POULTRY CONSUMPTION AND ARSENIC EXPOSURE IN THE U.S. POPULATION

by
Anne E. Nigra

A thesis submitted to Johns Hopkins University in conformity with the requirements for the degree of Master of Science (ScM)

Baltimore, Maryland
April 2016

ABSTRACT

Background: Arsenicals (roxarsone and nitarsone) used in poultry production likely increase inorganic arsenic (iAs) concentrations in poultry meat. The association between poultry intake and iAs exposure, as reflected in elevated urinary arsenic concentrations, however, is unknown.

Objectives: Evaluate the association between 24-hour dietary recall of poultry consumption and iAs exposure, as reflected in increased urine arsenic concentrations, in the U.S. population. We hypothesized that the association between turkey intake and increased urine arsenic concentrations would be modified by season, reflecting seasonal use of nitarsone.

Methods: We evaluated 3,329 participants ≥6 years old from the 2003-2010 National Health and Nutrition Examination Survey (NHANES) with urine arsenic available and undetectable urine arsenobetaine levels. Geometric mean ratios (GMR) of urine total arsenic and dimethylarsinic acid (DMA) were compared across increasing levels of poultry intake.

Results: After adjustment, participants in the highest quartile of poultry consumption had urine total arsenic 1.12 (95% CI 1.04, 1.22) and DMA 1.13 (1.06, 1.20) times higher than non-consumers. During the fall/winter participants in the highest quartile of turkey intake had urine total arsenic and DMA 1.17 (0.99, 1.39, p-trend=0.02) and 1.13 (0.99, 1.30, p-trend=0.03) times higher, respectively, than non-consumers. Past 24-hour consumption of turkey was not associated with total arsenic or DMA during the spring/summer.

Conclusions: Poultry intake was associated with increased urine total arsenic and DMA in NHANES 2003-2010, reflecting iAs exposure. Seasonally stratified analyses by poultry type provide strong suggestive evidence that the historical use of arsenic-based poultry drugs contributed to iAs exposure in the U.S. population, and support the banning of arsenic-based poultry drugs internationally.

Acknowledgements:

Coauthors: Keeve E. Nachman, PhD[2,3,4], David C. Love, PhD[2,3], Maria Grau-Perez, MS[2], Ana Navas-Acien, MD, PhD[1,2]

[1]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; [2]Department of Environmental Health Sciences, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; [3]Center for a Livable Future, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; [4]Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

I would like to thank Ana and Keeve for their wonderful mentoring and support, and Maria for all of her help with R. This research was supported by R01ES021367 and R01ES025216 and a directed research grant from the Johns Hopkins Center for a Livable Future.

Table of Contents

INTRODUCTION

In populations with low arsenic levels in drinking water, exposure to iAs occurs mainly through diet, particularly rice and other grains, as well as some juices and wine (Davis et al. 2012; DeCastro et al. 2014; FDA 2014a; Navas-Acien et al. 2011). Inorganic arsenic is a toxic and carcinogenic metalloid naturally occurring in water, air, and soil that enters the food supply through geological releases, contaminated water, and anthropogenic sources such as pesticide residue, non-ferrous metal smelting, and waste incineration (ATSDR 2007). Little is known, however, about the potential contribution of poultry intake to iAs exposure in human populations.

Arsenic-based drugs (roxarsone for chickens and nitarsone for turkey) were deliberately used in United States poultry production for decades, potentially representing an unnecessary and easily controllable source of iAs exposure in the population (Silbergeld and Nachman 2008). The FDA withdrew marketing approvals for roxarsone and two other arsenic-based feed additives in 2013, and withdrew approval for nitarsone, used to prevent histomoniasis in turkeys, in December of 2015. (FDA 2014b; Abraham et al. 2013; FDA 2015). Historical use of nitarsone in turkey production and roxarsone in chicken production may thus have been a chronic source of iAs exposure for the U.S. population, and is likely on-going in other parts of the world.

In 2010, it was estimated that ~88% of broiler chickens available at market had been treated with roxarsone (Nachman et al. 2012). A similar estimate is not available for nitarsone, but turkey industry representatives have reported that nitarsone was used seasonally during hot-weather months in young turkeys that were consumed during the fall/winter (Aubrey 2013). Analyses of chicken meat have shown that the use of roxarsone during chicken production likely contributes to elevated iAs, DMA, and other unknown arsenic species in chicken meat, and that the concentration of iAs increases with cooking (Nachman et al. 2013). Analyses of turkey meat have also shown that the use of nitarsone during turkey production likely contributes to elevated iAs, monomethylarsonate (MMA), and other unknown arsenic species in turkey meat (Nachman KE, oral communication, November 2015). It is unknown, however, if consumption of poultry exposed to arsenic-based drugs results in increased iAs exposure and internal dose in the population, as reflected in urinary excretion.

The National Health and Nutrition Examination Survey (NHANES) collects 24-hour dietary recall information the same day a spot urine sample is collected for total and speciated arsenic analysis (NCHS 2014). We evaluated whether consumption of poultry in the past 24-hours was associated with increased iAs exposure, as measured in urine by total arsenic and DMA during a time period when arsenic-based poultry drugs were approved for use in the U.S.

We hypothesized a priori that the association between turkey intake and elevated urine total arsenic and DMA would be modified by season (strongest for turkey consumed during the fall/winter and null for turkey consumed during the spring/summer), while the association for chicken intake would persist across seasons. To our knowledge, this is the first study to evaluate the association between recent poultry consumption and iAs exposure, as reflected in urine total arsenic and DMA concentrations.

METHODS

Study population

We analyzed data from the 2003-2010 cycles of the NHANES, conducted by the U.S. National Center for Health Statistics. NHANES is a multi-stage, nationally-representative sample of the non-institutionalized population (NCHS 2014). Our study uses data from the demographic questionnaire, the 24-hour dietary recall, the clinical examination, and the laboratory examination. All NHANES protocols were approved by the U.S. National Center for Health Statistics institutional review board and all participants gave written informed consent (NCHS 2011a). Our study was exempt from IRB approval because we used de-identified, publically-available data. To capture a time period when urine arsenic measures were available and roxarsone, nitarsone, and other arsenic-based drugs were still available in poultry production, we restricted our analysis to 2003-2010 NHANES cycles.

Urine arsenic was measured in a one-third subsample of all participants ≥ 6 years of age. From 10,451 participants in the NHANES 2003-2010 urine arsenic subsamples, we excluded 387 missing total urine arsenic, arsenobetaine, or DMA; 229 who were pregnant; 880 missing BMI, cotinine, urinary creatinine, or education information; and 5,626 with detectable arsenobetaine, as seafood arsenicals markedly contribute to total arsenic exposure and DMA and make it difficult to evaluate the contribution of other foods to iAs exposure (Navas-Acien et al. 2011). The final sample size was 3,329 participants 6 years and older. The response rate across the entire survey period was 76.5% (NCHS 2013).

Urine arsenic

Spot urine samples were collected during examination, poured in 5-mL cryovial vessels, frozen at ≤-20º C, and shipped within one week on dry ice to the National Center for Environmental Health at the Center for Disease Control and Prevention for analysis (NCHS 2005). Total arsenic concentrations were determined via quadrupole inductively coupled-plasma mass spectrometry with dynamic reaction cell (ICP-DRC-MS). Speciated arsenic concentrations (arsenite, arsenate, MMA, DMA and arsenobetaine) were determined via HPLC coupled to ICP-DRC-MS (NCHS 2007, 2009a, 2011b, 2011c).

We used total arsenic and DMA as proxies for inorganic arsenic internal dose (ideally measured as the sum of iAs and metabolites MMA and DMA), as the limits of detection (LOD) and percent of analytic sample below the LOD for arsenite (1.2 µg/L, 97.7%), arsenate (1.0 µg/L, 96.8%), and MMA (0.9 µg/L, 74.0%) were high compared to some other studies evaluating urinary arsenic levels, and most samples were largely undetectable (Cubadda et al. 2012; NCHS 2007, 2009a, 2011b, 2011c; Scheer et al. 2012). Although total arsenic and DMA reflect organic and inorganic arsenic exposure, restricting to participants with undetectable arsenobetaine likely removed the effect of organic arsenicals, which are thought to be largely non-toxic and which are attributable to seafood intake (Navas-Acien et al. 2011).

The LOD for total arsenic ranged from 0.60 µg/L to 0.74 µg/L across the entire survey period, with an inter-assay coefficient of variation ranging from 3.0% to 19.4% for lots with mean concentrations of 3.6 µg/L to 8.15 µg/L (NCEH 2006a, 2007, 2008, 2010). For DMA across the entire survey period, the LOD was 1.7 µg/L with an inter-assay coefficient of variation ranging from 4.6% to 6.6% for lots with mean concentrations of 4.12 μg/L to 6.85 μg/L (NCEH 2004, 2006b, 2008, 2010). The percent of participants in the analytic sample below the LOD for poultry consumers and non-consumers was 1.2% and 4.0%, respectively, for urine total arsenic and 28.2% and 32.0%, respectively, for DMA. Values below the LOD for total arsenic and DMA were replaced by the LOD divided by the square root of two. The LOD for arsenobetaine was <0.4 μg/L across the entire survey period (NCEH 2004, 2006b, 2008, 2010).

