An Exposure Assessment for Methylmercury from Seafood for Consumers in the United States

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Abstract

An exposure model was developed to relate seafood consumption to levels of methyl mercury (reported as mercury) in blood and hair in the U.S. population, and two subpopulations defined as children aged 2 to 5 and women aged 18 to 45. Seafood consumption was initially modeled using short-term (3 day) U.S. consumption surveys that recorded the amount of fish eaten per meal. Since longer exposure periods include more eaters with a lower daily mean intake, the consumption distribution was adjusted by broadening the distribution to include more eaters and reducing the distribution mean to keep total population intake constant. The estimate for the total number of eaters was based on long-term purchase diaries. Levels of mercury in canned tuna, swordfish, and shark were based on FDA survey data. The distribution of mercury levels in other species was based on reported mean levels, with the frequency of consumption of each species based on market share. The shape distribution for the given mean was based on the range of variation encountered among shark, tuna, and swordfish. These distributions were integrated with a simulation that estimated average daily intake over a 360-day period, with 10000 simulated individuals and 1000 uncertainty iterations. The results of this simulation were then used as an input to a second simulation that modeled levels of mercury in blood and hair. The relationship between dietary intake and mercury blood in a population was modeled from data obtained from a 90-day study with controlled seafood intake. The relationship between blood and hair mercury in a population was modeled from data obtained from several sources. The biomarker simulation employed 2000 simulated individuals and 1000 uncertainty iterations. These results were then compared to the recent National Health and Nutrition Examination Survey (NHANES) that tabulated blood and hair mercury levels in a cross section of the U.S. population. The output of the model and NHANES results were similar for both children and adult women with predicted mercury biomarker concentrations within a factor of two or less of NHANES biomarker results. However, the model tended to under-predict blood levels for women and over-predict blood and hair levels for children.

Keywords: Methylmercury, Dietary Exposure, Biomarkers

Introduction

Methylmercury (MeHg) is a toxicant found in the aquatic environment that originates from anthropogenic and natural sources and can accumulate in fish and other marine species, particularly in long-lived and larger predators. MeHg exposure can cause neurological symptoms such as paresthesia, ataxia, dysarthyria, hearing defects, and death, and has also been associated with developmental delays in children whose mothers were exposed during pregnancy (WHO, 1990). Much of the information about the effects of MeHg comes from high-level poisoning episodes in Minimata and Nigata, Japan (Irukayama, 1977) and in Iraq (Bakir et al, 1973). However, there is also concern that MeHg can cause developmental delays or other neurological effects at lower levels of exposure more consistent with the usual patterns of fish consumption (Davidson et al, 1995, Grandjean et al, 1997).

Although significant uncertainty remains about the occurrence and levels of mercury in the environment, it appears that the global movement of mercury primarily involves inorganic forms (WHO, 1990). Elemental forms of mercury that arise from degassing from the earth's crust and oceans, generally do not accumulate in food. It is the conversion of inorganic mercury to the methylated form in the aquatic ecosystem that is of critical importance in terms of mercury in food. The methylation of inorganic mercury occurs primarily as a result of microbial activity. MeHg is enriched in aquatic food with the highest levels occurring in predatory fishes, particularly those at the top of the aquatic food chain. MeHg is also incorporated in the terrestrial environment by species that feed on aquatic organisms; however, enrichment does not occur to the same extent in the terrestrial food chain. Indeed, MeHg in fish and fish products is the predominant source of mercury in food, and, correspondingly, seafood intake is the primary source of concern for methylmercury exposure in the U.S.

In the present assessment, a model for MeHg exposure in the U.S. population was developed that yields estimates for blood and hair tissue levels resulting from seafood consumption (see Figure 1). Most of the model components are two-dimensional, with a statistical distribution describing the frequency of occurrence among individuals in the population and a parameter range and/or a probability tree to represent the uncertainty in the prediction. The components of the model were integrated with two separate two-dimensional Monte-Carlo simulations. First, a chronic exposure simulation was designed to produce an intake estimate for the U.S. population over a one-year period. This simulation employed distributions describing short-term (3-day) seafood consumption, methylmercury levels in various seafood species, and per capita consumption of individual species. The results of the exposure assessment were then used in a second biomarker simulation that employed distributions describing the relationship between average dietary MeHg intake and concentration in blood, and the relationship between blood and hair mercury. The results of the tissue concentration estimates were then compared to empirical results obtained from a recent survey of blood and mercury values in the United States (CDC, 2001).

Data and Model Development

Seafood Consumption

Estimates of daily seafood consumption were developed from data taken from the U S Department of Agriculture Continuing Survey of Food Intake by Individuals (CSFII) survey (USDA, 1998). The data used were accumulated between 1989 and 1991, which tabulated consumption over a three-day period. Records for all seafood consumption events were selected for all individuals for which a full three-day record was taken. Records for 3525 individuals were obtained. Two subpopulations were drawn from this set: women aged 18-44 (823 individuals) and children aged 2-5 (215 individuals). The survey data were provided with demographic weights that were used to project the survey to the U.S. population.

Short-term surveys often do not provide accurate estimates of long-term food consumption (Pastenbach, 2000). In particular, they tend to misrepresent infrequent consumers since they will either not count a consumer who did not eat during the survey period or they will project a higher average intake for an infrequent consumer who did. As a result, a short-term survey will underestimate the number of eaters and overestimate average daily intake for eaters for longer periods of time since they fail to count many consumers who consume a product infrequently. Furthermore, the survey may also not accurately reflect the pattern of seafood consumption. That is, individuals who consume a particular species during the survey period may consume other species over a longer period of time.

To compensate for the inaccuracy of short-term food intake surveys, several adjustments were made. First, the number of seafood consumption events was decreased and the number of eaters increased by a Short Term-Long Term Eater Ratio (LTSTCR) with an uncertain range of 2.1 to 2.6, which results in an estimated number of seafood consumers in a given year of 70 to 90% (see Table 1). The upper end of this range roughly corresponds to the value reported in a national purchase diary survey[1], in which 87.5% of the households interviewed reported consuming seafood at some point during the year. Since equal and opposite LTSTCRs were applied to the frequency of consumption and number of consumers, the per capita mean consumption of seafood was held constant (see Figure 2.)

However, because short term surveys are better at monitoring consumption patterns for frequent consumers, the LTSTCR in serving frequency was reduced for frequent seafood consumers using an exponential function that reduced the LTSTCR as the number of servings increased:

$$AS = \frac{D3S * 122}{LTSTCR^{\frac{x}{D3S}}}$$

where

[1] From unpublished study conducted by the Home Testing Institute (New York) on behalf of the National Fisheries Institute, released May, 1987

AS = Annual Servings
D3S = 3 Day Servings
LTSTCR = Long Term-Short Term Consumer Ratio
x = exponential slope

With x equal to -1, the reduction in the LTSTCR for high end consumers resulted in an increase in the per capita mean consumption of about 35% (the range was 29 to 42 %). Increasing the value of x will reduce the mean consumption. Because mean consumption depends on the distribution of short term consumption event serving frequencies in the data set used, the value of x required to maintain the per capita mean consumption will vary among surveys and foods. In this assessment, a value of 1.5 for x resulted in a mean per capita seafood consumption that is very close (the mean is increased by about 3%) to those obtained from the 3 day survey. The resulting relationship between 3-day servings and projected annual servings is presented in the last column of Table 3.

Short-term surveys also may also fail to portray variation in the types of seafood consumed. For example, an individual who consumes a particular species for every day of a three-day survey may consume other species at other times during the year. Since the levels of mercury in seafood vary considerably by species (see next section), this may significantly influence the exposure estimate for an individual. Therefore, individual exposure estimates employed both the survey data and per capita market share information to build a consumption pattern for each individual. Specifically, 20 to 80% (an uncertain range) of the species assignment for a given serving (see the exposure simulation section) came from the CSFII survey, while the remaining 80 to 20% was based on random assignment from a distribution based on market share (see Table 4).

