

**Probabilistic Modeling of Dietary Arsenic Exposure and Dose
And Evaluation with 2003-2004 NHANES Data**

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Competing Interests Declaration

All authors declare no potential competing financial interests.

List of Abbreviations and Definitions

ADME: absorption, distribution, metabolism, and excretion

As: Arsenic

iAS: Inorganic As

oAS: Organic AS

tAs: Total As

AsBetaine: Arsenobetaine, an organic form of As

CSFII: Continuing Survey of Food Intakes by Individuals

DMA: Dimethylarsonic

EOHSI: Environmental and Occupational Health Sciences Institute

EPA: U.S. Environmental Protection Agency

FDA: Food and Drug Administration

FCID: Food Consumption Intake Database

MENTOR: Modeling ENvironment for TOtal Risk Studies

MMA: Monomethylarsonic acid

NERL: National Exposure Research Laboratory

NHANES: National Health and Nutrition Examination Survey

NHEXAS: National Human Exposure Assessment Survey

OPP: Office of Pesticide Programs

ORD: Office of Research and Development

PBPK: physiologically-based pharmacokinetic

SHEDS: Stochastic Human Exposure and Dose Simulation

TDS: Total Diet Survey

US: United States

ABSTRACT

BACKGROUND: Dietary exposure from food to toxic inorganic arsenic (iAs) in the general US population has not been well studied.

OBJECTIVES: This research quantifies dietary As exposure, and analyzes the major contributors to total As (tAs) and iAs. Another objective was to compare model predictions to observed data.

METHODS: Probabilistic exposure modeling for dietary As was conducted with the SHEDS-Dietary model, based on data from the NHANES. The dose modeling was conducted by combining the SHEDS-Dietary model with the MENTOR-3P system. Model evaluation was conducted via comparing exposure and dose modeling predictions against duplicate diet data and biomarker measurements, respectively, for the same individuals.

RESULTS: The mean modeled tAs exposure from food is 0.38 ug/kg/day, which is ~14 times higher than the mean As exposures from the drinking water. The mean iAs exposure from food is 0.05 ug/kg/day (1.96 ug/day), which is ~2 times higher than the mean iAs exposures from the drinking water. The modeled exposure and dose estimates matched well with the duplicate diet data and measured As biomarkers. The major food contributors to iAs exposure were the following: vegetables (24%); fruit juices and fruits (18%); rice (17%); beer and wine (12%); and flour, corn, and wheat (11%). Approximately 10% of tAs exposure from foods is the toxic iAs form.

CONCLUSIONS: The general US population may be exposed to tAs and iAs more from eating some foods than from drinking water. In addition, this model evaluation effort provides more confidence in the exposure assessment tools used.

Introduction

Human exposure to As can occur via different routes. A well-known early medical report about As exposure and adverse health effects discussed cancer associated with dermal exposure to As-containing medication used

for treating some forms of skin diseases (Hutchinson 1887). Later studies on occupational populations exposed to As compounds in industrial environments demonstrated that respiratory inhalation is a primary route of occupational As exposure, but ingestion and dermal exposure can be significant in particular situations (OSHA 2005; WHO 2004).

Compared with the simpler As chemistry and easily-identified As exposure in medical and occupational fields, As chemistry and exposure routes for the general population are much more complex. General population As exposure varies according to local geochemistry, environmental pollution, living conditions, life styles, and activity patterns of the exposed populations. Better characterization of environmental As levels and human activity patterns is critical for accurately assessing the human exposure to As in the general population, and related health risks.

Many efforts in studying As exposure to and regulating As intake by the general population have been focused on the ingestion of As contaminated water (NRC 2001; Abernathy et al. 1999; Abernathy et al. 2003; Anetor et al. 2007; Chen et al. 1988a; Chen et al. 1988b; Chiou et al. 2001; Tchounwou et al. 2003). This drinking water-focused As regulation also reflects a common understanding that inorganic As (iAs) is more harmful than organic As (oAs) (Tchounwou et al. 2003). A recent publication concluded that typical and high-end background exposures to iAs in U.S. population do not present elevated risks of carcinogenicity (Boyce et al. 2008). However, there are also some reports which show significant dietary intake of iAs via food, and even show food as a greater source of iAs intake than drinking water (Schoof et al., 1999a,b; Meacher et al. 2002). A study has estimated dietary intake of iAs in U.S children as 3.2 ug/day on average (Yost et al. 2004). A recent study shows that, in three US counties, the food intake pathway is the dominant contributor to tAs exposure and dose (Georgopoulos et al. 2008).

