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Associations between socioeconomic status and environmental toxicant concentrations in adults in the USA: NHANES 2001–2010☆

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ABSTRACT

Low level chronic exposure to toxicants is associated with a range of adverse health effects. Understanding the various factors that influence the chemical burden of an individual is of critical importance to public health strategies. We investigated the relationships between socioeconomic status (SES) and bio-monitored chemical concentration in five cross-sectional waves of the U.S. National Health and Nutrition Examination Survey (NHANES).

We utilised adjusted linear regression models to investigate the association between 179 toxicants and the poverty income ratio (PIR) for five NHANES waves. We then selected a subset of chemicals associated with PIR in 3 or more NHANES waves and investigated potential mediating factors using structural equation modelling.

PIR was associated with 18 chemicals in 3 or more NHANES waves. Higher SES individuals had higher burdens of serum and urinary mercury, arsenic, caesium, thallium, perfluorooctanoic acid, perfluorononanoic acid, mono(carboxyoctyl) phthalate and benzophenone-3. Inverse associations were noted between PIR and serum and urinary lead and cadmium, antimony, bisphenol A and three phthalates (mono-benzyl, mono-isobutyl, mono-n-butyl). Key mediators included fish and shellfish consumption for the PIR, mercury, arsenic, thallium and perfluorononanoic acid associations. Sunscreen use was an important mediator in the benzophenone-3/PIR relationship. The association between PIR and cadmium or lead was partially mediated by smoking, occupation and diet.

These results provide a comprehensive analysis of exposure patterns as a function of socioeconomic status in US adults, providing important information to guide future public health remediation measures to decrease toxicant and disease burdens within society.

1. Introduction

Environmental exposure to contaminants has increasingly been acknowledged to play an important role in a wide range of common chronic diseases, including complex and multifactorial conditions (Edwards and Myers, 2007). Understanding the interplay between genetic susceptibility, lifestyle and environmental exposure that underlies these conditions is becoming an increasingly important and expanding area of research (Wild, 2009).

The Environment Justice Hypothesis, which is part of the Environmental Justice Movement, states that hazards in the physical and chemical environment disproportionately affect those individuals and households that also face hazards in their social environment (Brown, 1995). The Environmental Justice Movement emerged in the 1980s and strives for fair treatment and meaningful involvement of all people regardless of race, colour, national origin, or income with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies (Environmental Protection Agency, 2012). The US Environmental Protection Agency is working towards environmental justice for all Americans, attempting to ensure that no specific group of people should bear a disproportionate burden of environmental harm and risks.

The major focus of the Environmental Justice Movement remains on individuals in lower socioeconomic groups, as there is a significant evidence base that these individuals have greater burdens of environmental toxicants. Health outcomes and disease burdens (e.g. asthma, cancer and diabetes) are known to associate with low socioeconomic status (SES) (Jemal et al., 2008; Zheng and Land, 2012), and this is hypothesised to relate to increased exposure to environmental contaminants. Evidence suggests that there is social and racial disparity in toxicant burden with higher exposure to lead (Iqbal et al., 2008),

Abbreviations: NHANES, National Health and Nutrition Examination Survey; PIR, Poverty Income Ratio; SES, Socio-economic status.

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pesticides (Cox et al., 2007) and polychlorinated biphenyls (PCBs) (Borrell et al., 2004; Vrijheid et al., 2012) noted. However, given the increasing list of chemicals found in our environment, there is currently a limited understanding of the relationship between toxicant burden and demographic parameters.