Mercury Levels in Seafood

Distributions were constructed for 24 groups that represented 92% of the seafood consumed in the United States (see Table 4). Distributions for tuna, shark, and swordfish were generated empirically by directly sampling from FDA surveillance data (see Figure 3). Distributions for other species, where empirical distributions are unavailable, were generated with modeled distributions that reflected reported arithmetic mean values published from a National Marine Fisheries survey (NMFS, 1978) for each group and a range analogous to the ranges obtained from tuna, shark, and swordfish. Lognormal and Gamma distributions were used to represent the data, with each model assigned a probability of 0.5 to represent the model uncertainty. The magnitude of the shape parameters (the geometric standard deviation of the lognormal distribution and the beta parameter of the gamma distribution) were represented as uniform distributions that encompassed the range of values resulting from fitting the shark, swordfish, and tuna data (see Figure 3 and Table 5). The 7% of the seafood market not included in the top 24 species were assumed to follow the same distribution as the rest of the seafood market.

In order to combine the information concerning seafood consumption with the levels of mercury in seafood, it was necessary to map the 268 food codes employed in the consumer survey with the 24 groups used for reporting methylmercury levels. In most cases, the

correspondence was either direct or the seafood ingredient in the survey food code was a member of a MeHg contamination group. In a few cases, an analog was chosen. If there was no clear analog, several new distributions were created that combined multiple MeHg contamination groups. Specifically, groups were created for crabs, lobster, shellfish, finfish, and all seafood. Per capita market share was used to assign histogram frequencies for each group member.

Diet-Blood Relationship

While there are many studies that have attempted to relate dietary exposure to blood mercury levels, in most cases the correlation is very poor, with r values of 0.3 or less. This lack of correlation may be attributed in large part to the failure of short-term measurements of mercury exposure to gauge long-term dietary exposure (Sherlock and Quinn, 1981). The most suitable study for this assessment is that of Sherlock *et al.* (1984), in which male volunteers consumed controlled seafood diets with known mercury concentrations over a 100-day exposure period. After monitoring mercury blood values for the duration of the study, equilibrium values for a chronic diet-blood relationship were projected for each of the 20 individuals in the study. The mean body weight for the subjects in this study was 71 kg, with a range of 52 to 102. The relationship between dietary exposure and mercury blood level appeared to be linear with respect to dose. Although the ratio of mercury blood level to dietary exposure was inversely related to body weight, it was not directly proportional to body weight. Sherlock et al (1984) suggested a body weight dose metric of $BW^{1/3}$.

Sherlock et al (1984) extrapolated steady-state blood levels from two other parameters (a and b). Since the extrapolated steady-state levels that were reported in the papers were not corrected for body weight, the values for each of the 20 subjects were recalculated using $BW^{1/3}$ to normalize all values to a BW of 70 kg. In order to characterize the measurement error for each subject, 40 bootstrap data sets were generated from the standard deviations reported for each parameter estimate. Each bootstrap set was then fit by 10 different frequency distributions using least squares regression. Three weighted models were retained per bootstrap, which were assigned probabilities on the basis of goodness-of fit and number of parameters (Carrington, 1996). The resulting 120 models were then employed as a probability tree to characterize uncertainty from measurement error and model selection (see Figure 4 and Table 6).

Blood-Hair Relationship

Individual subject data were obtained from two studies in which blood and hair measurements were taken from the same subjects. The first study is from a population of adult males (Sherlock et al, 1982). A linear regression analysis of the two variables indicated a slope of 0.367 ppm in hair per ppb in blood, with a correlation coefficient of 0.837. Sherlock et al (1984) indicated that the blood mercury measurements reported in their earlier paper were 30% below levels obtained with other methods. Hair/blood ratios from Sherlock et al (1982) are plotted in Figure 5 with the blood values multiplied by a factor of 1.3.

A second study reported hair and blood measurements from a population of pregnant women with a high rate of fish consumption (Marsh et al, 1996b). Individual subject data were obtained from the authors. Blood/hair ratios from this study are also plotted in Figure 5. The hair/blood ratios and variance appear to be somewhat higher for the subjects from the Sherlock study with relatively low blood mercury levels. This may be attributed to low-level environmental contamination of hair with inorganic mercury and possibly other sources of measurement error that have much greater impact at low levels (Sherlock et al, 1982). The contribution from environmental mercury may be somewhat greater in the Sherlock study, since the hair samples were not washed prior to assay. At higher levels of exposure, the results of the studies appear to be quite similar.

For the purposes of predicting hair levels from given blood levels, an empirical distribution was constructed by pooling data from both the studies. Out of concern for the apparent measurement errors associated with the low-level measurements from the Sherlock et al (1982) study, values from individual subjects with blood value below 10 ppb were excluded. The resulting data set contained 159 observations.

Simulations

Simulation models were constructed in Microsoft Excel and are available from the authors on request.

Exposure Simulation

The exposure assessment was constructed around the individuals in the survey. This strategy maintained the information about individual characteristics associated with each estimate of mercury exposure. It also retained the limited information present in the 3-day survey about long-term consumption patterns.

The simulation consisted of three iterative loops that with the following logical structure:

Begin Uncertainty Loop
- Resample Distribution for MeHg Concentration
- Resample % Consumers (70-90%), Calculate 1 Year/3 Day Eater Ratio
- Resample Fish Consumption Pattern (% CSFII vs Per Capita)
- Begin Individual Variability Loop
  - Calculate Average Exposure for Individual
  - Calculate Annual Servings
  - Begin Inner Loop: 1 Year Simulation of Seafood Intake
    - Resample Fish Species
    - Resample MeHg Concentration
    - Calculate and Sum MeHg Intake
  - Next Serving
  - Calculate and Record Average Daily MeHg Intake
- Next Individual

Calculate and Record Per Capita Population Distributions
Next Uncertainty Iteration

The Uncertainty loop consisted of 200 iterations and contained the uncertainty distributions developed for MeHg concentration in seafood and projection of the short-term consumer survey to long-term seafood consumption patterns were re-sampled within this loop. The random numbers used for each iteration were generated prior to running the simulation. This allows post-hoc investigation of individual results and allowed the Consumer Ratio to be carried forward to the biomarker simulation. Each iteration of the second Variability loop consisted of an individual from the CSFII survey who consumed one or more servings of seafood during the 3-day survey. The number of servings and average serving size for each individual are calculated at this step.

The annual number of servings was then used to set the number of iterations for the third loop, in which in each iteration simulated a seafood consumption event. First, a random number was used to select the information source (CSFII or per capita) to be used for the serving. Specifically, if the random number is less than the percentile ranging from 0.2 to 0.8 selected at the outset of the uncertainty iterations, a randomly selected CSFII record for the individual was used to identify the species and the serving size. Otherwise, a species was randomly selected from a histogram distribution based on per capita disappearance rate, and the average serving size for the individual was used. Second, the mercury concentration for the species consumed by randomly sampling from either an empirical distribution (shark, swordfish, and tuna) or a modeled distribution using a mean value from NMFS data and a distribution selected at the outset of the uncertainty iteration. MeHg intake from the serving was then calculated by multiplying serving size by concentration. After completion of the specified number of servings, total MeHg intake for the year was summed from all the servings, and then divided by 366 to yield an average daily MeHg exposure. This number was recorded along with the age, sex, body weight, and demographic weight for the individual. After completion of the middle and outer loops, a two- dimensional array was produced with dimensions of 200 uncertainty iterations by 3525 variability iterations. These were stored and used as the basis for the biomarker simulation (see next section).

