al. 2003), i.e., Σ16PCB50%, the sum of all congeners found in 50% or more of the MAWBs sample (CBs 52, 70, 74, 84, 87, 95, 99, 101[+90], 105, 110, 118, 138[+163+164], 149[+123], 153, 180, 187); Σ8PerPCB: the sum of 8 persistent PCBs, again found in 50% or

more of the MAWBs sample (CBs 74, 99, 105, 118, 138[+163+164], 153, 180, 187); and Σ6NonPerPCB: those congeners generally considered to be non-persistent (CBs 52, 84, 95, 101[+90], 110, and 149[+123]), also detected in 50% or more of the MAWBs sample. While there is debate over some classification schemes that include CBs 87 and 70 as moderately persistent (Hansen 2001), other data suggest that they should be fairly readily metabolized in humans and should be considered non-persistent (Brown 1994). Because of this uncertainty, they were excluded from both the persistent and non-persistent congener variables. PCB congeners for which all reported values were below the laboratory LOD in MAWBS included CBs 1, 3, 6, 63, 67 and 185 and in YAWBs included CBs 3, 6, 63, and 67; these were not included in any calculations (for more detail see Schell et al. 2003; Gallo et al. 2011). Only negligible levels of mirex were found in YAWBs, therefore mirex was not considered in this analysis (Gallo et al. 2011).

2.5 Statistical methodologies

Statistical analyses were conducted with SPSS v.20 (IBM 2012) and Stata/IC v. 12.1 for Windows (StataCorp 2011). While our focal product is unbiased elimination half-lives, we initially report and interpret descriptive measures of percent annual change in PCBs (Σ16PCB50%, Σ8PerPCBs, Σ6NonPerPCBs, and CBs 105, 118, 138[+163+164], and 153) and toxicants (*p*,*p*′-DDE and HCB) between the two studies, scaling the anticipated decline in a toxicant from its initial level in adolescence to its follow-up level in young adulthood as an expected positive value.

While description based on observed annual percent change is interesting and important, toxicokinetic fate modeling in which half-life calculations are derived from elimination rates requires a higher standard of assessment. It is well known that half-life estimates will be artificially high if they fail to account for continuing exposure and the effect of host-related factors on elimination (Shirai and Kissell 1996; Milbrath et al. 2009). Therefore, common practice in prior research utilizing longitudinal data estimates the elimination rate constant, under an exponential decay model, from the derivative (slope) in a linear regression of first-difference in log serum concentration between initial and follow-up on the first-difference in time between follow-up and initial measurement, adjusted for change in relevant host-related factors such as mass of fat or BMI (cf. Yakushiji et al. 1984; Grandjean et al. 2008; Milbrath et al. 2009). This form of regression is the well-known “fixed effects” model. It has desirable properties for causal inference, based in large part on its exclusive use of within-individual variation, but it is still highly susceptible to inconsistent estimates of elimination due to continuing exposure, including prediction of negative values of the rate of change, heteroscedastic errors, and influential outliers. These violations follow from the assumption that the data generating process is an exponential decay model for each individual:

$$Y_{it}=Y_{i0}\times exp\left(-k_i\times t_i+\varepsilon_{it}\right) \quad (1)$$

where Y_t is the toxicant concentration at time t, Y_0 is the initial concentration, and ε_t is a normally distributed error term for the i^{th} individual (Grandjean et al. 2008). This function cannot apply if $Y_t > Y_0$.

We propose that a censored normal regression model to account for ongoing exposure can offer a conceptual match to the problem of estimating intrinsic elimination rates using serum concentrations thought to follow an exponential decay by treating individuals with non-positive difference in log-transformed concentrations between initial and follow-up individuals as censored observations. In the absence of ongoing exposure, non-positive change in log concentration is a logical impossibility and half-life calculation would be undefined. In a population under any background exposure some proportion of cases, typically observations near the lower limit of y at Y_0, will show non-positive change. We make use of this condition to approximate the proportion of $ln(Y_0) - ln(Y_t)$ that is free from ongoing exposure by the estimated probability of being uncensored. The decomposition of the censored normal regression model in the next section will show that the estimated probability accounts for ongoing exposure by weighting the elimination rate parameter.

2.6 The Tobit model

The structural equation in the Tobit model is

$$y_i^* = X_i \beta_x + u_i \quad (2)$$

where u_i is an independently distributed error term assumed to be normal with zero mean and constant variance σ^2 and y_i^* is a latent variable that is observed for values greater than τ, where τ is the point, or limit, of censoring (Tobin 1958; McDonald and Moffitt 1980). In our application y_i^* is a positive-valued difference in log-transformed concentrations at initial and follow-up measurements, X_i is the duration between measurements, and β_x is the elimination rate parameter.

The observed y is defined in the measurement equation:

$$y_i = \begin{cases} y^* \; if \; y^* > \tau | k \\ \tau_y \; if \; y^* \leq \tau | k \end{cases} \quad (3)$$

We assume that $\tau = 0$, that is, that the data are censored at 0, thus increasing levels between initial (MAWBs) and follow-up (YAWBs) measurement are precluded from directly entering our calculations of the unbiased elimination rate and half-life. Our recognition that y_i cannot include non-positive values of y_i^*, even though non-positive difference in log-transformed concentrations at initial and follow-up measurements are measured, is an unusual operationalization of the latent variable in the censored normal regression model. Typically censoring means that values at the limit are unmeasured. Our definition of y_i^* is based on elimination kinetics, not on the presence or absence of non-missing values.