This paper extends findings from the previous studies by (1) assessing the total and inorganic dietary As exposure using the peer-reviewed EPA SHEDS model (SHEDS, 2007), (2) using more recent and larger databases representative of the US population for food consumption and As concentrations in food and drinking water, and (3) conducting model evaluation using food consumption and biomarker data. We used a population-based dietary exposure model, one module of the Stochastic Human Exposure and Dose Simulation

(SHEDS) model (SHEDS 2007; Xue et al. 2006; Zartarian et al. 2006), to estimate the exposure of As (tAs and iAs) from both food and drinking water. The total predicted exposure was linked with the Modeling ENvironment for TOtal Risk with Physiologically based Pharmacokinetic modeling for Populations (MENTOR-3P) system (Georgopoulos and Liou, 2006) to estimate the speciated As in urine. The model results were compared with biomarkers of tAs and As species measured in the 2003-2004 National Health and Nutrition Examination Survey (NHANES 2003-2004). Using large data sets of food consumption from NHANES, As concentrations in drinking water and various foods from FDA and NRDC databases, and urinary biomarkers from NHANES (same individuals as for food consumption data), we demonstrate that dietary exposure can be a significant route for human exposure to both tAs and iAs.

Materials and Methods

Food consumption data. National Health and Nutrition Examination Survey (NHANES) data from 2003-2004 (NHANES 2003-2004) were used for model inputs regarding the amount of food and water consumed by individuals. This database contains 16,934 person-days of real-time dietary consumption data, i.e. amounts of food and drinking water recorded instantly by individuals for each separate eating occasion. The average number of eating occasions is ~4.8 times per person per day. The U.S. Environmental Protection Agency's Food Consumption Intake Database (FCID) containing a recipe file with 553 food commodities was applied where needed to break down NHANES food reported into raw agricultural commodities (RAC).

Total and inorganic Arsenic (As) concentrations in food and drinking water. Total arsenic residue data from the Food and Drug Administration (FDA)'s ongoing Total Dietary Survey (TDS), also known as the market basket study (FDA 1991-2004), were used. TDS collects and analyzes ~280 foods for pesticide residues, industrial chemicals, and toxic and nutrient elements. Foods collected in the TDS are prepared as "table-ready," i.e. as would be consumed, for realistic estimates of dietary intake of those targeted components. As water concentrations recorded in the Natural Resources Defense Council database (Natural Resources Defense

Council 2000) were used and assumed to be tAs. This database reported average and maximum As concentrations (a total of 8970 records) in water from 25 states in the US. The As drinking water concentration data were weighted by population and fitted for the best distribution, to yield a lognormal distribution with 1.03 ppb as the geometric mean and 4.06 ppb as the geometric standard deviation. We derived inorganic As (iAs) concentration in each food commodity by using iAs percentage in the same food category as reported by Schoof et al.(1999 a,b).

Biomarker data for As exposure. Urinary biomarker data from the same individuals for consumption data (2573 records) from the NHANES were used for comparing against model predictions during the same time period as the consumption data were collected. Detection rates for tAs, dimethylarsinic acid (DMA), Arsenobetaine (AsBetaine), and monomethylarsonic acid (MMA) were 98.9, 87.4, 66.7 and 36.2 percent, respectively. Because the detection rates for iAs and other species were very low (1 to 7 percent) our model evaluation study using biomarker data focused primarily on tAs.

Models used. A Stochastic Human Exposure and Dose Simulation (SHEDS) model developed by US EPA's Office of Research and Development (ORD)'s National Exposure Research Laboratory (NERL) (SHEDS 2007; Xue et al. 2006; Zartarian et al. 2006) was used for calculating dietary and drinking water As exposures for each eating occasion of individuals; estimating the ranges of population dietary exposures; identifying key factors and contributions of food types and chemicals; and quantifying uncertainties. The exposure outputs from this SHEDS-Dietary model were used for providing input for deriving target tissue doses and biomarker levels in the population-oriented physiologically based pharmacokinetic (PBPK) modeling of MENTOR-3P developed by the Environmental and Occupational Health Sciences Institute (EOHSI) and UMDNJ, R.W. Johnson Medical School and Rutgers University (Georgopoulos and Liroy, 2006).

Exposure modeling. For estimating daily dietary As exposure, the detailed NHANES food diaries were used by the SHEDS-Dietary model to simulate food ingestion exposures by separate eating occasions for a simulated

individual (Figure 1). SHEDS-Dietary can use residues for food items as consumed, as well as residues of raw agricultural commodities (RAC). The reported NHANES food items were matched with food items in the TDS where possible (see step 1 in Figure 1). If TDS residues for As were available for a particular food (e.g., rice, chicken), then SHEDS-Dietary randomly drew a TDS tAs or iAs residue from that corresponding residue distribution of the same food. Otherwise, the model applied the FCID recipe files to the NHANES food items and randomly selected a residue for each of the RAC ingredients according to the recipe (see step 2 in Figure 1).

Through the recipe files, the unmatched foods consumed were matched by RAC so that residues for those foods could be calculated. The SHEDS-Dietary model drew the same residue value if that RAC was found in the same foods. Assignment of residues for non-detect values depended on the commodity: if there was at least 1 detection, $\frac{1}{2}$ the limit of detection was assigned; if no As values were detected, zero values were assigned. For each NHANES food diary, SHEDS-Dietary was applied using Monte-Carlo simulation by selecting a residue value from an empirical distribution for each TDS food or RAC. While a particular commodity may be used in multiple foods, the cooking method may differ, and thus, it will have a different food form. Process factors can then be applied (see step 3 in Figure 1). These factors account for food changes and related concentration changes due to dilution, drying, etc., but were not used here due to the lack of sufficient such information for our study. Each simulated individual's exposure for each commodity was calculated by multiplying total daily consumption with corresponding residues. Aggregate daily exposure was calculated by summing exposures across all commodities (Equation 1). Summation of As exposures from every eating occasion for one day yielded the individual's daily tAs exposure (see step 4 in Figure 1). In principle, both food residues as well as drinking water concentrations may vary by eating occasion and/or across foods consumed within an eating occasion.