Understanding factors which determine an individual's risk of exposure to a range of toxicants is of critical importance in minimising the health burden of these chemicals. Analytical techniques have improved in sensitivity and reproducibility and decreased in cost, allowing measurement of environmental chemicals in blood, urine and biological samples from large population studies (Stokstad, 2004). The combination of increased measurement sensitivity and larger study cohorts has led to the discovery of associations between environmental contaminants and chronic disease. For example perfluorooctanoic acid (PFOA) is associated with increased risk of thyroid disease (Melzer et al., 2010a) and bisphenol A has been linked with an increased risk of heart disease (OR per z-score increase in BPA: 1.42, CI: 1.17 to 1.72, $P = 0.001$) (Melzer et al., 2010b). Epidemiological evidence suggests that higher levels of methyl-mercury are associated with cardiovascular disease (Valera et al., 2012) and despite being phased out in the 1970s, lead is associated with high blood pressure (Scinicariello et al., 2011). It is therefore imperative that we utilise these more accurate analytical techniques to investigate what influences toxicant burden, to ensure that any arising public health issues can be appropriately addressed.

The National Health and Nutrition Examination Survey (NHANES) is designed to assess the health and nutritional status of adults and children located across the United States, and measures around 5000 people each year (10,000 per wave). NHANES remains the world's largest biomonitoring effort (Hyattsville, 2011), with over 200 chemicals monitored in representative samples of the US population over (currently) 6 repeated waves between 1999 and 2010. As such it provides a unique resource for investigating the relationships between SES and toxicant burden. The toxicants selected for monitoring in NHANES are those considered potentially harmful for human health.

This study aimed to investigate associations between concentrations of environmental toxicants with SES in five waves of NHANES. By investigating association in multiple waves, with up to 5 data points for each chemical, from cross sectional studies, we were able to identify chemicals which were robustly associated with SES in more than one dataset, thus increasing the validity of our findings. Based on the current literature and the Environment Justice Hypothesis (Brown, 1995; Environmental Protection Agency, 2012), we anticipated that the majority of chemical toxicants would be associated with lower SES.

2. Methods

2.1. Study population

Data were drawn from five independent cross-sectional waves of NHANES (2001–2002, 2003–2004, 2005–2006, 2007–2008 and 2009–2010). NHANES assesses the health and diet of the non-institutionalized civilian population of the United States and is administered by the US National Center for Health Statistics, Centers for Disease Control and Prevention (CDC). The NHANES protocol and design were approved by the National Centers for Health Statistics Institutional Review Board (Hyattsville, 2011). NHANES is an internationally recognized, nationally representative study, for research into the health of the US population (Yang et al., 2012).

2.2. Chemical analyses

The US National Toxicology Program (CDC, Atlanta), selected a range of potentially harmful chemicals for human health, for further study in specimens from NHANES respondents. Blood and urine specimens were taken from random subgroups (as selected by NHANES) of eligible sample members during the mobile examination centre visit. More information about the selection of subgroups and analyses run for each class of chemical toxicant is available on the NHANES website (NHANES). We included 179 chemical toxicants in this analysis which were measured in at least 2 NHANES waves. As a result of the subsampling in NHANES different compounds were measured in different random sub-samples and in different NHANES waves, and as such numbers of respondents included in our analyses vary.

2.3. Participant selection

Data were included on respondents aged 18 to 74 years. We excluded children and adolescents as we wanted to investigate toxicant burden in adults only. The elderly (>75 years of age) were excluded as the NHANES sample does not include people in care homes and as such is not representative of the elderly US population. Whilst racial disparities are important in toxicant burden we only included Mexican Hispanics, Non-Hispanic Whites and Non-Hispanic Blacks in this study as there were very few Non-Mexican Hispanics and other ethnicity groups in the dataset.

2.4. Statistical analysis

2.4.1. Investigating the association between poverty income ratio and chemical toxicants

We investigated the association between poverty income ratio (PIR) and 179 chemical toxicants measured in NHANES using linear regression. The chemical toxicants were log transformed prior to analysis. PIR is the ratio of the family's self-reported income to the family's appropriate poverty threshold (US Census Bureau) (Webster and Bishaw, 2005). It should be noted that the poverty threshold varies annually and thus for each wave. However, the PIR values are comparable across the waves, with a PIR of less than 1.00 representing those below the official poverty threshold and PIR values of 1.00 or greater (up to 5) indicating people above the poverty threshold. PIR was used as a continuous measure in the initial screen of 179 chemicals. We included the standard covariates age, sex, race and waist circumference in the regression models. Urinary creatinine was also included if the toxicant was measured in urine to account for dilution factors. *P*-values of less than 0.05 were considered to be statistically significant. Chemicals noted to associate with PIR in more than one wave were investigated in more detail, therefore our *P*-values were not adjusted for multiple testing.

