

Modeling Blood Organic Mercury as a Function of Usual Fish Consumption and Demographics, Using NHANES Data

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Abstract

EPA is interested in understanding the relationship between usual (long-term average) fish consumption and blood organic mercury concentration. The publicly available NHANES survey files have dietary intake data from two 24-hour periods and measurements of blood total mercury and inorganic mercury. Recent NHANES releases also have organic mercury measurements. For earlier releases, calculation of organic mercury concentrations from total and inorganic concentrations using subtraction gives some negative values and is complicated by non-detects. As a result, organic concentrations were imputed using a Bayesian model. The National Cancer Institute (NCI) provides SAS macros for calculating regression calibration estimates of usual fish consumption; however, those macros can be very slow when using many predictors and may not converge. To complete the calculations within a reasonable time, we have used various approximations when imputing the organic mercury concentrations and fitting the NCI-model. This paper presents the modeling results and compares them to a Bayesian model that combines the estimation of usual fish consumption and imputation of organic mercury.

Key Words: Multiple imputation, Non-detects, NCI method, Box-Cox transformation, Skew-normal, Bayes MCMC

1. Introduction and Objectives

Mercury released into the environment is converted to organic methyl mercury in sediments and in the water column and bioaccumulates through aquatic food webs. This bioaccumulation leads to increased levels of methyl mercury in larger, older, predatory fish. In the U.S., exposure to methyl mercury in humans is largely through the consumption of fish (NRC, 2000). Methyl mercury exposure *in utero* is associated with adverse health effects, e.g., neurodevelopmental deficits such as IQ and motor function deficits in children (Mergler et al, 2007; NRC, 2000).

EPA is interested in the relationship between long-term (“usual”) fish consumption and blood organic mercury concentrations in women of child-bearing age (16–49). Mercury in the body has a half-life on the order of 45 to 70 days (Kershaw, Clarkson, and Dhahir, 1980; Sherlock, Hislop, Newton, Topping, and Whittle, 1984; Smith et al., 1994; Smith and Farris, 1996; Clarkson & Magos, 2006) and therefore average long-term fish mercury intake is thought to be a better measure of risk from eating fish than recent (prior 24-hour) exposure. For this work, we modeled the relationship between usual intake of mercury from fish and blood organic mercury, and evaluated the sensitivity of the results to the modeling assumptions.

2. Data

The data come from two sources, 1) NHANES survey data collected from 1999 to 2012; and 2) reported concentrations of mercury by fish species. Table 1 summarizes the NHANES data used in the analysis.

Table 1: NHANES variables used in the analysis

Variable	Transformations or categories	Model use
Blood mercury	Impute log-transformed organic mercury	All models
Fish consumption	Derived from the NHANES 24-hour dietary recall data (see below)	All models: used to calculate usual intake
Reported number of meals with fish in last 30 days	Recoded as: 0, 1, 2, 3, 4 to 5, 6 to 9, 10 to 15, More than 15	All models: used to calculate usual intake
Survey release	1999-2000, 2001-2002, 2003-2004, 2005-2006, 2007-2008, 2009-2010, 2011-2012	All models
Race Ethnicity	Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, Other Race - Including Multi-Racial	All models
Body weight	Log-transformed and centered	All models
Hematocrit	Log-transformed and centered	All models
Income	Under \$20,000, \$20,000 to \$44,999, \$45,000 to \$74,999, \$75,000 and Over, Over \$20,000, Refused/Don't know, Multifamily HH	Full model
Education	Less than, more than, or equal to the median education for the respondents age	Full model
Age	Converted to age in decades and centered	Full model
Cotinine	Log-transformed, entered as a cubic function	Full model
Alcohol consumption	Age less than 20, Fewer than 12 drinks per year, 12 or more drinks per year	Full model
Region of the country	US Census Regions: Northeast, Midwest, West, and South	Full model
Coastal versus non-coastal areas	Coastal areas are defined as counties bordering the Atlantic, Gulf, and Pacific coasts and the Great Lakes.	Full model

Variables above were included because they were found to be important in other analyses. We considered BMI, and height; however, these variables were not significant when body weight was in the model. Stepwise regression was used to assess possible interactions. The full model was fit at the NCHS data center. A simplified model with the most significant predictors from the full was used for comparing alternative model assumptions.

2.1 Processing the Dietary Recall Data to Calculate Mercury Intake from Fish

The NHANES 24-hour recall data include the U.S. Department of Agriculture (USDA) food codes from the Food and Nutrient Database for Dietary Studies (FNDDS) and amount consumed in grams for every item of food eaten by the respondent in the 24 hours immediately preceding the interview. All records in the 24-hour data file for women aged 16-49 years that were for fish-containing food codes were extracted. The

recipe file and 24-hour recall data were merged to calculate quantity of “as prepared” fish consumed. Raw fish weight conversion was based on the likely moisture loss due to cooking.

To estimate the amount of mercury ingested, for each species, the geometric mean mercury concentration in raw fish tissue was multiplied by the amount of raw fish consumed. We obtained fish tissue concentration data from states, the U.S. Food and Drug Administration, the National Oceanic and Atmospheric Administration, EPA Region 10, and studies published in the peer-reviewed literature. For most species we were able to find data within the 1999-2012 time period. However, for abalone and crayfish we used data from the Mercury Report to Congress (U.S. EPA 1997). The geometric mean was estimated using a mixed linear model predicting log-transformed fish tissue mercury concentrations, treating the data source as a random effect and modeling the error variance as a power function of the number of samples averaged to obtain the reported value. The average mercury concentration weighted by 30-day consumption frequency was used for unspecified fish species.

