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Contribution of breast milk and formula to arsenic exposure during the first year of life in a U.S. prospective cohort

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Abstract

Arsenic is a carcinogen that can also affect the cardiac, respiratory, neurological and immune systems. Children have higher dietary arsenic exposure than adults due to their more restricted diets and greater intake per unit body mass. We evaluated the potential contributions of breast milk and formula to arsenic exposure throughout the first year of life for 356 infants in the prospective New Hampshire Birth Cohort Study (NHBCS) using infant diets reported by telephone at 4, 8 and 12 months of age; measured household water arsenic concentrations; and literature data. Based on our central-tendency models, population-wide geometric mean (GM) estimated arsenic exposures in the NHBCS were relatively low, decreasing from 0.1 μg kg^{-1} d^{-1} at 4 months of age to 0.07 μg kg^{-1} d^{-1} at 12 months of age. At all three time points, exclusively formula-fed infants had GM arsenic exposures ~8 times higher than exclusively breastfed infants due to arsenic in both tap water and formula powder. Estimated maximum exposures reached 9 μg kg^{-1} d^{-1} among exclusively formula-fed infants in households with high tap water arsenic (80 μg/L). Overall, modeled arsenic exposures via breast milk and formula were low throughout the first year of life, unless formula was prepared with arsenic-contaminated tap water.

Keywords

breastfeeding; child; cohort studies; diet; environmental exposure; infant formula

INTRODUCTION

Early life is a period of heightened vulnerability to arsenic exposure[1]. Arsenic is a known human carcinogen that can also adversely affect the neurological, respiratory, cardiovascular,

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immunological and endocrine systems[2]. Most studies have investigated populations with chronic exposure to high concentrations of arsenic via drinking water, such as those in Bangladesh, Chile, and Taiwan, where concentrations of arsenic in drinking water can be substantially higher than 50 μg/L[3,4]. In such populations, early life exposure has been associated with increased fetal mortality[3,4], decreased birth weight[4], and diminished cognitive function[5,6], although results are not always consistent across studies[7]. Moreover, effects of chronic early-life exposure can manifest in adulthood with increased occurrences and/or severity of lung disease, cardiovascular disease and cancer[1,2,8]. Although less is known about the short- and long-term consequences of exposure below the current U.S. EPA and World Health Organization maximum contaminant level (MCL) of 10 μg/L[9], *in utero* low-dose exposure has been associated with increased infant respiratory infections and the severity of these infections[10].

There are two primary pathways for arsenic exposure in the U.S. population: water and food. Arsenic is a naturally occurring element in aquifer bedrock and as a result is found in well water throughout the world[11-15]. Drinking water primarily contains As^{III} and As^{V}, inorganic forms of arsenic (iAs) with known toxicity[16]. Foods can contain iAs; organic metabolites of iAs such as dimethylarsinic acid (DMA) and monomethylarsonic acid (MMA); and arsenobetaine, arsenosugars, and arsenolipids[17,18]. Arsenobetaine is considered non-toxic and passes through the body unmetabolized[19]. Evidence from *in vitro* studies suggests that trivalent forms of MMA and DMA may have toxic and potentially carcinogenic properties[20-23], whereas the effects of the pentavalent forms of these compounds are less certain[24], especially when consumed in food[25].

Dietary exposure to arsenic is expected to be about three times higher for infants and young children than for adults[26], in part because their intake per unit body mass is higher[27] and their dietary diversity is lower than adults[26]. For example, newborn infants subsist on a diet of breast milk and/or formula. Powdered infant formula contains some arsenic[28-31], including in the inorganic form[31,32], and can contribute to exposure, especially when reconstituted with arsenic-contaminated water[33]. In contrast, we recently reported low levels of arsenic in breast milk from New Hampshire mothers with low exposure to arsenic in drinking water (median=0.26 μg/L)[33]. Other studies have found that arsenic in breast milk is low regardless of arsenic exposure via drinking water[34-39]. The dominant species of arsenic in breast milk is currently unclear, but may depend on the source or magnitude of exposure. In a Bangladeshi population exposed to high arsenic in drinking water (median=78 μg/L)[40], breast milk samples (n=79) contained predominantly inorganic arsenic[37], whereas only organic arsenic was detectable in breast milk from a small sample of Swedish mothers (n=3) who had no known source of arsenic in their drinking water[34].

