

Article

Maternal Mercury Exposure, Season of Conception and Adverse Birth Outcomes in an Urban Immigrant Community in Brooklyn, New York, U.S.A.

Cynthia J. Bashore¹, Laura A. Geer^{2,*}, Xin He³, Robin Puett¹, Patrick J. Parsons^{4,5}, Christopher D. Palmer^{4,5}, Amy J. Steuerwald⁴, Ovadia Abulafia⁶, Mudar Dalloul⁶ and Amir Sapkota¹

¹ Maryland Institute for Applied Environmental Health, University of Maryland School of Public Health, College Park, Room 2234F, College Park, MD 20742–2611, USA;

E-Mails: cbashore@umd.edu (C.J.B.); rpuett@umd.edu (R.P.); amirsap@umd.edu (A.S.)

² Department of Environmental and Occupational Health Sciences, Downstate School of Public Health, State University of New York, Box 43,450 Clarkson Ave., Brooklyn, NY 11203–2533, USA

³ Department of Epidemiology and Biostatistics, University of Maryland College Park School of Public Health, 2234H SPH Building, College Park, MD 20742–2611, USA;

E-Mail: xinhe@umd.edu

⁴ Laboratory of Inorganic and Nuclear Chemistry, Wadsworth Center, Department of Health, New York State University, Albany, NY 12201–0509, USA; E-Mails: pparsons@wadsworth.org (P.J.P.); palmer@wadsworth.org (C.D.P.); asteuerw@wadsworth.org (A.J.S.)

⁵ Department of Environmental Health Sciences, University at Albany School of Public Health, Albany, NY 12201, USA

⁶ Department of Obstetrics and Gynecology, State University of New York Downstate Medical Center, 445 Lenox Road, Brooklyn, NY 11203, USA; E-Mails: ovadia.abulafia@downstate.edu (O.A.); mudar.dalloul@downstate.edu (M.D.)

* Author to whom correspondence should be addressed; E-Mail: laura.geer@downstate.edu; Tel.: +718-221-5267; Fax: +718-221-5154.

Received: 26 May 2014; in revised form: 23 July 2014 / Accepted: 4 August 2014 /

Published: 18 August 2014

Abstract: Adverse birth outcomes including preterm birth (PTB: <37 weeks gestation) and low birth weight (LBW: <2500 g) can result in severe infant morbidity and mortality. In the United States, there are racial and ethnic differences in the prevalence of PTB and

LBW. We investigated the association between PTB and LBW with prenatal mercury (Hg) exposure and season of conception in an urban immigrant community in Brooklyn, New York. We recruited 191 pregnant women aged 18–45 in a Brooklyn Prenatal Clinic and followed them until delivery. Urine specimens were collected from the participants during the 6th to 9th month of pregnancy. Cord blood specimens and neonate anthropometric data were collected at birth. We used multivariate logistic regression models to investigate the odds of LBW or PTB with either maternal urinary mercury or neonate cord blood mercury. We used linear regression models to investigate the association between continuous anthropometric outcomes and maternal urinary mercury or neonate cord blood mercury. We also examined the association between LBW and PTB and the season that pregnancy began. Results showed higher rates of PTB and LBW in this cohort of women compared to other studies. Pregnancies beginning in winter (December, January, February) were at increased odds of LBW births compared with births from pregnancies that began in all other months (OR7.52 [95% CI 1.65, 34.29]). We observed no association between maternal exposure to Hg, and either LBW or PTB. The apparent lack of association is consistent with other studies. Further examination of seasonal association with LBW is warranted.

Keywords: preterm birth; low birth weight; mercury; season of conception; urban immigrant

1. Introduction

Adverse birth outcomes including preterm birth (PTB: <37 weeks gestation) and low birth weight (LBW: <2500 g) result in severe infant morbidity and mortality [1,2]. Risk factors for PTB include increased maternal age, black race, infections, toxicant exposure (e.g., cigarette smoke and illicit drug use), stress, over/underweight, underlying maternal health conditions (hypertension, obesity, and diabetes), clinical depression, and multiple gestations and prior PTB [3]. Genetic, demographic, and socioeconomic factors, pre-existing medical conditions, complications during pregnancy, inadequacies in prenatal care, as well as consumption of tobacco, caffeine, illicit drugs and alcohol are associated with the risk of LBW [4–8]. Prenatal exposures to pollutants such as organochlorines, formaldehyde, nitrogen dioxide (NO₂), and particulate matter (PM_{2.5}, PM₁₀) have been shown to be associated with altered fetal growth or PTB [8–14].

In the United States, there are racial and ethnic differences in the prevalence of LBW and infant mortality [2,15–19]. For example, non-Hispanic blacks have the highest PTB rates (15%–18%) compared with other racial ethnic groups [3]. Similarly, for immigrant women, maternal country of birth can predict adverse birth outcomes [20]. In some cases, recent immigrants had lower rates of adverse birth outcomes [15,21,22], but this advantage decreased with increasing years of residence and acculturation [23]. A plausible explanation for this observation may be changes in lifestyle, including dietary habits. For example, in terms of fish consumption, various recent immigrant groups such as Chinese and Caribbean's have been shown to consume fish more frequently. Larger meal size could also contribute to higher mercury exposures [24].

Fish consumption is associated with an increased exposure to mercury (Hg), and specifically methyl mercury (MeHg) which has the potential to cross the placenta and exert its toxic effects on the developing fetus. *In utero* Hg exposure has been linked to fetal malformations and decreased fetal survival in high-dose animal toxicology studies. One proposed mechanism is oxidative stress on the fetus [25]. Neuro-developmental disorders resulting from prenatal exposure to Hg have been documented previously [26–30], however the impact of Hg and frequency of fish consumption on adverse birth outcomes is not clearly defined or understood [31,32]. There is limited evidence of Hg effects on fetal growth and birth outcomes, and specifically birthweight [33,34] and some studies demonstrate no effects [35–37]. Others have reported an inverse association between Hg exposure and neonates' attained weight during the first 24 months of life, suggesting that effects may extend beyond parturition [32]. Fish consumption could serve as a proxy for exposure to other bioaccumulative contaminants (such as PCBs) that could have adverse impacts on birthweight [38]. Alternately, the positive benefits of omega-3 fatty acids can be a proxy for healthy behavior/nutritional status in general that could impart a positive impact on birthweight [38].

Studies have shown that, in addition to environmental and behavioral risk factors, season of conception and birth have been associated with adverse birth outcomes [39,40]. Temperature, air pollution, and increased industrial activity, as well as nutritional habits and food intake surrounding harvest periods or times of low food availability are examples of exposures that vary seasonally and may influence birth outcomes [39,41–43]. Thus season of conception or birth can be a proxy for exposures that vary temporally throughout the year. Seasonal association with PTB and LBW varies according to geographic latitude, national economic development status, predominant infectious diseases [39], and Vitamin D exposure [44]. Studies of racial ethnic groups in New York City have reported increased odds of LBW and PTB in some racial ethnic groups including immigrant communities such as Puerto Ricans and other Latino groups as well as in infants of mothers from the Sub-Saharan African region [19]. In this study, we examined the association of prenatal Hg exposure and season of conception with PTB and LBW in a high-risk population of African-American, Caribbean and West Indian women in an urban immigrant community in Brooklyn, New York. We further examined the association of prenatal Hg exposure with neonate anthropometric data.

2. Materials and Methods

2.1. Study Population and Questionnaire Assessment

A prospective study of pregnant women was conducted at the University Hospital of Brooklyn's Prenatal Clinic to investigate the association between maternal exposure to several pollutants and risk of adverse birth outcomes. The full study details are described elsewhere [45]. Briefly, a convenience sample of 191 pregnant women between the ages of 18 and 45 were recruited during the 6–9th month of pregnancy from October 2007 to December 2009. Data were collected with a pretested, culturally appropriate questionnaire designed in cooperation with local community groups, including Caribbean physicians. The questionnaire assessed demographic and lifestyle factors that may contribute to Hg exposure such as dietary factors, use of Hg-containing products in the home, use of skin-lightening creams, occupational exposures, number of dental amalgams, and use of Hg in folk

medicine practices. Results of the assessment of environmental risk factors for Hg exposure are described in the parent study [45]. Fish and shellfish consumption was estimated by showing participants a pictorial chart of various fish and shellfish species and asking the women about frequency of consumption and type of fish consumed during the current pregnancy. All women were provided with educational materials that described environmental sources of Hg and methods for avoiding Hg exposure.

2.2. Collection and Measurement of Maternal Urinary and Neonate Cord Blood Hg

During the 6th to 9th month of pregnancy participants provided a “spot” urine specimen for Hg and creatinine measurement. At delivery a physician or a midwife collected a neonatal cord blood specimen for total Hg determination. Chart review at birth provided demographic data including mother’s age, country of birth and date of immigration, race and ethnic origin, marital status and education level. The initial study protocol was approved by the SUNY Downstate Institutional Review Board (IRB) and by the New York State Department of Health’s IRB. An informed consent was received and signed by participants prior to participation.