24-hour poultry intake assessment

Poultry intake during the past 24-hours was collected via multiple-pass dietary recall during the in person questionnaire. Multiple-pass dietary recall is the validated method of choice for food recall, and is conducted in five steps: 1) easily remembered foods; 2) frequently forgotten foods; 3) time and occasion of meals; 4) detailed descriptions, eating locations, portions; and 5) final review probe (Conway et al. 2004; NCHS 2009b). To estimate portion size, participants are given 2- and 3-dimensional measuring guides (NCHS 2010). Food and drink items are reported in grams of intake and linked to 8-digit U.S. Department of Agriculture (USDA) food codes. Because USDA food codes often contain multiple food components (e.g. chicken sandwich), we used Food Commodity Index Database (FCID) codes to determine the weight of each USDA food item attributable to poultry meat (See Supplementary Material: Table S1) (EPA 2010a). The FCID was developed by the Environmental Protection Agency's (EPA) Office of Pesticide Programs. FCID codes convert the weight of each USDA food item into the respective weights of all commodities included in the item. For each participant, FCID commodity codes are summed across all USDA food items. We analyzed FCID commodity codes for “Turkey, meat” and “Chicken, meat,” and defined poultry intake as the sum of chicken and turkey meat intake, in g/kg bodyweight per day.

To control for potential confounding by other foods that contain substantial amounts of iAs, we used FCID commodity codes corresponding to rice, wine, and juice intake (Table S1) (FDA 2014a). Because no FCID commodity codes exist for cereals, we used corresponding USDA food codes (See Supplementary Material: Table S2).

Other variables

Questionnaire data (age, sex, race/ethnicity, education, smoking status, poverty-income ratio), examination data (body mass index, urine creatinine, serum cotinine) and tap water source were also available from NHANES. We categorized race/ethnicity as non-Hispanic white/non-Hispanic black/Mexican-American/other, including multiple races. Smoking status in adults was defined as never/former/current by self-report. Children (<20 years old) who never smoked a whole cigarette were categorized as “never” smokers; children who smoked a whole cigarette, but not in the past 30 days, were categorized as “former” smokers; children who smoked a cigarette in the last 30 days were categorized as “current” smokers. All participants with serum cotinine ≥10 ng/mL were re-categorized as “current” smokers, and children missing self-reported smoking status with serum cotinine <10 ng/mL were categorized as “never” smokers.

Statistical analysis

All statistical analyses were performed using the ‘survey’ package in R to account for NHANES complex survey design and sampling weights (Lumley 2014). Both urine total arsenic and DMA were right skewed and log-transformed for analysis.

We compared the geometric mean ratios (GMR) and corresponding 95% confidence intervals for both total arsenic and DMA by poultry intake using multiple linear regression across categories of intake for poultry and for chicken and turkey separately, comparing quartiles of intake within those who reported consuming poultry, chicken, or turkey to a reference category that included those who did not report any poultry, chicken, or turkey intake, respectively. Model 1 adjusted for urine creatinine (log-transformed continuous), age (continuous), sex (male/female), race/ethnicity (non-Hispanic white/non-Hispanic black/Mexican-American/other, including multiple), education (less than high school/high school or equivalent/greater than high school), poverty-income ratio (continuous), body mass index (continuous), smoking status (never/former/current), serum cotinine (log-transformed continuous), and tap water source (community supply/well or cistern/spring/other/no tap water). We were unable to exclude participants living in areas with high iAs levels in drinking water, as no information about participant location or geography was publically available. Model 2 further adjusted for past 24-hour intake of rice, cereal, juice, and wine (g/kg bodyweight, continuous). To allow a more flexible dose-response analysis, we also analyzed poultry intake as log-transformed continuous with restricted quadratic splines at the 10^{th}, 50^{th}, and 90th percentiles of poultry consumption among consumers, defining those who reported no poultry consumption as the reference group.

We also conducted subgroup analyses for poultry consumption by age, sex, race/ethnicity and rice consumption using multiple linear regression on total arsenic and DMA as log-transformed, with interaction terms for each subgroup. We then estimated the GMR of total arsenic and DMA comparing the 75th to 25th percentile of the poultry intake distribution, including non-consumers, by subgroup. To determine if season modified the relationship between intake and urine arsenic for turkey, but not chicken, we stratified our analyses by fall/winter (November 1st – April 30th) and spring/summer (May 1st – October 31st). We hypothesized that for turkey meat, but not chicken meat, the association would attenuate in the spring/summer but remain positive in the fall/winter, reflecting the seasonal use of nitarsone in turkey production and yearlong use of roxarsone in chicken production. Specifically, we hypothesized that summer use of nitarsone in turkey production would result in iAs exposure, as reflected in elevated urine total arsenic and DMA levels, in consumers during the fall/winter only.

RESULTS

Participant characteristics by poultry consumption

The weighted prevalence of poultry intake in the last 24-h was 52% overall and 50% among those with undetectable arsenobetaine (Table 1). Poultry consumers were younger, more likely to belong to racial/ethnic minority groups, more likely to report consuming rice and juice in the past 24-hours, and less likely to report consuming cereals in the past 24-hours. Among those with undetectable arsenobetaine, the median concentration of urine total arsenic and DMA were 4.18 and 2.56 µg/L, respectively, among poultry-consumers and 3.99 and 2.42 µg/L, respectively, among non-consumers.

Urine arsenic by poultry intake

After full adjustment, the GMRs (95% CIs) comparing the highest quartile of poultry intake among consumers (>1.61 g/kg bodyweight per day) to non-consumers were 1.12 (1.04, 1.22) for total arsenic and 1.13 (1.06, 1.20) for DMA (Table 2). When stratified by the type of poultry, the corresponding GMRs for total arsenic and DMA were 1.15 (1.06, 1.25) and 1.13 (1.06, 1.21) for chicken and 1.09 (0.99, 1.20) and 1.10 (1.01, 1.20) for turkey. In restricted quadratic spline models, both total arsenic and DMA increased significantly with increasing poultry intake beyond approximately 1.0 g/kg bodyweight (Figure 1). We found no difference in GMRs of total arsenic or DMA by poultry intake across age, sex, race/ethnicity and rice consumption subgroups (Figure 2).

Stratified analysis by season

In analyses stratified by season (winter vs. summer), the association between chicken intake and urine total arsenic and DMA remained similar for both seasons (p-value for interaction 0.76 for total arsenic and 0.24 for DMA). For turkey intake, however, the interaction was statistically significant for total arsenic (p-value for interaction 0.04 and borderline for DMA (0.07)), with strong associations for total arsenic and DMA in the fall/winter (p-for trend=0.02 and 0.03, respectively), but not in the spring/summer (p-for trend= 0.70 and 0.99, respectively) (Table 3).

DISCUSSION

In this representative study of the U.S. population conducted when roxarsone, nitarsone, and other arsenicals were widely used in poultry production, past 24-hour consumption of poultry was associated with elevated total arsenic and DMA concentrations in urine, reflecting iAs exposure (Chapman and Johnson 2002; Nachman et al. 2012). As hypothesized, chicken consumption was associated with increased urine total arsenic and DMA year-round, while only turkey consumption during the fall/winter, but not spring/summer, was associated with increased total arsenic and DMA in urine. These findings are consistent with the reported seasonal use of nitarsone in turkey production and the yearlong use of roxarsone in chicken production, and add to a growing body of literature suggesting that the use of arsenicals in poultry feed results in iAs exposure for poultry consumers (Aubrey 2013).

Arsenic-based drugs were used in U.S. poultry production for decades to prevent histomoniasis (blackhead disease) and coccidiosis (parasitic infection) and to improve weight gain and meat pigmentation (Abraham et al. 2013; Chapman and Johnson 2002; Silbergeld and Nachman 2008). Our results strongly support the decision of the FDA to withdraw approval for nitarsone sales in the U.S. beginning in December of 2015, and for roxarsone and other arsenicals in 2013. However, there is no indication that the marketing and use of arsenicals will be discontinued internationally (FDA 2015).

Inorganic arsenic is an established human carcinogen, causing cancers of the lung, skin, and bladder and maybe cancers of the liver and kidney (ATSDR 2007; IARC 2009). Increasing evidence supports that chronic low- to moderate iAs exposure levels results in numerous non-cancerous health effects, including cardiovascular, kidney and respiratory disease and diabetes, and cognitive and reproductive defects (Ahmad et al. 2011; Chen et al. 2011; Farzan et al. 2013; Farzan et al. 2015; Moon et al. 2012; Moon et al. 2013; Navas-Acien et al. 2008; Rahman et al. 2009; Tolins et al. 2014; Zheng et al. 2014). In 2011, the FDA concluded that any animal feed additive that contributed to increased iAs levels in poultry tissues was of concern (FDA 2011). The EPA's Integrated Risk Information System (IRIS) is currently reevaluating iAs risk assessment; a draft appearing on the EPA website proposed an updated lung and bladder cancer potency factor of 25.7 for the U.S. population, citing the increased susceptibility of women (EPA 2010b). Using this proposed cancer potency factor and intake rates from NHANES 2003-2006, Nachman et al. (2013) estimated that, assuming roxarsone use in chickens, a typical consumer of conventionally-produced chicken would receive an average daily iAs dose of 1.44 x 10^{-6} mg/kg bodyweight, resulting in an excess 124 bladder and/or lung cancer cases per year in the U.S.