Here, we quantify the potential arsenic exposure via breast milk and formula for individual infants in the New Hampshire Birth Cohort Study (NHBCS) over their first year of life. Our goals are to use exposure modeling to (1) provide insight into the relative contribution of breast milk vs. formula to exposure, assuming use of home tap water to reconstitute infant formula, and (2) explore how population-wide exposure varies as breastfeeding prevalence decreases and formula use increases during the period from birth to one year of age. Given that breast milk is expected to be lower in arsenic than formula, we hypothesized that arsenic exposure would increase during infancy due to the increased prevalence of formula feeding[41].

SUBJECTS AND METHODS

The New Hampshire Birth Cohort Study (NHBCS)

In January 2009, we began recruiting pregnant women ranging in age from 18–45 who were receiving prenatal care at study clinics in New Hampshire, USA, as described previously[10,42]. Enrollment criteria included a singleton pregnancy; the use of a private, unregulated well in the home since their last menstrual period; and plans to stay in the current residence through delivery. This study was reviewed and approved by the Committee for the Protection of Human Subjects (CPHS) at Dartmouth College, Hanover, NH, and all participants in the study provided informed consent in accordance with CPHS guidelines. Household tap water arsenic was measured in samples returned by subjects after enrollment[10,33,42].

Maternal Questionnaire

Women who agreed to participate were asked to complete a prenatal medical history and lifestyle questionnaire that included questions about sociodemographic factors, health history, personal habits, home water source, and home water consumption.

Infant feeding

At 4, 8 and 12 months postpartum, participants were contacted for a brief telephone interview that included questions about feeding practices on an average day, such as frequency of breastfeeding, amount of formula consumed, and type of water used to reconstitute powdered formula (e.g., home tap vs. bottled). Based on these responses, we assigned infants to one of three feeding categories for their liquid diet: Breastfed (fed only breast milk), Formula-fed (fed only formula), or Mixed (fed both breast milk and formula). We assumed that all formula was prepared using home tap water and that infants in the Mixed feeding type received exactly half breast milk and half formula. This was done in the absence of more detailed data on infant feeding practices and local data on bottled water arsenic, and to better reflect potential upper-bound exposures among New Hampshire infants.

Arsenic exposure estimates via breast milk and formula for NHBCS infants

We calculated potential arsenic exposure for each NHBCS infant at 4, 8 and 12 months of age based on (1) current feeding type (Breastfed, Mixed or Formula-fed, as described above); (2) the measured concentration of arsenic in household tap water (Supplemental Material, Table S1) for Mixed and Formula-fed infants; and (3) literature-based values for age-specific breast milk ingestion rate (IR_{BW}, reported in the U.S. EPA Child Specific Exposure Factors Handbook[43] Table 15-4) and the arsenic concentration in breast milk[33] or formula powder[31]. The feeding type of each individual was allowed to vary at each time point (4, 8, and 12 months) depending on parental reports.

For each infant at each time point, we used two different models to estimate the distribution of potential arsenic exposure among NHBCS infants due to ingestion of breast milk and/or formula – a *central tendency model* and an *upper bound model* – based on individual-level concentrations of arsenic in household tap water and reported feeding type at 4, 8 and 12 months of age. Exposures were estimated using the equations in the Supplemental Material, Appendix 1 and the following numeric values:

(1) The central tendency model multiplied the median concentration of arsenic in breast milk (0.31 μg/L)[33] and/or reconstituted formula (1.1 μg/L from powder[31] plus the measured household tap water arsenic)[33] by the mean IR_{BW}[43] (0.112 L kg^{-1} d^{-1} at 4 months, 0.075 L kg^{-1} d^{-1} at 8 months, and 0.047 L kg^{-1} d^{-1} at 12 months).

(2) The upper bound model multiplied the maximum concentration of arsenic in breast milk (0.62 μg/L)[33] and/or reconstituted formula (1.8 μg/L from powder[31] plus the measured household tap water arsenic)[33] times the upper percentile IR_{BW}[43] (defined as the mean plus 2 standard deviations: 0.148 L kg^{-1} d^{-1} at 4 months, 0.125 L kg^{-1} d^{-1} at 8, and 0.101 L kg^{-1} d^{-1} at 12 months). This model is likely best for estimating short-term upper bound exposures, since data for upper bound IR_{BW} were collected over short periods (i.e., 3-10 days).