2.2 Sample Size

Following the NHANES analysis guidelines, for the analysis we used the MEC sampling weight to represent the non-institutionalized population in the United States. Of the 13,069 women aged 16 to 49 with MEC weights, 1,714 (16.2%) were excluded due to missing values in some analysis variables, leaving 11,355 for the analysis. The proportion of missing cases varied among demographic categories ($p < 0.05$). For the analysis reported in this paper, the data was not reweighted to adjust for the missing values.

3. Statistical Analysis

The statistical analysis was performed using SAS Institute Inc. Cary, NC, USA, software versions 9.3 and 9.4. 95% confidence intervals are presented for assessing precision. Statistically significant differences, when used, are based on 5% significance levels.

The statistical model assumes the log-transformed blood organic mercury concentration is a linear function of transformed usual intake of fish mercury and other predictors. However, the NHANES data have organic (methyl) mercury measurements for only the most recent release (2011-2012). For all releases the data include measurements of total and inorganic mercury. To fit the models, we imputed organic mercury measurements and calculated usual intake of mercury from fish for each respondent, creating 20 imputed data sets. Replicate weights were created using the JK2 method.

The National Cancer Institute (NCI) provides SAS macros for calculating regression calibration estimates of transformed usual fish consumption; however, those macros can be very slow when using many predictors and may not converge. To complete the calculations within a reasonable time, we have used various approximations when imputing the organic mercury concentrations and fitting the NCI model. The following subsections provide additional details.

3.1 Estimation of Usual Fish Mercury Intake

For the NCI method, consumption amounts reported in a 24-hour dietary recall are assumed to be unbiased estimates of the fish intakes. As a result, the blood mercury is assumed to be a function of the long-term arithmetic mean fish mercury intake.

Reported 24-hour fish and fish mercury consumption provide imprecise measures of usual intake. The two NHANES 24-hour recalls provide the opportunity to estimate the magnitude of the measurement error and adjust for the effect of measurement error in order to estimate the relationship between usual intake of fish mercury and blood organic mercury. The adjustment is based on a statistical model and is reasonable to the extent that the model is appropriate for describing the data and the measurement error.

The NCI method models the usual intake for individual i by modeling the probability that an individual consumes fish in any 24-hour recall period (P_i) and modeling the average amount of fish (or mercury from fish) consumed in a 24-hour recall period in which some fish was consumed (A_i). The models have random effects for each individual representing variation of an individual's probability or consumption amounts around the predicted population means. The random effects may be independent or correlated. Whether an individual consumes fish in a 24-hour recall r ($AteFish_{ir}$) is a binomial random variable with probability P_i . When fish is consumed in a 24-hour recall, the NCI model assumes the transformed amount consumed ($T(Amount_{ir})$) varies around the individual's long term mean in the transformed scale (M_i). In the NCI method, $T(\cdot)$ is a Box-Cox transformation. The long-term mean amount consumed is:

$$A_i = T^{-1}(M_i) E(T^{-1}(e_{ir}))$$

where $E(T^{-1}(e_{ir}))$ is the expected value of the within person random errors in the untransformed scale. With this adjustment, the estimated usual intake is an unbiased estimate of long-term fish or fish mercury intake. An individual's usual intake is:

$$U_i = P_i A_i$$

The usual intake can be used to predict log-transformed blood organic mercury concentrations using the following model:

$$\ln(OrgHg_i) = \sum_{j=1}^J X_{ji} \beta_j + F(U_i) \beta_U + e_i$$

where J is the number of predictors excluding usual intake and $F(U_i)$ is a transformation of usual intake.

NCI provides the MIXTRAN macro to fit the probability and amount models and the INDIVINT macro to estimate the expected value of the Box-Cox transformed usual intake to use in the regression model above. However, the NCI MIXTRAN macro was not used because:

- 1) The calculations for the full model were performed offsite at the NCHS data center with time constraints and, with many predictors and data from many respondents, the calculations took too long to complete;
- 2) With many predictors, the algorithms may fail to converge; and

- 3) When using NHANES survey weights and estimating the correlation between the random effects, the algorithms sometimes failed to converge.

As a result, we developed a method to approximate the NCI model fit, referred to as the EPA method (USEPA, 2014). The EPA method involves the following steps:

- 1) Fit a logistic regression to predict $Logit(AteFish_{ir})$ using the NHANES survey weights, but without the random effects, and saving the predicted logit values, Y_i .
- 2) To estimate the random effects for the probability model, fit the a model with one predictor and a random effect for each person (δ_{P_i}) (note: the intercept is set to zero):

$$Logit(AteFish_{ir}) = \delta_{P_i} + Y_i \beta_P$$

- 3) Fit a linear regression to predict $T(Amount_{ir})$ using the NHANES survey weights, but without the random effects, and saving the predicted values, Z_i .
- 4) To estimate the random effects for the amount model, fit the following model with one predictor and a random effect for each person (δ_{A_i}) (note: the intercept is set to zero and the slope is set to one):

$$T(Amount_{ir}) = \delta_{A_i} + Z_i + e_{ir}$$

3.2 Adjusting for Measurement Error

One approach for adjusting for measurement error is to jointly impute estimates of organic mercury and usual intake for each individual using a Bayesian model that models the measurement error process. By creating multiple imputed datasets, each with a different imputation of usual intake, we can calculate the parameter estimates and standard errors adjusted for the uncertainty due to measurement error adjustment and imputation (Rubin, 1987).