Urine specimens were collected and analyzed for creatinine at SUNY Downstate and for total Hg by the Trace Elements Section of the Laboratory of Inorganic and Nuclear Chemistry, Wadsworth Center, NYS Department of Health (DOH) using methods described previously [45]. Urine collected at SUNY was separated onsite into 2 mL and 10 mL aliquots. To adjust for diurnal variations in urine dilution, the 2 mL aliquot of urine was measured at SUNY for creatinine using the Alkaline Picrate Method and a Beckman Olympus Analyzer, Model AU-2700 (Beckman Coulter, Inc., Brea, CA, USA). The 10 mL aliquot was transferred into a trace element collection tube containing Triton X-100 and sulfamic acid preservative to prevent losses of inorganic Hg. At the NYS DOH, total urinary Hg was determined using a Perkin Elmer Model DRC II (Perkin Elmer Life Sciences, Shelton CT, USA) inductively coupled plasma–mass spectrometer (ICP-MS) as previously described [45]. Cord blood specimens were analyzed for total Hg by ICP-MS, as described previously [46]. During analysis, it was noted that some of the cord blood specimens developed fibrin clots, which is quite common for cord blood. In such instances, the blood specimens were sonicated for one hour in an ultrasonic-bath, which was found to be sufficient to dissipate the micro-clots, and permit the analysis to proceed. The method limits of detection (LOD) were 0.24 and 0.09 $\mu\text{g/L}$ cord blood Hg and urinary Hg, respectively [45]. All specimens that were found to be below the detection limit were assigned $\frac{1}{2}$ LOD values.

2.3. Statistical Analysis

The study database included 191 mother-neonate pairs. For the purpose of this study, data analysis was restricted to singleton births ($n = 187$). Observations that included only gender ($n = 2$), contained no infant data ($n = 20$), or did not include data for the number of weeks gestation ($n = 6$), neonate birth weight ($n = 1$), and either cord blood Hg or urine Hg and urine creatinine ($n = 1$) were excluded, resulting in a final database of 159 singleton births.

Creatinine-corrected values for urine Hg expressed in units of $\mu\text{g Hg}$ per gram creatinine ($\mu\text{g/g}$) were used in all regression analyses. In linear regression models, appropriate transformations were applied to meet the normality assumption. For instance, cord blood and creatinine-corrected urine Hg

were natural log transformed, neonate head circumference was raised to the third power, and neonate length was squared. Three outliers, one extremely preterm and small neonate (27 weeks gestation, 33 cm length and 1105 g) and two other neonates (36 weeks, 54 cm length and 4355 g, and 39 weeks, 54 cm and 4570 g) were removed from the birth weight and head circumference linear regressions, as such values were deemed beyond the range of possible values.

The Kruskal-Wallis test was used to determine if the distributions of cord blood and/or maternal urinary Hg levels differed by LBW, PTB and/or maternal race/ethnicity. We used univariate linear regression to test the associations between maternal characteristics and birth weight, head circumference, and infant length, and multivariate linear regression to investigate the association of neonate cord blood or maternal urinary Hg level with birth weight, head circumference, and body length. Models were adjusted for previously identified risk factors impacting birthweight including maternal age, educational attainment, race/ethnicity, living with partner/spouse [3], and in the case of birthweight models, term of birth. Individual cell size was limited and thus we were unable to analyze dietary intake of specific predatory fish species. The outcome measures included in the logistic regression (LBW, PTB) were dichotomous, while those used in the linear regression (birthweight, head circumference) were continuous. In addition, age, education, and race were coded as categorical variables, while both cord blood and urinary Hg (including corrected for creatinine) were continuous variables. Logistic analyses were adjusted for a reduced number of study variables (maternal age and racial/ethnic group) due to the small number of adverse birth outcomes in the dataset. The association between the season of conception and the odds of LBW or PTB was also examined using logistic regression and comparison of sequential three-month intervals with the remainder of the year. The “season of conception” was determined by estimating the date that pregnancy began, calculated as the number of weeks of gestation multiplied by 7 days per week, and counted back from the infant’s day of birth. Mann-Whitney and chi-square tests were used to evaluate whether the characteristics of the study subjects included in the analyses were similar to the characteristics of the subjects excluded due to missing data for model covariates.

3. Results

Two racial/ethnic groups (African-American: 46% and Caribbean/West Indian: 39%) accounted for the majority of the study population (Table 1).

The frequency of fish consumption during pregnancy was high, with 15% of the population reporting consumption several times per week, while the prevalence of alcohol and tobacco use was low (4% and 3%, respectively). Even after coding species consumed into “low”, “high” and “extremely high” mercury exposure levels based on species ranking by the NYC Department of Health and Mental Hygiene [47], we did not have sufficient sample size to include type of species consumed into our models. We did, however, find that some participants were consuming fish high in mercury such as tuna and shark. The prevalence of alcohol and tobacco use was low (4% and 3%, respectively). Nineteen percent of neonates were born preterm (<37 weeks) and 14% were LBW (<2500 g). Median, 25th and 75th percentiles for cord blood and creatinine-corrected urinary Hg are reported in Table 2.

Table 1. Study population characteristics.

Participant Characteristics	N (Percent)	Mean Infant Birthweight (Grams) (SD)	Mean Number of Weeks Gestation (SD)
<i>Race/Ethnicity</i>			
African-American	73 (46)	3006 (546)	37.6 (2.2)
Caribbean/West Indian	62 (39)	3104 (602)	37.9 (2.2)
From African Continent (4), Latino/Hispanic (13) & Other (5)	22 (14)	3120 (476)	38.0 (1.6)
Did not answer	2 (1)	3673 (237)	39.5 (0.7)
<i>Age group</i>			
Less than 25 year	61 (38)	3133 (469)	38.2 (2.0)
25 to 29 year	37 (23)	3001 (579)	37.9 (2.1)
30 to 34 year	39 (25)	3037 (620)	37.5 (2.4)
35 and over	22 (14)	3059 (621)	37.1 (2.0)
<i>Educational attainment</i>			
Some high school or less	36 (23)	3052 (541)	37.7 (2.2)
High school certificate	50 (31)	3028 (602)	37.8 (2.2)
Technical school, some college or more	73 (46)	3104 (545)	37.8 (2.1)
<i>Live with spouse/Partner</i>			
No	81 (51)	3057 (596)	37.7 (2.3)
Yes	77 (48)	3080 (527)	37.9 (2.0)
Did not answer	1 (1)	3110	38
<i>Frequency of fish intake during this pregnancy</i>			
Almost never or never	54 (34)	3019 (451)	37.7 (1.9)
1–3 times per month	58 (36.5)	3117 (555)	37.9 (2.2)
4–7 times per month	23 (14.5)	3122 (404)	38.2 (1.6)
Several times per week	24 (15)	3013 (865)	37.3 (2.9)
<i>Number of dental amalgams</i>			
None	85 (53)	3100 (523)	37.9 (1.9)
1 to 3	40 (25)	2998 (692)	37.3 (2.7)
4 to 6	25 (16)	3097 (499)	38.1 (2.0)
7 or more	8 (5)	3117 (314)	38.5 (1.7)
Did not answer	1 (1)	2120	36
<i>Born outside the United States</i>			
No	84 (53)	3025 (524)	37.7 (2.1)
Yes	75 (47)	3117 (598)	37.9 (2.2)
<i>Special product use</i>			
No	147 (92)	3067 (568)	37.8 (2.2)
Yes	9 (6)	3198 (422)	38.1 (1.8)
Did not answer	3 (2)	2753 (558)	38.0 (2.0)
<i>Visited botanica * during pregnancy</i>			
No	150 (94)	3065 (555)	37.8 (2.2)
Yes	8 (5)	3248 (591)	38.6 (0.7)
Did not answer	1 (1)	2120	36

Table 1. Cont.

Participant Characteristics	N (Percent)	Mean Infant Birthweight (Grams) (SD)	Mean Number of Weeks Gestation (SD)
<i>Alcohol use</i>			
No	151 (95)	3084 (556)	37.8 (2.2)
Yes	6 (4)	2656 (624)	37.2 (1.9)
Did not answer	2 (1)	3170 (431)	38 (0)
<i>Tobacco use</i>			
No	152 (96)	3074 (565)	37.8 (2.2)
Yes	5 (3)	2872 (476)	37.6 (1.7)
Did not answer	2 (1)	3170 (431)	38 (0)
<i>Season of conception</i>			
Spring	43 (27)	3143.3(503.7)	38.3 (1.8)
Summer	56 (35)	3109.5 (573.1)	37.7 (2.1)
Fall	33 (21)	3066.9 (527.4)	37.6 (1.9)
Winter	27 (17)	2867.3 (636.4)	37.3 (2.7)
<i>Birth weight</i>			
Less than 2500 g	23 (14)	2132 (360)	34.8 (2.9)
2500 g and over	136 (86)	3227 (414)	38.3 (1.5)
<i>Term of birth</i>			
Preterm (less than 37 weeks)	30 (19)	2436 (616)	34.5 (2.2)
Term (37 to 42weeks)	129 (81)	3216 (431)	38.6 (1.2)

* A *botanica* is defined as a retail store that sells folk medicine, religious candles, and other products regarded as magical or alternative medicine.