At the end of each variability loop, per capita population percentiles were calculated. This was accomplished by generating a frequency histogram from the 3525 estimates where the width is proportional to the demographic weight provided with the survey. Individuals not consuming seafood were included in the distribution by introducing a value of zero for the fraction of non-consumers. The percentage of seafood consumers was calculated by multiplying the number of consumers in the three-day survey by the Consumer Ratio for the current uncertainty iteration. Subtraction of the resulting value from one yielded the fraction of non-consumers. The results of the simulation are presented in Table 7.

Biomarker Simulations

Three biomarker simulations were constructed to predict population distributions for

mercury in blood and hair. Each simulation consisted of a two-dimensional Monte-Carlo routine with an outer uncertainty loop and an inner variability loop with the following logical structure:

Begin Uncertainty Loop
    Randomly Select Uncertainty Iteration from Exposure Asssessment
    Randomly Select Population Model for Diet-Blood Ratio
    Begin Individual Variability Loop
        Randomly Select Individual from Exposure Assessment
        Randomly select Diet-Blood Ratio from Population Model
        Randomly select Blood-Hair Ratio from Empirical Distribution
        Calculate and Record Predicted Blood Value
        Calculate and Record Predicted Hair Value
    Next Individual
    Calculate Population Distributions
Next Uncertainty Iteration

A simulation for the entire population was run with 10000 variability iterations and 1000 uncertainty iterations. Two simulations were also run with subsets of the exposure simulation corresponding to women aged 18-44 and children aged 2-5 with 5000 variability iterations and 1000 uncertainty iterations.

At the outset of each uncertainty iteration, one of the 200 uncertainty iterations from the exposure assessment and a population model for the diet to blood ratio were randomly selected. The variability loops were then run with random selection of the individual from the exposure assessment, the diet/blood ratio from the population model, and the blood/hair ratio from the empirical distribution. Random numbers for the variability iterations were generated prior to the simulation and the same set of values were used for each uncertainty iteration. These values were then used to calculate blood and hair values for each individual. At the conclusion of each variability loop, per capita population percentiles were calculated in the same manner the percentiles for daily MeHg intake.

Results

Levels of Mercury in Blood

Estimates for levels of mercury in blood are given in Table 8. The primary percentiles are estimates of the variability in mercury levels while the confidence intervals reflect the range of estimates produced by the uncertainty analysis.

Comparison of a subset of these percentiles to values obtained from a recent national survey (CDC, 2001) are given in Table 9 for adult women and children. The age ranges for the population groups are similar, but not exactly the same. The correspondence between the model and the survey values are within a factor of two at all percentiles for both women and children. However, when compared to the survey values, the estimates are consistently lower for women and consistently higher for children (see Figure 7).

Levels of Mercury in Hair

Estimates for levels of MeHg in hair are given in Table 9. The primary percentiles are estimates of the variability in mercury levels while the confidence intervals reflect the range of estimates produced by the uncertainty analysis.

Comparison of a subset of these percentiles to values obtained from a recent national survey (CDC, 2001) are given in Table 11 for adult women and children with similar age ranges. The correspondence between the model and the survey values is much better for adult women than for young children. For adult women the central values are very close and the confidence intervals overlap at all percentiles. For children, although there is overlap of the confidence intervals, the central values differ by a factor of 2 at both the 75th and 90^{th} percentiles (see Figure 8).

Discussion

The primary motivation for the development of these simulations is to provide an analytical tool that relates methylmercury intake from seafood to blood and hair levels in the U.S. population. The exposure analysis establishes a baseline analysis of current conditions and compares the simulation results with data obtained from a recent national human mercury biomaker survey (CDC, 2001). The simulation results indicate a close approximation to the biomarker survey data, with predicted mercury levels in both matrices within a factor of 2 for the range of distribution compared (up to the 90^{th} percentile).

For several reasons, it would be difficult to construct a chronic diet to biomarker exposure assessment with the same accuracy for most other environmental contaminants, since the quality of consumption and residue information is usually not as good. First, while MeHg exposure is largely restricted to seafood, the sources of exposure to many environmental contaminants are often more widely distributed (e.g. lead and dioxin). Second, the levels

of other contaminants in various foods are usually much less well characterized. Although models were employed to extrapolate the distributions for some species, the fact that the model has enough data to describe differences among species is a luxury that is not available for other environmental contaminants. Third, for the relationships between dietary exposure and biological indices there are insufficient data to characterize a population distribution as well as central tendency.

Still, better data could improve the exposure assessment. The most significant need is for better characterization of long-term seafood consumption habits. Without the adjustment to high frequency consumers in the short-term survey, the projected biomarker levels from long-term seafood consumption are under-predicted at the higher percentiles. Although there is an intuitive basis for the adjustment (short-term surveys better characterize frequent consumers), the adjustment itself is arbitrary. Adding an adjustable parameter to the exponential function might improve the fit of the model to the NHANES data. However, the wider distribution for the biomarkers might also be attributed to other sources of variation. In particular, the species consumption patterns for each consumer may be more highly correlated than is specified in this assessment. Furthermore, all species may not have the same degree of correlation. For example, many individuals may eat primarily tuna, while other species are more uniformly distributed.

The exposure model in this assessment uses a scaling factor of body weight to the one-third power to adjust predicted blood levels for individuals of varying size. Although this factor was suggested by Sherlock et al (1984), the primary justification for using it is empirical – the exposure assessment over-predicts the blood concentrations for children, if the more traditional practice of scaling directly to body weight is employed. However, the assessment still over-predicts children. Since the high frequency adjustment to the calculation of the number of annual servings of seafood resulted in an elevation of the per capita mean intake of about 35%, reducing the entire distribution by 26% might be justified. However, since the same factor would need to be applied for all three populations, the estimates for adults would then be too low. A reduction in the estimate for children could be obtained by further reducing or eliminating the influence of the weight variable in the diet to blood simulation.

The blood levels reported by NHANES are measurements taken at a single time point. As a result, they do not represent steady state levels. Individuals who consumed seafood shortly before the blood samples were collected may have had levels that were considerably higher than steady state. This may account for the under prediction of blood levels in adult women. The fact that NHANES hair levels were predicted more accurately than blood levels supports this interpretation.

Irrespective of the influence of recent seafood consumption, the model also clearly under-predicts NHANES blood levels at lower percentiles in adult women. This may be attributed to mischaracterization of seafood consumption patterns by low-frequency consumers or the omission of other low level sources of mercury exposure. Since the NHANES measurements (like most of the other mercury determinations used for the analysis) report total mercury, the lower levels may partially reflect exposure to inorganic

mercury. Since exposure to inorganic mercury largely comes from sources other than seafood (WHO, 1990), this exposure is not included in this assessment. However, as long as the decisions involving dietary exposure to mercury are driven by higher exposures, the low-level biomarker predictions are of little practical significance.

Since the survey estimates are probably more reliable than the prediction resulting from the simulation, the purpose of this exposure assessment is not to produce estimates of mercury in blood and hair. Instead, the intent is to relate those mercury tissue levels to seafood consumption and methylmercury levels in seafood across the U.S. population. The model may then be used to relate putative interventions designed to alter either the amount of seafood consumed or levels of methylmercury in seafood to expected changes in human mercury tissue levels. When combined with a dose-response function (e.g. Carrington and Bolger , 2000) the assessment may be expanded to calculate both initial risk, and predict the change in risk that may be expected as a result of appropriate risk management intervention. This exposure assessment should be particularly useful for use as part of an analysis that is intended to balance two or more risks, costs, or benefits (e.g. Ponce *et al*, 2000)

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References

Bakir F, Damliji SF, Amin-Zaki L, Murtadha M, Khalidi A, Al-Rawi NY, Tikriti S, Dhahir HI, Clarkson TW, Smith JC, and Doherty TW. (1973). MeHg Poisoning in Iraq. *Science 181*:230-241.