Regression calibration is another approach for adjusting for measurement error. The NCI macros include the INDIVINT macro to calculate the regression calibration estimate of Box-Cox transformed usual intake. For an individual's data, the regression calibration estimate is the expected value of the Box-Cox transformed usual intake for that individual. The regression calibration estimate of Box-Cox transformed usual intake can be written as $F(U_i) = RC(BC(U_i, \lambda))$, where λ is the parameter for transforming usual intake in the model predicting blood mercury. The parameter estimates for transformed usual intake should be relatively unbiased if log-transformed blood mercury is a linear function of $RC(BC(U_i, \lambda))$. Thus, for the full model λ was set to 0.7 so that the regression parameter for $RC(BC(U_i, \lambda))^2$, if included in the model, was small and not statistically significant. The regression calibration estimate of usual intake using the full sample survey weight was used as a predictor when imputing blood organic mercury.

The steps for fitting the regression calibration (R) model are:

- For each replicate weight w :

- Use the EPA method to fit a weighted model predicting usual intake.
- Calculate regression calibration estimate of transformed usual intake, $RC_w(BC(U_i, \lambda))$, using the NCI INDIVINT macro.
- Impute organic mercury as a function of $RC_0(BC(U_i, \lambda))$ for full sample weight and other predictors.
- For each combination of imputed dataset and replicate weight, predict log-transformed imputed organic mercury as a function of $RC_w(BC(U_i, \lambda))$ and other predictors
- Calculate the parameter covariance for each imputed data set (using the replicate weights) and the overall parameters and standard errors across imputed data sets (using the SAS MIANALYZE procedure).

The steps when using Bayesian joint imputation (B) are:

- Jointly impute usual intake and organic mercury using an unweighted Bayesian model fitting the probability, amount, and mercury models.
- For each combination of imputed dataset and replicate weight, predict log-transformed imputed organic mercury as a function of transformed imputed usual intake and other predictors.
- Calculate the parameter covariance for each imputed data set (using the replicate weights) and the overall parameters and standard errors across imputed data sets (using the SAS MIANALYZE procedure).

The following sections provide detail on assumptions regarding the distribution of reported consumption amounts, methods of imputing the organic mercury concentrations, and transformations of usual intake.

3.3 Distribution of Random Effects

Table 2 describes the four distributional assumptions considered for modeling the variance components in the amount model. In all cases, the variance components are assumed to be additive in the transformed units.

Table 2: Variance component assumptions

Label	Description
BC	After a suitable Box-Cox transformation, the within and between person variance components are assumed to be normally distributed.
SS	After a log-transformation, the two components are assumed to have a skew-normal distribution with common skewness parameter.
NS	After a log-transformation, the between person component is assumed to have a normal distribution and the within person component has a skew-normal distribution.
NN	After a log-transformation, the two components are assumed to have a normal distribution.

3.4 Transformations of Usual Intake

Table 3 shows transformations of usual intake used in different models.

Table 3: Transformations of usual intake

Label	Description
Q	A quadratic function of log-transformed usual intake.
B7	A Box-Cox transformation with $\lambda = .70$.
B0	A Box-Cox transformation with $\lambda = .01$ (the minimum λ for INDIVINT).
BL	A Box-Cox transformation for which λ is fit in the Bayesian model.

3.5 Imputation of Organic Mercury

Measurements of blood organic (methyl) mercury are only available from the most recent NHANES survey release (2011-2012). All years have measurements of total (THg) and inorganic (IHg) mercury. However, many of the inorganic and a few of the total mercury measurements are below the detection limit. Table 4 summarizes three methods that were considered for imputing blood organic mercury data for all respondents. Method 4 can only be applied if organic mercury (in this case methyl mercury) measurements are available for at least some respondents.

Table 4: Methods for imputing blood organic mercury

Imputation method	The imputed value estimates:	Details
1	Total mercury measurements with imputed non-detects	Non-detects are imputed assuming all measurements have a lognormal distribution
2	Approximate imputed organic mercury measurements	Non-detects for total and inorganic mercury are imputed as in method 1, then $Dif = THg - IHg$ $organic\ mercury = \frac{Dif + \sqrt{Dif^2 + .04}}{2}$
4	Imputed organic mercury true concentrations	Assume the true mercury concentration is the sum of the true organic and inorganic mercury concentrations and the organic and inorganic concentrations have a lognormal distribution. Assume the total, inorganic, and organic mercury measurements, after imputing non-detects, are equal to the corresponding true concentrations with additional multiplicative log-normally distributed measurement error.

3.6 Models Fit

Table 5 shows the models that we fit in order to evaluate the sensitivity of the results to different modeling assumptions. These models used the most significant predictors of those used in the full model. The model designations concatenate labels for the measurement error adjustment method, the variance component assumption, the imputation method for organic mercury and the transformation for usual intake.