In making these calculations, we assumed that arsenic concentrations did not vary across formula brands based on published reports of comparable arsenic concentrations across brands and products[31]; moreover, the median concentration used (1.1 μg/L) was similar to concentrations reported by the FDA[32] (1 μg/L of total arsenic when converted from μg/g of formula powder assuming arsenic-free water). Similarly, median and maximum concentrations of arsenic in breast milk were applied from our previous study of NHBCS mothers (n=9) whose home tap water arsenic concentrations ranged from <0.01 to 8.9 μg/L, a concentration range that represents approximately 90% of our study population[33]. Other studies around the world also report low concentrations of arsenic in breast milk relative to drinking water[34-39].

To test the effect of assuming that milk ingestion rates were consistent across feeding types, we performed two sensitivity analyses. First, we calculated the IR_{BW} for a subset of Formula-fed NHBCS infants for whom data on both daily formula consumption rates and body weight were available (n=34, 48, and 58 for 4, 8 and 12 months, respectively), and compared these values to the modeled inputs. We then estimated exposure for the Formula-fed and Mixed-fed infants using summary statistics for this NHBCS-specific formula IR_{BW}[43], instead of the breast milk IR_{BW}. In addition, we estimated exposure using the tap water IR_{BW} determined by the U.S. EPA[43], which also includes water intake other than formula (i.e., mixing with cereal).

RESULTS

NHBCS Characteristics

We selected 356 infants from the NHBCS with complete records of feeding type at the 4, 8 and 12 month time-points (Table 1). In this subset, mean (SD) maternal age was 31.5 (4.6) years at the time of delivery. Most of the mothers were college graduates (39%) or had attended some postgraduate schooling (31%), and the majority reported being married (85%). Slightly more than half of the infants were female (55%) and all were white (100%). Less than half of the infants attended daycare at 4, 8 and 12 months (33%, 38% and 41%, respectively). Demographics of the larger cohort are similar to this subset (data not shown).

Tap water arsenic within the study subset was generally low: 86% of the families had household tap water arsenic concentrations <10 μg/L, the current U.S. EPA MCL (Table 1). However, the maximum household tap water arsenic for the NHBCS reached levels 8 times the MCL (79.7 μg/L), with some differences among feeding types and time points (Supplemental Material Table S1).

Infant Feeding Patterns in the NHBCS

The predominant feeding type shifted from Breastfed to Formula-fed over the first year of life (Figure 1; Supplemental Material Tables S2, S3). At 4 months of age, 45% of mothers reported that their infants were Breastfed, 23% were Mixed-fed, and 32% were Formula-fed. By 12 months of age, the percentage of Breastfed infants had decreased to 21% and the percentage of Formula-fed infants had nearly doubled to 66%.

Among Formula-fed infants, formula ingestion rates reported by parents decreased as infants got older (Supplemental Material Table S2). The average reported volume of formula consumed by Formula-fed infants decreased from 839 mL d^{-1} at 4 months to 710 mL d^{-1} at 12 months of age. Estimates of IR_{BW} for the subset of Formula-fed NHBCS infants were similar to the values recommended by the U.S. EPA Child Specific Exposure Factors Handbook for exclusively breastfed babies (Table 15-4)[43] at 4 months (n = 34; mean = 0.13 L kg^{-1} d^{-1}; mean + 2 SD = 0.20 L kg^{-1} d^{-1}), 8 months (n = 48; mean = 0.08 L kg^{-1} d^{-1}; mean + 2 SD = 0.15 L kg^{-1} d^{-1}) and 12 months of age (n=58; mean = 0.06 L kg^{-1} d^{-1}; mean + 2 SD = 0.14 L kg^{-1} d^{-1}) (Supplemental Material Table S4). For infants receiving both breast milk and formula, the average reported volume of formula decreased from 337 mL d^{-1} and 6 breast-feedings d^{-1} at 4 months to 277 mL d^{-1} and 4 breast-feedings per day at 12 months of age (Supplemental Material Table S2, S3). Breastfed infants had an average of 7 feedings d^{-1} at 4 months; by 12 months this decreased to 4 feedings d^{-1} (Supplemental Material Table S3).