Food is the primary source of unregulated arsenic exposure, highlighting the importance of eliminating or reducing dietary iAs exposures where possible (Georgopoulos et al. 2008). Specifically, rice, wine, juices, and cereals contribute to iAs exposure and rice can also contribute to DMA exposure, while seafood contributes to low-toxicity organic arsenicals (Davis et al. 2012; Jackson et al. 2012; Navas-Acien et al. 2011; Schoof et al. 1999; Tariba 2011). Contamination of rice, grain, and grape products is likely attributable to the historical application of arsenic-based pesticides, naturally occurring ground water contamination, and especially for rice, the accumulation and deposition of arsenic into the rice grain (Carey et al. 2012; Chen et al. 2015; Robinson et al. 2007; Tariba 2011; Wilson et al. 2012). There are also some reports of poultry waste being used to fertilize rice paddies and roxarsone potentially contributing to iAs in the rice (Alter vs. Pfizer Inc. 2012). Non-toxic, organic arsenicals (arsenobetaine, arsenosugars, arsenolipids) in seafood likely arise from the metabolism of naturally occurring arsenic in sea animals and plants (Sabbioni et al. 1991). Although phytoremediation by arsenic-accumulating plants can successfully remediate arsenic contaminated crop areas, remediation may require multiple cycles over long periods of time (Hettick et al. 2015). In contrast, eliminating the unnecessary and deliberate use of arsenic-based drugs in poultry production is an easily controlled method of reducing dietary iAs exposure.

Our seasonally stratified analysis provides strong suggestive evidence that iAs exposure from poultry consumption was the result of arsenic-based drug use. Multiple studies have shown that roxarsone is transformed into inorganic and other arsenic species under particular environmental conditions (Arai et al. 2003; Garbarino et al. 2003; Jackson et al. 2001). Moreover, elevated total and inorganic arsenic is found in poultry tissues and meat after treatment with arsenicals (Conklin et al. 2012; FDA 2011), and conventionally produced poultry is known to have higher levels of total and inorganic arsenic compared to organic and antibiotic-free poultry (Nachman et al. 2013). It is possible, however, that other arsenic sources are responsible for elevated arsenic in poultry tissue, such as accidental or naturally-occurring contamination of the soil, water, food supply, or packaging process (Hettick et al. 2015).

Our study has several limitations. We were unable to differentiate between poultry produced with and without arsenicals, as information regarding the consumption of organic or antibiotic-free poultry was not available and we were unable to quantify the amount of iAs present in the consumed poultry meat. Although consumption of poultry produced without arsenic-based drugs differs across socioeconomic groups, our analysis found no differences in urine total arsenic and DMA by poultry intake across racial/ethnic groups (Figure 1), poverty-income ratio (≤ 1 vs. >1), or education (data not shown) (Onyango et al. 2007). The LODs for total arsenic and arsenic species in NHANES are relatively high. Also, neither roxarsone nor nitarsone species were analyzed in urine. Additionally, our analysis was limited to poultry consumption in the past 24-hours, and urine arsenic may reflect dietary consumption over the last 1-4 days (CDC 2013). Because urine DMA has a shorter half-life than total arsenic, urine DMA is more likely to reflect past 24-hour dietary consumption (Fowler et al. 2007). We controlled for other dietary sources of arsenic exposure, including rice, wine, juices, cereals, and seafood. Restricting to participants with undetectable arsenobetaine likely removed the contribution of non-toxic organic seafood arsenicals and their metabolites, which, at very high concentrations, can overwhelm the evaluation of other dietary sources of arsenic. Although restriction markedly reduced the sample size, population characteristics before and after restriction remained similar (Table 1), and our results remained robust after full adjustment for both sociodemographic and dietary factors (Table 2).

CONCLUSIONS

Consistent with a growing body of literature establishing diet as an unregulated yet important source of iAs exposure in the U.S. population (Tariba 2011; Jackson et al. 2012), our results support that the use of arsenicals in poultry production resulted in iAs exposure to poultry consumers, as measured in elevated urine total arsenic and DMA. Historical seasonal use of nitarsone in turkey production and yearlong use of roxarsone in chicken production may represent an important source of chronic iAs exposure in the U.S. population. Future research should evaluate if the relationship between poultry consumption and elevated urine total arsenic and DMA is attenuated in years after the withdrawal of arsenic-based drugs from the U.S. market. Our study provides strong evidence to support the FDA's recent decision to withdraw approval for nitarsone, and to extend the banning of arsenic-based drugs in food production to all countries around the world.

REFERENCES

Abraham M, McDougald L, Beckstead R. 2013. Blackhead disease: Reduced sensitivity of Histomonas meleagridis to nitarsone in vitro and in vivo. Avian Dis 58(1):60-63.

Ahmad SA, Sayed MH, Barua S, Khan MH, Faruquee MH, Jalil A, et al. 2001. Arsenic in drinking water and pregnancy outcomes. Environ Health Perspect 109(6):629-631.

Alter v. Pfizer Inc. 2012. Case No. CV-2012-67. Arkansas County Circuit Court, September 24, 2012. Available: http://www.hwnn.com/images/stories/hwnn/amended_complaint.pdf [accessed 28 October 2015].

Arai Y, Lanzirotti A, Sutton S, Davis J, Sparks D. 2003. Arsenic speciation and reactivity in poultry litter. Environ Sci Technol 37(18):4083-4090.

ATSDR (Agency for Toxic Substances and Disease Registry). 2007. Toxicological profile for arsenic. Available: http://www.atsdr.cdc.gov/ToxProfiles/tp2.pdf. 2007 [accessed 30 July 2015].

Aubrey, A. NPR (National Public Radio). How trace amounts of arsenic end up in grocery store meat. 2013. Available: http://www.npr.org/sections/thesalt/2013/05/15/184261664/how-trace-amounts-of-arsenic-end-up-in-grocery-store-meat [accessed 22 October 2015].

Carey AM, Lombi E, Donner E, deJonge MD, Punshon T, Jackson BP, et al. 2012. A review of recent developments in the speciation and location of arsenic and selenium in rice grain. Anal Bioanal Chem 402(10):3275-3286.

CDC (Center for Disease Control and Prevention) National Biomonitoring Program. 2013. Biomonitoring Summary: Arsenic. Available: http://www.cdc.gov/biomonitoring/Arsenic_BiomonitoringSummary.html [accessed 13 August 2015].

CDC (Center for Disease Control and Prevention). 2014. Fourth Report on Human Exposures to Environmental Chemicals. Biomonitoring summary: Arsenic. Available: http://www.cdc.gov/exposurereport/pdf/fourthreport.pdf [accessed 13 August 2015].

Chapman HD, Johnson ZB. 2002. Use of antibiotics and roxarsone in broiler chickens in the USA: analysis for the years 1995 to 2000. Poult Sci 81(3):356-364.

Chen Y, Graziano JH, Parvez F, Admed A, Eunus M, McClintock TR, et al. 2011. Arsenic exposure from drinking water and mortality from cardiovascular disease in Bangladesh: prospective cohort study. Br Med J 342:d2431. doi: 10.1136/bmj.d2431.

Chen Y, Moore KL, Miller AJ, McGrath SP, Ma JF, Zhao FJ. 2015. The role of nodes in arsenic storage and distribution in rice. J Exp Bot 66(13):3717-3724.

Conklin SD, Shockey N, Kubachka K, Howard KD, Carson MC. 2012. Development of an ion chromatography–inductively coupled plasma–mass spectrometry method to determine inorganic arsenic in liver from chickens treated with roxarsone. J Agric Food Chem 60(37):9394-9404.

Conway JM, Ingwersen LA, Moshfegh AJ. 2004. Accuracy of dietary recall using the USDA five-step multiple-pass method in men: An observational validation study. J Am Diet Assoc 104(4):595-603.

Cubadda F, Aureli F, D'Amato M, Raggi A, Turco AC, Mantovani A. 2012. Speciated urinary arsenic as a biomarker of dietary exposure to inorganic arsenic in residents living in high-arsenic areas in Latium, Italy. Pure Appl Chem 84(2):203-214.

Davis MA, Mackenzie TA, Cottingham KL, Gilbert-Diamond D, Punshon T, Karagas MR. 2012. Rice consumption and urinary arsenic concentrations in U.S. children. Environ Health Perspect 120(10):1418-1424. doi:10.1289/ehp.1205014.