Table 5: Models fit to assess sensitivity of the results to the assumed model

Model designation	Transformation of amount	Distribution of variance components		Organic mercury Imputation method	Transformation of usual intake
		Between Person	Within Person		
RBC2B0	BC($\lambda = .16$)	Normal	Normal	2	BC($\lambda = .01$)
RBC2B7	BC($\lambda = .16$)	Normal	Normal	2	BC($\lambda = .70$)
BBC1B7	BC($\lambda = .16$)	Normal	Normal	1	BC($\lambda = .70$)
BBC1BL	BC($\lambda = .16$)	Normal	Normal	1	BC($\lambda = \text{Fit}$)
BBC1Q	BC($\lambda = .16$)	Normal	Normal	1	Quadratic
BBC2Q	BC($\lambda = .16$)	Normal	Normal	2	Quadratic
BNN1Q	Log	Normal	Normal	1	Quadratic
BNS1Q	Log	Normal	Skew-normal	1	Quadratic
BSS1Q	Log	Skew-normal	Skew-normal	1	Quadratic
BSS2Q	Log	Skew-normal	Skew-normal	2	Quadratic
BSS4Q	Log	Skew-normal	Skew-normal	4	Quadratic

4. Results

4.1 Relationship between Usual Intake of Fish and Log-transformed Blood Organic Mercury

Figure 1 summarizes the full model fit using the EPA method and regression calibration (equivalent to the RBC2B7 model) and all predictors, including region and the coastal indicator that are available only at the NCHS computing center. The horizontal axis is scaled based on the Box-Cox transformation of usual intake in order to show the linear relationships fit in the model. The histogram shows the distribution of usual intake derived from the model fit. The slope between usual intake and blood organic mercury differs by race/ethnicity and body weight. For this model, non-Hispanic whites are more sensitive to fish mercury intake and Mexican Americans are less sensitive, relative to other race/ethnicity groups.

Figure 2 illustrates the significant effect of main effects after adjusting for the effects related to usual intake. Based on this model, there are significant organic mercury concentration differences across time related to survey release date, significant regional and coastal differences, and a significant increase in blood organic mercury associated with increasing education and increasing hematocrit.

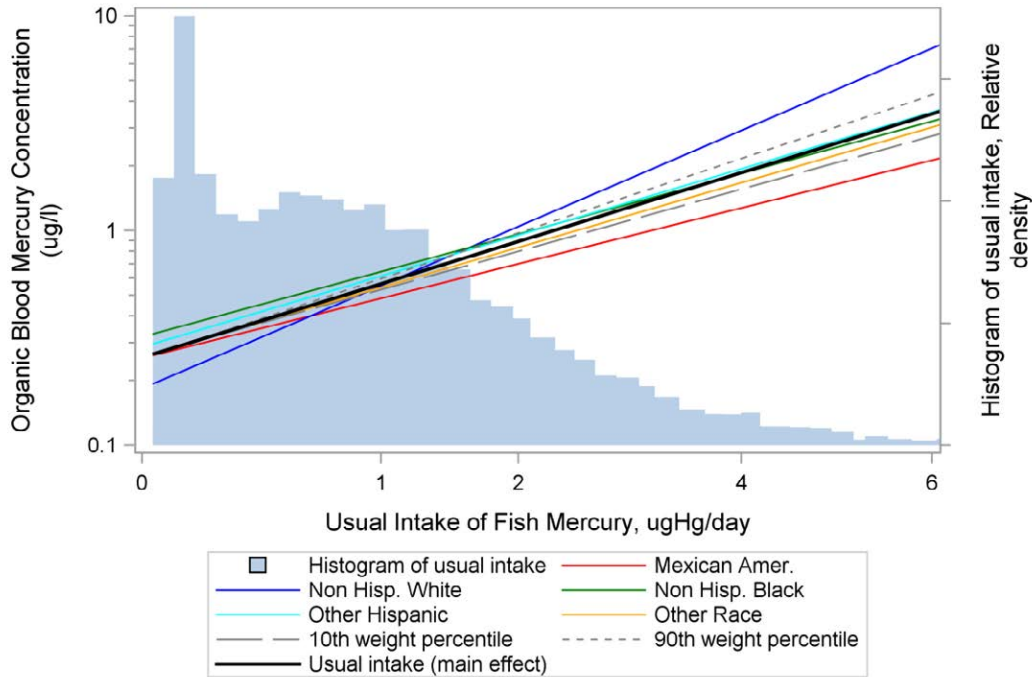


Figure 1: Predicted relationship between blood organic mercury and usual fish mercury intake after adjusting for other main effects.