Our models assumed all formula was made with tap water in order to estimate potential exposure among users of private wells. Many families reported using home tap water to reconstitute formula powder, and the use of home tap water increased slightly over the first year of life. Among Formula-fed infants, the percentage of mothers who reported always using tap water to prepare formula increased from 57% at 4 months to 65% at 12 months. However, there were some differences in tap water arsenic concentrations by use of tap water to prepare formula: a higher geometric mean tap water arsenic concentration was found among those who reported never using tap water to prepare formula (0.88 µg/L) compared to than those who reported using tap water to mix formula most of the time at 8 months of age (0.45 µg/L; P=0.04) and 12 months of age (1.11 vs. 0.36 µg/L; P=0.002), but not at 4 months of age (0.71 vs. 0.54 µg/L, P=0.42).

Arsenic exposure estimates for NHBCS infants via breast milk and formula made with home tap water

Results from both the central tendency and upper bound models have distributions due to the use of individual-level data on feeding type and the concentration of arsenic in household tap water (Breastfed, Mixed or Formula-fed) at 4, 8 and 12 months. Based on the central tendency model, geometric mean (GM) estimated arsenic exposure across the NHBCS population was relatively low, ranging from 0.1 µg kg^{-1} d^{-1} at 4 months of age to 0.07 µg kg^{-1} d^{-1} at 12 months of age (Table 2). However, GM estimated exposure from this model was approximately 8 times higher for Formula-fed infants than for Breastfed infants at all time points (Table 2, Supplemental Material Figure S1), due to the presence of low concentrations of arsenic in both the formula powder and household tap water (Table 3). GM exposure among Formula-fed, Mixed and Breastfed infants was 55%, 67% and 58% lower at 12 months compared to 4 months, respectively. Including all feeding types, population-wide GM exposure decreased approximately 27% from 4 to 12 months due to decreasing IR_{BW} (Figure 2A).

Based on the upper-bound model, GM estimated arsenic exposures were slightly higher across time points, ranging from 0.22 µg kg^{-1} d^{-1} at 4 months of age to 0.24 µg kg^{-1} d^{-1} at 12 months of age (Table 2). GM estimated exposures were 5-6 times higher for Formula-fed infants than for Breastfed infants (Table 2, Supplemental Material Figure S1), and exposures decreased from 4 to 12 months in all feeding types. Unlike the central tendency model, population-wide GM exposure from the upper bound model *increased* 8% from 4 to 12 months of age in conjunction with increased prevalence of formula consumption at the population level (Figure 2B).

Variability in estimated exposure among Formula-fed infants was due to the concentration of arsenic in household tap water. The most exposed Formula-fed infant from our central tendency model was estimated to be exposed to 73 times more arsenic per kg body mass per day than the least exposed Formula-fed infant (Supplemental Material Table S5), and over 300 times more arsenic than Breastfed infants (Table 2, Supplemental Material Table S5). At low concentrations of tap water arsenic, approximately half of exposure among Formula-fed infants was attributable to the formula powder itself (Table 3).

Using the central tendency model but excluding the 14% of infants whose tap water exceeded the current U.S. EPA MCL of 10 µg/L, GM exposure among Formula-fed infants was ~30% lower than for the full subset (0.19 µg kg^{-1} d^{-1} at 4 months and 0.09 µg kg^{-1} d^{-1} at 12 months of age; Supplemental Material Table S6), and 6-9 times higher for Formula-fed infants compared to Breastfed infants (Table 2, Supplemental Material Table S7).

DISCUSSION

Estimated GM arsenic exposures in the NHBCS were generally low regardless of feeding type and exposure model. However, the estimated upper bound exposures for infants fed exclusively formula reflected the elevated arsenic concentrations in tap water, which reached 80 μg/L. The 8X increase in arsenic exposure among Formula-fed compared to Breastfed infants is consistent with our previous finding for 6-week old NHBCS infants[33], with approximately half of exposure attributable to the powdered component of formula when the arsenic concentration in mixing water was relatively low (~1 μg/L). Importantly, GM exposures were similar even when the analysis was restricted to infants whose tap water arsenic was below the current MCL of 10 μg/L, suggesting that this finding is generalizable to the U.S. infant population consuming formula reconstituted with water from regulated sources. The reduction in exposure within each feeding type from 4 to 12 months reflects the decrease in liquid consumption per unit body weight over the first year of life, due both to growth and the introduction of solid foods. However, this decrease was attenuated at the population level, when all feeding types were included, due to the 35% increase in the percentage of formula-fed infants in the population from 4 to 12 months.