Equation [1]. Exposure Equation Used by SHEDS-Dietary

$$Exposure [mass\ chemical/ eating\ occasion] = \sum amount\ of\ food\ item\ consumed [mass] \times As\ concentration\ in\ the\ food\ item [mass\ chemical/ mass\ food] \times process\ factors$$

For modeling drinking water As exposures, we utilized the NHANES data to assess the timing and amounts of direct and indirect drinking water intake within a simulated person-day. Total drinking water consumed (both direct and indirect water, from tap, bottled, and other sources) was assumed to contain the same concentration level – i.e., only one concentration value was selected in the Monte Carlo simulation for each eating occasion. Water used in cooking is one example of indirect water. The modeled drinking water exposure algorithm in SHEDS-Dietary is similar to that used for food exposure (Equation 1). One residue value is randomly selected and multiplied by total water intake to obtain drinking water exposures. Although SHEDS-Dietary can be used to model longitudinal dietary exposure as well as cross-sectional exposure, this paper addressed only the cross-sectional exposure based on single day data.

PBPK modeling. MENTOR-3P was used to represent absorption, distribution, metabolism, and excretion (ADME) processes of As inside the human body by lumping together similar tissues as a set of physiological compartments. A “flow-limited” PBPK formulation, representing a simplification of a generalized PBPK Model of MENTOR-3P (Figure 2), was adopted here. This simplified PBPK model for As employed the model parameters in the work of Yu (1999a,b) including fractional blood flow rates, metabolism parameters, and tissue/blood partition coefficients. The modification of calculating tissue volumes and blood flow rate based on body weight was added to this simplified population-oriented PBPK model (see Georgopoulos et al., 2008 and references therein), such that the interindividual variability of these physiological parameters can be captured. The dynamics of four arsenic circulating species in body compartments — arsenates (AsV), arsenites (AsIII) and two As metabolites, MMA and DMA — were captured using this PBPK model. Also characterized were the corresponding biomarker levels in urine.

Model results evaluation. Two types of model evaluation were conducted: (1) SHEDS-Dietary predictions were compared to National Human Exposure Assessment Survey (NHEXAS) duplicate diet data; and (2) linked SHEDS-MENTOR predictions were compared to NHANES biomonitoring data. 156 duplicate food study

subjects in NHEXAS were matched by age, gender, and location with modeled results from SHEDS-Dietary (based on NHANES consumption diaries). To account for variability, the model was run 200 times for 156 matched subjects, and three cumulative distribution functions (CDFs) were selected according the 5th, 50th and 95th percentiles of the 200 simulations. Modeled estimates of tAs dose from the linked SHEDS-MENTOR predictions were compared with the NHANES urinary biomarker data for tAs. For the matched NHANES dietary consumption with NHANES biomarker data, 2355 records were available.

RESULTS Using the SHEDS-Dietary model it was calculated that the tAs exposure from food is 0.36, 1.28 and 1.40 ug/kg/day for the mean, the standard deviation, and the 95th percentile, respectively, for the whole simulated population (Table 1). The tAs exposure from food by young children (age 5 and younger) is higher (means ranged between 0.54 and 0.62) than that shown for other age groups (means ranged between 0.25 and 0.37) (Table 1). Based on mean values in Tables 1 and 2, the tAs exposure from food predicted by SHEDS-Dietary is, on average, ~14 times higher than the tAs exposure from drinking water. Arsenic exposures (iAs) from drinking water are 0.025, 0.104, and 0.107 ug/kg/day for the mean, the standard deviation, and the 95th percentile, respectively (Table 2). There is no clear age group difference in the drinking water As exposure.

The iAs exposure from food by young children (age 5 and younger) is higher (means ranged between 0.08 and 0.23) than that shown for other age groups (means ranged between 0.03 and 0.04) (Table 1). The iAs exposure from food predicted by SHEDS-Dietary model (Table 1) is on average 2 times higher than the tAs exposure from drinking water (Table 2). Thus, even if we assume all As in the drinking water exists in the iAs forms, the dietary food iAS exposure by the modeled general US population is still greater than the drinking water exposure. Summarizing the iAs contribution by food commodities, we estimate that about 10% of tAs exposure from foods is the toxic iAs form.

Among biomarkers analyzed for As exposure in the NHANES subjects, Arsenobetaine and DMA were shown at high concentrations with a mean as 8.4 and 5.4 ug/L, respectively, while the mean concentration for tAs in the urine was 18.4 ug/L (Table 4 supplement).