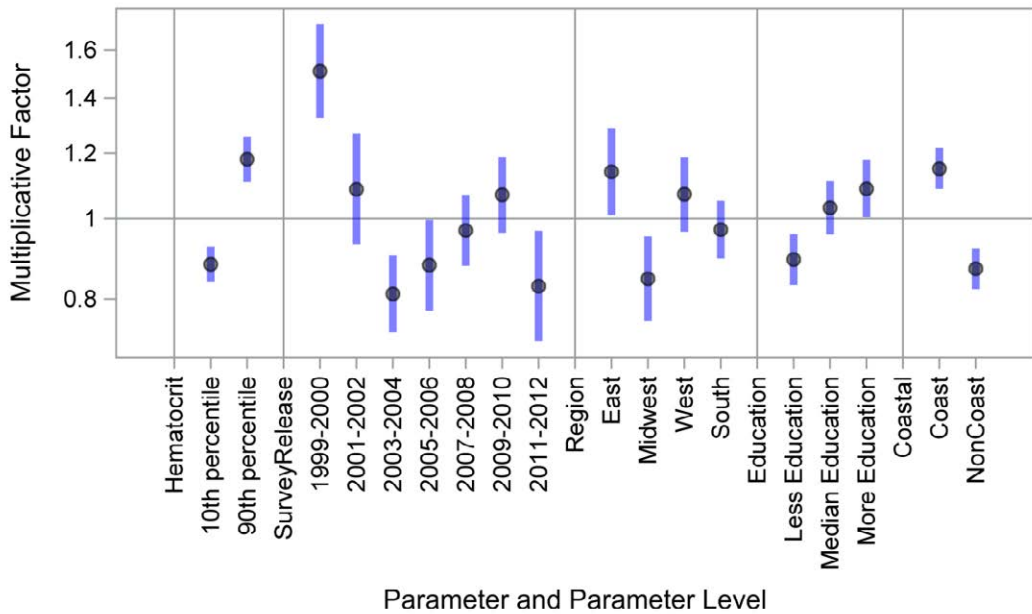


Figure 2: Predicted relationship between blood organic mercury and main effects after adjusting for usual fish mercury intake (only significant relationships are shown).

4.2 Sensitivity of the Model Results to Different Model Assumptions

The models provide information on characteristics of the data that cannot be directly observed, including: the distribution of usual intake, the distribution of organic mercury, and the relationship between these two. The following discusses these characteristics for the models that were fit.

The distribution of imputed usual intake depends in part on whether usual intake is imputed jointly with organic mercury. With joint imputation, the relationship between usual intake and organic mercury affects the imputation of usual intake. Figure 3 shows histograms of imputed log-transformed usual intake for four models which are variations on the model fit using all parameters:

- A regression calibration model similar to the full model (RBC2B7)
- A Bayesian joint imputation model that is essentially equivalent to the full model (BBC1B7) (it uses total instead of organic mercury)
- A Bayesian joint imputation model in which the Box-Cox transformation parameter is fit by the Bayesian model (BBC1BL). The fitted value suggested that a log transformation should be used, i.e., $\lambda=0$.
- A regression calibration model with $\lambda=0.01$ (RBC1B0)

The distribution for the regression calibrations models are essentially the same, as expected, because the transformation of usual intake when predicting organic mercury does not affect the regression calibration estimate of usual intake. The distribution of usual intake for the Bayesian BBC1B7 model is similar to that for the regression calibration models because 1) the same transformations are used and 2) $\lambda=-.7$ was selected so that the log-transformed organic mercury concentration is a linear function of transformed usual intake. However, when letting the Bayesian model select the best Box-Cox transformation of usual intake for predicting log-transformed organic mercury, a log-transformation is selected ($\lambda=0$). The distribution of imputed usual intake under this model is more normally distributed with a smaller standard deviation.

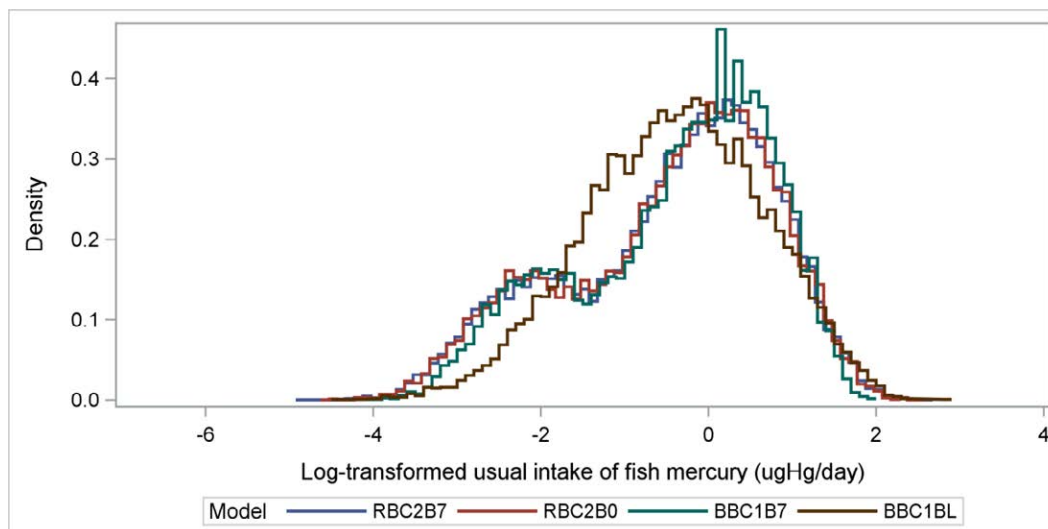


Figure 3: Distribution of imputed usual intake for models closely related to the full model.

Figure 4 shows the histograms of imputed usual intake in models with joint imputation of usual intake and organic mercury for which the Bayesian model selects of optimal quadratic transformation of log-transformed usual intake for predicting log-transformed

organic mercury. With joint imputation and a quadratic function, the distributions of imputed usual intake are roughly normally distributed. The distribution under the BBC2Q model has notably smaller variance for, as yet, unidentified reasons.