It is important to recognize that Tobin's model uses all observations, both those that are at the limit (censored) and those above it, to estimate a regression line, by assuming that there is an underlying, stochastic index equal to $(X_i \beta + u_i)$ which is observed only when it is positive (i.e., above the limiting value). There are actually three expected values that can be derived from the Tobit model: the expected value of the latent variable, $E[y^*]$, the expected

value of the uncensored observations, $E[y \mid y > \tau]$, and the expected value of y. The expected value of y in the model is

$$E[y] = X\beta F(z) + \sigma f(z) \quad (4)$$

where $z = X\beta/\sigma$, $f(z)$ is the unit normal density, and $F(z)$ is the cumulative normal distribution function. This is the probability of being uncensored multiplied by the expected value of y given y is uncensored. In addition we can show that the marginal effect on the expected value of y (censored and uncensored) is:

$$\frac{\partial E[y]}{\partial x_k} = \Phi\left(\frac{X_i\beta}{\sigma}\right)\beta_x = P(y>0)\frac{\partial E[y|y>0]}{\partial x_k} + (E[y|y>0])\frac{\partial P[y>0]}{\partial x_k} \quad (5)$$

McDonald and Moffitt argue that in most applications the decomposition is necessary to locate the effect of interest. The first form of the decomposition in eq. 5, with X defined as the duration between blood draws, shows that the estimated probability of observing an uncensored (positive-valued) observation at each value (duration) of X is a factor that scales the parameter (β_x) that alters the latent dependent variable. The second form of the decomposition in eq. 5 allows us to see that a change in X affects the conditional mean of the latent dependent variable, y_i^*, in the positive part of the distribution and it affects the probability that the observation will fall in that part of the distribution. The corresponding estimator of intrinsic elimination half-life follows accordingly:

$$intrinsic\ half\ life = ln(2)/\Phi\left(\frac{X_i\beta}{\sigma}\right)\beta_x \quad (6)$$

We report the associated half-lives, estimated with and without statistical controls for sources of exposure and host-related characteristics. We also provide estimated half-lives derived from linear regressions with statistical controls to facilitate comparison against previous attempts to account for continuing exposure by including covariates for sources of intake and from a subsample that excludes individuals whose levels increased or were unchanged over the follow up period (cf. Grandjean et al. 2008; Knobeloch et al. 2008). We use non-lipid adjusted measures of PCBs, CBs, and toxicants because statistical controls include lipid-based or related covariates (as described in the following section).

2.7 Exploratory factor analysis

Exploratory factor analysis (EFA) is a popular and effective means of identifying the number and nature of the underlying factors responsible for covariation in a set of data (Hatcher 1994; Fabrigar et al. 1999). We applied the principal factor method with promax rotation to 15 measures of consumption and a variety of other physical and behavioral characteristics using squared multiple correlations as prior commonality estimates. Items entered into the factor analysis included years between blood draws between projects, whether the participant was born in 1985 or later vs. 1984 (*i.e.*, before or after fish consumption advisories were issued by the New York State Department of Health), maternal

fish and fowl consumption before and during pregnancy (number of reported meals and number of reported meals divided into top- and bottom-feeding fish), dietary intake (total caloric, fat and protein intake), age (in years), sexual maturation stage as determined by Tanner (Tanner 1990), weight (kg), height (cm), BMI (kg/m^2), each measured at the initial wave (MAWBs). These covariates were selected based on literature review (Arisawa et al. 2011; Blanck et al. 2000; Burns et al. 2011; Dhooge et al. 2010; Fitzgerald et al. 2010; Leijs et al. 2009; Patel et al. 2010), on our earlier findings (Denham et al. 2005; Gallo et al. 2002, 2005, 2011; Schell et al. 2009), and on correlations with toxicant levels at $p \leq 0.20$. Preliminary analyses found that two measures of breast feeding (duration of breast feeding and a simple indicator of whether or not the respondent had ever breast fed), maternal smoking during pregnancy, gravidity (Gallo et al. 2011), levels of three clinical analytes (triglycerides, cholesterol, glucose), and a proxy for socioeconomic status (SES),[1] did not load on any factor. These items were removed from the EFA, but were reintroduced, along with sex of the respondent, as individual covariates to adjust our regression estimates of elimination rates.

3. Results

3.1 Description of MAWBs and YAWBs samples

Basic descriptive statistics from the initial wave of this project (MAWBs) and at follow-up (YAWBs) for all items entered into the EFA and other candidate characteristics are shown in Table 1.

The median age of the 151 individuals included in this analysis during the MAWBs wave was 13.5 years. The average body mass index (BMI) was 23.9 kg/m^2 and was significantly higher in males (25.4 kg/m^2; $p \leq 0.001$) than females (23.1 kg/m^2). Approximately half of respondents were breastfed, with an average duration of just over three months, and about 40% of respondents' mothers smoked during their pregnancy.