A significant number of respondents were missing data for cord blood Hg (92 observations) or urinary Hg (11 observations). Almost all (98.5%) of cord blood Hg levels and 82.7% of urinary Hg levels were above the method LOD. There was a significant positive correlation between maternal urinary Hg and cord blood Hg ($r = 0.47$, 95% CI 0.34–0.60, $n = 75$) [45]. Caribbean/West Indian women and neonates had the highest cord blood and maternal urinary Hg levels (2.23 $\mu\text{g/L}$ and 0.48 $\mu\text{g/g}$, respectively), but they were not significantly different from African-American, African-continent or Latina women. LBW neonates did not significantly differ in cord blood or maternal urinary Hg levels compared to neonates weighing over 2500 g (1.70 $\mu\text{g/L}$ and 0.39 $\mu\text{g/g}$ compared to 1.96 $\mu\text{g/L}$ and 0.38 $\mu\text{g/g}$, $p > 0.05$). Similarly, cord blood or maternal urinary Hg levels did not differ by timing of birth (1.50 $\mu\text{g/L}$ and 0.45 $\mu\text{g/g}$ (PTB) compared to 1.98 $\mu\text{g/L}$ and 0.35 $\mu\text{g/g}$ (term birth group), $p > 0.05$). Maternal urinary Hg levels were lowest in the summer and these findings were statistically significantly different from the fall ($p = 0.01$). When the observations were restricted to only those observations included in the LBW and PTB seasonal models, no significant seasonal difference in maternal urinary Hg occurred ($p = 0.06$, data not shown). We observed no increase in the odds of LBW or PTB associated with either neonate cord blood Hg or maternal urinary Hg (Refer to Table 3). There was no association of LBW or PTB associated with neonate cord blood Hg or maternal urinary Hg when stratified by season (data not shown).

Table 2. Cord Blood Hg and Creatinine Corrected Maternal Urinary Hg.

Participant Characteristics	Cord Blood Hg ($\mu\text{g/L}$)				Urinary Hg ($\mu\text{g/g}$ Creatinine)			
	<i>N</i>	Median	[Q1, Q3] ^a	<i>p</i> -Value ^b	<i>N</i>	Median	[Q1, Q3]	<i>p</i> -Value ^b
<i>Race/Ethnicity</i>								
African-American	29	1.49	[0.9, 2.64]	0.10	63	0.35	[0.11, 0.78]	0.22
Caribbean/West Indian	26	2.23	[1.78, 4.20]		59	0.48	[0.16, 0.83]	
From African continent, Latino/Hispanic & Other	11	1.44	[0.8, 5.02]		22	0.28	[0.07, 0.63]	
<i>Neonate birth weight</i>								
Less than 2500 g	10	1.70	[1.30, 2.04]	0.63	21	0.39	[0.08, 0.67]	0.60
2500g and over	57	1.96	[1.15, 3.65]		125	0.38	[0.14, 0.80]	
<i>Week of gestation at birth</i>								
Less than 37	11	1.50	[1.30, 2.04]	0.19	28	0.45	[0.19, 0.74]	0.69
37 to 42	56	1.98	[1.20, 4.70]		118	0.35	[0.12, 0.79]	
<i>Season of conception</i>								
Spring	21	2.27	[1.11, 4.90]	0.20	42	0.33	[0.14, 0.74]	0.04
Summer	14	1.47	[0.81, 1.80]		53	0.28	[0.07, 0.61]	
Fall	14	2.13	[1.37, 3.65]		28	0.66	[0.25, 0.89]	
Winter	18	1.91	[1.25, 4.95]		23	0.44	[0.26, 0.80]	

^a Q1 = 25th percentile, Q3 = 75th percentile; ^b Kruskal-Wallis ANOVA *p*-value.

Similarly, there was no significant change in birth weight, body length, or head circumference with changes in neonate cord blood or maternal urinary Hg (Table 4). Adjustment for fish consumption (data not shown) in linear and logistic models did not change results considerably.

The overall findings did not change when the analysis was stratified by presence or absence of dental amalgams (data not shown).

Table 3. Association of cord blood Hg and urinary Hg with preterm birth and low birth weight (LBW).

Logistic Regressions ^a	Odds Ratio	95% Confidence Interval (CI)	<i>p</i> -Value ^b
<i>LBW</i>			
Cord blood Hg (<i>n</i> = 66)	1.07	[0.72, 1.61]	0.73
Creatinine-corrected urine Hg (<i>n</i> = 144)	0.51	[0.14, 1.87]	0.27
<i>PTB</i>			
Cord blood Hg (<i>n</i> = 66)	0.65	[0.38, 1.12]	0.04
Creatinine-corrected urine Hg (<i>n</i> = 144)	0.78	[0.38, 1.59]	0.48

^a Logistic regressions were adjusted for maternal age group and racial ethnic group. LBW model included term of birth. ^b Likelihood ratio test *p*-values. Models including either cord blood Hg or creatinine-corrected urine Hg did not provide better fit than reduced models not containing either cord blood Hg or creatinine-corrected urine Hg variable (Likelihood ratio test *p* > 0.05) except for the PTB cord blood Hg model (LR *p* = 0.03); however, all women (*n* = 10) who reported consuming fish 4–7 times per month and who had neonate cord blood Hg measurements had term deliveries and were dropped from the logistic regression analysis for PTB.

Table 4. Association of cord blood Hg and urinary Hg with neonate birth weight, head circumference and length.

Linear Regressions	β Coefficients ^a	95% CI	<i>p</i> -Value ^b
<i>Birth weight (in grams)</i>			
Cord blood Hg (<i>n</i> = 64)	4.42	[−7.38, 16.22]	<0.01
Creatinine-corrected urine Hg (<i>n</i> = 140)	−1.23	[−7.35, 4.88]	<0.01
<i>Head Circumference (cubed, in cm³)</i>			
Cord blood Hg (<i>n</i> = 64)	61.16	[−66.25, 188.57]	0.05
Creatinine-corrected urine Hg (<i>n</i> = 137)	3.63	[−66.84, 74.10]	<0.01
<i>Length (squared, in cm²)</i>			
Cord blood Hg (<i>n</i> = 62)	−0.24	[−10.46, 9.98]	0.16
Creatinine-corrected urine Hg (<i>n</i> = 133)	−1.74	[−6.20, 2.71]	<0.01

Linear regressions were adjusted for age group, education attainment, racial/ethnic group, and living with partner/ spouse. Birth weight models also included term of birth. ^a β -coefficients represent the change in outcome variable (birth weight (g), head circumference (cm³), and length (cm²)) with each 10% increase in cord blood or maternal urine Hg; ^b Likelihood ratio test *p*-values.

Mann-Whitney and chi-square tests were used to evaluate whether the characteristics of the study subjects included in the multivariate analysis were similar to the characteristics of the subjects excluded due to missing data for model covariates. Refer to Appendix Tables A1–A8. For the LBW and PTB logistic regressions which included the cord blood mercury variable, excluded subjects were more likely than included subjects to live with a spouse or partner (55% and 39%, respectively, *p* = 0.05) and report alcohol use (6.5% and 0%, respectively, *p* = 0.03). For the linear regressions that included the cord blood mercury variable, none of the study subjects included in the analysis reported alcohol use, which was statistically significantly different than the excluded population (0% and 6.5%, respectively, *p* = 0.04). For the logistic and linear regressions that included the maternal urinary mercury variable, the excluded subject group included a higher percentage of African-American women in comparison to Caribbean/West Indian women (for example, 77% African-American and 23% Caribbean/West Indian in the excluded group compared to 44% and 41%, respectively for the subjects included in the PTB and LBW analysis, *p* = 0.02). There were no other statistical differences between the groups in regards to participant characteristics.

Figure 1 shows higher percentages of LBW births during the months of December through March. Odds ratios for season of conception derived based on 3 month groupings is provided in Table 5. The largest OR is found in the three-month aggregate of December, January, and February adjusted for maternal age and racial/ethnic group were OR: 7.52 [95% CI 1.65, 34.29] (Table 5).

The association of season of conception and PTB was similar, but not significant (winter versus all other seasons OR: 1.33 [95% CI 0.46, 3.80]).

Figure 1. Percent of neonates with low birthweight by month of conception.

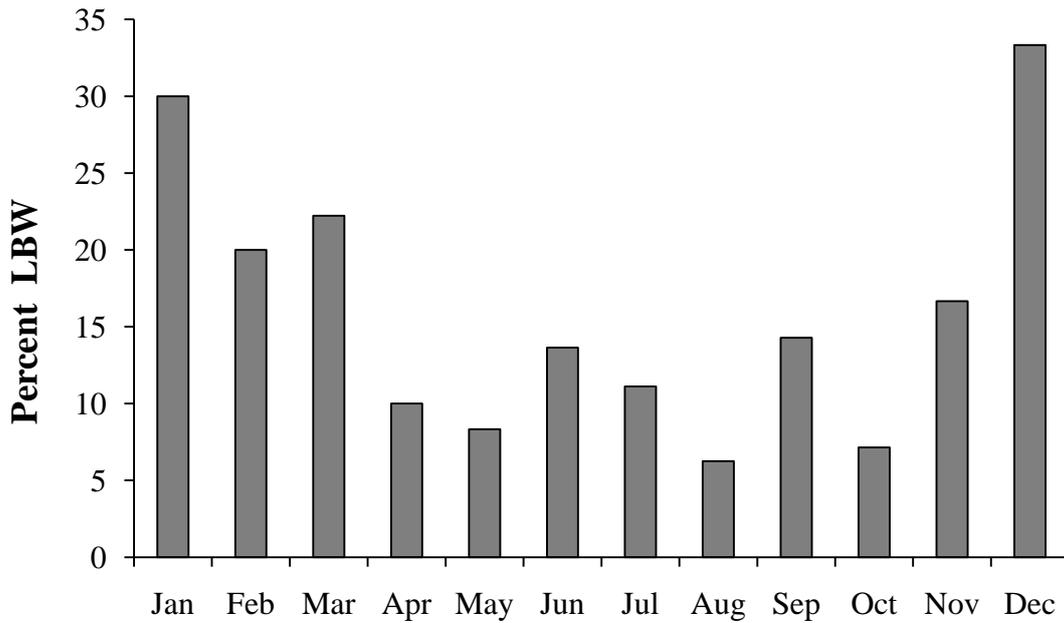


Table 5. Association of season of conception with adverse birth outcomes.