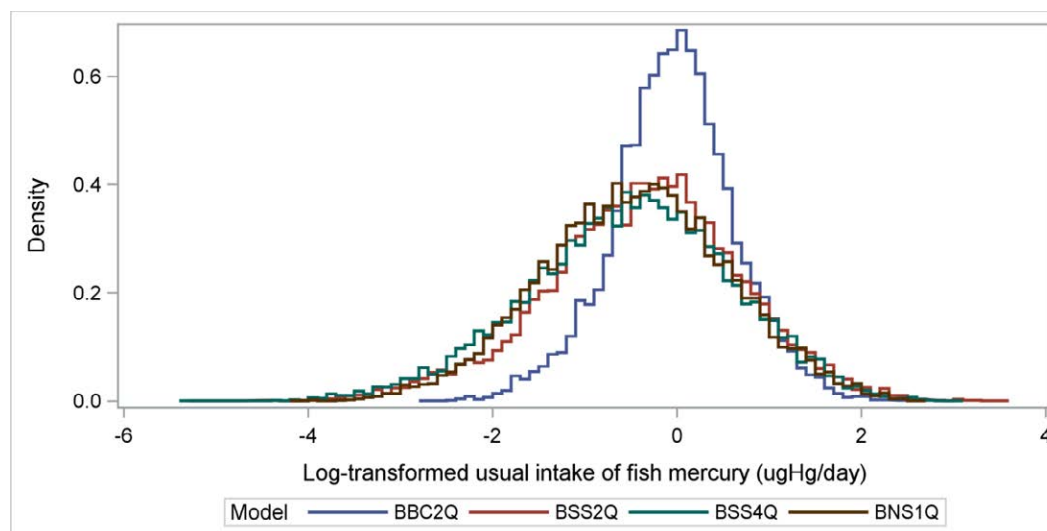


Figure 4: Distribution of imputed usual intake with joint imputation of organic mercury.

Although the distributions in Figures 3 and 4 differ somewhat in spread and shape, the upper percentiles of the distributions are relatively similar. Thus, estimates of upper percentiles of usual intake may be relatively insensitive to the modeling assumptions.

The distributions of organic mercury (not shown) are roughly normally distributed with similar distributions across models. Thus, the distribution of imputed organic mercury is relatively insensitive to the model assumptions.

Figures 5 and 6 show the modeled relationship between usual intake and blood organic mercury using different models. As with the full model shown in Figure 1, each relationship depends on the race/ethnicity category, more so for some models than others. These figures show the average relationship across race/ethnicity groups. If all mercury comes from fish consumption and the relationship between usual intake and blood mercury concentrations is linear, we would expect that doubling mercury intake would result in doubling blood mercury concentrations. This corresponds to a linear relationship between log-transformed usual intake and log-transformed blood organic mercury with a slope of 1.0. If some mercury comes from other sources, we would expect a slope less than 1.0. For reference, the figures show a line with slope = 1.0. The lines for each relationship extend from the first to the 99th percentile of the imputed usual intake for that model. All the curves shown in the figures are highly significant.

Of particular interest is the effect of different organic mercury imputation methods on the relationship between fish consumption and organic mercury. Figure 5 shows the modeled relationship for three imputation methods, all assume skew-normal variance components. If usual intake is most closely associated with organic mercury (as opposed to total mercury, as for the BSS1Q model), we would expect a stronger relationship and a higher slope for the relationship between imputed blood organic mercury and usual intake, as for BSS2Q and BSS4Q. Those slopes are close to 1.0 and suggest that most organic mercury can be attributed to intake of mercury from fish.

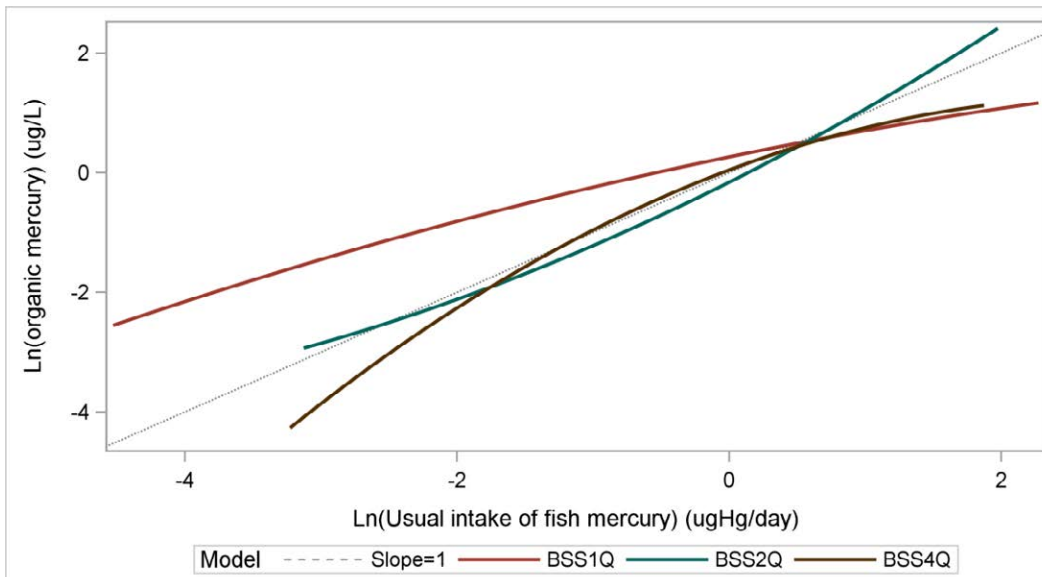


Figure 5: Relationship between usual intake and blood organic mercury, for different methods of imputing organic mercury.