In comparing with the NHEXAS duplicate diet data, our SHEDS-Dietary modeling of tAs exposure from foods performed reasonably well (Figure 3). Among 156 paired comparisons, the mean \pm standard deviation of SHEDS-Dietary estimates for tAs exposure from food was 0.192 ± 0.561 ug/kg/day, as compared with 0.185 ± 0.3 shown by the duplicate diet analysis (Figure 3 insert table).

The linked SHEDS-MENTOR model also predicted well the tAs in urine (Figure 4). The SAS regression analysis showed a good fit with a slope of 1.4 and R^2 of 0.91 for the logarithmic-transformed predicted and measured values. The means of model predictions and NHANES urine measurements of tAs are 18.32 and 18.06 ug/L, respectively (Figure 4 insert table).

The five major food contributors to tAs exposure were fish (60%), shellfish (9%), rice (7%), fruit juices and fruits (5%), and meats (5%) (Figure 1 supplement). The major food contributors to iAs exposure were vegetables (24%), fruit juices and fruits (18%), rice (17%), beer and wine (12%), and flour, corn, and wheat (11%) (Figure 5).

DISCUSSION

It is challenging to study As exposure in the general human population because there are many variables affecting the processes and numerous limitations on obtaining relevant information. Unlike the study of occupational As exposure, where populations are relatively homogeneous, As compounds are easy to identify, and exposure routes are limited, As exposure in the general population is complicated with subject heterogeneity, different As species, and multiple exposure routes. Some information easily obtainable from industrial settings may be difficult or too expensive to obtain in general environmental settings. Another challenge is that As from the diet exists in many forms, most in organic form which is much less toxic than the inorganic form. Thus, it is important to consider the different As species in As exposure and risk analysis. Using some modeling approaches to estimate general human exposure to As and to identify some data gaps or assumption deficiencies is helpful for understanding As exposure in the general population.

Previous studies have shown that, for most people in the general population, diet may be the largest source of exposure to As (MacIntosh et al. 1996). For example, MacIntosh et al. reported that mean dietary intakes of

tAs is 50.6 ug/day for females and 58.5 ug/day for males (MacIntosh et al. 1997). Some recent studies suggested that dietary exposure to As may exceed the maximum As intake from drinking water in areas where elevated As levels were found in rice (Williams et al. 2007). Other studies have shown a greater intake of toxic iAs from food as compared with that from drinking water (e.g., Meacher et al. 2002). Schoof et al. (1999a,b) estimated that intake of inorganic As (iAs) in the US diet ranges from 1 to 20 ug/day, with a mean of 3.2 ug/day. An estimation of dietary iAs intake by U.S children was also made to be 3.2 ug/day on average, with a range of 1.6 to 6.2 (Yost et al. 2004). These estimations are close to values reported in another study which showed the average intake of iAs ranges from 1.34 ug/day in infants to 12.54 ug/day in 60-65 year-olds (Tao and Bolger 1998). However, these studies of dietary As exposure are usually based on the same assumed food intake values per person, and thus lack characterization of inter-individual variability of exposures. It was reported that lack of data about the actual amount of food consumed accounted for at least 80% of the total uncertainty for As exposure estimation (MacIntosh et al. 1996). MacIntosh et al. 1997 also pointed out that the food consumption-food composition approach adopted in the earlier MacIntosh et al., 1996 study did not capture all the As exposure as reflected from the empirical weight approach using toenail As concentration data as a validation.

In this study we used data from National Health and Nutrition Examination Survey (NHANES). NHANES is so far the most comprehensive survey including food intakes and has the unique advantage of containing biomarker information for the same subjects in the survey (NHANES 2003-2004). Biomarkers of exposure are independent measurements that can be used to evaluate the validity of dietary assessment methods and food composition data. Using the biomarker data from the same survey for model evaluation is more reliable, because it does not suffer from other complications such as differences between study groups related to location, lifestyle, living conditions, and other potential confounding factors.

The NHANES data are also more recent than data such as the Continuing Survey of Food Intakes by Individuals (CSFII) (ARS 1994-96) used in previous studies. In comparison with previous As exposure modeling, the Stochastic Human Exposure and Dose Simulation (SHEDS)-Dietary model used in this study

performed food item matching and incorporated usage factors in the modeling. The dietary intake estimation was also based on actual eating occasions (Figure 1).

Our modeling approach yielded estimates that are very compatible with the duplicate diet data (Figure 3). The mean and 95th percentile of modeled tAs exposure (0.192 and 0.723, respectively) were very comparable with As intakes from the NHEXAS duplicate food study (0.185 and 0.612 ug/kg/day, respectively) for the same age, gender, and location. The combination of the SHEDS-Dietary model with MENTOR-3P also predicted the urine tAs concentration that compares well with biomarker monitoring data in the NHANES (Figure 4). It predicted the tAs in urine very well (slope= 1.4 and $R^2 = 0.91$ with logarithmic-transformed data). Thus, it seems that our modeling approach has overcome some previous deficiencies and yielded more reliable estimates.