Season of Conception	OR	95% CI	<i>p</i> -value ^a
<i>LBW</i>			
Winter (December, January, February) vs. all other months	7.52	[1.65, 34.29]	<i>p</i> = 0.01
Spring (March, April, May) vs. all other months	0.59	[0.15, 2.29]	<i>p</i> = 0.44
Summer (June, July, August) vs. all other months	0.75	[0.21, 2.61]	<i>p</i> = 0.65
Fall (September, October, November) vs. all other months	0.42	[0.09, 1.89]	<i>p</i> = 0.24
<i>Preterm Birth</i>			
Winter (December, January, February) vs. all other months	1.33	[0.46, 3.80]	<i>p</i> = 0.60
Spring (March, April, May) vs. all other months	1.01	[0.39, 2.62]	<i>p</i> = 0.98
Summer (June, July, August) vs. all other months	0.62	[0.25, 1.56]	<i>p</i> = 0.30
Fall (September, October, November) vs. all other months	1.39	[0.53, 3.66]	<i>p</i> = 0.51

LBW models were adjusted for term of birth, maternal age group and race/ethnicity. PTB models were adjusted for maternal age group and race/ethnicity. Dates are coded as Spring (1 March–31 May), Summer (1 June–31 August), Fall (1 September–31 November) and Winter (1 December–28/9 February). *N* = 157 for all models, there were 23 LBW neonates and 30 PTB neonates in total. ^a Likelihood ratio test *p*-values. Models containing the seasonal variable did not provide a significantly better fit than the reduced models (Likelihood ratio test *p* > 0.05) except for the LBW winter model (LR *p* = 0.01).

4. Discussion

PTB and LBW disproportionately affect minority populations and result in acute and chronic health impacts. Previous studies report that cultural practices may increase exposure to Hg through dietary consumption [48]. Fish consumption habits reported in this study, such as higher reported consumption in certain racial/ethnic groups, were in line with those reported in McKelvey *et al.* (2011) [49] in the NYC population. This study found no association between neonate cord blood Hg or maternal urinary Hg levels and LBW or continuous anthropometric outcomes, and no association of maternal urinary Hg with PTB. This could suggest that though these women were exposed to Hg, fish consumption had a beneficial effect on gestation length as seen in prior studies [50,51], or could indicate sampling error due to the small sample size. The cord blood Hg levels found in this study were lower than in other studies reporting an association between decreased birth weight with increased Hg exposure. In a study of women exposed to Hg through consumption of traditional diets in Greenland, Foldspang and Hanson (1990) [52] reported decreased birth weight with increasing maternal and neonate cord blood levels, but neonate cord blood Hg levels ranged from 2 to 136 $\mu\text{g/L}$, with a mean of 21.0 $\mu\text{g/L}$ [52]. Consumption habits and consequent MeHg levels from this population certainly cannot be considered within the “normal” range of most fish-consuming populations, such as in most areas of the USA [48]. Ramon *et al* (2009) [33] also reported a negative association between cord blood Hg and mean birth weight, but maternal fish consumption was also much higher (only 1.6% of women reported rarely or never eating fish compared to 34% in this cohort) and 72% of the neonates had cord blood Hg levels $>5.8 \mu\text{g/L}$ [33]. Maternal urinary Hg in this study ranged from 0.24 to 3.50 $\mu\text{g/g}$ with a geometric mean of 0.32 $\mu\text{g/g}$ and 95th percentile of 1.9 $\mu\text{g/g}$. In a comparison study, the population-weighted geometric mean and 95th percentile of 0.63 and 0.83 $\mu\text{g/g}$, and 1.13 and 1.45 $\mu\text{g/g}$, respectively, was reported in Non-Hispanic Blacks and Caribbean-born Non-Hispanic Blacks in New York City [49]. Thus findings from our study are in line with levels found in large population-based studies in the USA.

Differences in Hg levels may be attributed to cultural differences in quantity of meal or type of fish consumed as well as local availability of various types of fish. The lack of association between total blood Hg exposure, mainly MeHg, and birth outcomes in this study is consistent with other studies of low-level Hg exposure that have also found no association [18]. Sample size limitations could contribute to lack of association found, as well as use of maternal urinary Hg in our birth outcomes models, a less accurate measure of MeHg exposure than total Hg in blood [53] which was the main measure of exposure used in comparable studies examining birthweight. Accounting for varying levels of fish consumption, which has been done in prior studies, had no measureable effect on model results.

Our study revealed increased odds of LBW neonates for pregnancies that began in December, January and February. In an Australian study, Ford (2011) [54] found a similar association of small for gestational age neonates and season of conception (2×2 contingency test, $p = 0.01$). Of 401 live births born to 585 couples enrolled in a prospective study, 11 of the neonates had birth weights lower than the 3rd percentile of national weights. Six of these neonates were conceived in winter, while 5 were conceived in spring [54]. Other studies that examine the association of birth weight with season of birth have found elevated rates of LBW in summer and autumn compared to winter and spring [19], which would be consistent with a season of conception in fall and winter.

This study did not find an association between the season of conception and PTB. In contrast, Bodnar and Simhan (2008) [55] found that the peak prevalence of PTB in a retrospective cohort study of 82,213 singleton livebirths. The present study is not sufficiently powered to identify small differences in prevalence of PTB as identified in the Bodnar and Simhan study [55]. Season serves as a proxy for geophysical conditions, environmental exposures, and psychosocial events such as annual religious holidays [56,57]. The observed association may also be due to lower Vitamin D uptake during winter months. Season can also serve as a proxy for exposure to air pollutants that vary, particularly those related to petroleum products and vehicle exhaust such as 1,3 butadiene, benzene, xylene and cadmium, increase in the winter [58]. Additional combustion byproducts of fuel consumption released during winter could include PM and other possible co-varying pollutants such as SO₂, both of which have been associated with effects on birthweight [59,60]. Levels of indoor and outdoor non-volatile polycyclic aromatic hydrocarbons (PAHs) have been shown to increase during the heating season in New York City [60] and levels of ambient volatile organic compounds benzo[a]pyrene, toluene, ethylbenzene, and xylene were higher in winter in a Camden, New Jersey study [61]. The increased incidence of infectious diseases in the winter also cannot be ruled out. In contrast, several studies show a seasonal effect of elevated blood lead levels in summer months due to increased play in outdoor contaminated areas, increased hand to mouth activity, and possibly even physiologic factors [62].

This study is the first to examine exposure to Hg and season of conception with risk of LBW and PTB birth in this New York City community. In a prior study in this same population, Lijinian *et al* (1997) [63] found an association between preterm labor and high heat-humidity index, stressing the need for further study of seasonality effects on timing of birth. Seasonal variability in birth weight has been associated with temperature in previous studies [64,65]. Strengths of this study include the prospective study design and the inclusion of a population at high risk for adverse birth outcomes and increased fish consumption. The use of individual-level measures of maternal and neonate Hg exposures removes bias by providing an independent level of measurement that is not subject to recall bias or misclassification error that can occur if exposure is solely determined by a diet history. Medical records provided neonate anthropometric data as well as immigration history for the non-US born women. One of the limitations of the study is convenience sampling, which may have resulted in selection bias. It is possible that the lack of an association between Hg exposure and adverse birth outcomes is due to beneficial actions of ω -3 fatty acids available through fish consumption. Though levels of ω -3 fatty acids were not measured directly in these women, we adjusted models for fish consumption (data not shown) to account for possible nutritional benefits and as a proxy for healthy lifestyle effects on birthweight. Adjustment for fish consumption did not measurably change model results. The measures of prenatal exposure were limited to two different time points, and thus could have led to inaccurate characterization of exposure. Additionally, the small sample size may have limited our ability to detect an association. The season of conception may have been misclassified during calculation of the date of conception, as estimation of gestational age using either a woman's recall of the first day of her last menstrual period, or ultra-sound dating that may be inaccurate [66,67]. Classifying pregnancies that began within a few days of the end of the season may have biased the association, since the majority of the beginning of the first trimester would have occurred during the adjacent season. Other parameters that may have influenced birth weight such as parity, maternal height, weight and body mass index [68,69] were unavailable and were not included in regression

models. Neighborhood-level effects such as the level of neighborhood organization, ethnic density and other psychosocial factors have been associated with PTB and/or LBW but were not examined in this study [70–73]. Since season of conception and season of birth are not independent, seasonal exposures during other seasons may be driving the association seen in this study.

In conclusion, this study is consistent with others that do not show an association between prenatal Hg exposure and adverse birth outcomes. Further examination of the factors that may influence the seasonal association with LBW is needed.

Acknowledgments

The authors would like to acknowledge that the analytical work in this study was supported by funding from Grant No U38EH000-464-01 from the National Center for Environmental Health, US CDC to the Wadsworth Center. Human study protocol was approved by the SUNY Downstate Institutional Review Board (IRB) and by the New York State Department of Health's IRB. This initial study was funded by the New York Community Trust. The sponsors had no role in the study outside of funding.