While our models are for total arsenic and did not explicitly consider arsenic speciation, the majority of arsenic in tap water is inorganic As. Thus, we expect that much of the exposure to arsenic via formula could be in the more toxic, inorganic form, especially for infants receiving formula made with water high in arsenic. Estimates of iAs in formula powder range from at least 50%, an assumption applied by the FDA[32], to nearly 100% inorganic[31]. In contrast, the dominant form of arsenic in breast milk is currently unclear: we were unable to measure the percentage of iAs in breast milk due to the low total arsenic concentrations[33] and previous studies have reported contradictory findings[34,37].

The presence of inorganic arsenic in reconstituted infant formula is of particular concern because at 4 months of age, we estimate that 16% of our study population (29% when restricted to Mixed- and Formula-fed infants) exceeded the reference dose (RfD) for chronic oral ingestion of arsenic calculated by the U.S. EPA[44] – 0.3 μg kg^{-1} d^{-1} – using the central tendency model. While a useful benchmark, it must be acknowledged that the EPA RfD is based on a no-effect level calculated for adult intake per body weight over adult chronic lifetime exposure to arsenic in drinking water and does not indicate potential cancer risks. The U.S. EPA is in the process of re-evaluating the arsenic RfD based on additional data that allow a more comprehensive assessment of potential non-cancer risks of arsenic for vulnerable early life stages as well as for lifetime exposure[45].

Our exposure models included a number of assumptions that were applied in the absence of subject-specific body weights and precise measurements of breast milk consumption, and were selected with the aim of estimating potential exposure for the population. These assumptions lead to expected under- and over-estimates of true exposure, which we evaluate below using sensitivity analysis and/or qualitative discussion:

(1) Our models assumed that all formula was prepared using home tap water, whereas 30% of mothers in our study population reported using primarily bottled water to prepare formula. Because bottled water is regulated to have arsenic concentrations below the current MCL[46], this assumption would lead to an expected overestimate in our upper percentile estimates from either model. However, it is expected to have minimal impact on our GM estimates because 86% of our study population had tap water concentrations below the MCL and our findings were robust to the inclusion of NBHCS infants with home tap water arsenic concentrations above the MCL (Supplementary Material Tables S6, S7). Also, this assumption is expected to improve generalizability of our findings to the general population of New Hampshire infants from homes with residential wells, as our study population was provided with their tap water results and thus may have been less likely to mix formula using tap water containing elevated concentrations of arsenic than the typical New Hampshire family.

(2) Our models assumed that Mixed-fed infants received 50% breast milk, which would lead to an expected overestimate of exposure in this feeding type at 4 months, but an underestimate at 12 months, due to a switch from predominantly breast milk at 4 months of age to predominantly formula at 12 months of age (Supplemental Material Tables S2, S3).

(3) Our models applied the IR_{BW} for breast milk[43] to all feeding types and generally assumed no exposure to tap water other than via formula. These assumptions may underestimate exposure since the IR_{BW} – and thus arsenic exposure – may be higher for formula, as confirmed by our sensitivity analysis using the calculated IR_{BW} for the subset of Formula-fed NHBCS infants that had data available for both ingestion rate and body weight. In models using this NHBCS-derivd IR_{BW}, central tendency estimated exposures were 11 to 35% higher than estimates from the primary models (Supplemental Material, Table S6).

(4) The IR_{BW} applied in the upper bound model (mean + 2 SD) for all feeding types may lead to an expected overestimate since this rate is based on a 24-hour timeframe, and extreme values in the short-term will not be maintained.

(5) The maximum concentration of arsenic in breast milk may be underestimated as it is based on a small sample and the maximum concentration of arsenic in home tap water in that sample (8.9 μg/L) was lower than in our study population (79.9 μg/L). However, populations with high exposures, such as those in Bangladesh and Chile, have also reported low levels in breast milk[34-39], suggesting that the impact of this underestimate on exposures from our upper bound model would be relatively small.

Finally, the concentrations of arsenic in breast milk and formula powder used in our model were taken from previous studies in the absence of individual-level data. However, our confidence in the appropriateness of these data for our study population is high as they were measured for the NHBCS population and values are comparable to those from previous studies: total arsenic concentrations in formula were similar to those reported by the U.S. FDA[32] and concentrations in breast milk were similar to reports from other countries[34-39].