Due to the low detection rates of iAs (1 to 7 percent) in the NHANES urine data, the evaluation of SHEDS-MENTOR modeling results for iAs could not be conducted. However, the Yu PBPK model adapted for MENTOR-3P has been evaluated against experimental observations from the literature for urinary biomarker levels of speciated arsenic (see Yu 1999a,b and references therein). Since the TDS study only provided tAs concentrations in foods, the iAs percentage in the same food category as reported by Schoof et al., 1999a,b was used to derive iAs food concentrations. This assumption could result in uncertainties of estimated inorganic arsenic exposure from foods, which could be carried onto the subsequent PBPK modeling analysis for estimating target tissue doses and biomarker levels of iAs.

Our results in general are consistent with those reported in previous studies. For example, a duplicate diet study of children in Germany showed 6.9 and 3.1 ug/day tAs exposure for the mean and median, respectively (Wilhelm et al., 2003), which are compatible with our estimates of 7.2 and 3.5 ug/day for 1-2 year-olds and 10.8 and 4.1 ug/day for 3-5 year-olds. Another study showed that average intake of tAs for the general US population estimated by the Dietary Exposure Potential Model (DEPM) is 0.653 ug/kg/day (Moschandreas et al. 2002), which is similar to our result of 0.39 ug/kg/day for the same population. Even when inorganic As (iAs) is specifically considered, our results are also within the wider range of iAs exposures reported in previous such studies. For example, the iAs intake from US diet was estimated to be 1 to 20 ug/day with a mean of 3.2 ug/day

by Schoof et al. (Schoof et al. 1999a,b), and was reported as 1.34 ug/day in infants and 12.54 ug/day in 60-65 years old (Tao and Bolger 1998). Our results of the major food contributors to As exposure are consistent with the As levels measured in various foods in US markets (Tao and Bolger 1998).

Our modeling assessment advances the science by using the large and recent data bases from NHANES, TDS, NHEXAS, and states to estimate As intake for the US general population from food and drinking water. Other unique aspects of research presented in this paper are evaluation of tAs intake estimates using duplicate food survey data from NHEXAS, and using urine biomarker data from NHANES to evaluate the SHEDS-MENTOR model predictions. The integrated exposure and dose modeling application presented in this paper for As has not been attempted before for a large general population (such as the NHANES population), to our knowledge, in the exposure-related literature. The SHEDS-Dietary model and the linked SHEDS-Dietary/MENTOR-3P model predictions compared well to the measured duplicate diet data and urine biomarker data, respectively; thus, this was an important model evaluation effort to provide more confidence in these predictive exposure assessment tools.

Conclusions

The relationship between As intake from drinking water and related health effects has been well studied previously. Using rich data sets and state-of-the science models, we found that the general US population may be exposed to tAs and toxic iAs through the dietary route more from eating some As-containing foods than from drinking As-containing water. The major food contributors to tAs exposure were found to be fish, shellfish, rice, fruit juices and fruits, and meats; the major food contributors to iAs exposure were vegetables, fruit juices and fruits, rice, beer and wine, and flour, corn, and wheat. Approximately 10% of tAs exposure from foods is the toxic iAs form.

Our study reinforces and expands upon previous observations that dietary As exposure via food is an important route for As intake by the general population and, sometimes, it can be even a greater source of As exposure than drinking water. Thus, for complete exposure analysis and risk assessment in the general population, iAs intake from food should be considered in addition to iAs intake from drinking water.

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Table 1. SHEDS modeled As exposure from food using 2003-2004 NHANES data (ug/kg/day)

Age Group	n	mean	std	p5	p25	p50	p75	p95	p99
Total As									
0 < 1 years	757	0.62	0.53	0.05	0.27	0.56	0.84	1.45	2.08
1-2 years	1068	0.54	1.23	0.05	0.13	0.26	0.46	2.06	5.06
3-5 years	953	0.54	1.74	0.03	0.11	0.20	0.36	2.20	5.60
6-12 years	2190	0.37	1.69	0.02	0.05	0.10	0.22	1.24	4.28
13-19 years	3576	0.25	1.04	0.01	0.03	0.06	0.14	1.02	3.58
20-49 years	4221	0.33	1.09	0.01	0.03	0.07	0.17	1.41	4.12
50+ years	3804	0.32	1.20	0.01	0.03	0.05	0.15	1.35	4.91
all ages	16931	0.36	1.28	0.01	0.04	0.08	0.24	1.40	4.45
Inorganic As									
0 < 1 years	757	0.23	0.19	0.01	0.09	0.21	0.31	0.53	0.80
1-2 years	1068	0.10	0.12	0.01	0.04	0.07	0.12	0.29	0.59
3-5 years	953	0.08	0.11	0.01	0.03	0.05	0.09	0.21	0.40
6-12 years	2190	0.04	0.06	0	0.01	0.03	0.05	0.13	0.25
13-19 years	3576	0.03	0.05	0	0.01	0.01	0.03	0.09	0.21
20-49 years	4221	0.03	0.07	0	0.01	0.02	0.04	0.11	0.28
50+ years	3804	0.03	0.07	0	0.01	0.01	0.03	0.09	0.22
all ages	16931	0.05	0.09	0	0.01	0.02	0.05	0.19	0.41