Carrington, C.D. (1996). Logical Probability and Risk Assessment. *Human Ecol Risk Assesst 2*:62-78.

Carrington, C.D. and Bolger, P.M. (2000). A Pooled Analysis of the Iraqi and Seychelles Methylmercury Studies. *Human Ecol Risk Assess 6*:323-340.

CDC (Center for Disease Control and Prevention) (2001). Blood and Hair Mercury Levels in Young Children and Women of Childbearing Age -- United States, 1999. *MMWR 50*:140-3

Cox, C., Clarkson, T.W., Marsh,D.O., Amin-Zaki, L., Tikriti, S., and Myers, G. (1989). Dose-response analysis of infants prenatally exposed to methylmercury: An application of a single compartment model to single strand hair analysis. *Environ Res 49*:318-332.

Cox, C., Marsh, D.O., Myers, G.J., and Clarkson, T.W. (1995). Analysis of data on delayed development from the 1971-1972 outbreak of methylmercury poisoning in Iraq: Assessment of influential points. *Neurotoxicol 16*:727-730.

Crump, K., Viren, J., Silvers, A., Clewell, III H., Gearhart, J., and Shipp, A. (1995). Reanalysis of dose-response data from the Iraqi methylmercury poisoning episode. *Risk Anal 15*:523-532.

Davidson, P., Myers, G. Cox, C., Shamlaye, C., Clarkson, T., Marsh, D., Tanner, M., Berlin, M., Sloane-Reves, J., Cernichiari, E., Choisy, O.and Chor, A. (1995). Longitudinal Neurodevelopmental Study of Seychellois Children Following In Utero Exposure to MeHg from Maternal fish Ingestion: Outcomes at 19 and29 Months. *Neurotoxicol 16*: 677-688.

Evans, M. Hastings, N., and Peacock, B. (1993). *Statistical Distributions, 2nd Ed.* John Wiley & Sons, New York.

Grandjean, P, Weihe, P., and White. R., (1995). Milestone Development in Infants Exposed to MeHg from Human Milk. *Neurotoxicol 16*: 27-34. ,

Grandjean, P., Weihe, P. White, R., Debes, F., Araki, S., Yokoyama, K., Murata, K., Sorensen, N., Dahl, R. and Jorgensen, P. (1997). Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. *Neurotoxicol Teratol. 19*:417-428.

Irukayama K, Tsubaki T, Shirakawa K, Hirota K, Kondo, K, Sato T, and Kanbayashi K (1977). History and Background. In*: Minamata Disease,* Tsubaki T and Irukayama K (Eds), pp. 1-102.

Kjellstrom, T., Kennedy, P., Wallis, S. and Mantell, C. (1986). Physical and mental development of children with prenatal exposure to mercury from fish. Stage 1: preliminary tests at age 4. National Swedish Environmental Protection Board Report 3080.

Marsh, D., Clarkson TW, Cox C, Myers GJ, Amin-Zaki L, and Al-Tikriti S. (1987). Fetal MeHg poisoning. Comparison of mercury levels in maternal blood, fetal cord blood, and placental tissues. *Arch Neurol 44*:1017-1022.

Marsh D., Clarkson TW, Myers GJ, Davidson PW, Cox C, Cernichiari E, Tanner MA, Lednar W, Shamlaye CF, Choisy O, Hoareau C, and Berlin M. (1995a). The Seychelles Study of Fetal MeHg Exposure and Child Development. *Neurotoxicol 16*:583-596.

Marsh D., Turner MD, Smith JC, Perez VMH, andAllen P, and Richdale N (1995b). Fetal MeHg study in a Peruvian fish eating population. *Neurotoxicol 16*:717-726.

Myers, G.J., Davidson ,P.W., Shamlaye, C.F., Axtell, C.D., Cernichiari, E, Choisy, O., Choi, A., Cox ,C., and Clarkson, T.W. (1997). Effects of prenatal methylmercury exposure from a high fish diet on developmental milestones in the Seychelles child development study. *Neurotoxicol 18*:819-830.

NMFS (National Marine Fisheries Service Survey of Trace Elements in Fishery Resource), NOAA Technical Report NMFS SSRF-721, 1978.

Pastenbach, D.J. (2000). The practice of exposure assessment: A state-of-the-art review. *J. Toxicol Environ Hlth B 3*:179-291.

Ponce, R., Bartell, S., LaFlamme, D., Carrington, C., Lee, R., Faustman, E. and Bolger, M (2000).: Quantitative analysis of risks and benefits for public health decisions applied to fish consumption: use of QALY weighted dose-response modeling. *Risk Anal 20*:529-542.

Sherlock JC, Lindsay DG, Hislop JE, Evans WH, and Collier TR (1982). Duplication diet study on mercury intake by consumers in the United Kingdom. *Arch Environ Health 37*:271-278.

Sherlock JC, Hislop J, Newton D, Topping G., and Whittle K (1984). Elevation of mercury in human blood from controlled chronic ingestion of MeHg in fish. *Hum Toxicol 3*:117-131.

Sherlock JC and Quinn M (1988). Underestimation of dose-response relationship with particular reference to the relationship between the dietary intake of mercury and its concentration in blood. *Hum Toxicol 7*:129-132.

U.S. Department of Agriculture, Agricultural Research Service (1998). 1989-91 Continuing Survey of Food Intakes by Individuals and 1989-91 Diet and Health Knowledge Survey on CD-ROM. Accession Number: PB96-501747

Yess, N (1993). U.S. Food and Drug Administration survey of methyl mercury in canned tuna. Journal AOAC International 76:36-38

World Health Organization (WHO), International Program on Chemical Safety, *Environmental Health Criteria 1*, 1976

World Health Organization (WHO), International Program on Chemical Safety, Environmental Health Criteria 101, 1990.

Table 1: Projected Seafood Consumers for a One Year Period

Population	*3-day Consumers in Survey*	*Projected 1 Year Consumers*
All Persons	33.5%	70 - 90%
Adult Women	35.7%	75 - 93%
Children 2-5	27.9%	58 - 72%

The projected values were obtained by multiplying the 3-day values by a range of 2.1 to 2.6, which was chosen to generate a range of 70-90% in the total population.

Table 2: Annual Servings Projected From 3-Day Surveys

Servings Survey		Projected Servings	
3 Day Servings	Servings per Day	Annual Servings	Servings per Day
1	0.33	29 to 40	0.08 to 0.11
2	0.66	119 to140	0.33 to 0.38
3	1	227 to 257	0.62 to 0.69
4	1.33	341 to 369	0.93 to 1.01

The range for the annual survey projections reflects the range for the LTSTCR.

Table 3: Selected Percentiles for Estimated Daily Seafood Consumption

Frequency	*Consumers=70%*	*Consumers=90%*	*With High Frequency Adjustment*
10^{th} Percentile	0.0	0.0	0.0 (0.0, 0.0)
25^{th} Percentile	0.0	5.0	1.6 (0.0, 3.7)
Median	8.9	10.4	6.8 (5.0, 8.8)
75^{h} Percentile	21.2	20.7	17.2 (14.0, 20.8)
90^{th} Percentile	37.9	33.7	41.5 (36.9, 47.0)
95^{th} Percentile	39.9	34.8	62.7 (56.2, 69.2)
99^{th} Percentile	51.0	44.5	123.2 (112.8, 131.3)
99.5^{th} Percentile	90.4	73.1	141.3 (135.1, 148.4)
99.9^{th} Percentile	110.5	90.9	206.6 (196.8, 218.8)

All units are g seafood-day. The first two columns give the range resulting from the Short-Term to Long-Term Eater Ratio Adjustment (LTSTCR). The third column gives the median and confidence intervals for the estimated seafood intake after the phase out of the LTSTCR for high frequency consumers. The frequency distributions are tabulated on a per capita basis, which includes non-consumers.