2.4.2. Mediators of the PIR-toxicant association

To try and further our understanding of the robust associations noted between PIR and toxicants we attempted to identify mediators of the association. We initially investigated the scientific literature for potential mediators and where available investigated their role in the NHANES data. Structural equation modelling (SEM) was utilised to investigate the indirect effect (through the potential mediator) of PIR on the concentration of the toxicant of interest in the NHANES waves were a significant association was noted between PIR and the chemical toxicant. We used SEM, as it enables testing of non-straightforward patterns of relationships, and is therefore well suited to the management of cross-sectional data for inferential purposes. The total, direct and indirect effects were estimated using the post-estimation command “estat teffects”. The indirect effect of PIR on the toxicant of interest was recorded for a range of potential mediators. The regression coefficient for the indirect effect represents the change in toxicant concentration for every unit change in PIR that is driven by the mediator. We also calculated the proportion of the effect attributable to the mediator. This was calculated by dividing the coefficient of the studied effect (i.e. through the specific mediator)

by the coefficient of the total effect of PIR on toxicant concentration. If the indirect effect was significant (i.e. $P < 0.05$) for two or more NHANES waves the mediator was considered to be important in the interaction.

The mediators investigated included fish and shellfish consumption in the last 30 days, sunscreen use frequency, occupation (only available in 2001/2 and 2003/4), smoking (monitored as serum cotinine (Vartiainen et al., 2002)) and dietary factors including total protein, calcium and iron.

Where possible we included multiple mediators within one model, as this controls for correlated mediators. However, due to the nature of data being collected in different NHANES waves, this was only possible for a subset of chemicals where all potential mediators were measured in all waves. It should also be noted that due subsampling some mediators were only monitored in a third of participants, reducing the power of analyses if all mediators were combined using SEM.

The model fit was analysed by investigating the standardised root mean residual (SRMR) which is an absolute fit indicator, with a value of less than 0.05 indicating good model fit. The coefficient of determination (CD) was also monitored, with larger values indicating better model fit. These parameters were computed for each model in STATA using the estat gof, stat(residual) option. SRMR and CD were the only goodness of fit parameters available when using survey weighted data.

NHANES uses a complex cluster sample design. Individual weights were provided with each toxicant group sub-sample data and these weights were used along with the NHANES primary sampling unit and strata. All statistical analyses were conducted using STATA IC Version 12.1 (Stata Corp., College Station, US).

3. Results

Across the five NHANES waves there was an increase in the proportion of individuals living below the poverty threshold, an increase in the average BMI and fluctuations in average age and proportion of participants within specific ethnic groups ($P < 0.001$; Table 1).

3.1. Association between PIR and chemical toxicant

We investigated whether an association existed between toxicant concentration and PIR for 179 chemicals using adjusted linear regression models (Table 2). Twenty-eight (16%) chemicals (across 8 chemical classes) were noted to vary significantly in two or more NHANES waves. Positive correlation (higher toxicant concentration as PIR increases) was observed in 12 chemicals (43% of all robust associations) in our adjusted models (shown in bold in Table 2). Negative correlation was observed in 16 chemicals (57%) in our adjusted models (Table 2).

We further investigated a subset of these chemicals ($n = 18$) which were associated with PIR in three or more waves. Nine (50%) of these were positively associated with PIR, including arsenic, perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), mono(carboxyoctyl) phthalate, urinary caesium, mercury and thallium, serum mercury and benzophenone-3. Negative associations were noted in at least 3 NHANES waves for the phthalates (mono-benzyl, mono-isobutyl, mono-n-butyl), urinary antimony, cadmium and lead, serum cadmium and lead, and bisphenol A (BPA). The mean concentration of these toxicants varied over the decade of monitoring, although different chemicals displayed different trends (data not shown). Of note serum lead and urinary mercury significantly decreased ($P < 0.001$) over the decade, whilst BP3 significantly increased ($P < 0.001$).