DeCastro BR, Caldwell KL, Jones RL, Blount BC, Pan Y, Ward C, et al. 2014. Dietary sources of methylated arsenic species in urine of the United States population, NHANES 2003–2010. PLoS ONE 9(9):e108098, doi:10.1371/journal.pone.0108098.

EPA (Environmental Protection Agency) 2010a. Food Commodity Intake Database. Available: http://www.fcid.foodrisk.org [accessed 30 July 2015].

EPA (Environmental Protection Agency). 2010b. IRIS Toxicological Review of Ingested Inorganic Arsenic (2010 External Review Draft). EPA/635/R-10/001. Available:

http://cfpub.epa.gov/ncea/iris_drafts/ recordisplay.cfm?deid=219111 [accessed 13 August 2015].

Farzan SF, Karagas MR, Chen Y. 2013. In utero and early life arsenic exposure in relation to long-term health and disease. Toxicol Appl Pharmacol 272(2):384-390.

Farzan SF, Li Z, Korrick SA, Spiegelman D, Enelow R, Nadeau K, et al. 2015. Infant Infections and Respiratory Symptoms in Relation to Arsenic Exposure in a U.S. Cohort. Environ Health Perspect; doi: 10.1289/ehp.1409282 [Online 11 September 2015].

FDA (Food and Drug Administration). 2011. Provide data on various arsenic species present in broilers treated with roxarsone: Comparison with untreated birds. Available: http://www.fda.gov.ezp.welch.jhmi.edu/downloads/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/UCM257545.pdf [accessed 12 August 2015].

FDA (Food and Drug Administration). 2014a. Total Diet Study: Elements Results Summary Statistics, Market baskets 2006 through 2011. Available: http://www.fda.gov/downloads/Food/FoodScienceResearch/TotalDietStudy/UCM184301.pdf [accessed 30 July 2015].

FDA (Food and Drug Administration). 2014b. Withdrawal of Approval of New Animal Drug Applications for Combination Drug Medicated Feeds Containing an Arsenical Drug. Fed Reg 78:70062. Available: http://www.gpo.gov/fdsys/pkg/FR-2014-02-27/pdf/2014-02617.pdf [accessed 30 July 2015].

FDA (Food and Drug Administration). 2015. FDA announces pending approval of withdrawal of nitarsone. Available: http://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm440668.htm [accessed 30 July 2015].

Fowler BA, Nordberg M, Jones RL, Chen CJ. 2007. Arsenic. In: Handbook on the toxicology of metals, Third edition (Nordberg GF, Fowler BA, Nordberg M, Friberg LT, eds). Burlington, MA:Elsevier, 367-406.

Garbarino J, Bednar A, Rutherford D, Beyer R, Wershaw R. 2003. Environmental fate of roxarsone in poultry litter: degradation of roxarsone during composting. Environ Sci Technol 37(8):1509-1514.

Georgopoulos PG, Wang S, Yang Y, Xue J, Zartarian VG, McCurdy T, et al. 2008. Biologically based modeling of multimedia, multipathway, multiroute population exposures to arsenic. J Expo Sci Environ Epidemiol 18(5):462-476.

Hettick BE, Cañas-Carrell JE, French AD, Klein DM. 2015. Arsenic: A review of the element's toxicity, plant interactions, and potential methods of remediation. J Agric Food Chem 63(32):7097-7107.

IARC (International Agency for Research on Cancer) Working Group on the Evaluation of Carcinogenic Risks to Humans. 2009. A review of human carcinogens. Part C: Arsenic, metals, fibres, and dusts. Available: http://monographs.iarc.fr/ENG/Monographs/vol100C/mono100C.pdf [accessed 30 July 2015].

Jackson BP, Bertsch PM. 2001. Determination of arsenic speciation in poultry wastes by IC-ICP-MS. Environ Sci Technol 35(24):4868-4873.

Jackson BP, Taylor VF, Karagas MR, Punshon T, Cottingham KL. 2012. Arsenic, organic foods, and brown rice syrup. Environ Health Perspect 120(5):623-626.

Lumley T. 2014. "survey: analysis of complex survey samples." R package version 3.30.

Moon KA, Guallar E, Navas-Acien A. 2012. Arsenic exposure and cardiovascular disease: an updated systematic review. Curr Atheroscler Rep 14(6):542-555.

Moon KA, Guallar E, Umans JG, Devereux RB, Best LG, Francesconi KA, et al. 2013. Association between exposure to low to moderate arsenic levels and incident cardiovascular disease: a prospective cohort study. Ann Intern Med 159(10):649-659.

Nachman K, Raber G, Francesconi K, Navas-Acien A, Love D. 2012. Arsenic species in poultry feather meal. Sci Total Environ 417:183-188.

Nachman KE, Baron PA, Raber G, Francesconi KA, Navas-Acien A, Love DC. 2013. Roxarsone, inorganic arsenic, and other arsenic species in chicken: a U.S.-based market basket sample. Environ Health Perspect 121(7):818-824.

Navas-Acien A, Francesconi KA, Silbergeld EK, Guallar E. 2011. Seafood intake and urine concentrations of total arsenic, dimethylarsinate and arsenobetaine in the US population. Environ Res 111(1):110-118.

Navas-Acien A, Silbergeld EK, Pastor-Barriuso R, Guallar E. 2008. Arsenic exposure and prevalence of type 2 diabetes in US adults. JAMA Intern Med 300(7):814-822.

NCEH (National Center for Environmental Health). 2004. Laboratory Procedure Manual: Urine arsenic speciation. Available: http://www.cdc.gov/nchs/data/nhanes/nhanes_03_04/l06uas_c_met_arsenic_speciated.pdf [accessed 30 July 2015].

NCEH (National Center for Environmental Health). 2006a. Laboratory Procedure Manual: Total Arsenic. Available: http://www.cdc.gov/nchs/data/nhanes/nhanes_05_06/uas_d_met.pdf [accessed 30 July 2015].

NCEH (National Center for Environmental Health). 2006b. Laboratory Procedure Manual: Urine arsenic speciation. Available: http://www.cdc.gov/nchs/data/nhanes/nhanes_05_06/l06uas_d_met_arsenic_speciated.pdf [accessed 30 July 2015].

NCEH (National Center for Environmental Health). 2007. Laboratory Procedure Manual: Total Arsenic. Available: http://www.cdc.gov/nchs/data/nhanes/nhanes_03_04/l06uas_c_met_arsenic_total.pdf [accessed 30 July 2015].

NCEH (National Center for Environmental Health). 2008. Laboratory Procedure Manual: Urine arsenic speciation. Available: http://www.cdc.gov/nchs/data/nhanes/nhanes_07_08/uas_e_met_arsenic.pdf [accessed 30 July 2015].

NCEH (National Center for Environmental Health). 2010. Laboratory Procedure Manual: Urine arsenic speciation. Available: http://www.cdc.gov/nchs/data/nhanes/nhanes_09_10/uas_f_met_arsenic.pdf [accessed 30 July 2015].

NCHS (National Center for Health Statistics). 2005. Laboratory Procedure Manual. Available: http://www.cdc.gov/nchs/data/nhanes/nhanes_05_06/lab.pdf [accessed 30 July 2015].

NCHS (National Center for Health Statistics). 2007. 2003-2004 Data Documentation, Codebook, and Frequencies. Available: http://wwwn.cdc.gov/Nchs/Nhanes/2003-2004/L06UAS_C.htm [accessed 30 July 2015].

NCHS (National Center for Health Statistics). 2009a. 2005-5006 Data Documentation, Codebook, and Frequencies. Available: http://wwwn.cdc.gov/Nchs/Nhanes/2005-2006/UAS_D.htm [accessed 30 July 2015].

NCHS (National Center for Health Statistics). 2009b. MEC-in person dietary interviewers procedures manual. Available: http://www.cdc.gov/nchs/data/nhanes/nhanes_09_10/DietaryInterviewers_Inperson.pdf [accessed 30 July 2015].

NCHS (National Center for Health Statistics). 2010. Measuring guides for the dietary recall interview. Available: http://www.cdc.gov/nchs/nhanes/measuring_guides_dri/measuringguides02.htm [accessed 30 July 2015].

NCHS (National Center for Health Statistics). 2011a. Participants: Informed consent. Available: http://www.cdc.gov/nchs/nhanes/genetics/genetic_participants.htm [accessed 30 July 2015].

NCHS (National Center for Health Statistics). 2011b. 2009-2010 Data Documentation, Codebook, and Frequencies. Available: http://wwwn.cdc.gov/Nchs/Nhanes/2009-2010/UAS_F.htm [accessed 30 July 2015].

NCHS (National Center for Health Statistics). 2011c. 2007-2008 Data Documentation, Codebook, and Frequencies. Available: http://wwwn.cdc.gov/Nchs/Nhanes/2007-2008/UAS_E.htm [accessed 30 July 2015].

NCHS (National Center for Health Statistics). 2013. NHANES Response Rates and Population Totals. Available: http://www.cdc.gov/nchs/nhanes/response_rates_cps.htm [accessed 22 October 2015].