Table 4: Share of Seafood Market by Top 20 Species

SPECIES	*POUNDS PER CAPITA*	*% OF MARKET*	*MEAN HG (ppm)*
CATFISH (AQUACULTURE)	1.02	0.0689	0.05
CLAMS	0.46	0.0311	0.02
COD	1.057	0.0714	0.12
CRABS-BLUE	0.24	0.0162	0.15
CRABS-DUNGENESS	0.054	0.0036	0.17
CRABS-KING	0.037	0.0025	0.09
CRABS-SNOW	0.092	0.0062	0.15
CRAWFISH (AQUACULTURE)	0.065	0.0044	0.05
FLATFISH	0.33	0.0223	0.09
HALIBUT	0.286	0.0193	0.31
LOBSTERS (AMERICAN)	0.093	0.0063	0.46
LOBSTERS (SPINY)	0.093	0.0063	0.12
OCEAN PERCH	0.056	0.0038	0.06
OYSTERS	0.22	0.0149	0.05
POLLOCK	1.64	0.1108	0.15
ROCKFISH	0.127	0.0086	0.20
SABLE FISH	0.024	0.0016	0.27
SALMON	1.299	0.0878	0.05
SARDINES	0.18	0.0122	0.03
SCALLOPS	0.25	0.0169	0.04
SHARK	0.02	0.0014	0.96
SHRIMP	2.7	0.1824	0.05
SWORDFISH	0.08	0.0054	1.07
TUNA, CANNED	3.1	0.2095	0.17

Table 5: Fitted Distribution Parameters for Shark, Swordfish, and Tuna

	Lognormal		Gamma	
Species	Mean	GSD	alpha	beta
Shark	0.78	0.59	3.16	0.28
Swordfish	0.81	0.37	7.59	0.11
Tuna	0.134	1.07	1.02	0.19

The distributions were fit by minimizing least squares for the residuals of the predicted distribution percentiles (see Figure 3). Although empirical distributions were used for the three species listed above, the range of GSD and beta values obtained with these three species were used to describe the distribution of MeHg concentrations in other species.

Table 6: Sample Output for Modeled Diet (μg/day) / Blood (ppb) Ratio

Cumulative Frequency	Model Prediction
Median	0.80 (0.78, 0.84))
90th Percentile	0.94 (0.88, 0.99)
95th Percentile	0.93 (0.91, 1.04)
99th Percentile	1.01 (0.94, 1.18)

Sample output from the function used to predict dietary blood levels from a given daily dietary MeHg exposure. Values are given for the median estimate with the 5th and 95th percentiles as confidence intervals.

Table 7: Estimated Methylmercury Exposure from Seafood for Three U.S. Populations

Cumulative Frequency	*All Persons*	*Women 18-44*	*Children 2-5*
25th Percentile	0.2 (0.0, 0.4)	0.2 (0.0, 0.3)	0.0 (0.0, 0.0)
Median	0.8 (0.6, 1.0)	0.8 (0.7, 0.8)	0.3 (0.2, 0.3)
75th Percentile	2.0 (1.6, 2.5)	2.0 (1.9, 2.1)	0.9 (0.8, 1.0)
90th Percentile	4.9 (4.3, 5.5)	4.6 (4.4, 4.8)	2.2 (1.9, 2.5)
95th Percentile	7.1 (6.4, 7.8)	6.5 (6.1, 6.9)	3.5 (3.1, 3.9)
99th Percentile	12.7 (11.6, 14.1)	11.3 (10.0, 12.6)	6.4 (5.6, 7.4)
99.5th Percentile	15.3 (13.9, 17.1)	12.9 (11.8, 14.6)	7.2 (6.3, 8.8)

All units are median values for the entire uncertainty distribution, with 5th and 95th percentiles of the uncertainty distributions (confidence intervals) given in parentheses. The units are μg MeHg/ day.

Table 8: Estimated Blood Mercury Levels for Three U.S. Populations

	All Persons	*Women 18-44*	*Children 2-5*
10th Percentile	0.0 (0.0, 0.0)	0.0 (0.0, 0.1)	0.0 (0.0, 0.0)
25th Percentile	0.1 (0.0, 0.3)	0.2 (0.0, 0.3)	0.0 (0.0, 0.0)
Median	0.6 (0.6, 0.7)	0.7 (0.6, 0.7)	0.3 (0.2, 0.4)
75th Percentile	1.7 (1.6, 1.8)	1.7 (1.6, 1.8)	1.2 (1.1, 1.4)
90th Percentile	4.0 (3.9, 4.2)	3.7 (3.4, 3.9)	2.1 (1.8, 2.5)
95th Percentile	5.7 (5.4, 6.0)	5.0 (4.7, 5.4)	3.4 (3.0, 4.0)
99th Percentile	10.0 (9.2, 10.6)	9.9 (8.8, 11.4)	8.2 (7.2, 9.4)

All units are median values for the entire uncertainty distribution, with 5th and 95th percentiles of the uncertainty distributions (confidence intervals) given in parentheses. The units are ppb MeHg.

Table 9: Comparison of Estimated Blood Mercury Levels to NHANES IV Blood Mercury Levels

	Women 18-44	***Women 16-49***	***Children 2-5***	***Children 1-5***
	Simulation	**NHANES**	**Simulation**	**NHANES**
10th Percentile	0.0 (0.0, 0.1)	0.2 (0.1,0.3)	0.0 (0.0, 0.0)	<LOD
25th Percentile	0.2 (0.0, 0.3)	0.5 (0.4,0.7)	0.0 (0.0, 0.0)	<LOD
Median	0.7 (0.6, 0.7)	1.2 (0.8,1.6)	0.3 (0.2, 0.4)	0.2 (0.2,0.3)
75th Percentile	1.7 (1.6, 1.8)	2.7 (1.8,4.5)	1.2 (1.1, 1.4)	0.5 (0.4,0.8)
90th Percentile	3.7 (3.4, 3.9)	6.2(4.7,7.9)	2.1 (1.8, 2.5)	1.4 (0.7,4.8)

The simulation values (ppb MeHg) are median estimates with confidence intervals given in parentheses. The mean values and confidence intervals for the NHANES survey are taken from MMWR (2001).

Table 10: Estimated Hair Mercury Levels for Three U.S. Populations

	All Persons	*Women 18-44*	*Children 2-5*
10th Percentile	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)
25th Percentile	0.0 (0.0, 0.1)	0.1 (0.0, 0.1)	0.0 (0.0, 0.0)
Median	0.2 (0.2, 0.2)	0.2 (0.2, 0.2)	0.1 (0.1, 0.2)
75th Percentile	0.5 (0.5, 0.6)	0.5 (0.5, 0.6)	0.4 (0.3, 0.4)
90th Percentile	1.3 (1.3, 1.4)	1.2 (1.1, 1.3)	0.8 (0.7, 0.9)
95th Percentile	2.0 (1.9, 2.1)	1.8 (1.7, 1.9)	1.2 (1.1, 1.4)
99th Percentile	3.8 (3.6, 4.1)	3.4 (3.1, 3.9)	2.1 (1.7, 2.4)

All units are median values for the entire uncertainty distribution, with 5th and 95th percentiles of the uncertainty distributions (confidence intervals) given in parentheses. The units are ppm MeHg.