3.2. Mediation analysis

We investigated these associations in more detail, identifying potential mediators, which may drive the association between the chemical toxicant and PIR (Table 3). Mediators that were available in NHANES were investigated in more detail. We utilised structural equation modelling to identify mediators. All models demonstrated a SRMR of <0.05 and the CD was greater than 0.48 in all models.

A number of mediators were identified in at least 2 NHANES waves for some of the chemical toxicants (Table 4). The relationship between PIR and serum and urinary mercury was mediated to some extent by fish and shellfish consumption (Table 4). The indirect effect of fish and shellfish consumption explained between 5 and 23% of the PIR variance. Fish and shellfish consumptions were also mediators in the relationship between urinary arsenic and PIR (variance explained by indirect effect 13–100%). The relationship between arsenic and fish and shellfish consumption was not altered when both were included in the same models. The relationship between PFNA, thallium and PIR was mediated to some extent by shellfish consumption (15–48% and 19% respectively). For BP3 the relationship PIR-sunscreen-BP3 was investigated. In 2003/4 and 2005/6 sunscreen was noted to mediate the relationship between BP3 and PIR explaining 70% and 37% of the variance respectively.

Smoking was a key mediator in the inverse relationship between PIR and serum/urinary lead and cadmium. In all 5 NHANES waves investigated the relationship between serum and urinary cadmium was partially mediated by smoking (Table 4; 44–64% and 22–44% respectively). Smoking was also important in the PIR and lead relationship (serum 24–47% and urine 16–21%). Occupation was also noted to be a mediator in the association between PIR and serum/urinary lead and cadmium. Occupation accounted for approximately 30% of the total effect in the association between PIR and serum cadmium or serum lead (Table 4). Specific dietary variables were also identified as potential mediators for the association between lead or cadmium and PIR, including total iron and total calcium, although these variables only accounted for a small percentage of the variance (<5%).

Table 1
Demographic data for each NHANES wave for all adults aged between 18 and 74 years with poverty income ratio (PIR) data available.

	NHANES cycle					*P* value
	2001/2	2003/4	2005/6	2007/8	2009/10	
N	4756	4449	4356	4196	4404	
Sex: male (%)	2292 (48.2)	2150 (48.3)	2098 (48.2)	2090 (49.8)	2166 (49.2)	0.445
Mean age in years (CI)	41.9 (41.4–42.3)	42.2 (41.7–42.7)	41.2 (40.7–41.7)	45.2 (44.7–45.7)	44.6 (44.1–45.1)	<0.001
Race (%)						
Mexican Hispanics	1239 (26.1)	1062 (23.9)	1040 (23.9)	916 (21.8)	1000 (22.7)	<0.001
Non-Hispanic Whites	2411 (50.7)	2282 (51.3)	2101 (48.2)	2175 (51.8)	2419 (54.9)	
Non-Hispanic Blacks	1106 (23.2)	1105 (24.8)	1215 (27.9)	1105 (26.3)	985 (22.4)	
Education (%)						
Less than high school	1518 (31.9)	1285 (28.9)	1176 (27.0)	1233 (29.4)	1187 (27.0)	<0.001
High school/GED	1166 (24.5)	1187 (26.7)	1103 (25.3)	1037 (24.7)	1076 (24.4)	
Some college	1190 (25.0)	1252 (28.1)	1281 (29.4)	1143 (27.2)	1279 (29.0)	
College graduate	882 (18.5)	725 (16.3)	796 (18.3)	783 (18.7)	862 (19.6)	
Mean poverty income ratio (CI)	2.7 (2.7–2.8)	2.5 (2.5–2.6)	2.6 (2.6–2.7)	2.6 (2.5–2.6)	2.4 (2.4–2.5)	<0.001
Mean BMI kg m^{-2} (CI)	28.1 (27.9–28.3)	28.5 (28.3–28.7)	28.8 (28.6–29.0)	29.2 (28.9–29.4)	29.4 (29.2–29.7)	<0.001

Table 2
Results from adjusted regression analysis of chemical toxicant concentration against poverty income ratio (PIR). Only chemicals demonstrating an association with PIR in 2 or more waves were reported. When the chemical toxicant was not measured in certain NHANES waves the term "no data" was utilised. Chemicals shown in bold were noted to demonstrate a positive association with PIR. All others listed demonstrated significant negative associations.