NCHS (National Center for Health Statistics). 2014. About the National Health and Nutrition Examination Survey. Available: http://www.cdc.gov/nchs/nhanes/about_nhanes.htm [accessed 30 July 2015].

Onyango BM, Hallman WK, Bellows AC. 2007. Purchasing organic food in US food systems: A study of attitudes and practice. Br Food J 109(5):399-411.

Rahman A, Vahter M, Smith AH, Nermell B, Yunus M, El Arifeen S, et al. 2009. Arsenic exposure during pregnancy and size at birth: a prospective cohort study in Bangladesh. Am J Epidemiol 169(3):304-312.

Robinson GR, Larkins P, Boughton CJ, Reed BW, Sibrell PL. 2007. Assessment of contamination from arsenical pesticide use on orchards in the Great Valley region, Virginia and West Virginia, USA. J Environ Qual 36(3):654-663.

Sabbioni E, Fischbach M, Pozzi G, Pietra R, Gallorini M, Piette JL. 1991. Cellular retention, toxicity and carcinogenic potential of seafood arsenic. I. Lack of cytotoxicity and transforming activity of arsenobetaine in the BALB/3T3 cell line. Carcinogenesis 12(7):1287-1291.

Schoof R, Yost L, Eickhoff J, Crecelius EA, Cragin DW, Meacher DM, et al. 1999. A market basket survey of inorganic arsenic in food. Food Chem Toxico 37(8):839-846.

Scheer J, Findenig S, Goessler W, Francesconi KA, Howard B, Umans JG, et al. 2012. Arsenic species and selected metals in human urine: validation of HPLC/ICPMS and ICPMS procedures for a long-term population-based epidemiological study. Anal Methods 4(2):406-413.

Silbergeld EK, Nachman K. 2008. The environmental and public health risks associated with arsenical use in animal feeds. Ann N Y Acad Sci 1140(1):346-357.

Tariba B. 2011. Metals in wine—impact on wine quality and health outcomes. Biol Trace Elem Res 144(1-3):143-156.

Tolins M, Ruchirawat M, Landrigan P. 2014. The developmental neurotoxicity of arsenic: cognitive and behavioral consequences of early life exposure. Ann Glob Health 80(4):303-314.

Wilson D, Hooper C, Shi X. 2012. Arsenic and lead in juice: apple, citrus, and apple-base. J Environ Health 75(5):14-20.

Zheng L, Kuo C, Fadrowski J, Agnew J, Weaver VM, Navas-Acien A. 2014. Arsenic and chronic kidney disease: A systematic review. Curr Envir Health Rpt 1(3):192-207.

TABLES

Table 1. Participant characteristics by arsenobetaine and poultry intake, 2003-2010

	Participants with undetectable arsenobetaine (N= 3,329)		**All participants (N= 8,955)**	
	Poultry intake past 24-hours		**Poultry intake past 24-hours**	
	Yes	**No**	**Yes**	**No**
N (%)[a]	1740 (50.1)	1589 (49.9)	4773 (52.0)	4182 (48.0)
Age (yr) - mean (SE)	35.2 (0.6)	38.2 (0.8)	39.3 (0.4)	41.8 (0.5)
Sex - % female (SE)	53.9 (1.5)	53.8 (1.7)	50.4 (1.1)	50.6 (1.0)
Race/ethnicity - % (SE)				
non-Hispanic white	70.0 (2.2)	76.2 (2.0)	65.4 (2.0)	73.7 (1.8)
non-Hispanic black	10.4 (1.1)	7.5 (0.9)	13.6 (1.1)	9.2 (0.7)
Mexican-American	11.6 (1.5)	9.0 (1.0)	9.7 (1.1)	8.7 (0.9)
Other, including multiple	7.9 (0.9)	7.3 (1.0)	11.3 (1.0)	8.4 (0.8)
Education - % (SE)				
<High school	22.0 (1.5)	20.0 (1.4)	19.0 (1.0)	18.7 (1.0)
HS or equivalent	26.7 (1.6)	28.8 (1.7)	23.8 (0.8)	26.9 (0.9)
>HS	51.4 (2.0)	51.2 (1.9)	54.4 (1.2)	57.2 (1.2)
Smoking - % (SE)				
Never	58.3 (1.9)	59.0 (1.9)	57.5 (1.2)	52.8 (1.1)
Former	15.9 (1.1)	15.5 (1.4)	19.1 (0.8)	19.9 (0.9)
Current	25.8 (1.9)	25.4 (1.7)	23.4 (0.9)	27.3 (1.0)
Cotinine (nmol/L)	0.07 (0.02, 6.80)	0.08 (0.02, 3.78)	0.06 (0.02, 2.17)	0.07 (0.02, 13.80)
BMI - mean (SE)	26.2 (0.2)	26.3 (0.2)	27.1 (0.1)	27.2 (0.2)
Chicken past 24-hr - N (%)	1622 (93.5)	-	4459 (93.7)	-
Turkey past 24-hr - N (%)	752 (46.3)	-	2093 (47.0)	-
Both past 24-hr - N(%)	634 (39.8)	-	1779 (40.7)	-

Seafood past 24-hr - % (SE)	3.4 (0.6)	2.2 (0.5)	16.7 (0.8)	16.8 (0.9)
Rice past 24-hr - % (SE)	18.9 (1.2)	10.7 (1.2)	26.7 (1.1)	14.9 (1.0)
Juice past 24-hr - % (SE)	19.8 (1.2)	16.3 (1.4)	17.8 (0.7)	15.2 (0.7)
Wine past 24-hr - % (SE)	3.2 (0.7)	3.6 (0.6)	6.4 (0.6)	6.1 (0.6)
Cereal past 24-hr - % (SE)	29.2 (1.7)	33.0 (2.2)	29.7 (0.9)	31.5 (1.2)
Total urine arsenic (µg/L)	4.18 (2.47, 6.97)	3.99 (2.21, 6.30)	8.22 (4.35, 16.49)	7.63 (4.00, 16.17)
Urine DMA (µg/L)	2.56 (1.20, 4.26)	2.42 (1.20, 3.93)	3.73 (2.11, 6.00)	3.52 (2.00, 5.93)
Urine arsenobetaine (AB) (µg/L)	-	-	1.20 (0.28, 5.89)	0.94 (0.28, 5.38)
Total arsenic minus AB (µg/L)	-	-	6.10 (3.34, 10.70)	5.77 (3.12, 10.47)

Cotinine, total urine arsenic, dimethylarsinate (DMA), arsenobetaine (AB), and total arsenic minus AB are median (interquartile range).

[a] All percentages are weighted to account for NHANES complex sampling design and weights.

Table 2. Urine arsenic concentrations by poultry intake in the past 24-hrs (N=3,329)

		Total arsenic			DMA		
	N (%)[a]	Geometric mean (95% CI)	Model 1[c] GMR (95% CI)	Model 2[d] GMR (95% CI)	Geometric mean (95% CI)	Model 1[c] GMR (95% CI)	Model 2[d] GMR (95% CI)
Poultry intake (g/kg bodyweight)							
0	1589 (49.9)	3.72 (3.45, 4.01)	1 (reference)	1 (reference)	2.53 (2.40, 2.67)	1 (reference)	1 (reference)
0.001 - 0.42	435 (12.6)	3.63 (3.29, 4.01)	1.06 (0.99, 1.14)	1.05 (0.99, 1.13)	2.39 (2.24, 2.55)	1.02 (0.95, 1.08)	1.01 (0.95, 1.07)
0.421 - 0.90	435 (12.3)	4.11 (3.64, 4.64)	1.13 (1.04, 1.23)	1.12 (1.04, 1.22)	2.64 (2.39, 2.93)	1.08 (1.00, 1.16)	1.07 (0.99, 1.16)
0.901 - 1.61	435 (13.0)	4.12 (3.84, 4.43)	1.12 (1.04, 1.21)	1.12 (1.05, 1.21)	2.65 (2.46, 2.85)	1.08 (1.01, 1.17)	1.08 (1.01, 1.16)
1.611 +	435 (12.1)	4.60 (4.16, 5.09)	1.17 (1.08, 1.28)	1.12 (1.04, 1.22)	3.03 (2.81, 3.28)	1.17 (1.10, 1.25)	1.13 (1.06, 1.20)
[b] p-trend			<0.001	<0.001		<0.001	<0.001
Chicken intake (g/kg bodyweight)							
0	1707 (53.2)	3.74 (3.48, 4.02)	1 (reference)	1 (reference)	2.54 (2.41, 2.67)	1 (reference)	1 (reference)
0.001 - 0.30	406 (12.2)	3.44 (3.12, 3.79)	1.02 (0.94, 1.10)	1.02 (0.95, 1.09)	2.28 (2.12, 2.46)	0.99 (0.92, 1.05)	0.98 (0.93, 1.04)
0.30 - 0.79	405 (11.4)	4.16 (3.77, 4.60)	1.13 (1.04, 1.23)	1.12 (1.04, 1.20)	2.70 (2.45, 2.97)	1.09 (1.02, 1.17)	1.08 (1.01, 1.15)
0.79 - 1.44	406 (12.3)	4.24 (3.91, 4.60)	1.17 (1.08, 1.26)	1.16 (1.08, 1.25)	2.73 (2.52, 2.97)	1.12 (1.05, 1.21)	1.12 (1.04, 1.20)
1.44+	405 (10.9)	4.72 (4.23, 5.27)	1.19 (1.09, 1.30)	1.15, (1.06, 1.25)	3.07 (2.83, 3.34)	1.17 (1.09, 1.25)	1.13 (1.06, 1.21)
[b] p-trend			<0.001	<0.001		<0.001	<0.001
Turkey intake (g/kg bodyweight)							
0	2577 (76.8)	3.86 (3.61, 4.12)	1 (reference)	1 (reference)	2.58 (2.45, 2.71)	1 (reference)	1 (reference)
0.001 - 0.14	188 (5.6)	3.79 (3.30, 4.36)	1.06 (0.98, 1.14)	1.04 (0.95, 1.14)	2.62 (2.33, 2.94)	1.07 (0.99, 1.17)	1.06 (0.97, 1.15)
0.14 - 0.29	188 (5.2)	3.93 (3.48, 4.43)	1.04 (0.94, 1.14)	1.07 (0.97, 1.17)	2.44 (2.22, 2.68)	0.98 (0.91, 1.06)	1.01 (0.94, 1.08)
0.29 - 0.54	188 (5.8)	3.98 (3.41, 4.65)	1.06 (0.96, 1.18)	1.06 (0.96, 1.17)	2.53 (2.19, 2.92)	1.02 (0.91, 1.14)	1.01 (0.91, 1.13)
0.54+	188 (6.5)	4.55 (3.94, 5.25)	1.12 (1.00, 1.25)	1.09 (0.99, 1.20)	3.00 (2.63, 3.42)	1.13 (1.02, 1.26)	1.10 (1.01, 1.20)
[b] p-trend			0.04	0.04		0.07	0.08