Author Contributions

Cynthia J. Bashore was responsible for drafting of the overall manuscript and data analysis. Xin He supervised statistical analysis for the manuscript under consideration. Robin Puett helped with the analysis plan, and drafting of the manuscript. Laura A. Geer and Amir Sapkota assisted with the overall planning of the manuscript, statistical analysis and drafting of the manuscript. Ovadia Abulafia and Mudar Dalloul supervised all clinical aspects of the original research and participated in the review of manuscript drafts. Patrick J. Parsons and his laboratory (including Christopher D. Palmer and Amy J. Steuerwald) participated in the specimen analysis and interpretation of the data, and the drafting of various sections of the manuscript. All co-authors were involved in final approval of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Goldenberg, R.L.; Culhane, J.F. Low birth weight in the United States. *Am. J. Clin. Nutr.* **2007**, *85*, 584–590.
2. Infant Mortality Statistics from the 2007 Period Linked Birth/Infant Death Data Set. Available online: http://www.cdc.gov/nchs/data/nvsr/nvsr59/nvsr59_06.pdf (accessed on 13 August 2014).
3. Goldenberg, R.L.; Culhane, J.F.; Iams, J.D.; Romero, R. Preterm birth 1: Epidemiology and causes of preterm birth. *Lancet* **2008**, *371*, 75–84.
4. Jaddoe, V.W.V.; Troe, E.-J.W.M.; Hofman, A.; Mackenbach, J.P.; Moll, H.A.; Steegers, E.A.; Witteman, J.C.M. Active and passive maternal smoking during pregnancy and the risks of low birthweight and preterm birth: The Generation R study. *Paediatr. Perinat. Epidemiol.* **2008**, *22*, 162–171.

5. Janjua, N.Z.; Delzell, E.; Larson, R.R.; Meleth, S.; Kristensen, S.; Kabagambe, E.; Sathiakumar, N. Determinants of low birth weight in urban Pakistan. *Public Health Nutr.* **2008**, *12*, 789–798.
6. Reichman, N.E.; Hamilton, E.R.; Hummer, R.A.; Padilla, Y.C. Racial and ethnic disparities in low birthweight among urban unmarried mothers. *Matern. Child Health J.* **2008**, *12*, 204–215.
7. Stillerman, K.P.; Mattison, D.R.; Giudice, L.C.; Woodruff, T.J. Environmental exposures and adverse pregnancy outcomes: A review of the science. *Reprod. Sci.* **2008**, *25*, 631–650.
8. Valero de Bernabe, J.; Soriano, T.; Albaladejo, R.; Juarranz, M.; Calle, M.E.; Martinez, D.; Dominguez-Rojas, V. Risk factors for low birth weight: A review. *Eur. J. Obstet. Gynecol. Reprod. Biol.* **2004**, *116*, 3–15.
9. Bellinger, D.C. Teratogen update: Lead and pregnancy. *Birth Defects Res.* **2005**, *73*, 409–420.
10. Chang, H.H.; Reich, B.J.; Miranda, M.L. Time-to-Event analysis of fine particle air pollution and preterm birth: Results from North Carolina, 2001–2005. *Am. J. Epidemiol.* **2012**, *175*, 91–98.
11. Llanos, M.N.; Ronco, A.M. Fetal growth restriction is related to placental levels of cadmium, lead and arsenic but not with antioxidant activities. *Reprod. Toxicol.* **2009**, *27*, 88–92.
12. Sapkota, A.; Chelikowsky, A.P.; Nachman, K.E.; Cohen, A.J.; Ritz, B. Exposure to particulate matter and adverse birth outcomes: A comprehensive review and meta-analysis. *Air Qual. Atmos. Health* **2012**, *5*, 369–381.
13. Van den Hooven, E.H.; Pierik, F.H.; de Kluizenaar, Y.; Willemsen, S.P.; Hofman, A.; van Rantigen, S.W.; Zandveld, P.Y.J.; Mackenbach, J.P.; Seegers, E.A.P.; Miedema, H.M.E.; *et al.* Air pollution exposure during pregnancy, ultrasound measures of fetal growth, and adverse birth outcomes: A prospective cohort study. *Environ. Health Perspect.* **2012**, *120*, 150–156.
14. Zhu, M.; Fitzgerald, E.F.; Gelberg, K.H.; Lin, S.; Druschel, C.M. Maternal low-level lead exposure and fetal growth. *Environ. Health Perspect.* **2010**, *118*, 1471–1475.
15. Fang, J.; Madhavan, S.; Alderman, M.H. Low birth weight: Race and maternal nativity—Impact of community income. *Pediatrics* **1999**, *103*, e5. PMID: 9917485.
16. Field, T.; Deogo, M.; Hernandez-Reif, M.; Deeds, O.; Holder, V.; Schanberg, S.; Kuhn, C. Depressed pregnant black women have a greater incidence of prematurity and low birthweight outcomes. *Infant Behav. Dev.* **2009**, *32*, 10–18.
17. Janevic, T.; Stein, C.R.; Savitz, D.A.; Kaufman, J.S.; Mason, S.M.; Herring, A.H. Neighborhood deprivation and adverse birth outcomes among diverse ethnic groups. *Ann. Epidemiol.* **2010**, *20*, 445–451.
18. Karagas, M.R.; Choi, A.L.; Oken, E.; Horvat, M.; Schoeny, R.; Kamai, E.; Cowell, W.; Grandjean, P.; Korrick, S. Evidence on the human health effects of low-level methylmercury exposure. *Environ. Health Perspect.* **2012**, *120*, 799–806.
19. Stein, C.R.; Savitz, D.A.; Janevic, T.; Ananth, C.V.; Kaufman, J.S.; Herring, A.H.; Engel, S.M. Maternal ethnic ancestry and adverse perinatal outcomes in New York City. *Am. J. Obstet. Gynecol.* **2009**, *584*, 1–9.
20. Bollini, P.; Pampallona, S.; Wanner, P.; Kupelnick, B. Pregnancy outcome of migrant women and integration policy: A systematic review of the international literature. *Soc. Sci. Med.* **2009**, *68*, 452–461.
21. Fornia, F.; Jamieson, D.J.; Sanders, D.; Lindsay, M.K. Pregnancy outcomes in foreign-born and US-born women. *Int. J. Gynaecol. Obstet.* **2003**, *83*, 257–265.

22. Howard, D.L.; Marshall, S.S.; Kaufman, J.S.; Savitz, D.A. Variations in low birth weight and preterm delivery among blacks in relation to ancestry and nativity: New York City, 1998–2002. *Pediatrics* **2006**, *118*, 1399–1405.
23. Datta-Nemdharry, P.; Dattani, N.; Macfarlane, A.J. Birth outcomes for African and Caribbean babies in England and Wales: Retrospective analysis of routinely collected data. *BMJ Open* **2012**, *2*, doi:10.1136/bmjopen-2012-001088.
24. Ortiz-Roque, C.; Yadiris, L.-R. Mercury contamination in reproductive age women in a Caribbean island: Vieques. *J. Epidemiol. Commun. Health* **2004**, *58*, 756–757.
25. Lee, B.E.; Hong, Y.C.; Park, H.; Ha, M.; Koo, B.S.; Chang, N.; Roh, Y.M.; Kim, B.N.; Kim, Y.J.; Kim, B.M.; *et al.* Interaction between GSTM1/GSTT1 polymorphism and blood mercury on birth weight. *Environ. Health Perspect.* **2010**, *118*, 437–443.
26. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Mercury*; ATSDR: Atlanta, GA, USA, 1999.
27. Budtz-Jorgensen, E.; Grandjean, P.; Weihe, P. Separation of risks and benefits of seafood intake. *Environ. Health Perspect.* **2007**, *115*, 323–327.
28. Mahaffey, K.R. Mercury exposure: Medical and public health issues. *Trans. Am. Clin. Climatol. Assoc.* **2005**, *116*, 127–154.
29. Mahaffey, K.R.; Sunderland, E.M.; Chan, H.M.; Choi, A.L.; Grandjean, P.; Marien, K.; Oken, E.; Sakamoto, M.; Schoeny, R.; Weihe, P.; *et al.* Balancing the benefits of n-3 polyunsaturated fatty acids and the risks of methylmercury exposure from fish consumption. *Nutr. Rev.* **2011**, *69*, 493–508.
30. Winjgaarden, E.; Beck, C.; Shamlaye, C.F.; Cernichiari, E.; Davidson, P.W.; Myers, G.J.; Clarkson, T.W. Benchmark concentrations for methyl mercury obtained from the 9-year followup of the Seychelles Child Development Study. *Neurotoxicology* **2006**, *27*, 702–709.
31. Gundacker, C.; Frohlich, S.; Graf-Rohrmeister, K.; Eibenberger, B.; Jessenig, V.; Gicic, D.; Prinz, S.; Wittmann, K.J.; Zeisler, H.; Vallant, B.; *et al.* Perinatal lead and mercury exposure in Austria. *Sci. Total Environ.* **2010**, *408*, 5744–5749.
32. Kim, B.-M.; Lee, B.-E.; Hong, Y.-C.; Park, H.; Ha, M.; Kim, Y.-J.; Kim, Y.; Chang, M.; Kim, B.-N.; Oh, S.-Y.; *et al.* Mercury levels in maternal and cord blood and attained weight through the 24 months of life. *Sci. Total Environ.* **2011**, *410–411*, 26–33.
33. Ramon, R.; Ballester, F.; Aguinagalde, X.; Amurrio, A.; Vioque, J.; Lacasana, M.; Rebagliato, M.; Murcia, M.; Iniguez, C. Fish consumption during pregnancy, prenatal mercury exposure, and anthropometric measures at birth in a prospective mother-infant cohort study from Spain. *Am. J. Clin. Nutr.* **2009**, *90*, 1047–1055.
34. Sikorski, R.; Paszkowski, T.; Szprengier-Juszkiewicz, T. Mercury in neonatal scalp hair. *Sci. Total Environ.* **1986**, *57*, 105–110.
35. Daniels, J.L.; Rowland, A.S.; Longnecker, M.P.; Crawford, P.; Golding, J.; Team, A.S. Maternal dental history, child's birth outcome and early cognitive development. *Paediatr. Perinat. Epidemiol.* **2007**, *21*, 448–457.