Table 2. SHEDS modeled As exposure from drinking water (ug/kg/day)

Age Group	n	mean	std	p5	p25	p50	p75	p95	p99
00 < 1 years	756	0.014	0.083	0.000	0.000	0.000	0.000	0.053	0.412
01-2 years	1064	0.031	0.108	0.000	0.000	0.002	0.019	0.150	0.397
03-5 years	944	0.036	0.150	0.000	0.000	0.004	0.021	0.152	0.539
06-12 years	2179	0.030	0.156	0.000	0.000	0.003	0.016	0.108	0.441
13-19 years	3566	0.019	0.092	0.000	0.000	0.002	0.011	0.076	0.281
20-49 years	4218	0.026	0.087	0.000	0.000	0.002	0.016	0.113	0.414
50+ years	3797	0.025	0.084	0.000	0.000	0.004	0.019	0.107	0.344
all ages	16883	0.025	0.104	0.000	0.000	0.002	0.016	0.107	0.374

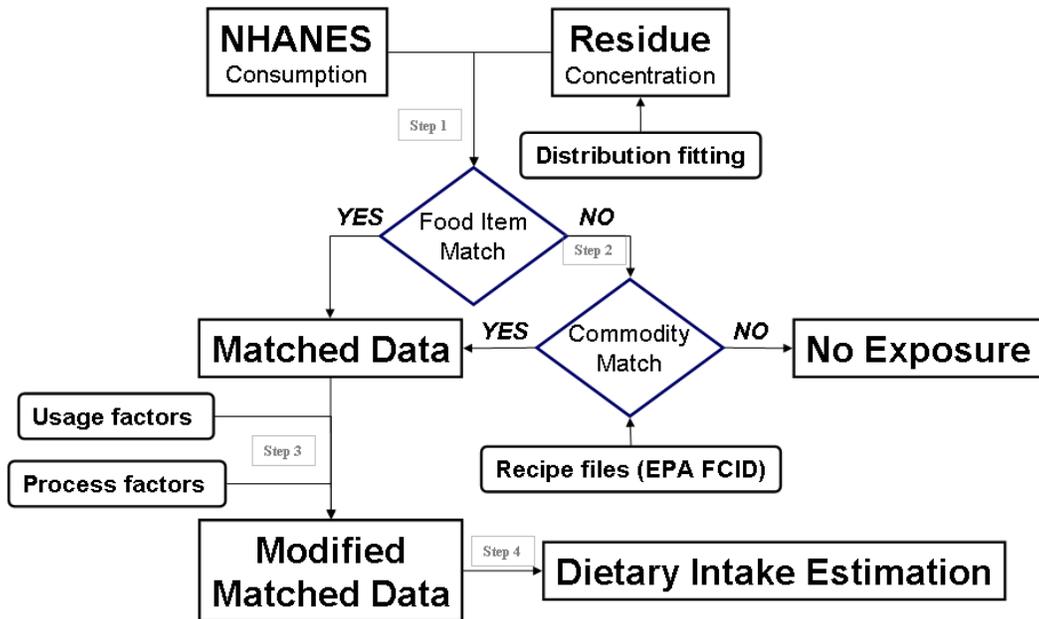
Figure 1. SHEDS dietary module overview

Figure 2. Structure of PBPK modeling of exposure to arsenic in the EOHSI's MENTOR framework