GMR = geometric mean ratio. Poultry defined as chicken and/or turkey.

[a] All percentages are weighted to account for NHANES complex sampling design and weights.

[b] p-trend obtained from adding quartile of poultry intake as continuous variable to model.

[c] Model 1 adjusted for urine creatinine (log-transformed continuous), age (continuous), sex (male/female), race/ethnicity (non-Hispanic white/non-Hispanic black/Mexican-American/Other, including multiple), education (<high school/ high school or equivalent/ >high school), body mass index (continuous), smoking status (never/former/current), serum cotinine (log-transformed continuous), poverty income ratio (PIR, continuous), and tap water source (community supply/well,cistern/spring/other/no tap water).

[d] Model 2 further adjusted for past 24-hr intake of rice, cereal, juice, and wine (g/kg bodyweight, continuous).

Table 3. Urine arsenic concentrations by poultry intake in the past 24-hrs - stratified by season (N= 3,329)

		Total arsenic			DMA		
Intake (g/kg bodyweight)	N (%)[e]	Geometric mean (95% CI)	Model 1[h] GMR (95% CI)	Model 2[i] GMR (95% CI)	Geometric mean (95% CI)	Model 1[h] GMR (95% CI)	Model 2[i] GMR (95% CI)
Turkey intake				*Spring/summer season*			
0	1410 (77.5)	3.71 (3.40, 4.05)	1 (reference)	1 (reference)	2.50 (2.35, 2.66)	1 (reference)	1 (reference)
0.001 - 0.15	104 (6.0)	3.65 (3.00, 4.44)	1.02 (0.90, 1.14)	1.00 (0.88, 1.14)	2.61 (2.24, 3.05)	1.10 (0.98, 1.23)	1.08 (0.96, 1.23)
0.15 - 0.29	101 (4.9)	3.69 (3.13, 4.33)	0.99 (0.84, 1.16)	1.02 (0.88, 1.17)	2.27 (1.99, 2.58)	0.93 (0.81, 1.08)	0.95 (0.84, 1.08)
0.29 - 0.53	102 (6.0)	3.64 (3.00, 4.42)	1.02 (0.89, 1.16)	1.02 (0.90, 1.16)	2.28 (1.94, 2.68)	0.93 (0.82, 1.06)	0.94 (0.82, 1.07)
0.53+	102 (5.6)	3.94 (3.29, 4.70)	1.02 (0.91, 1.14)	1.01 (0.92, 1.12)	2.65 (2.26, 3.12)	1.07 (0.95, 1.20)	1.06 (0.96, 1.17)
[f] p-trend			0.75	0.70		0.98	0.99
				Fall/winter season			
0	1167 (75.6)	4.12 (3.80, 4.47)	1 (reference)	1 (reference)	2.74 (2.57, 2.92)	1 (reference)	1 (reference)
0.001 - 0.14	86 (5.2)	4.23 (3.60, 4.97)	1.13 (1.00, 1.27)	1.11 (1.00, 1.24)	2.68 (2.26, 3.18)	1.04 (0.92, 1.18)	1.03 (0.92, 1.15)
0.14 - 0.28	86 (5.9)	4.13 (3.57, 4.79)	1.13 (0.96, 1.32)	1.16 (1.00, 1.34)	2.65 (2.36, 2.98)	1.08 (0.97, 1.21)	1.11 (1.02, 1.22)
0.28 - 0.56	85 (5.3)	4.79 (3.82, 6.00)	1.10 (0.91, 1.32)	1.06 (0.90, 1.26)	3.07 (2.41, 3.90)	1.13 (0.93, 1.37)	1.09 (0.92, 1.30)
0.56+	86 (7.9)	5.38 (4.33, 6.69)	1.22 (1.01, 1.48)	1.17 (0.99, 1.39)	3.47 (2.87, 4.20)	1.19 (1.00, 1.40)	1.13 (0.99, 1.30)
[f] p-trend			0.013	0.018		0.02	0.03
[g] p-interaction			0.030	0.044		0.05	0.07
Chicken intake				*Spring/summer season*			
0	994 (55.8)	3.63 (3.30, 3.99)	1 (reference)	1 (reference)	2.48 (2.32, 2.64)	1 (reference)	1 (reference)
0.001 - 0.26	209 (11.4)	3.31 (2.90, 3.78)	1.02 (0.93, 1.12)	1.01 (0.94, 1.10)	2.21 (2.02, 2.42)	0.97 (0.91, 1.05)	0.97 (0.90, 1.04)
0.26 - 0.77	204 (10.8)	3.87 (3.31, 4.53)	1.10 (1.00, 1.22)	1.10 (1.00, 1.21)	2.56 (2.17, 3.02)	1.07 (0.96, 1.20)	1.07 (0.96, 1.18)
0.77 - 1.41	205 (11.7)	3.91 (3.57, 4.29)	1.16 (1.06, 1.27)	1.17 (1.07, 1.28)	2.54 (2.30, 2.80)	1.12 (1.04, 1.20)	1.12 (1.04, 1.20)
1.41+	207 (10.4)	4.30 (3.74, 4.96)	1.17 (1.05, 1.30)	1.12 (1.02, 1.24)	2.73 (2.44, 3.06)	1.11 (1.02, 1.21)	1.08 (1.00, 1.17)
[f] p-trend			<0.001	0.003		0.001	0.007
				Fall/winter season			
0	713 (48.9)	3.97 (3.59, 4.39)	1 (reference)	1 (reference)	2.65 (2.45, 2.87)	1 (reference)	1 (reference)
0.001 - 0.34	201 (13.6)	3.77 (3.33, 4.28)	1.04 (0.93, 1.15)	1.04 (0.94, 1.15)	2.43 (2.19, 2.70)	1.00 (0.91, 1.09)	1.01 (0.93, 1.09)
0.34 - 0.81	198 (12.6)	4.56 (4.06, 5.13)	1.22 (1.08, 1.37)	1.16 (1.04, 1.30)	2.89 (2.54, 3.29)	1.14 (1.03, 1.27)	1.09 (0.99, 1.19)

0.81 - 1.48	198 (12.8)	4.79 (4.21, 5.46)	1.13 (0.99, 1.28)	1.09 (0.97, 1.23)	3.11 (2.75, 3.52)	1.11 (0.96, 1.27)	1.07 (0.93, 1.22)
1.48+	200 (12.3)	5.22 (4.42, 6.17)	1.17 (1.01, 1.34)	1.13 (0.99, 1.28)	3.50 (3.13, 3.92)	1.24 (1.12, 1.36)	1.20 (1.09, 1.31)
[f] p-trend			0.003	0.010		0.002	0.009
[g] p-interaction			0.540	0.762		0.240	0.240

[e] All percentages are weighted to account for NHANES complex sampling design and weights.

[f] p-trend obtained from adding quartile of poultry intake as continuous variable to model.

[g] p-interaction obtained from Model 2, adding poultry intake as log-transformed continuous, season (fall,winter/spring,summer), and an interaction term for season and poultry intake.