The top three locally caught types of fish most often consumed by Akwesasne women were perch, walleye, and bullhead (see Figure 1). Less than 6% ate catfish, eel, or trout either before or during pregnancy. Waterfowl consumption was negligible with only a few women consuming any wild duck or goose (8% and 4% respectively) before pregnancy, and during pregnancy not one woman ate goose, and only 2% consumed any duck. Average maternal fish consumption before pregnancy was significantly greater than consumption during pregnancy (p=0.001). Average number of locally-caught fish meals ranged from 9 to over 190 meals over the course of a pregnancy, a significant decrease from 28 to 358 meals per year before pregnancy.

At follow-up, the mean age in the YAWBs wave was 18.1 years. Nearly 50% of the young adults reported that they currently smoked cigarettes, and 95% consumed alcohol in the past year. Males had a significantly higher BMI (27.6 kg/m2; p≤ 0.001) than females. For a more comprehensive description of YAWBs characteristics, see Gallo et al. 2011.

[1]We acknowledge that estimating SES is difficult, especially in a Native American population. Nevertheless, we calculated a weighted variable, which included maternal education, maternal employment and marital status, and size of residence.

3.2 Initial and follow-up toxicant levels and change

Levels of PCB groupings, *p,p′*-DDE and HCB, and individual PCB congeners of the participants as youth and again as young adults are shown in Table 2. CBs 118, 138[+163+164] and 153 were detected in nearly all participants in YAWBs (GM: 0.05 ppb, 0.07 ppb, 0.08 ppb, respectively), while CBs 105, 180, and 70 had the highest rate of detection in the earlier study (GM: 0.03 ppb, 0.03 ppb, and 0.02 ppb respectively; results not shown).

Levels of PCBs in all groups and *p,p′*-DDE decreased from 15 to more than 40 percent. Levels of the non-persistent congeners had the sharpest decline (median 0.11 ppb; 48% decrease). In contrast, levels of HCB were unchanged from MAWBs to YAWBs.

In both studies, HCB and *p,p′*-DDE were found in nearly 100% of the sample; only HCB was significantly higher in males (p=0.05) in the YAWBs wave data. In general, levels of all PCB groups and other toxicants did not differ significantly by sex. In YAWBs, breastfed individuals (n=73) had significantly higher levels of Σ16PCB50%, and Σ8PerPCBs, CBs# 52, 74, 138, 153, and 187 ($p \leq 0.05$). In MAWBs, significantly higher levels of Σ16PCB50%, Σ8PerPCBs, *p,p′*-DDE, HCB, and CBs# 52, 74, 118, 153, 180, and 187 were found in breastfed youth ($p \leq 0.03$). Levels of *p,p′*-DDE were significantly reduced in those who had been breastfed as infants ($p \leq 0.001$). Further statistical testing determined that levels of *p,p′*-DDE and the three PCB groupings were reduced significantly less in proportion to the length of time the individual was breastfed (p=0.04). HCB was unrelated to breastfeeding duration. Mean time elapsed between blood draws in each study was 4.1 years, and there were slight, non-significant differences in mean interval by sex (males=3.9 years, females = 4.1 years), and breast feeding status (BF= 4.3 years, NBF = 3.9 years).

A substantial percentage of respondents had higher absolute levels at follow-up (YAWBs) than in the initial (MAWBs) wave (Table 2). Forty-four percent of individuals increased their levels of HCB and 34% increased their *p,p′*-DDE level. Nine percent (n=14) of the sample had increased levels of Σ6NonPCBs. Most of these subjects demonstrated 25 – 35% higher absolute levels in young adulthood than in adolescence. Given the large percentage of respondents with an absolute increase, Table 3 supplements the information given in Table 2 by disaggregating annual percent change for each PCB grouping, congener, and other toxicants for the subsample of individuals whose levels decreased from their initial blood draw versus the full sample. Table 3 underscores the impact of ongoing exposure in our sample.

3.3. The number and nature of host-related characteristics and vectors of dietary intake

To understand the factor structure underlying our data, we employed exploratory factor analysis (EFA). We used several criteria to determine that seven factors would be retained for rotation to a final solution, including the Kaiser criterion; the scree test; proportion of common variance accounted for; and interpretability, including conceptual clarity of the factor structure. Four of the 15 items were found to load on the first factor (a variable was said to load on a given factor if the loading was 0.4 or greater), accounting for approximately 30% of the common variance among the 15 items. This is an age/maturation

and period-related factor, consisting of an indicator of whether the adolescent was born before 1985 or after (the year fish advisories were issued), adolescents' age in years, the years between the first and second blood draws, and adolescents' Tanner Stage (an earlier Tanner stage in an adolescent indicate more maturation occurred between studies).