36. Drouillet-Pinard, P.; Huel, G.; Slama, R.; Forhan, A.; Sahuquillo, J.; Goua, V.; Thiebaugeorges, O.; Foliguet, B.; Mgnin, G.; *et al.* Prenatal mercury contamination: Relationship with maternal seafood consumption during pregnancy and fetal growth in the “EDEN mother-child” cohort. *Br. J. Nutr.* **2010**, *104*, 1096–1100.
37. Lederman, S.A.; Jones, R.L.; Caldwell, K.L.; Rauh, V.; Sheets, S.E.; Tang, D.; Viswanathan, S.; Becker, M.; Stein, J.L.; Wang, R.Y.; *et al.* Relation between cord blood mercury levels and early child development in a World Trade Center cohort. *Environ. Health Perspect.* **2008**, *116*, 1085–1091.
38. Oken, E.; Choi, A.L.; Karagas, M.R.; Mari  n, K.; Rheinberger, C.M.; Schoeny, R.; Sunderland, E.; Korrick, S. Which fish should I eat? Perspectives influencing fish consumption choices. *Environ. Health Perspect.* **2012**, *120*, 790–798.
39. Chodick, G.; Flash, S.; Deitch, Y.; Shalev, V. Seasonality in birth weight: Review of global patterns and potential causes. *Hum. Biol.* **2009**, *81*, 463–477.
40. Lee, S.J.; Steer, P.J.; Filippi, V. Seasonal patterns and preterm birth: A systemic review and an analysis in a London-based cohort. *BJOG* **2006**, *113*, 1280–1288.
41. Olsson, D.; Ekstrom, M.; Forsberg, B. Temporal variation in air pollution concentrations and preterm birth—A population based epidemiological study. *Int. J. Env. Res. Public Health* **2012**, *9*, 272–285.
42. Strand, L.B.; Barnett, A.G.; Tong, S.L. The influence of season and ambient temperature on birth outcomes: A review of the epidemiological literature. *Environ. Res.* **2011**, *111*, 451–462.
43. Strand, L.B.; Barnett, A.G.; Tong, S.L. Maternal exposure to ambient temperature and the risks of preterm birth and stillbirth in Brisbane, Australia. *Am. J. Epidemiol.* **2012**, *175*, 99–107.
44. Leffelaar, E.R.; Vrijkotte, T.G.M.; van Eijsden, M. Maternal early pregnancy vitamin D status in relation to fetal and neonatal growth: Results of the multi-ethnic Amsterdam born children and their development cohort. *Br. J. Nutr.* **2010**, *104*, 108–117.
45. Geer, L.A.; Persad, M.D.; Palmer, C.D.; Steuerwald, A.J.; Dalloul, M.; Abulafia, O.; Parsons, P.J. Assessment of prenatal mercury exposure in a predominately Caribbean immigrant community in Brooklyn, NY. *J. Environ. Monit.* **2012**, *14*, 1035–1043.
46. Palmer, C.D.; Lewis, M.E., Jr.; Geraghty, C.M.; Barbosa, F., Jr.; Parsons, P.J. Determination of lead, cadmium and mercury in blood for assessment of environmental exposure: a comparison between inductively coupled plasma-mass spectrometry and atomic absorption spectrometry. *Spectrochim. Acta Part B* **2006**, *61*, 980–990.
47. Understanding Mercury Levels. Available online: http://www.health.ny.gov/environmental/chemicals/hsees/mercury/mercury_exposure_levels.htm. (accessed on 4 September 2012).
48. Xue, J.; Zartarian, V.G.; Liu, S.V.; Geller, A.M. Methyl mercury exposure from fish consumption in vulnerable racial/ethnic populations: Probabilistic SHEDS-Dietary model analyses using 1999–2006 NHANES and 1990–2002 TDS data. *Sci. Total Environ.* **2012**, *414*, 373–379.
49. McKelvey, W.; Jeffery, N.; Clark, N.; Kass, D.; Parsons, P.J. Population-Based inorganic mercury biomonitoring and the identification of skin care products as a source of exposure in New York city. *Environ. Health Perspect.* **2011**, *119*, 203–209.

50. Grandjean, P.; Bjerve, K.S.; Weihe, P.; Steuerwald, U. Birthweight in a fishing community: Significance of essential fatty acids and marine food contaminants. *Int. J. Epidemiol.* **2001**, *30*, 1272–1278.
51. Lucas, M.; Dewailly, E.; Muckle, G.; Ayotte, P.; Bruneau, S.; Gingras, S.; Rhainds, M.; Holub, B.J. Gestational age and birth weight in relation to n-3 fatty acids among Inuit (Canada). *Lipids* **2004**, *39*, 617–626.
52. Foldspang, A.; Hansen, J.C. Dietary intake of methylmercury as a correlate of gestational length and birth weight among newborns in Greenland. *Am. J. Epidemiol.* **1990**, *132*, 310–317.
53. Grandjean, P.; Budtz-Jorgensen, E.; Jorgensen, P.J.; Weihe, P. Umbilical cord mercury concentration as biomarker of prenatal exposure to methylmercury. *Environ. Health Perspect.* **2005**, *113*, 905–908.
54. Ford, J.H. Preconception risk factors and SGA babies: Papilloma virus, omega 3 and fat soluble vitamin deficiencies. *Early Hum. Dev.* **2011**, *87*, 785–789.
55. Bodnar, L.M.; Simhan, H.N. The prevalence of preterm birth and season of conception. *Paediatr. Perinat. Epidemiol.* **2008**, *22*, 538–545.
56. Kloner, R.A. The “Merry Christmas Coronary” and “Happy New Year Heart Attack” phenomenon. *Circulation* **2004**, *110*, 3744–3745.
57. Phillips, D.P.; Jarvinen, J.R.; Abramson, I.S.; Phillips, R.R. Cardiac mortality is higher around Christmas and New Year’s than at any other time. *Circulation* **2004**, *110*, 3781–3788.
58. Touma, J.S.; Cox, W.M.; Tikvart, J.A. Spatial and temporal variability of ambient air toxics data. *J. Air Waste Manag. Assoc.* **2006**, *56*, 1716–1725.
59. Geer, L.A.; Weedon, J.; Bell, M.L. Ambient air pollution and term birth weight in Texas from 1998 to 2004. *J. Air Waste Manag. Assoc.* **2012**, *62*, 1285–1295.
60. Jung, K.H.; Yan, B.; Chillrud, S.N.; Perera, F.P.; Whyatt, R.; Camann, D.; Kinney, P.L.; Miller, R.L. Assessment of benzo(a)pyrene-equivalent carcinogenicity and mutagenicity of residential indoor vs. outdoor polycyclic aromatic hydrocarbons exposing young children in New York City. *Int. J. Environ. Res. Public Health* **2010**, *7*, 1889–1900.
61. Lioy, P.J.; Fan, Z.; Zhang, J.; Georgopoulos, P.; Wang, S.W.; Ohman-Strickland, P.; Wu, X.; Zhu, X.; Harrington, J.; Tang, X.; *et al.* Personal and ambient exposures to air toxics in Camden, New Jersey. *Res. Rep. Health Eff. Inst.* **2011**, *160*, 3–127, 129–151.
62. Kemp, F.W.; Neti, P.V.; Howell, R.W.; Wenger, P.; Louria, D.B.; Bogden, J.D. Elevated blood lead concentrations and vitamin D deficiency in winter and summer in young urban children. *Environ. Health Perspect* **2007**, *115*, 630–635.
63. Lajinian, S.; Hudson, S.; Applewhite, L.; Feldman, J.; Minkoff, H.L. An association between the heat-humidity index and preterm labor and delivery: A preliminary analysis. *Am J Public Health.* **1997**, *87*, 1205–1207.
64. Lawlor, D.A.; Ronalds, G.; Clark, H.; Smith, G.D.; Leon, D.A. Birth weight is inversely associated with incident coronary heart disease and stroke among individuals born in the 1950s: Findings from the Aberdeen Children of the 1950s prospective cohort study. *Circulation* **2005**, *112*, 1414–1418.
65. Murray, L.J.; O’Reilly, D.P.; Betts, N.; Patterson, C.C.; Davey Smith, G.; Evans, A.E. Season and outdoor ambient temperature: Effects on birth weight. *Obstet. Gynecol.* **2000**, *96*, 689–695.