[h] Model 1 adjusted for urine creatinine (log-transformed continuous), age (continuous), sex (male/female), race/ethnicity (non-Hispanic white/non-Hispanic black/Mexican-American/Other, including multiple), education (<high school/ high school or equivalent/ >high school), body mass index (continuous), smoking status (never/former/current), serum cotinine (log-transformed continuous), poverty income ratio (PIR, continuous), and tap water source (community supply/well,cistern/spring/other/no tap water).

[i] Model 2 further adjusted for past 24-hr intake of rice, cereal, juice, and wine (g/kg bodyweight, continuous).

FIGURE LEGENDS

Figure 1. Geometric mean ratio (95% confidence interval) of urine total arsenic and dimethylarsinate (DMA) by poultry intake in the past 24-hours.
Lines represent the geometric mean ratio of urinary arsenical concentrations of poultry consumers compared to non-consumers, based on restricted quadratic spline models with knots at the 10th, 50th, and 90th percentiles of log-transformed poultry intake. Polygons surrounding the lines represent 95% confidence intervals. The reference was set to non-poultry consumers. Geometric mean ratios were adjusted for urinary creatinine (log-transformed continuous), age (continuous), sex (male/female), race/ethnicity (non-Hispanic white/non-Hispanic black/Mexican-American/other, including multiple), education (<high school/ high school or equivalent/ >high school), body mass index (continuous), smoking status (never/former/current), serum cotinine (log-transformed continuous), poverty income ratio (PIR, continuous), and tap water source (community supply/well,cistern/spring/other/no tap water). Bars represent the distribution of poultry intake (g/kg bodyweight) within the study population.

Figure 2. Geometric mean ratio (95% confidence interval) of total arsenic and DMA comparing an interquartile range (75th to 25th percentile of poultry intake, g/kg bodyweight)
GMR = geometric mean ratio. CI = confidence interval.
Confidence intervals were obtained by comparing the 75th percentile vs the 25th percentile of the poultry intake distribution.

Figure 1. Geometric mean ratio (95% confidence interval) of urine total arsenic and dimethylarsinate (DMA) by poultry intake in the past 24-hours.

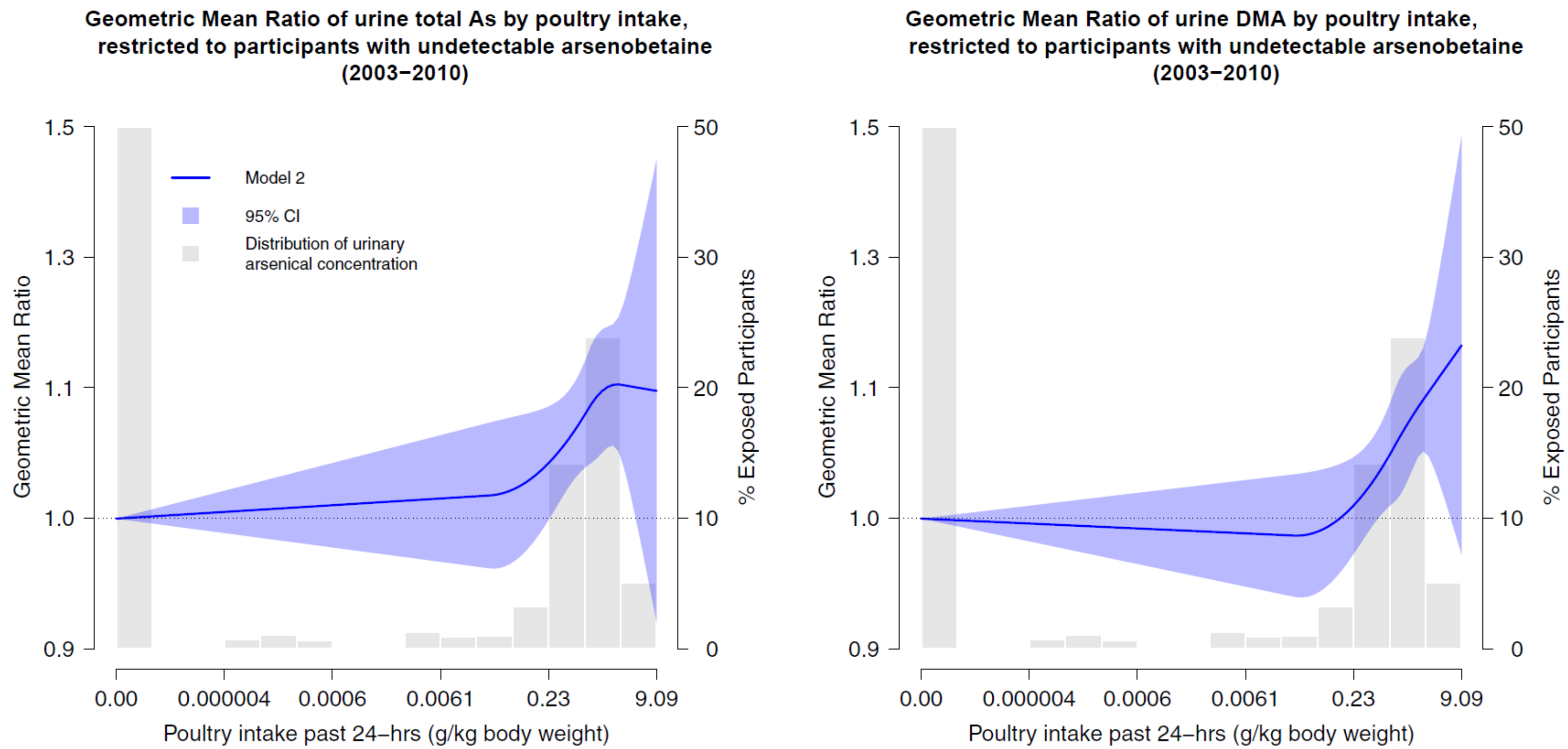
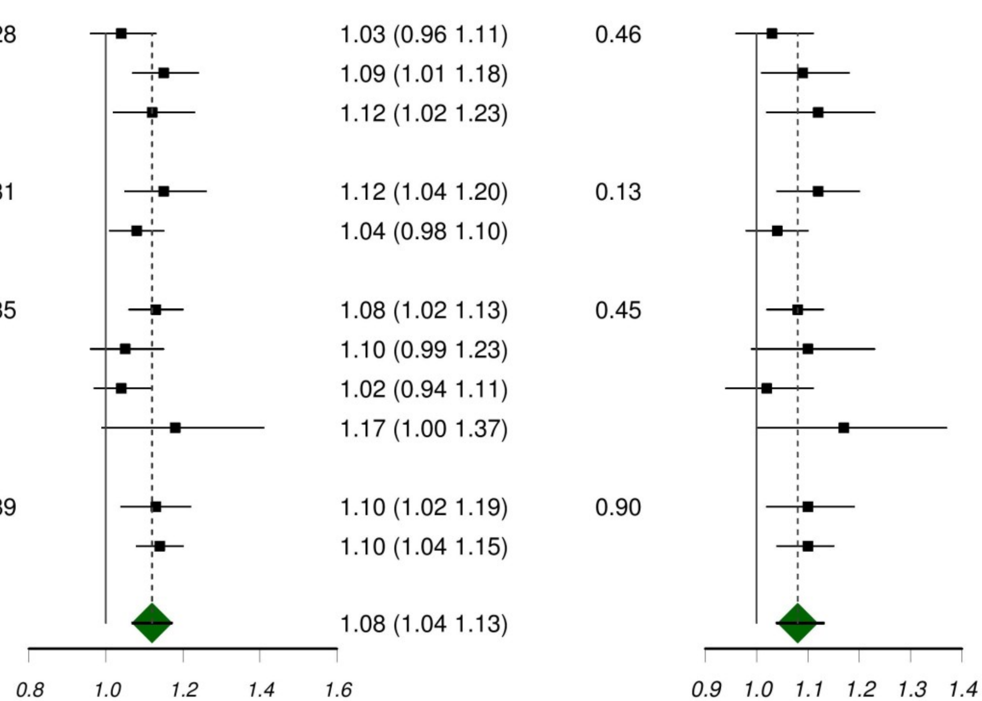


Figure 2. Geometric mean ratio (95% confidence interval) of total arsenic and DMA comparing an interquartile range (75th to 25th percentile of poultry intake, g/kg bodyweight)



Subgroup	GMR (95% CI)	P for Interaction	GMR (95% CI)	P for Interaction
Age (years)				
<=18	1.04 (0.96 1.13)	0.28	1.03 (0.96 1.11)	0.46
19 – 59	1.15 (1.07 1.24)		1.09 (1.01 1.18)	
60+	1.12 (1.02 1.23)		1.12 (1.02 1.23)	
Sex				
Male	1.15 (1.05 1.26)	0.31	1.12 (1.04 1.20)	0.13
Female	1.08 (1.01 1.15)		1.04 (0.98 1.10)	
Race/ethnicity				
White	1.13 (1.06 1.20)	0.35	1.08 (1.02 1.13)	0.45
Black	1.05 (0.96 1.15)		1.10 (0.99 1.23)	
Mexican−American	1.04 (0.97 1.12)		1.02 (0.94 1.11)	
Other	1.18 (0.99 1.41)		1.17 (1.00 1.37)	
Rice consumption				
No	1.13 (1.04 1.22)	0.89	1.10 (1.02 1.19)	0.90
Yes	1.14 (1.08 1.20)		1.10 (1.04 1.15)	
Overall	1.12 (1.07 1.17)		1.08 (1.04 1.13)	

SUPPLEMENTARY MATERIAL

Table S1. Food Commodity Index Database (FCID) commodity codes used to define intake variables.