Table 11: Comparison of Estimated Hair Mercury Levels to NHANES

	Women 18-44	***Women 16-49***	***Children 2-5***	***Children 1-5***
	Simulation	**NHANES**	**Simulation**	**NHANES**
10th Percentile	0.0 (0.0, 0.0)	<LOD	0.0 (0.0, 0.0)	<LOD
25th Percentile	0.1 (0.0, 0.1)	<LOD	0.0 (0.0, 0.0)	<LOD
Median	0.2 (0.2, 0.2)	0.2 (0.2,0.3)	0.1 (0.1, 0.2)	<LOD
75th Percentile	0.5 (0.5, 0.6)	0.5 (0.4,0.8)	0.4 (0.3, 0.4)	0.2 (0.1,0.4)
90th Percentile	1.2 (1.1, 1.3)	1.4 (0.9,1.7)	0.8 (0.7, 0.9)	0.4 (0.3,1.8)

The simulation values are median values with confidence intervals given in parentheses. The mean values and confidence intervals for the NHANES survey are taken from MMWR (2001).

Figure 1 : Strucure of the Exposure Assessment

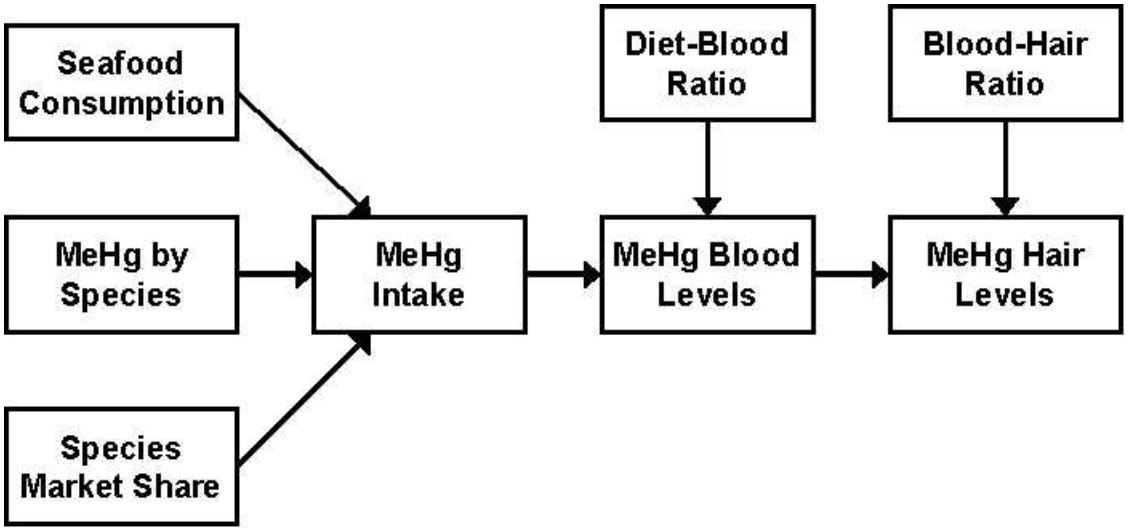
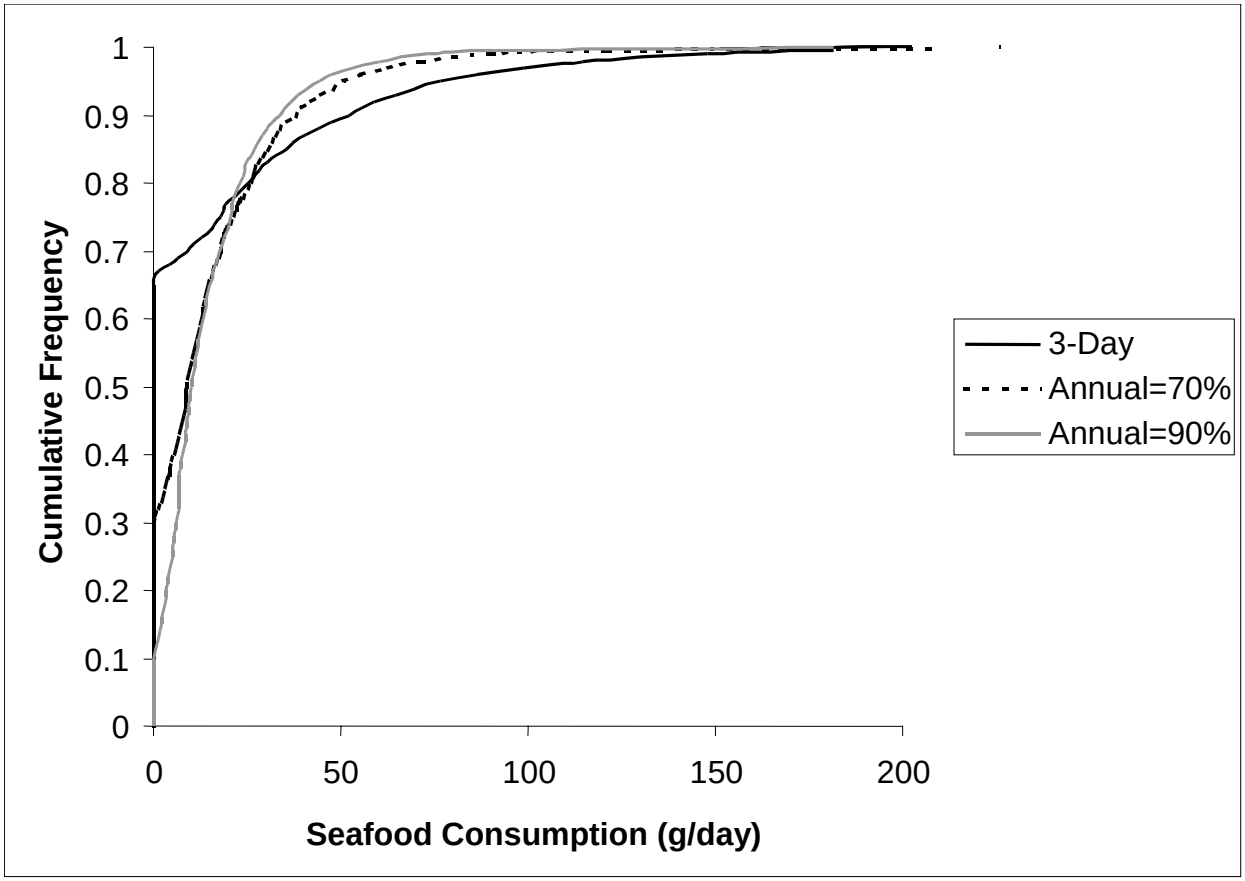
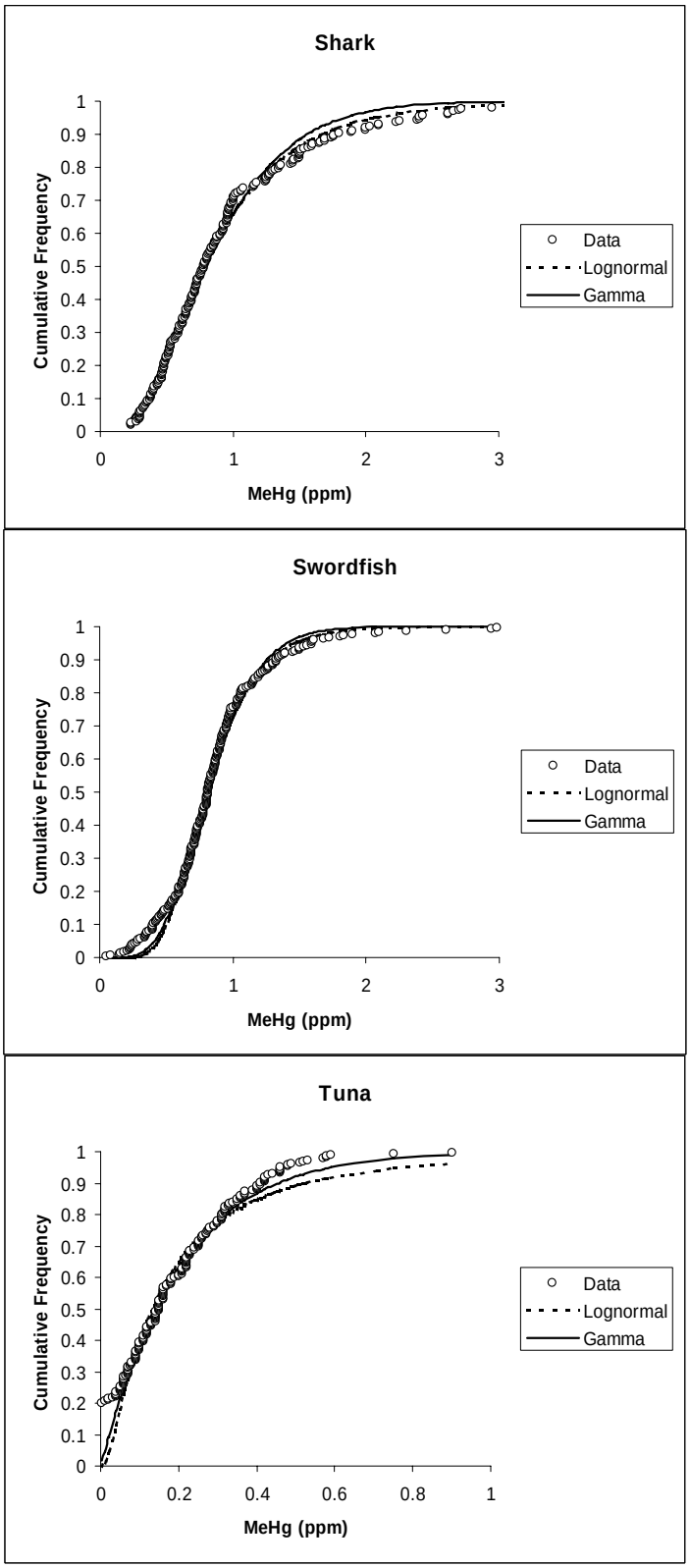