The second factor is a nutritional composite, indicating the adolescent's total caloric, protein and fat intake as measured by the NCI-FFQ. This factor accounts for approximately 25% of the common variance. The third factor is a "consumption prior to pregnancy" factor (annualized sum of fish and fowl meals consumed before pregnancy, annualized number of top-feeding fish meals consumed before pregnancy, and annualized number of bottom-feeding fish meals consumed before pregnancy). The third factor accounts for about 18% of the common variance. Factors four and five each explain about 10% of common variance. Factor four identifies fish and fowl consumption during pregnancy (same measurement, though during rather than before pregnancy, as in the third factor, but without bottom-feeding fish meals). Factors five and six describe body dimensions. Factor 5 consists of BMI and weight, while the sixth factor isolates height. The final factor, accounting for about three percent of common variance, is another fish consumption factor, but consists solely in the consumption of bottom-feeding fish before and during pregnancy.

A different perspective on how the variables are related to the factors is provided through an examination of the factor structure, the correlations of the 15 individual items with the seven factors. These correlations, along with the other covariates that were initially considered in the EFA and to be used as controls in our multiple regression estimates of intrinsic elimination rates, are reported in Table 4.

Examination of the factor structure helps to explain aspects of the rotated pattern matrix. The factor structure generally evidences a "simple structure" wherein most of the variables have relatively high factor loadings on only one factor and most of the factors have relatively high factor loadings for some variables, the "body dimension" variables. However, BMI, weight, and height drive several notable exceptions, as they evidence factorial complexity. Here we see that the first, age/period-related, factor is also substantially correlated with height and weight (but not BMI). Our fifth factor, that identified BMI and weight, also reveals substantial correlation with height, while our "height" (sixth) factor has moderate to strong correlations with weight, age, and Tanner Stage. Factors two, three, four, and seven, maintain their conceptual distinctiveness.

3.4 Tobit regression estimation of intrinsic elimination rates and half-lives

We estimate elimination rates, and their associated half-lives, by fitting Tobit regression models. Log-transformed change between studies in levels of four individual PCB congeners (CBs 105, 118, 138, and 153), three PCB groupings (Σ16PCB50%, Σ8PerPCBs, Σ6NonPerPCBs), and HCB and *p*,*p*′-DDE, with τ set to the maximum y_i that fails to exceed an exponential decay function of time between initial and follow-up blood draws, is regressed on duration of exposure between initial and follow-up blood draws, with and without adjustment for the seven latent constructs that underlie measures of consumption, sex of the respondent, and the other covariates described previously (see section 2.7 on exploratory factor analysis). We interpret the estimated regression slope, after applying the

McDonald-Moffitt decomposition, on the duration between blood draws as the intrinsic elimination rate. We report the unadjusted (Model 1) and adjusted (Model 2) half-lives in Table 5. The regression analyses also allow us to assess the contribution of the latent constructs and other covariates to the adjustment that gives the intrinsic half-lives. We also estimate half-lives using the conventional linear regression method, adjusting for the seven factors, sex, and other covariates, using all respondents (Model 3) and only respondents whose initial toxicant level exceeded their follow-up level (Model 4). These estimated half-lives provide a benchmark by which illustrate the impact of our censored normal regression method by comparison to previously used methods for dealing with ongoing exposure.

Comparison of the unadjusted (Model 1) Tobit regression with first-order rate constant only to adjusted (Model 2) Tobit regression with factors and other covariates in addition to first-order rate constant estimated half-lives showed mixed results. Estimated half-lives ranged from just five years (Σ6NonPerPCBs) to over 35 years (*p*,*p*′-DDE). The adjusted estimates produced a decrease in half-life for Σ16PCB50%, Σ6NonPerPCBs, and CBs 105 and 118, but increased half-life for Σ8PerPCBs, *p*,*p*′-DDE, HCB, and CBs 138 and 153. In some instances, the adjustments had trivial impact (e.g., estimated half-life of Σ16PCB50% decreased by five months, while Σ8PerPCBs' half-life increased by about seven months). The impact on HCB and *p*,*p*′-DDE half-lives was far more consequential and likely results not only from the effectiveness of our regression covariates, but also from selectivity in our study population to background concentration. HCB increased from about 67 years to over 78 years and *p*,*p*′-DDE half-life more than doubled. Ongoing exposure to HCB, *p*,*p*′-DDE, and some PCB congeners in our population is very high; recall that Table 2 shows that 44 and 34 percent of individuals had an absolute increase in HCB and *p*,*p*′-DDE, respectively, between blood draws.

The decompositions shown in section 2.6 should be clear that OLS regression on the full sample will produce inconsistent estimates because $E[y]$ is a non-linear function of X, β, and σ; and OLS assumes linearity. In addition, OLS regression on the uncensored sample (Model 4) will also produce inconsistent estimates because it omits relevant parts of the estimator of β. Regardless, a comparison of half-life estimates reported under Models 3 and 4 help reinforce the value of our method. Failure to account for ongoing exposure in the half-lives reported under Model 3 produces estimates that are all shorter than those in Model 2, except CB 138, which is three years longer. Estimated half-lives based on exclusion of individuals with non-positive values (Model 4) are far worse. Half-lives reported in Model 4 are all substantially less than those in Models 2 and 3; and the difference is clearly related to the proportion of cases with non-positive values (again refer to Table 2).