66. Dietz, P.M.; England, L.J.; Callaghan, W.M.; Pearl, M.; Wier, M.L.; Kharrazi, M. A comparison of LMP-based and ultrasound-based estimates of gestational age using linked California livebirth and prenatal screening records. *Paediatr. Perinat. Epidemiol.* **2007**, *21*, 62–71.
67. Lynch, C.D.; Zhang, J. The research implications of the selection of a gestational age estimation method. *Paediatr. Perinat. Epidemiol.* **2007**, *21*, 86–96.
68. Alexander, G.R.; Kogan, M.D.; Himes, J.H. 1994–1996 U.S. singleton birth weight percentiles for gestational age by race, Hispanic origin, and gender. *Matern. Child Health J.* **1999**, *3*, 225–321.
69. Frederick, I.O.; Williams, M.A.; Sales, A.E.; Martin, D.P.; Killien, M. Pre-Pregnancy body mass index, gestation weight gain, and other maternal characteristics in relation to infant birth weight. *Matern. Child Health J.* **2008**, *12*, 557–567.
70. Holland, M.L.; Kitzman, H.; Veazie, P. The effects of stress on birth weight in low-income, unmarried black women. *Womens Health Issues* **2009**, *19*, 390–397.
71. Mason, S.M.; Kaufman, J.S.; Daniels, J.L.; Emch, M.E.; Hogan, V.K.; Savitz, D.A. Black preterm birth risk in nonblack neighborhoods: Effects of Hispanic, Asian, and Non-Hispanic white ethnic densities. *Ann. Epidemiol.* **2011**, *21*, 631–638.
72. Mason, S.M.; Kaufman, J.S.; Daniels, J.L.; Emch, M.E.; Hogan, V.K.; Savitz, D.A. Neighborhood ethnic density and preterm birth across seven ethnic groups in New York City. *Health Place* **2011**, *17*, 280–288.
73. Mason, S.M.; Kaufman, J.S.; Emch, M.E.; Hogan, V.K.; Savitz, D.A. Ethnic density and preterm birth in African-, Caribbean-, and US-Born Non-Hispanic Black populations in New York City. *Am. J. Epidemiol.* **2010**, *172*, 800–888.

Appendix

Table A1. Comparison of included versus excluded cases for cord blood Hg and LBW and PTB models. CI= included in model, CE = excluded.

Participant Characteristics	CI (66)	CE (93)	p-Value
<i>Race/Ethnicity</i>			0.47
African-American	29	44	
Caribbean/West Indian	26	36	
From African Continent, Latino/Hispanic & Other	11	11	
Did not answer		2	
<i>Age group</i>			0.72
Less than 25 year	27	34	
25 to 29 year	14	23	
30 to 34 year	16	23	
35 and over	9	13	
<i>Educational attainment</i>			0.27
Some high school or less	17	19	
High school certificate	22	28	
Technical school, some college or more	27	46	
<i>Live with spouse/partner</i>			0.05
No	40 (61%)	41 (44%)	
Yes	26 (39%)	51 (55%)	
Did not answer	0	1	

Table A1. Cont.

Participant Characteristics	CI (66)	CE (93)	p-Value
<i>Frequency of fish intake during this pregnancy</i>			0.55
Almost never or never	21	33	
1–3 times per month	24	34	
4–7 times per month	10	13	
Several times per week	11	13	
<i>Number of dental amalgams</i>			0.92
None	35	50	
1 to 3	18	22	
4 to 6	7	18	
7 or more	5	3	
Did not answer	1		
<i>Born outside the United States</i>			0.21
No	31	53	
Yes	35	40	
<i>Special product use</i>			0.18
No	59	88	
Yes	6	3	
Did not answer	1	2	
<i>Visited botanica during pregnancy</i>			0.21
No	62	88	
Yes	3	5	
Did not answer	1		
No	66	85	
Yes	0 (0%)	6 (6.5%)	
Did not answer		2	
<i>Tobacco use</i>			
No	66	86	0.053
Yes	0 (0%)	5 (5.4%)	
Did not answer		2	
<i>Birth weight</i>			0.84
Less than 2500 g	10	13	
2500 g and over	56	80	
<i>Term of birth</i>			0.55
Preterm (less than 37 weeks)	11	19	
Term (37 to 42weeks)	55	74	

Table A2. Comparison of included versus excluded cases for urine Hg and LBW and PTB models. UI = included in model, UE = excluded.

Participant Characteristics	UI (144)	UE (15)	p-Value
<i>Race/Ethnicity</i>			0.02
African-American	63 (44%)	10 (77%)	14%exc
Caribbean/West Indian	59 (41%)	3 (23%)	5%exc
From African Continent,Latino/ Hispanic & Other	22	0	
Did not answer		2	
<i>Age group</i>			0.60
Less than 25 year	54	7	
25 to 29 y year	35	2	
30 to 34 year	34	5	
35 and over	21	1	
<i>Educational attainment</i>			0.11
Some high school or less	34	2	
High school certificate	47	3	
Technical school, some college or more	63	10	
<i>Live with spouse/partner</i>			0.36
No	75	6	
Yes	68	9	
Did not answer	1	0	
<i>Frequency of fish intake during this pregnancy</i>			0.56
Almost never or never	51	3	
1–3 times per month	50	8	
4–7 times per month	21	2	
Several times per week	22	2	
<i>Number of dental amalgams</i>			0.97
None	77	8	
1 to 3	37	3	
4 to 6	24	1	
7 or more	6	2	
Did not answer		1	
<i>Born outside the United States</i>			0.56
No	75	9	
Yes	69	6	
<i>Special product use</i>			0.50
No	135	12	
Yes	9	0	
Did not answer		3	
<i>Visited botanica during pregnancy</i>			0.37
No	62	88	
Yes	3	5	
Did not answer	1	0	

Table A2. Cont.

Participant Characteristics	UI (144)	UE (15)	p-Value
<i>Alcohol use</i>			<i>0.55</i>
No	137	14	
Yes	5	1	
Did not answer	2	0	
<i>Tobacco use</i>			<i>0.46</i>
No	137	15	
Yes	5	0	
Did not answer	2		
<i>Birth weight</i>			<i>0.90</i>
Less than 2500 g	21	2	
2500 g and over	123	13	
<i>Term of birth</i>			<i>0.57</i>
Preterm (less than 37 weeks)	28	2	
Term (37 to 42weeks)	116	13	

Table A3. Comparison of included *versus* excluded cases for linear regression of birthweight and urinary Hg. BWLRUI = included in model. BWLRUE = excluded.

Participant Characteristics	BWLRUI	BWLRUE	p-Value
<i>Race/Ethnicity</i>			<i>0.02</i>
African-American	61	12	
Caribbean/West Indian	57	5	
From African Continent, Latino/Hispanic & Other	22	0	
Did not answer		2	
<i>Age group</i>			<i>0.74</i>
Less than 25 year	54	7	
25 to 29 year	34	3	
30 to 34 year	32	7	
35 and over	20	2	
<i>Educational attainment</i>			<i>0.14</i>
Some high school or less	33	3	
High school certificate	46	4	
Technical school, some college or more	64	12	
<i>Live with spouse/partner</i>			<i>0.91</i>
No	72	9	
Yes	68	9	
Did not answer		1	
<i>Frequency of fish intake during this pregnancy</i>			<i>0.32</i>
Almost never or never	50	4	
1–3 times per month	49	9	
4–7 times per month	21	2	
Several times per week	20	4	

Table A3. Cont.

Participant Characteristics	BWLRUI	BWLRUE	p-Value
<i>Number of dental amalgams</i>			<i>0.87</i>
None	75	10	
1 to 3	35	5	
4 to 6	24	1	
7 or more	6	2	
Did not answer		1	
<i>Born outside the United States</i>			<i>0.64</i>
No	73	11	
Yes	67	8	
<i>Special product use</i>			<i>0.43</i>
No	129	18	
Yes	9	0	
Did not answer	2	1	
<i>Visited botanica during pregnancy</i>			<i>0.30</i>
No	132	18	
Yes	8	0	
Did not answer		1	
<i>Alcohol use</i>			<i>0.73</i>
No	133	18	
Yes	5	1	
Did not answer	2		
<i>Tobacco use</i>			<i>0.40</i>
No	133	19	
Yes	5	0	
Did not answer	2		
<i>Birth weight</i>			<i>0.86</i>
Less than 2500 g	20	3	
2500 g and over	120	16	
<i>Term of birth</i>			<i>0.80</i>
Preterm (less than 37 weeks)	26	4	
Term (37 to 42weeks)	114	15	

Table A4. Linear regression model of birthweight and cord blood Hg. BWLR CI = included in model, BWLR CE = excluded.

Participant Characteristics	BWLR CI	BWLR CE	p-Value
<i>Race/Ethnicity</i>			<i>0.43</i>
African- American	28	45	
Caribbean/West Indian	25	37	
From African Continent, Latino/Hispanic & Other	11	11	
Did not answer		2	

Table A4. Cont.