Figure 2: Adjustment for Short-term to Long-term Population Seafood Consumption



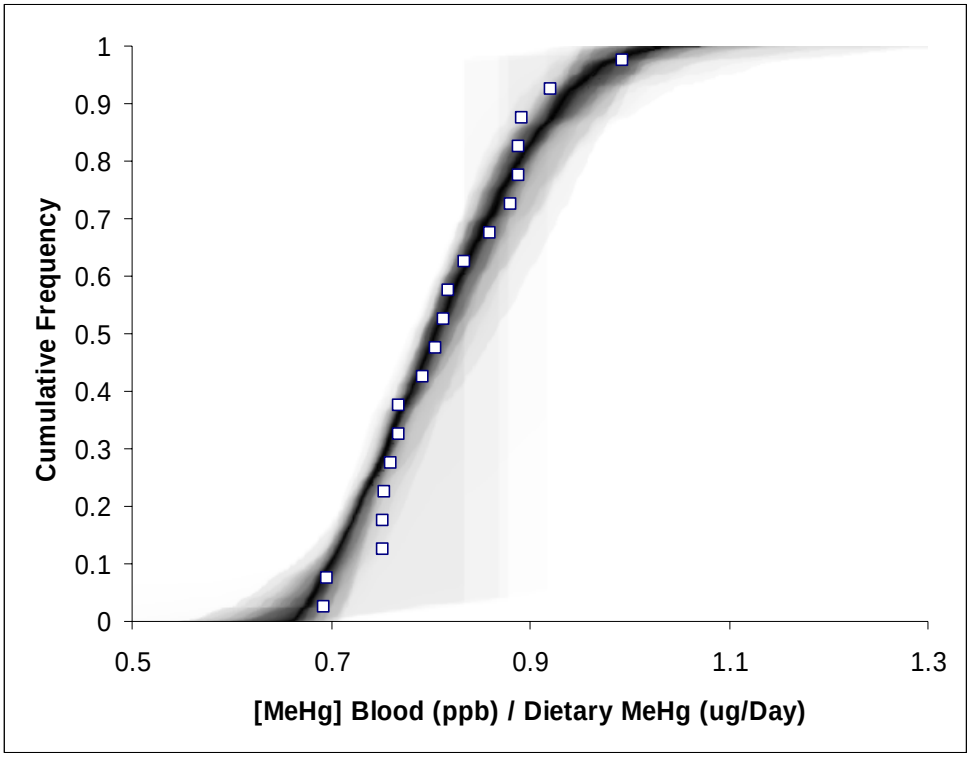
The dashed line reflects the results of a three day dietary consumption survey in which the number of adult women consuming seafood was about 33% of the total population. The other two lines represent uncertainty bounds where the number of persons consuming seafood at any time over a one year period is between 70 and 90%, with daily percapita intake held constant.

Figure 3: MeHg Concentrations in Shark, Swordfish, and Tuna



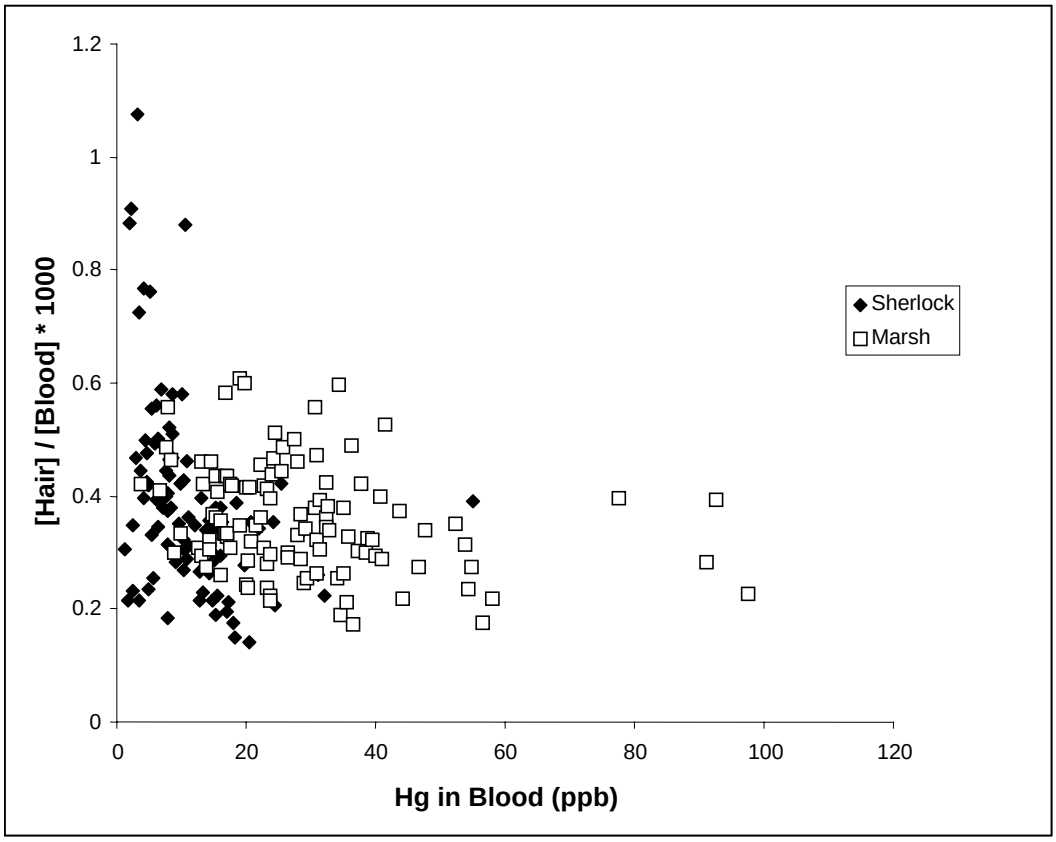
Cumulative distributions for MeHg in shark swordfish, and tuna, with fitted lognormal and gamma distributions. The tuna data we re previously published in Yess (1993). The shark and swordfish data are FDA surveillance samples collected in 1992-93 using the the same methodology.