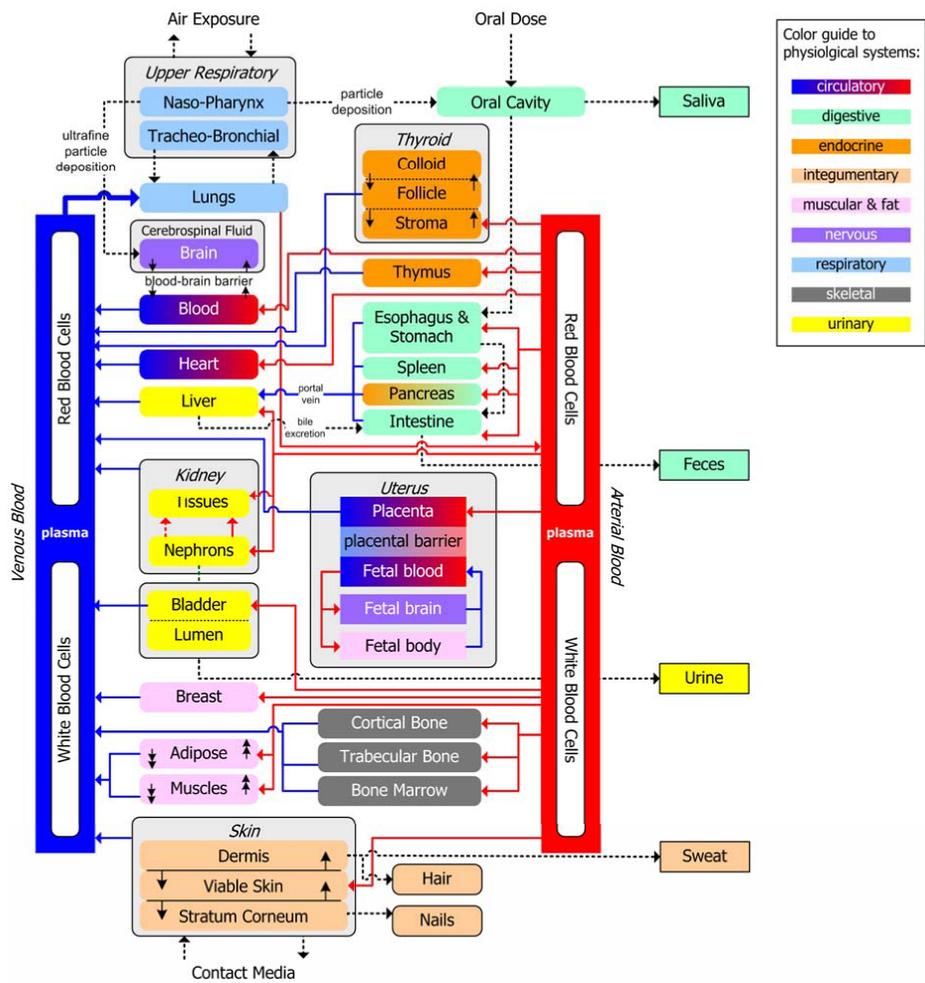
Figure 3. SHEDS dietary exposure model evaluation with duplicate food survey*

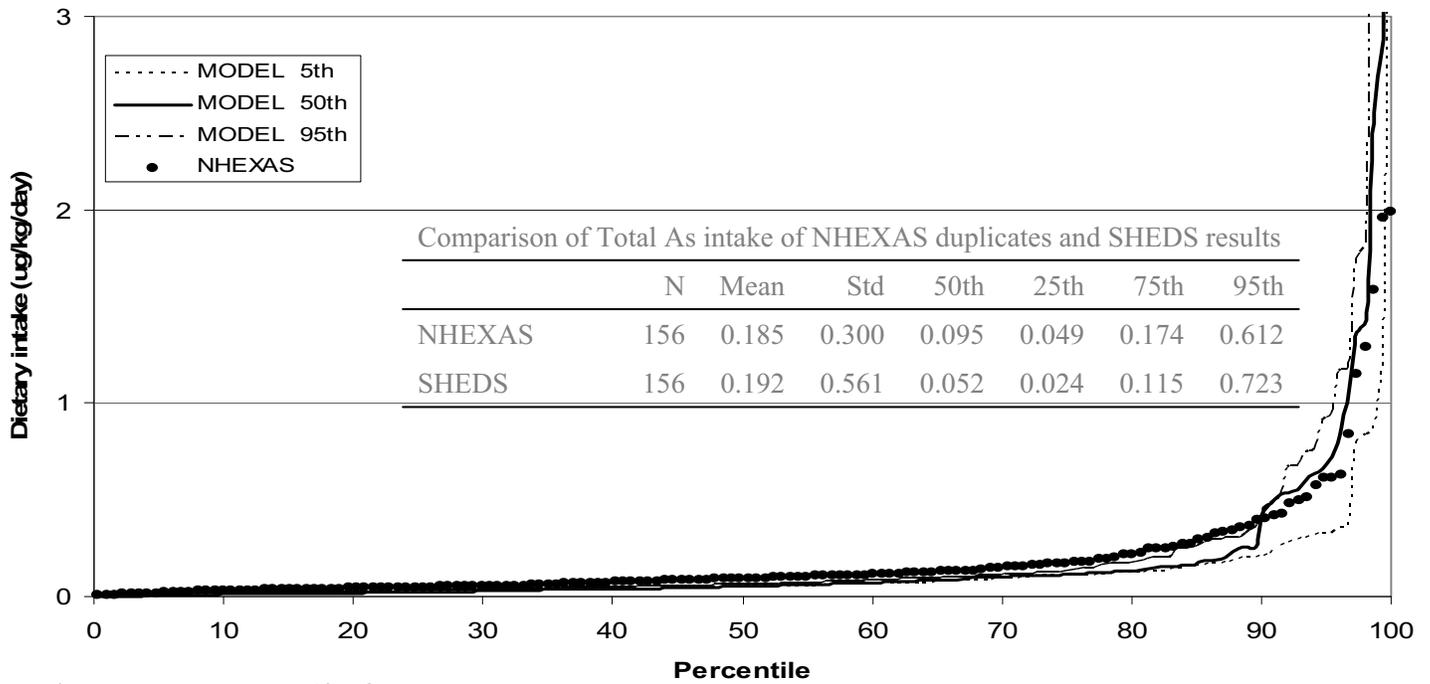
Figure 4. Total arsenic model evaluation for SHEDS and MENTOR PBPK with NHANES urine data