Of the seven factors identified in the EFA, only the "nutritional factor" (factor 2: caloric, protein, and fat intake) and fish/fowl consumption during pregnancy (factor 4) were not significantly related to any of the elimination rates. None of the factors or other covariates was significantly related to CB 138 half-life, although consumption before pregnancy (factor 3) was marginally significant (p=0.073). Consumption before pregnancy (factor 3) was significantly and negatively related to Σ16PCB50%, Σ8PerPCBs, and positively related to DDE. The factor that describes age and maturation (factor 1) was positively associated with Σ6NonPerPCBs and CB 118, suggesting the older the participant the greater the decline in

these two POP levels from initial measurement to follow-up. Body mass index and weight (factor 5) was found to have a negative adjustment on HCB and CB 153; bottom fish consumption (factor 7) was negatively associated with *p*,*p*′-DDE and CB 105. Height (factor 6) also showed a significant and negative effect on CB 105. An indicator of whether the respondent had been breastfed, gravidity, and triglycerides were the only controls found to significantly add to half-life prediction.

4. Discussion

While there are a number of cross sectional investigations that have identified factors associated with current organochlorine body burden, there is a paucity of reports on serial PCB data among humans, especially within the age bracket that we have considered here. To the best of our knowledge, this is the first report of serial congener-specific PCB data from adolescence to young adulthood. Thus, the current study provides an exceptional opportunity to examine changes in serum organochlorine levels of young Akwesasne men and women relative to late childhood and adolescent levels.

Akwesasne young adult toxicant levels were found to have decreased overall in the past four years, yet continue to be higher in the breastfed individuals than in the non-breastfed, with the exceptions of Σ6NONPerPCBs, HCB and CB 105. This is consistent with our earlier report on breastfed adolescents (Schell et al. 2003). This overall decrease suggests that there is less consumption of locally caught fish, fowl or wildlife, that body burden of these PCBs has been reduced via metabolism and excretion, and potentially lower levels of airborne congeners now than four years earlier.

Nearly 44%, 32%, and 36% of the young adults had increased HCB, CBs 105 and 138[+163+164] levels respectively, which would suggest continued exposure. This continued post-natal exposure would obfuscate any effect by breast-feeding. The Akwesasne community continues to live surrounded by industrial facilities, some recently closed, that have not been remediated and continue to leak residual toxicants into the air, soil and water.

While we concur with Megson et al. (2013) that accounting for the source and contaminant pathway is important when attempting to age date exposure, our investigation of the number and nature of vectors of dietary intake suggests that source and pathway also bear consequences within a narrow age range and historical period. We identified seven underlying factors for the type and timing of consumption and a set of physical and behavioral characteristics. The latent constructs included an age/maturation and period-related factor, a nutritional composite, consumption prior to pregnancy, fish and fowl consumed during pregnancy, factors distinguishing body mass and weight from height, and bottom-feeding fish consumption (see Table 4). Elimination rates and their half-lives are often adjusted for the body burden – age relationship (cf. (Quinn and Wania 2012), but our EFA has shown that distinct dietary routines are also underlying factors that should be part of the regression model specification.

A variety of potential solutions for bias in half-life estimates have been proposed for populations with continuing (background) exposure (Bartell 2012; Wong et al. 2013). We proposed and applied an alternative estimator, the Tobit model, to calculate unbiased half-

life expectation at mean levels of model covariates using all available information by separating cases whose change between initial measurement and follow-up exceeded change anticipated by the first-order rate constant. We also compared unadjusted against the adjusted estimated half-lives (see Table 5). In some instances, the adjustments had trivial impact, while in others the adjustment increased half-life by as much as a decade. In addition, the adjusted estimates produced a decrease in half-life for Σ16PCB50%, Σ6NonPerPCB, and CBs 105 and 118, but increased half-life for Σ8PerPCB, *p*,*p*′-DDE, HCB, and CBs 138 and 153. Of the seven factors identified in the EFA, only two were not significantly related to any of the elimination half-lives; and although fish/fowl consumption during pregnancy was not associated with half-lives, the other two dietary intake factors showed associations with several PCB groupings, CBs, and other POPs.

Estimated half-lives ranged from approximately five years (Σ6NonPerPCBs) to over 84 years (HCB). The level of the organochlorine HCB, a contaminant in several pesticides, remained virtually unchanged between studies, yet two factors, BMI/weight (factor 5) and, to a less extent, consumption prior to pregnancy (factor 3; p=0.079) were predictive of half-life. HCB is highly persistent due to its chemical stability and resistance to biodegradation, with an estimated half-life of over two years in the atmosphere, and over four years in soil. The average time between analyses of the participant's blood is slightly over four years, hence perhaps not long enough to find a substantial change in levels between these two projects.

5. Conclusion

This study utilized sequential measurements of persistent organic pollutants levels from adolescence to adulthood, a period of intense change in size and body composition to quantify individual-level change within a community exposed to environmental toxicants. We estimated unbiased elimination rates, or half-lives, ranging from five to over 84 years. While toxicant levels were found to have decreased overall in the past four years with the exception of HCB, many continue to be higher in the breastfed individuals than in the non-breastfed. The overall decrease suggests that body burden of these PCBs has been reduced via metabolism and excretion. Other possible contributors may be a reduction in the levels of airborne congeners from four years earlier, and the community's decreased consumption of locally caught fish, fowl or wildlife. Examination of the factors behind the continued increase in levels of some of these toxicants is warranted.