Figure 4: Variability in Diet/Blood Ratios



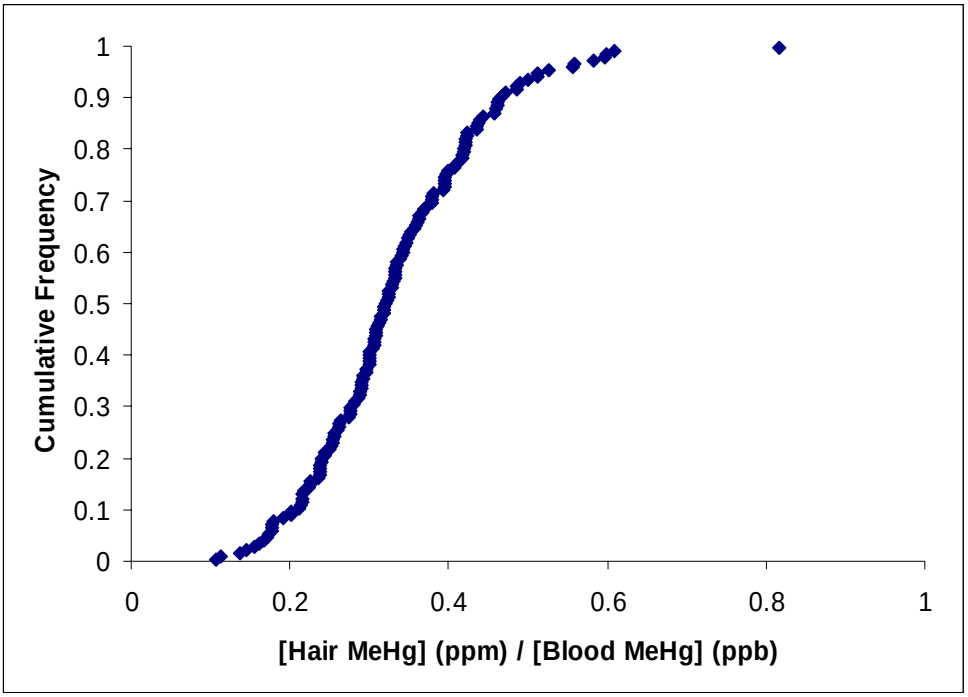
The points are the mean estimates taken from Sherlock et al (1984), while the gray-scale curve illustrates the probability function drawn from the data.

Figure 5: Mercury in Blood and Hair; Data from Two Studies



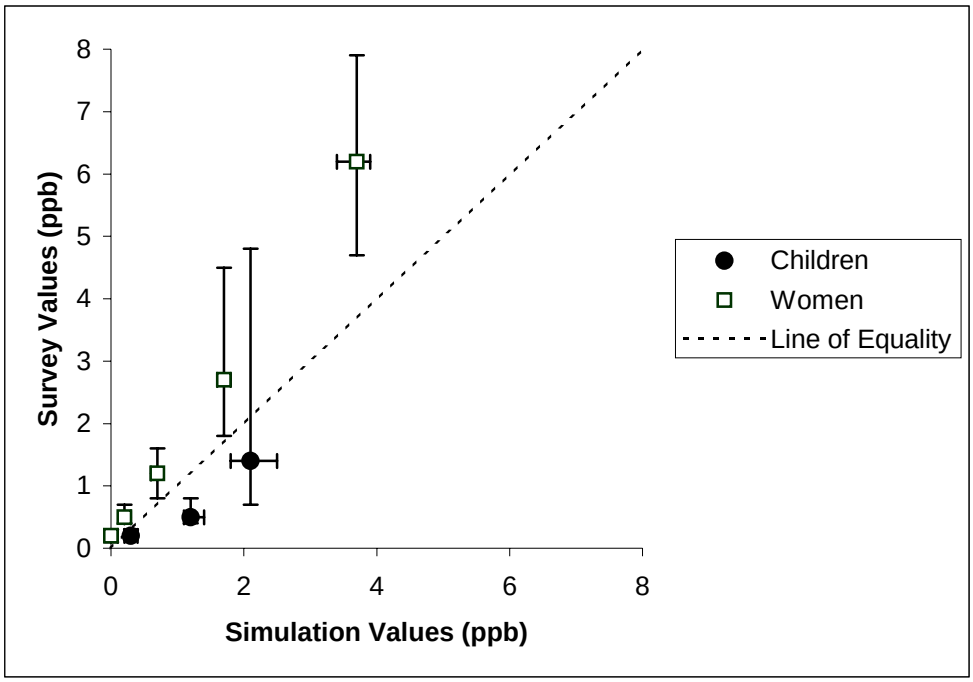
The data labeled “Scotland” taken from Sherlock et al (1982), while the data labeled “Peru”is from Marsh et al (1995b).

Figure 6: Empirical Distribution for Hair/Blood Ratios



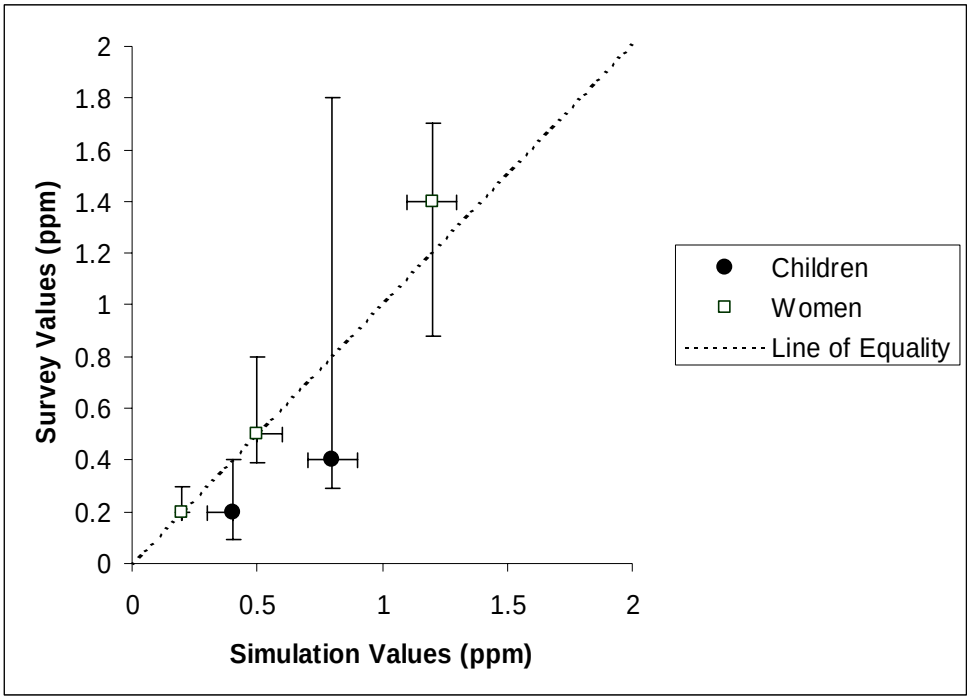
A plot of 159 observations pooled from Sherlock et al (1982) and Marsh at al (1996).

Figure 7: Quantile-Quantile Comparison for Blood Values



A quantile-quantile plot of the simulation predictions and NHANES survey values for mercury in blood. The units for both axes are ppb.

Figure 8: Quantile-Quantile Comparison for Hair Values



A quantile-quantile plot of the simulation predictions and NHANES survey values for mercury in hair. The units for both axes are ppm.