In conclusion, modeled arsenic exposures via breast milk and formula were relatively low throughout the first year of life, unless formula was prepared with arsenic-contaminated tap water. We expect that the transition to solid foods, which typically occurs beginning at ~6 months, presents an additional source of exposure to arsenic for the typical NHBC infant, since many foods commonly fed to infants during weaning, such as infant rice cereal, contain elevated concentrations of arsenic[31,47,48]. Thus, future work should seek to quantify daily arsenic intake during this critical period of development.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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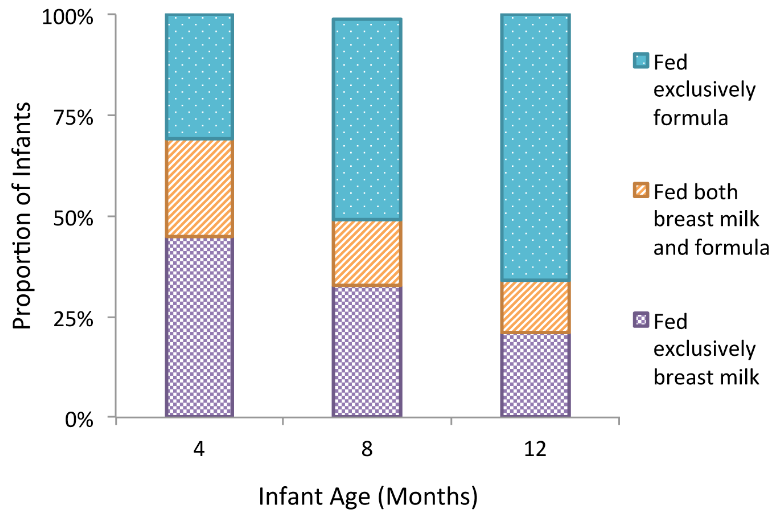

Figure 1.
Proportion of NHBCS infants fed formula and breast milk at 4, 8 and 12 months of age.

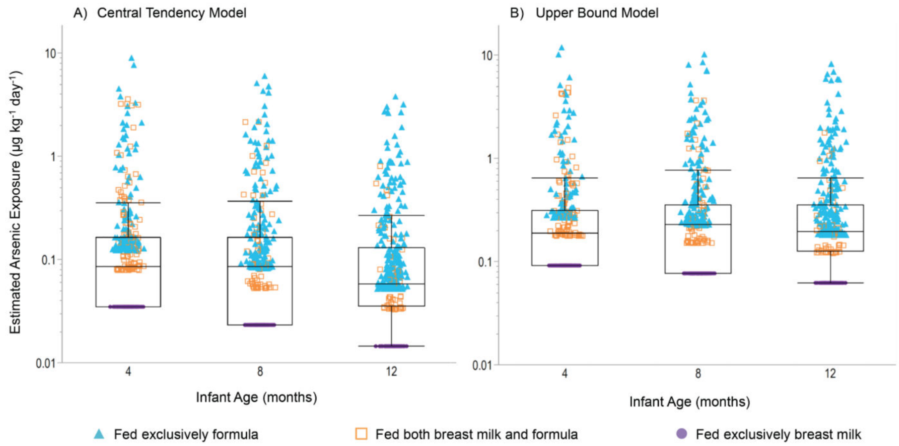

Figure 2.
Arsenic exposure (μg kg^{-1} d^{-1}) from formula and breast milk among NHBCS infants (n=356) at 4, 8 and 12 months of age using the A) central tendency model and B) upper bound model, which use central tendency or upper bound inputs, respectively, for the body-weight adjusted ingestion rate, infant formula powder, and breast milk. Variability between infants is due to individual-level data on feeding type and measured concentrations of arsenic in home tap water. Each symbol indicates one infant, the boxes denote the first and third quartile (Q1 and Q3) with the median as a line in the middle, and the whiskers denote points within 1.5 times the interquartile range of Q1 and Q3. There is no variability in Breastfed infants because all were modeled with the same inputs.

Table 1

Selected characteristics of mothers and infants in the New Hampshire Birth Cohort sub-study reported here (n=356).