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Abbreviations

AMN	Akwesasne Mohawk Nation
ΣPCB50%	Sum of IUPAC#s 52, 70, 74, 84, 87, 95, 99, 101[+90], 105, 110, 118, 138[+163+164], 149[+123], 153, 180, 187
ΣPERPCB8	Sum of IUPAC#s 74, 99, 105, 118, 138[+163+164], 153, 180, 187
ΣNONPER6	Sum of IUPAC#s 52, 84, 95, 101[+90], 110, and 149[+123], HCB, Hexachlorobenzene
MAWBs	Mohawk Adolescent Well Being study
p	*p*′-DDE, *p*,*p*′-dichlorophenyldichloroethylene
PCBs	Polychlorinated Biphenyls
POPs	Persistent organic pollutants
ppb	Parts per billion
ppt	Parts per trillion

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Highlights

1. We utilized sequential measurements of POPs to quantify individual-level change.
2. Unadjusted and adjusted half-lives are reported for PCBs, *p*,*p*′-DDE, and HCB.
3. Ongoing exposure was considered in estimation of POPs intrinsic elimination rate.
4. EFA identified individual-level host characteristics related to change in POP levels.
5. Change in toxicant levels was related to change in maturation and year of birth.

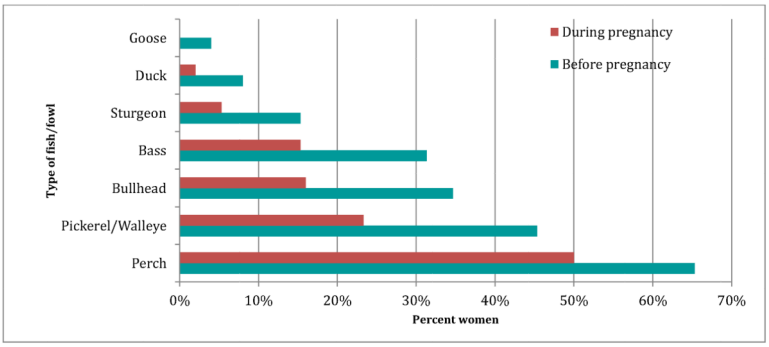

Figure 1.

Percent of women who consumed any locally caught fish or fowl before or during pregnancy.

Table 1

Characteristics of the sample during the first and second study (n=151).

	MAWBs (1995–2000)				YAWBs (2000–2005)			
Characteristic	**Mean**	**SD**	**Max**	**% yes**	**Mean**	**SD**	**Max**	**% yes**
Youth/Young adult								
Age (yrs)	13.5	1.74	16.9	-	18.1	1.09	21.4	
Born before issuance of fish advisories				60%				60%
Breast fed (Y/N)	-	-	-	48%	-	-	-	49%
Breast feeding duration (mos)	3.1	5.01	30.0	-	-	-	-	-
BMI (kg/m^2)	23.9	5.18	43.5	-	25.7	4.86	45.8	-
Height (cm)	157.7	10.53	185.1	-	167.6	9.04	190.5	-
Weight (kg)	60.4	16.92	116.1	-	72.8	17.47	128.8	-
Tanner Stage	3.3	1.05	5.0	-	-	-	-	-
Cholesterol (mg/dL)	157.1	27.53	243.0	-	-	-	-	-
Triglycerides (mg/dL)	86.5	39.93	207.0	-	-	-	-	-
Total caloric intake (kcal)	2669.7	1030.64	6620.8	-	2058.7	904.10	6413.7	-
Total fat intake (g/day)	119.4	55.60	402.3	-	87.9	42.66	300.7	-
Total protein intake (g/day)	92.5	37.54	240.2	-	76.5	35.53	271.8	-
Birth order position	2.4	1.53	8.0	-	-	-	-	-
1st born				36%				37%
Current cigarette use (Y/N)	-	-	-	17%	-	-	-	49%
Number of years between blood draw	-	-	-	-	4.1	1.35	7.1	-
Maternal								
Maternal cigarette use during pregnancy (Y/N)	-	-	-	42%	-	-	-	-
Socioeconomic index	24.4	5.61	37.0		-	-	-	-
					-	-	-	-
Maternal fish and fowl consumption before pregnancy (Y/N)	-	-	-	73%	-	-	-	-
Sum of reported fish and fowl meals consumed before pregnancy (#/12 mo)	28.3	56.54	359.5		-	-	-	-
					-	-	-	-
Maternal fish and fowl consumption during pregnancy (Y/N)	-	-	-	56%	-	-	-	-

Characteristic	MAWBs (1995–2000)				YAWBs (2000–2005)			
	Mean	SD	Max	% yes	Mean	SD	Max	% yes
Sum of reported fish and fowl meals consumed during pregnancy (#/9 mo)	8.7	23.34	191.0		-	-	-	-

Table 2

Summary and specific PCB congener levels within the Akwesasne Mohawk adolescent population (in ppb; n=151).