Figure 5. Contributions of inorganic arsenic intake by foods



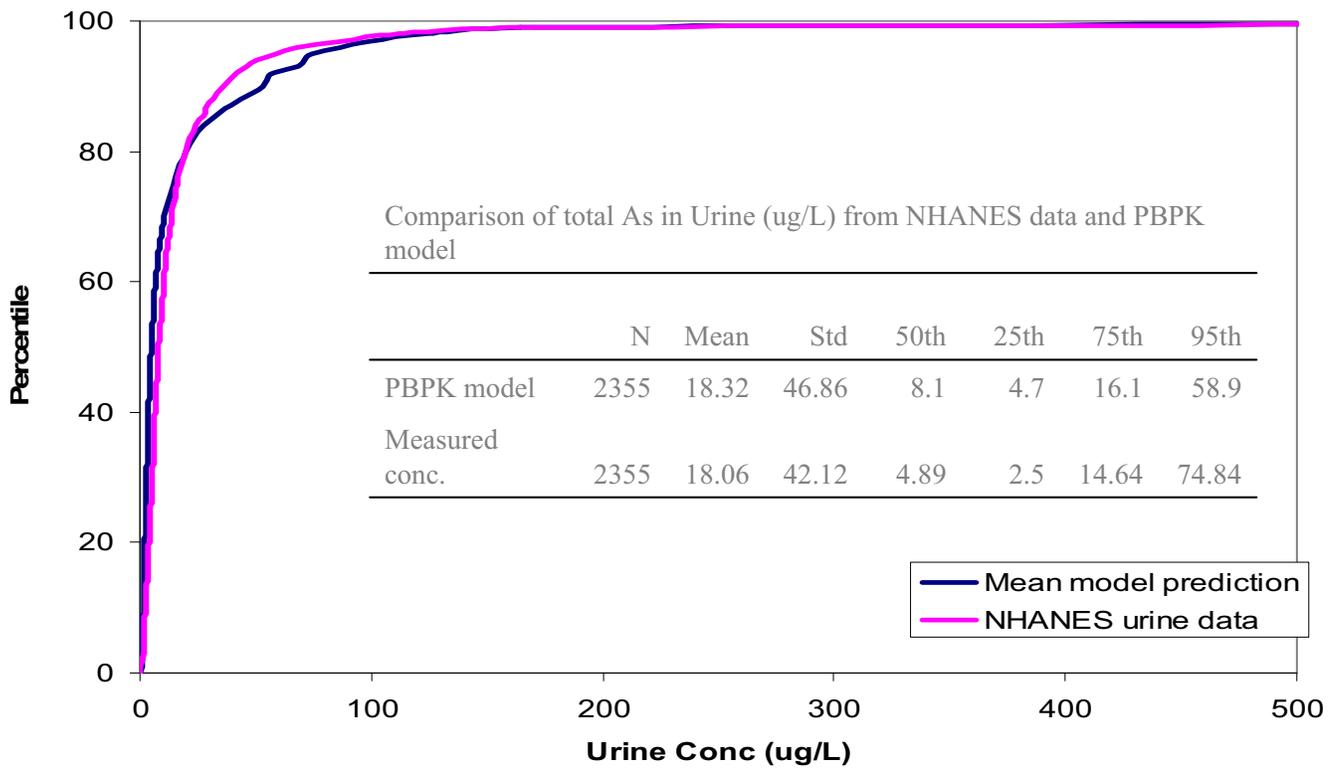
- NHANES Consumption: Food consumption data from NHAHES.
- Residue Concentration: Total As residue data by food item or commodity from TDS
- Distribution fitting: fittings of residue data into suitable statistical distribution
- Food Item: food products people in the survey consumed such pizza, raw apple
- Commodity: raw agriculture commodity (RAW)
- Usage factors: Pesticide usage percentages by RAW from USDA.
- Process factors: concentration or dilution factors due to processes of food from RAW into food products.
- Recipe files (EPA FCID): data base for percents of various RAWs for the food products.

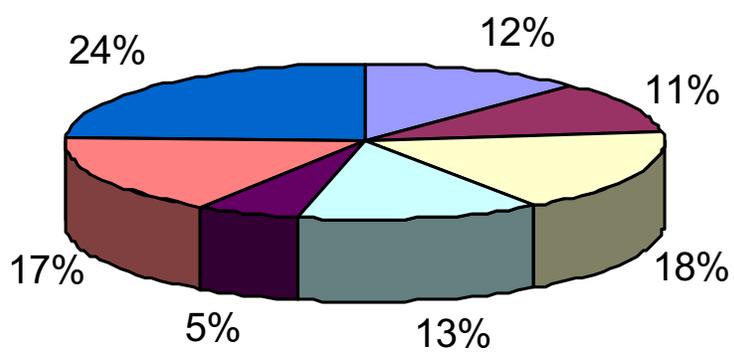




* Fill in no-detected with 1/2 LOD when As residue mean

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- Beer, Wine
- Flour, Corn, Wheat
- Fruit, Fruit Juice
- Others
- Poultry, pork, beef, egg
- Rice
- Vegetables