Population Characteristic	Mean (range) or n (%)[a]
Maternal variables	
Maternal age, years	31.5 (18.6–44.5)
<20	4 (1%)
20–29	104 (29%)
30–35	176 (49%)
>35	72 (20%)
Maternal education	
<11th grade	3 (1%)
High school graduate / GED	29 (8%)
Junior college, some college, technical school	70 (20%)
College graduate	135 (39%)
Postgraduate schooling	106 (31%)
Relationship status	
Single	37 (11%)
Married	292 (85%)
Separated or divorced	14 (4%)
Infant variables	
Infant Sex	
Male	161 (45%)
Female	195 (55%)
Infant Race	
White	337 (100%)
Other	0 (0%)
Attended day care	
4 months of age	118 (33%)
8 months of age	135 (38%)
12 months of age	147 (41%)
Household Tap Water [As]	0.48[b] (<0.01–80)
<1 μg/L	205 (58%)
1–10 μg/L	101 (28%)
>10 μg/L	50 (14%)

[a]Sum of subjects for the following variables are less than the total sample size (n missing): maternal education (13), relationship status (13) and infant race (19).

[b]Median concentration and range is reported, as data are log-normally distributed.

Table 2

Estimated exposure to arsenic (μg kg^{-1} d^{-1}) during the first year of life. These estimates were calculated using central tendency or upper-bound inputs for the body-weight adjusted ingestion rate, the concentration of arsenic in infant formula powder, and the concentration of arsenic in breast milk. Variability among infants is due to individual-level data on the concentration of arsenic in tap water (for Formula-fed and Mixed feeding infants) and change in feeding mode over time.

A) Central tendency model

	All		**Breastfed**		**Mixed**		**Formula Fed**	
	% (n)	**GM (95% CI)[a]**	**% (n)**	**Value[b]**	**% (n)**	**GM (95% CI)**	**% (n)**	**GM (95% CI)**
4 months	100 (356)	0.10 (0.09, 0.12)	45 (159)	0.03	24 (85)	0.20 (0.16, 0.25)	31 (112)	0.28 (0.23, 0.34)
8 months	100 (356)	0.09 (0.08, 0.10)	33 (119)	0.02	16 (58)	0.13 (0.10, 0.17)	50 (179)	0.20 (0.17, 0.24)
12 months	100 (356)	0.07 (0.07, 0.08)	21 (73)	0.01	13 (48)	0.07 (0.05, 0.09)	66 (235)	0.13 (0.11, 0.15)

B) Upper bound model

	All		Breastfed		Mixed		Formula Fed	
	% (n)	GM (95% CI)[a]	% (n)	Value[b]	% (n)	GM (95% CI)	% (n)	GM (95% CI)
4 months	100 (356)	0.22 (0.20, 0.24)	45 (159)	0.09	24 (85)	0.37 (0.30, 0.44)	31 (112)	0.51 (0.43, 0.61)
8 months	100 (356)	0.24 (0.21, 0.26)	33 (119)	0.08	16 (58)	0.30 (0.24, 0.38)	50 (179)	0.45 (0.40, 0.52)
12 months	100 (356)	0.24 (0.21, 0.26)	21 (73)	0.06	13 (48)	0.21 (0.17, 0.25)	66 (235)	0.37 (0.33, 0.41)

[a]GM=Geometric mean and 95% CI=95% confidence interval

[b]There is no distribution for breastfed infants because all infants had the same input values for body-weight adjusted ingestion rate

Table 3

Estimated exposure to arsenic (μg kg^{-1} d^{-1}) from formula powder compared to mixing water a mong exclusively formula-fed infants.

A) Central tendency model

	Formula Powder	Mixing Water		Total		% Powder	
		GM	Max	GM	Max	GM	Max
4 months	0.12	0.16	8.92	0.28	9.05	44%	1%
8 months	0.08	0.12	5.98	0.20	6.06	41%	1%
12 months	0.05	0.07	3.74	0.13	3.80	41%	1%

B) Upper bound model

	Formula Powder	Mixing Water		Total		% Powder	
		GM	Max	GM	Max	GM	Max
4 months	0.27	0.24	11.8	0.51	12.1	52%	2%
8 months	0.23	0.23	9.96	0.45	10.2	50%	2%
12 months	0.18	0.19	8.05	0.37	8.23	49%	2%

GM = geometric mean; Max = maximum value across individuals