	MAWBs					YAWBs					*p*-value	% with increased levels (n)
	ROD*	Mean	GM	SD	Max	ROD*	Mean	GM	SD	Max		
Σ16PCB50%[a,b]	-	0.77	0.70	0.371	2.71	-	0.50	0.46	0.287	2.66		
Σ of 8 Persistent PCBs[a,c]	-	0.46	0.41	0.276	2.45	-	0.35	0.31	0.228	1.89	***0.001***	25(37)
Σ of 6 Non-persistent PCBs[a,d]	-	0.24	0.21	0.124	0.72	-	0.12	0.11	0.082	0.74	***0.001***	9 (14)
p,p′-DDE (ppb)[a]	100 %	0.45	0.38	0.384	3.08	99%	0.39	0.33	0.237	1.61	***0.003***	34(52)
HCB (ppb)[a]	99%	0.04	0.03	0.019	0.19	100%	0.04	0.03	0.015	0.11	0.37	44(67)
PCB IUPAC#[a]												
105	67%	0.03	0.03	0.015	0.10	86%	0.02	0.01	0.021	0.10	***0.010***	32(49)
118	99%	0.08	0.07	0.040	0.28	100%	0.05	0.04	0.042	0.42	***0.001***	23(34)
138 [+163+164][e]	89%	0.08	0.07	0.058	0.47	100%	0.07	0.06	0.050	0.41	***0.010***	36(54)
153	97%	0.11	0.09	0.101	0.98	98%	0.08	0.07	0.056	0.45	***0.001***	30(45)

*ROD: Rates of detection as described in Schell et al. 2003, and Gallo et al. 2011

[a]All values below the YAWBs mdl was replaced by the YAWBs mdl and all values below the MAWBs mdl were replaced by the MAWBs mdl

[b]Congeners with ≥ 50% detection rate; Sum of IUPAC#s 52, 70, 74, 84, 87, 95, 99, 101[+90], 105, 110, 118, 138[+163+164], 149[+123], 153, 180, 187

[c]Sum of IUPAC#s: 74, 99, 105, 118, 138[+163+164], 153, 180, 187

[d]Sum of IUPAC#s: 52, 84, 95, 101[+90], 110, and 149[+123]

[e]Bracket indicates ‘minor’ congener based on Aroclor concentration (Hansen, 1999).

Table 3

Annual percent change[a] of PCB grouping and specific congeners, *p,p′*-DDE, and HCB between studies.

	All individuals						Individuals with decreased levels only					
	n	**Mean**	**Median**	**SD**	**Min**	**Max**	***n***	**Mean**	**Median**	**SD**	**Min**	**Max**
Annual percent change												
Σ16PCB50%[b]	151	6.8	7.8	13.24	−84.3	51.7	128	10.3	9.4	7.28	0.1	51.7
Σ8PerPCBs[c]	151	3.4	5.8	15.02	−105.5	49.0	114	8.9	8.3	6.74	0.3	49.0
Σ6NONPerPCBs[d]	151	10.5	11.1	14.91	−81.4	55.3	137	13.5	12.6	8.90	0.3	55.3
p,p′-DDE	151	1.0	3.2	10.96	−35.6	24.2	99	7.0	5.7	5.26	0.4	24.2
HCB	151	−1.7	2.0	14.68	−90.4	21.8	84	7.1	6.4	4.56	0.5	21.8
PCB IUPAC#												
105	151	1.1	8.9	30.40	−187.1	60.9	102	16.3	14.6	10.90	0.7	60.9
118	151	5.2	9.3	22.70	−195.4	54.4	117	12.5	12.2	7.91	1.2	54.4
138 [+163+164][e]	151	−3.6	3.8	26.67	−145.3	47.4	97	9.5	9.2	7.04	0.4	47.4
153	151	0.9	5.9	21.10	−151.3	48.9	106	9.8	9.4	6.73	0.3	48.9

[a] $$Annual\ percent\ change = \frac{(MAWBs\ level - YAWBs\ level)/MAWBs\ level}{time\ interval\ between\ blood\ draws\ in\ years} \times 100$$

[b] Congeners with ≥ 50% detection rate in MAWBs;IUPAC #s: 52, 70, 74, 84, 87, 95, 99, 101[+90], 105, 110, 118, 149[+123], 138[+163+164], 153, 180, 187.

[c] Sum of IUPAC#s: 74, 99, 105, 118, 138[+163+164], 153, 180, 187

[d] Sum of IUPAC#s: 52,84,95,101,110,123[+149].

[e] Bracket indicates ‘minor’ congener based on aroclor concentration (Hansen, 1999).