Participant Characteristics	BWLRCI	BWLRCE	p-Value
<i>Age group</i>			0.45
Less than 25 year	27	34	
25 to 29 year	14	23	
30 to 34 year	15	24	
35 and over	8	14	
<i>Educational attainment</i>			0.23
Some high school or less	17	19	
High school certificate	21	29	
Technical school, some college or more	26	47	
<i>Live with spouse/partner</i>			0.09
No	38	43	
Yes	26	51	
Did not answer		1	
<i>Frequency of fish intake during this pregnancy</i>			0.92
Almost never or never	21	33	
1–3 times per month	24	34	
4–7 times per month	10	13	
Several times per week	9	15	
<i>Number of dental amalgams</i>			0.95
None	34	51	
1 to 3	17	23	
4 to 6	7	18	
7 or more	5	3	
Did not answer	1		
<i>Born outside the United States</i>			0.22
No	30	54	
Yes	34	41	
<i>Special product use</i>			0.16
No	56	91	
Yes	6	3	
Did not answer	2	1	
<i>Visited botanica during pregnancy</i>			0.89
No	60	90	
Yes	3	5	
Did not answer	1	0	
<i>Alcohol use</i>			0.04
No	64	87	
Yes	0	6	
Did not answer		2	
<i>Tobacco use</i>			0.06
No	64	88	
Yes	0	5	
Did not answer		2	

Table A4. *Cont.*

Participant Characteristics	BWLRCI	BWLRCE	<i>p</i> -Value
<i>Birth weight</i>			0.73
Less than 2500 g	10	13	
2500 g and over	54	82	
<i>Term of birth</i>			0.40
Preterm (less than 37 weeks)	10	20	
Term (37 to 42weeks)	54	75	

Table A5. Linear regression model of head circumference and cord blood Hg. HCLRCI = included in model, HCLRCE = excluded.

Participant Characteristics	HCLRCI	HCLRCE	<i>p</i> -Value
<i>Race/Ethnicity</i>			0.42
African-American	28	45	
Caribbean/West Indian	25	37	
From African Continent, Latino/Hispanic & Other	11	11	
Did not answer			
<i>Age group</i>			0.45
Less than 25 y	27	34	
25 to 29 y	14	23	
30 to 34 y	15	24	
35 and over	8	14	
<i>Educational attainment</i>			0.23
Some high school or less	17	19	
High school certificate	21	29	
Technical school, some college or more	26	47	
<i>Live with spouse/partner</i>			0.09
No	38	43	
Yes	26	51	
Did not answer		1	
<i>Frequency of fish intake during this pregnancy</i>			0.91
Almost never or never	21	33	
1–3 times per month	34	34	
4–7 times per month	10	13	
Several times per week	9	15	
<i>Number of dental amalgams</i>			0.95
None	34	51	
1 to 3	17	23	
4 to 6	7	18	
7 or more	5	3	
Did not answer	1		
<i>Born outside the United States</i>			0.22
No	30	54	
Yes	34	41	

Table A5. Cont.

Participant Characteristics	HCLRCI	HCLRCE	p-Value
<i>Special product use</i>			<i>0.16</i>
No	56	91	
Yes	6	3	
Did not answer	2	1	
<i>Visited botanica during pregnancy</i>			<i>0.89</i>
No	60	90	
Yes	3	5	
Did not answer	1		
<i>Alcohol use</i>			<i>0.04</i>
No	64	87	
Yes	0	6	
Did not answer		2	
<i>Tobacco use</i>			
No	64	88	<i>0.06</i>
Yes	0	5	
Did not answer		2	
<i>Birth weight</i>			<i>0.73</i>
Less than 2500 g	10	13	
2500 g and over	54	82	
<i>Term of birth</i>			<i>0.39</i>
Preterm (less than 37 weeks)	10	20	
Term (37 to 42weeks)	54	75	

Table A6. Linear regression model of head circumference and urinary Hg. HCLRUI = included in model, HCLRUE = excluded.

Participant Characteristics	HCLRUI	HCLRUE	p-Value
<i>Race/Ethnicity</i>			
African-American	59	14	0.02
Caribbean/West Indian	57	5	
From African Continent, Latino/Hispanic & Other	21	1	
Did not answer		2	
<i>Age group</i>			<i>0.54</i>
Less than 25 year	53	8	
25 to 29 year	34	3	
30 to 34 year	31	8	
35 and over	19	3	
<i>Educational attainment</i>			<i>0.53</i>
Some high school or less	31	5	
High school certificate	45	5	
Technical school, some college or more	61	12	

Table A6. Cont.

Participant Characteristics	HCLRUI	HCLRUE	p-Value
<i>Live with spouse/partner</i>			0.72
No	71	10	
Yes	66	11	
Did not answer		1	
<i>Frequency of fish intake during this pregnancy</i>			0.36
Almost never or never	49	5	
1–3 times per month	48	10	
4–7 times per month	20	3	
Several times per week	20	4	
<i>Number of dental amalgams</i>			0.44
None	72	13	
1 to 3	35	5	
4 to 6	24	1	
7 or more	6	2	
Did not answer		1	
<i>Born outside the United States</i>			0.53
No	71	13	
Yes	66	9	
<i>Special product use</i>			0.96
No	127	20	
Yes	8	1	
Did not answer	2	1	
<i>Visited botanica during pregnancy</i>			0.26
No	129	21	
Yes	8	0	
Did not answer		1	
<i>Alcohol use</i>			0.85
No	130	21	
Yes	5	1	
Did not answer			
<i>Tobacco use</i>			0.36
No	130	22	
Yes	5	0	
Did not answer			
<i>Birth weight</i>			0.91
Less than 2500 g	20	3	
2500 g and over	117	19	
<i>Term of birth</i>			0.62
Preterm (less than 37 weeks)	25	5	
Term (37 to 42weeks)	112	17	

Table A7. Linear regression model of neonate length and urinary Hg. LLRUI = included in model, LLRUE = excluded.

Participant Characteristics	LLRUI	LLRUE	p-Value
<i>Race/Ethnicity</i>			0.04
African- American	57	16	
Caribbean/West Indian	56	3	
From African Continent, Latino/Hispanic & Other	20	2	
Did not answer		2	
<i>Age group</i>			0.86
Less than 25 year	50	11	
25 to 29 year	32	5	
30 to 34 year	33	6	
35 and over	18	4	
<i>Educational attainment</i>			0.26
Some high school or less	31	5	
High school certificate	44	6	
Technical school, some college or more	58	15	
<i>Live with spouse/partner</i>			0.72
No	69	12	
Yes	64	13	
Did not answer		1	
<i>Frequency of fish intake during this pregnancy</i>			0.52
Almost never or never	48	6	
1–3 times per month	45	13	
4–7 times per month	20	3	
Several times per week	20	4	
<i>Number of dental amalgams</i>			0.47
None	69	16	
1 to 3	36	4	
4 to 6	23	2	
7 or more	5	3	
Did not answer		1	
<i>Born outside the United States</i>			0.59
No	69	15	
Yes	64	11	
<i>Special product use</i>			0.46
No	124	23	
Yes	7	2	
Did not answer	2	1	
<i>Visited botanica during pregnancy</i>			0.79
No	126	24	
Yes	7	1	
Did not answer		1	

Table A7. Cont.

Participant Characteristics	LLRUI	LLRUE	p-Value
<i>Alcohol use</i>			0.26
No	127	24	
Yes	4	2	
Did not answer	2		
<i>Tobacco use</i>			0.83
No	127	25	
Yes	4	1	
Did not answer	2		
<i>Birth weight</i>			0.28
Less than 2500 g	21	2	
2500 g and over	112	24	
<i>Term of birth</i>			0.30
Preterm (less than 37 weeks)	27	3	
Term (37 to 42weeks)	106	23	

Table A8. Linear regression model of neonate length and cord blood Hg. LLRCI = included in model, LLRCE = excluded.

Participant Characteristics	LLRCI	LLRCE	p-Value
<i>Race/Ethnicity</i>			0.86
African-American	29	44	
Caribbean/West Indian	23	39	
From African Continent, Latino/Hispanic & Other	10	12	
Did not answer		2	
<i>Age group</i>			0.49
Less than 25 year	26	35	
25 to 29 year	13	24	
30 to 34 year	16	23	
35 and over	7	15	
<i>Educational attainment</i>			0.13
Some high school or less	17	19	
High school certificate	21	29	
Technical school, some college or more	24	49	
<i>Live with spouse/partner</i>			0.09
No	37	44	
Yes	25	52	
Did not answer		1	
<i>Frequency of fish intake during this pregnancy</i>			0.93
Almost never or never	21	33	
1–3 times per month	22	36	
4–7 times per month	10	13	
Several times per week	9	15	

Table A8. Cont.

Participant Characteristics	LLRCI	LLRCE	p-Value
<i>Number of dental amalgams</i>			0.83
None	33	52	
1 to 3	17	23	
4 to 6	7	18	
7 or more	4	4	
Did not answer			
<i>Born outside the United States</i>			0.57
No	31	53	
Yes	31	44	
<i>Special product use</i>			0.41
No	55	92	
Yes	5	4	
Did not answer	2	1	
<i>Visited botanica during pregnancy</i>			0.95
No	58	92	
Yes	3	5	
Did not answer	1		
<i>Alcohol use</i>			0.04
No	62	89	
Yes	0	6	
Did not answer		2	
<i>Tobacco use</i>			0.07
No	62	90	
Yes	0	5	
Did not answer		2	
<i>Birth weight</i>			0.63
Less than 2500 g	10	13	
2500 g and over	52	84	
<i>Term of birth</i>			0.77
Preterm (less than 37 weeks)	11	19	
Term (37 to 42weeks)	51	78	