Figure 6 shows the modeled relationship for the four models discussed in Figure 3. The full model (RBC2B7) shows a curved relationship between log-transformed blood organic mercury and log-transformed usual intake, as does the roughly equivalent Bayesian model (BBC1B7). When the Bayesian model fits the parameter for the Box-Cox transformation or the transformation of usual intake assumes $\lambda=.01$, the resulting curves are essentially straight lines (BBC1BL and RBC2B0). The choice of the function relating usual intake to organic mercury (quadratic, Box-Cox transformation with a fixed or variable parameter) constrains the model that is fit. We are still evaluating the alternative functions.

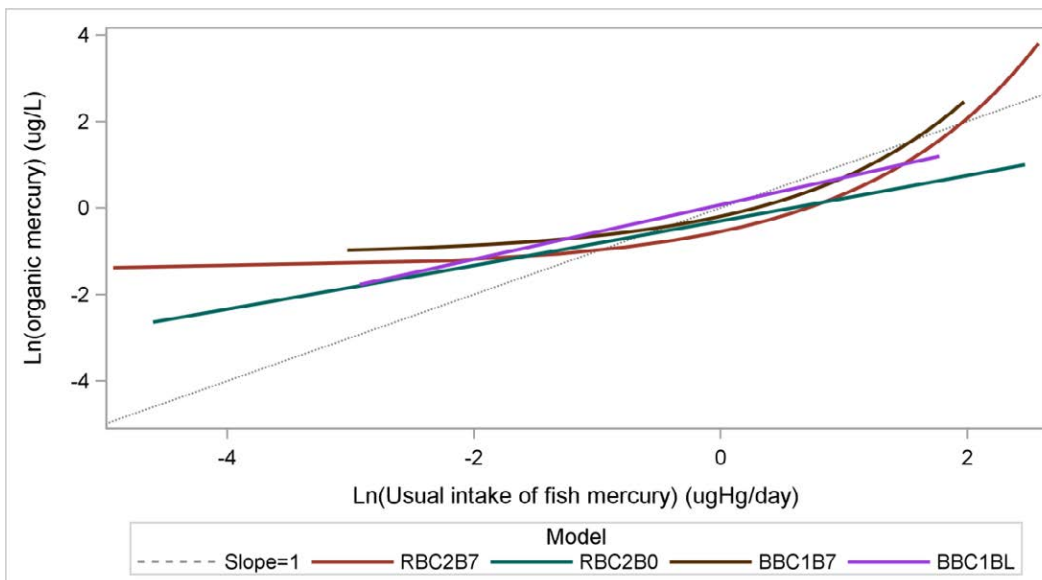


Figure 6: Relationship between usual intake and blood organic mercury, for model using imputation method 2.

The relationships using different variance component assumptions in the amount model are relatively similar and are not shown. Additional analysis is needed to evaluate the extent to which one set of assumptions is better than another.

Figure 7 compares the parameters for body weight, hematocrit, and survey releases for all models. Although the parameters are generally consistent across models, differences are larger than expected based on the confidence intervals. In general, blood mercury levels are highest in 1999-2000, relatively constant from 2001 to 2010, and a little lower in 2011-2012. However, specifics regarding trends over time will depend on both model assumptions and what trend is being assessed. Although blood mercury is generally inversely related to body weight, depending on the model, the slope is not always negative or significant. Hematocrit is positively related to blood organic mercury; however the slope is not always significant.

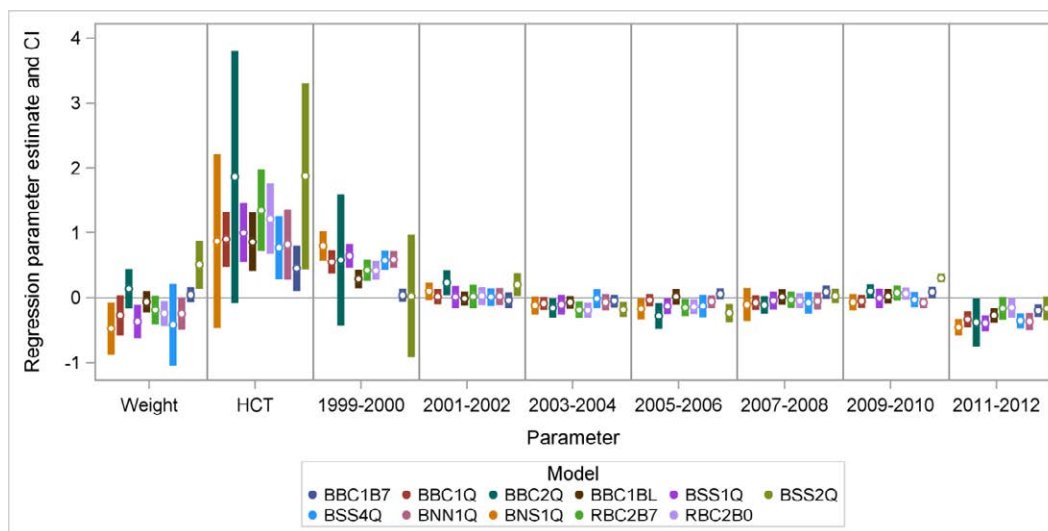


Figure 7: Main effect parameters and confidence intervals for all models.