Table 4

Correlations between PCA factors and characteristics of the sample measured at time of initial blood draw

	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6	Factor 7
	Pearson correlation						
Age (yrs)	***0.94*** **	0.09	0.02	0.12	0.30**	***0.57*** **	0.11
Sex	−0.05	−0.15	0.04	0.00	***−0.27*** **	***−0.30*** **	−0.10
Born before issuance of fish advisories	***−0.80*** **	−0.05	0.01	−0.03	−0.10	***−0.40*** **	−0.08
Breast fed (y/n)	−0.12	0.06	0.06	−0.15	−0.10	0.05	0.13
Breast feeding duration (mos)	−0.14	−0.03	***0.20*** *	−0.14	−0.11	0.00	***0.21*** **
BMI (kg/m^2)	***0.17*** *	0.10	−0.05	0.00	***0.98*** **	***0.25*** **	0.07
Height (cm)	***0.73*** **	0.15	−0.04	0.07	***0.42*** **	***0.97*** **	0.01
Weight (kg)	***0.45*** **	0.13	−0.05	0.03	***0.95*** **	***0.66*** **	0.06
Tanner Stage	***0.81*** **	0.06	0.02	0.11	***0.22*** **	***0.50*** **	−0.04
Cholesterol	***−0.23*** **	−0.08	0.04	0.01	−0.07	***−0.16*** *	0.12
Triglycerides (mg/dL)	−0.08	0.06	−0.07	−0.03	***0.24*** **	0.00	***0.17*** *
Total caloric intake	0.12	***0.99*** **	0.11	***0.19*** *	0.12	***0.17*** *	***0.17*** *
Total fat intake	0.05	***0.96*** **	0.05	0.15	0.13	0.09	0.18*
Total protein intake	0.13	***0.94*** **	0.09	***0.23*** **	0.07	0.11	0.08
Gravidity	−0.05	−0.02	***0.22*** **	−0.02	0.09	0.04	***0.29*** **
Number of years between blood draw	***−0.79*** **	−0.11	0.11	−0.09	***−0.22*** **	***−0.32*** **	0.02
Maternal cigarette use during pregnancy (y/n)	0.09	0.11	−0.05	−0.07	0.05	0.00	0.00
Socioeconomic index	0.00	−0.12	−0.07	−0.12	−0.07	0.05	0.11
Fish consumption before pregnancy							
Sum of reported bottom-feeding fish meals consumed before pregnancy (#/12 mo)	−0.06	0.04	***0.65*** **	−0.12	−0.11	0.03	***0.73*** **
Sum of reported top-feeding fish meals consumed before pregnancy (#/12 mo)	0.01	0.11	***0.94*** **	***0.51*** **	−0.02	−0.02	−0.11
Sum of reported fish and fowl meals consumed before pregnancy (#/12 mo)	−0.03	0.11	***0.99*** **	***0.40*** **	−0.05	0.00	0.15
Fish consumption during pregnancy							
Sum of reported bottom-feeding fish meals consumed during pregnancy (#/9 mo)	0.09	***0.17*** *	0.08	***0.18*** *	0.11	0.05	***0.44*** **
Sum of reported top-feeding fish meals consumed during pregnancy (#/9 mo)	0.14	***0.21*** *	***0.38*** **	***0.98*** **	0.01	0.01	***−0.21*** *
Sum of reported fish and fowl meals consumed during pregnancy (#/9 mo)	0.10	***0.22*** **	***0.37*** **	***0.98*** **	0.03	0.02	−0.08

Factor 1: Age and maturation - age (yrs), Tanner Stage, years between blood draws, Born before or after fish advisory

Factor 2: Nutrition - total protein, fat and caloric intake

Factor 3: Maternal consumption of local fish or fowl before pregnancy

Factor 4: Maternal consumption of local fish or fowl during pregnancy

Factor 5: Weight and BMI

Factor 6: Height

Factor 7: Maternal consumption of bottom feeding fish both before and during pregnancy

Table 5

Estimate of half-lives (in years) of PCB grouping and specific congeners, *p,p′*-DDE, and HCB.

	Model 1* Unadjusted Half-life	Model 2** Adjusted Half-life	Model 3*** Adjusted Half-life LR Method (all cases)	Model 4**** Adjusted Half-life LR Method (no increase cases)
	Mean	Mean	Mean	Mean
Σ16PCB50%[a]	8.4	7.91	6.64	5.15
Σ8PerPCBs[b]	12.54	13.19	10.35	6.18
Σ6NONPerPCBs[c]	5.46	4.5	4.08	3.5
p,p′-DDE	35.62	55.78	20.9	7.2
HCB	69.52	84.74	73.45	8.67
PCB IUPAC#[a]				
105	8.43	7.19	4.47	2.36
118	7.68	6.49	5.4	3.71
138 [+163+164][d]	22.32	24.67	27.75	5.82
153	14.13	16.32	13.18	5.55

* Half-life estimated with Tobit regression without adjusting for any covariates

** Half-life estimated with Tobit regression adjusted for vectors of intake and controls

*** Half-life estimated with linear regression (LR) using all respondents (adjusted for vectors of intake and controls)

**** Half-life estimated with linear regression (LR) eliminating respondents with increased POP level (adjusted for vectors of intake and controls)

[a] Congeners with ≥ 50% detection rate in MAWBs: IUPAC #s: 52, 70, 74, 84, 87, 95, 99, 101[+90], 105, 110, 118, 149[+123], 138[+163+164], 153, 180, 187

[b] Sum of IUPAC#s: 74, 99, 105, 118, 138[+163+164], 153, 180, 187

[c] Sum of IUPAC#s: 52,84,95,101,110,123[+149]

[d] Bracket indicates ‘minor’ congener based on aroclor concentration (Hansen, 1999)