Intake variable	FCID commodity codes	Description
Poultry	4000093000	Chicken, meat
	5000382000	Turkey, meat
Chicken	4000093000	Chicken, meat
Turkey	5000382000	Turkey, meat
Rice	1500323000	Rice, white
	1500324000	Rice, brown
	1500325000	Rice, bran
	1500326000	Rice, flour
Wine	1304179000	Grape, wine and sherry
Juice	1100010000	Apple, juice
	1304176000	Grape, juice
	1100268000	Pear, juice
	1203288000	Prune, juice
	1307132000	Cranberry, juice

Table S2. USDA food codes used to define cereal intake.

Intake variable	USDA food code	Description
Cereal	56200300 through 56203620	Pastas, cooked cereals, and rice
	56206970 through 57604100	Cereals, not specified as to cooked, or not cooked, ready-to-eat cereals, and cereal grains

ANNE NIGRA

Updated April 2016

PLACE OF BIRTH: Natrona Heights, PA
March 16, 1992

CONTACT: anigra1@jhu.edu
724-759-0109
403 Augusta St, Pittsburgh, PA 15211

EDUCATION

May 2016 — **Master of Science (ScM) in Epidemiology,** GPA: 3.93
Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
Department of Epidemiology
Concentration (Track): Environmental Epidemiology
Thesis: Poultry Consumption and Arsenic Exposure in the U.S. Population.
Certificate in Environmental and Occupational Health

May 2014 — **Bachelors of Arts (BA) in Biology (High Honors),** GPA: 3.69
Oberlin College, Oberlin, OH
Minor: Gender, Sexuality, and Feminist Studies
Honors Thesis: Tree Core Analysis for Heavy Metal Carcinogens in a Childhood Cancer Cluster

HONORS, AWARDS, and SCHOLARSHIPS

2015-2016	Master's Tuition Scholarship, JHSPH
May 2014	High Honors in Biology, Oberlin College
Spring 2014	Sigma Xi, Scientific Research Society, Associate Member
2010-2014	John F. Oberlin merit scholarship, Oberlin College

RESEARCH EXPERIENCE

June 2015 – Present — **RESEARCH ASSISTANT, Dr. Ana Navas-Acien.**
JHSPH Environmental Health Sciences Dept.

- Ongoing environmental epidemiology projects evaluating heavy metal exposure via food and water in the U.S. population using NHANES and cohort studies.
- Poultry Consumption and Arsenic Exposure in the U.S. Population: Cross-sectional analysis in NHANES of urinary arsenic concentrations by quartiles of recent poultry intake, during years when arsenic-based drugs were heavily used in poultry production.
- Urinary Tungsten and Incident Cardiovascular Disease in the Strong Heart Study: Prospective analysis of hazard ratio of incident cardiovascular disease by quartiles of urinary tungsten in cohort of American Indians.

- Inorganic Arsenic, Nitarsone and Other Arsenic Species in Turkey Meat: a US-based market basket sample and risk assessment using NHANES and USDA data: Calculated U.S. poultry intake rates for risk assessment.
- Currently evaluating association between urinary arsenic and mortality in NHANES using National Death Index follow-up data.

2012 – 2014 **RESEARCH/FIELD ASSISTANT, Mary C. Garvin.**
Oberlin College Biology Dept.

- Tree Core Analysis for Heavy Metal Carcinogens in a Childhood Cancer Cluster: Tree core sampling and aging, statistical analysis, and GIS.
- Chemical Cues of Bird-Mosquito Vector Interaction: Bird identification, handling, and netting, blood and uropygial sampling. Reared and maintained *Culex* mosquito colonies, ran PCR sexing reactions and analyses.

January 2013 **TRAINING IN ICP-MS, Johan Schijf Laboratory.**
Chesapeake Biological Laboratory, Maryland

- Training in clean lab technique, tree core digestion, and inductively coupled plasma-mass spectrometry analysis for heavy metal contaminants.

Summer 2012 **TRAINING IN DENDROCHRONOLOGY, Greg Wiles Laboratory.**
College of Wooster Geology Dept.

- Training in tree core preparation and COFECHA software (assesses quality of cross-dating and measurement).

PUBLIC HEALTH WORK

2012 – 2014 **COORDINATOR, HIV Peer Testing.**
Oberlin College Student Health Services

- Coordinated Oberlin College's free, confidential, anonymous HIV Peer Testing program.
- Oversaw hiring process, personnel evaluation, ongoing training and shadowing for testers.
- Managed administrative work, community outreach projects, and collaboration with the Lorain County Health Department, Lorain County AIDS Task Force, and Ohio Department of Health.
- Implemented state-sponsored Positive-Result Protocol Training for all testers.
- Oversaw transition to the first Ohio Department of Health-sanctioned college/university-testing site in 2012, allowing client utilization of state sponsored clinics and medical funds.

TEACHING EXPERIENCE

Fall 2015 **TEACHING ASSISTANT, Epidemiologic Methods 2 (EPI 752).**
JHSPH Epidemiology Dept.

Fall 2013 **TUTOR, Neurotoxicology and Neurodegeneration (NSCI 337).**
Oberlin Neuroscience Dept.

2012 and 2013 **WORKSHOP LEADER, Genetics, Evolution, and Ecology (BIOL 102).**
Oberlin Biology Dept.

- Ran collaborative peer learning workshops that emphasized active and varied learning techniques.

PUBLICATIONS and PROFESSIONAL DEVELOMENT

MANUSCRIPTS IN PREPARATION:

- **Nigra AE**, Nachman KE, Love DC, Grau-Perez M, Navas-Acien A. Poultry consumption and arsenic exposure in the U.S. population.
- **Nigra AE**, Howard BV, Umans JG, Best L, Francesconi KA, Goessler W, Devereux R, Navas-Acien A. Urinary tungsten and incident cardiovascular disease in the Strong Heart Study.
- Nachman KE, Love DC, Baron PA, **Nigra AE**, Raber G, Francesconi KA, Navas-Acien A. Inorganic arsenic, nitarsone and other arsenic species in turkey meat: a US-based market basket sample and risk assessment.
- Nachman KE, Ginsburg GL, Miller MD, Murray CJ, **Nigra AE,** Pendergrast CB. Practical considerations for addressing arsenic dietary exposure.

PRESENTATIONS:

April 2014 **Senior Symposium,** Oberlin College, OH.
"Tree Core Analysis for Heavy Metal Carcinogens in a Childhood Cancer Cluster."

PROFESSIONAL MEETINGS:

November 2-3, 2015 **C-FARR Consortium,** Dartmouth, NH.
(**Collaborative on Food with Arsenic and associated Risk and Regulation)**

- Meeting to draft a collection of six papers reviewing arsenic in food to be published in special edition journal.

ACADEMIC SERVICE

Present **EPIDEMIOLOGY DEPT. STUDENT COORDINATOR,** Joint EHS/Epi ESEE Journal Club.

September 2015 **NEW STUDENT NEIGHBORHOOD ORIENTATION GUIDE,** JHSPH.

COMMUNITY SERVICE

2011 – 2014 **TESTER AND COUNSELOR, HIV Peer Testing,** Oberlin College.

- Client-centered, LGBTQ-centered, and sex-positive testing and counseling to improve harm reduction.

January 2012 **SYRINGE EXCHANGE PROGRAM ASSISTANT,** Free Medical Clinic of Greater Cleveland.

- Packaged syringe-cleaning kits. General administrative assistant.

September 2011 **DAY OF SERVICE SITE COORDINATOR,** Lorain, OH.

- Coordinated student volunteer day at community garden system in Lorain, OH.
- Community farm upkeep and maintenance.

Summer 2011 **OBERLIN FRESHSTOP MANAGER,** CityFresh CSA.

- Community supported agriculture (CSA) with justice mission (limited income shares subsidized by full-income shares).
- Processed orders and payments (including state food assistance benefits), coordinated community outreach, promotion, and volunteers.
- Coordinated with local farmers regarding weekly produce shipments.

SKILLS

- R, GIS, NHANES analysis.
- PCR, gel electrophoresis, dendrochronology, tree core sampling.
- Bird identification, handling, netting, blood and uropygial sampling, mosquito colony rearing.
- Client centered counseling, harm-reduction counseling, sexual health education.