Overall measures of model fit are somewhat difficult to construct. The models can be easily compared on how the mean imputed usual intake compares to the mean reported intake across individuals. However, the distribution of usual intake is skewed to the high side and the mean may be sensitive to small changes in the upper tails of the distributions. For comparison, the weighted mean intake in the input data is 1.24 ugHg/day. Another measure is the overall F-test for the weighted regression fit predicting organic mercury from usual intake. Higher F values correspond to higher r-squared and a better fit. Table 6 shows mean of the log-transformed F-value across all replicate weights and the mean of imputed usual intake. The table is sorted from smallest to largest F-value (worst to best fit).

Based on the F-tests, the Bayesian joint imputation models fit better than the regression calibration model. This might be expected because regression calibration, as a procedure, is more general than imputation. Regression calibration provides estimates of usual intake that can be used for predicting a linear relationship between usual intake and many other dependent variables. On the other hand, the Bayesian joint imputation provides estimates of usual intake that are expected to work best when assessing the relationship between

variables used in the imputation. This is particularly true when the relationship between usual intake and organic mercury is strong, as in this data.

Table 6: Overall measures of model fit sorted from worst to best overall F

Model	Mean Ln(Overall F)	Mean Imputed usual intake
RBC2B0	5.81	1.13
RBC2B7	5.91	1.15
BBC1B7	6.17	1.10
BBC1BL	6.67	1.10
BNN1Q	6.83	1.62
BBC1Q	6.84	1.07
BNS1Q	6.85	0.96
BSS1Q	6.94	1.14
BSS4Q	7.90	1.04
BBC2Q	8.22	1.17
BSS2Q	8.32	1.17

Bayesian joint imputation models predicting organic mercury (imputation methods 2 and 4) fit better than similar models predicting total mercury (imputation method 1). This is consistent with the prevailing belief that fish consumption is more closely related to blood organic mercury concentrations than to total mercury concentrations.

5. Discussion

For the models considered in this paper, increasing intake of mercury from fish is associated with statistically significant increases in blood total and organic mercury measurements; although the slope and linearity of the relationship depends on the model assumptions. These general results are consistent with previous work.

The analysis in Birch, Bigler, Rogers, ZShuang, and Clickner (2014) used estimated 30-day mercury intake calculated from the reported number of fish meals in the past 30 days and the average weight of fish in those meals estimated from the 24-hour recall data. The imputation of organic mercury was similar to imputation method 2 in this paper. Although the estimate of fish mercury intake and the list of covariates were different, the basic conclusions were similar in that mercury intake was a highly significant predictor of blood mercury. The models reported here improve on the previous work by estimating long-term “usual” mercury intake from fish using a model which adjusts for measurement error.

The analysis reported in Rothenberg et al. (2016) was restricted to respondents that consumed fish in the first dietary recall. This subpopulation will have a higher proportion of frequent fish consumers than the NHANES population. The analysis used total blood mercury measurements as an approximation to organic mercury. Nonetheless, the analysis provides useful results and finds a highly significant relationship between recent fish mercury intake and blood total mercury measurements. Their analysis used both men and women and was not able to use the reported frequency of fish consumption as a predictor because it was not available for all respondents in the analysis. The focus of their analysis was the relationship between BMI and blood mercury. After adjusting for other predictors, they found a negative relationship which is consistent with the generally negative relationship we found between body weight and blood mercury.

The models fit in these two papers are more different from the model fit using the EPA method and regression calibrations than are the Bayesian joint imputation models considered in this paper. Differences between the results in this paper and the results in other papers or between the various models considered in this paper help to emphasize that 1) conclusions about a strong positive relationship between mercury intake from fish and blood mercury concentrations are robust, but specific conclusions about more marginal predictors depend on the model selection.

Based on the F-tests, when predicting organic mercury from fish consumption, it is better to use organic mercury concentrations (whether actual measurements or imputed concentrations) than approximate organic mercury with total mercury concentrations. When concerned about long-term “usual” intake or fish or fish mercury, the NCI method or EPA method can be used. Overall, the Bayesian joint imputation appears to provide the best fit. However, fitting the model to impute usual intake and organic mercury and fit the subsequent model to predict organic mercury from usual intake is complex and very time consuming. The Bayesian model program used for this analysis (the SAS MCMC program) also has limitations such that using many more predictors or data from many more respondents may not be feasible.

Determining that there is a positive relationship between reported fish consumption and blood mercury measurements (whether total or organic mercury) is relatively easy. Fitting a model relating usual intake to blood organic mercury concentrations is more difficult and requires a theoretical model. We tried several alternative models to assess the sensitivity of the results to the model specification. Although there are criteria for saying that some models fit better than others, the results are still dependent on significant assumptions about the relationships and distributions. With data from more than two dietary recalls and organic mercury measurements on all respondents, it may be possible to select a generally accepted or preferred model. Until that data is available, modellers should recognize that variation among models can be significantly greater than implied by the confidence intervals for the parameters.

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