Chemical group	Chemical	2001/2	2003/4	2005/6	2007/8	2009/10
Arsenics	**Arsenobetaine**	No data	0.01 (−0.05–0.07)	0.07 (−0.01–0.14)	0.08 (0.02–0.14)**	0.14 (0.06–0.22)**
	Total arsenic	No data	0.02 (−0.07–0.11)	0.04 (0.00–0.07)*	0.06 (0.02–0.10)**	0.10 (0.06–0.14)***
Polyfluorinated compounds	**PFOA**	No data	0.06 (0.04–0.09)***	0.06 (0.03–0.09)***	0.03 (0.02–0.05)***	0.03 (0.01–0.06)*
	PFOS	No data	0.04 (0.02–0.07)**	0.04 (0.01–0.07)**	0.02 (0.00–0.04)	0.01 (−0.02–0.05)
	PFNA	No data	0.05 (0.02–0.09)**	0.05 (0.01–0.09)*	0.03 (0.01–0.05)**	0.02 (−0.01–0.04)
Phthalates (PH)	Mono-benzyl PH	−0.11 (−0.15 to −0.08)***	−0.05 (−0.09 to −0.01)*	−0.08 (−0.13 to −0.04)**	−0.07 (−0.11 to −0.03)**	−0.08 (−0.13 to −0.04)**
	Mono-isobutyl PH	−0.05 (−0.09 to −0.01)*	−0.02 (−0.05–0.01)	−0.05 (−0.12–0.02)	−0.04 (−0.08 to −0.01)*	−0.04 (−0.07 to −0.02)**
	Mono-n-butyl PH	−0.05 (−0.08 to −0.01)*	−0.02 (−0.07–0.02)	−0.05 (−0.08 to −0.01)**	−0.03 (−0.07 to 0.00)*	−0.05 (−0.08 to −0.01)*
	Mono(carboxyoctyl) PH	No data	No data	0.07 (0.03–0.12)**	0.09 (0.03–0.14)**	0.13 (0.07–0.19)***
	Mono(carboxynonyl) PH	No data	No data	No data	0.06 (0.01–0.10)*	0.08 (0.05–0.11)***
Polycyclic aromatic hydrocarbons (PAHs)	2-Napthol	−0.17 (−0.22 to −0.12)***	−0.10 (−0.15 to −0.04)**	No data	No data	No data
	3-fluorene	−0.16 (−0.22 to −0.12)***	−0.12 (−0.18 to −0.06)**	No data	No data	No data
	2-Fluorene	−0.14 (−0.18 to −0.09)***	−0.11 (−0.16 to −0.07)***	No data	No data	No data
	3-Phenanthrene	−0.07 (−0.11 to −0.04)***	−0.05 (−0.07 to −0.02)**	No data	No data	No data
	2-Phenanthrene	−0.10 (−0.13 to −0.06)***	−0.04 (−0.06 to −0.01)*	No data	No data	No data
	1-Pyrene	−0.10 (−0.14 to −0.06)***	−0.08 (−0.11 to −0.04)**	No data	No data	No data
Dioxins, furans, and coplanar PCBS	1,2,3,4,6,7,8,9-Ocdd	−0.02 (−0.05 to −0.00)*	−0.03 (−0.06 to −0.01)*	No data	No data	No data
Urinary heavy metals	Antimony	−0.02 (−0.04–0.00)*	−0.03 (−0.06 to −0.00)*	−0.01 (−0.03–0.01)	−0.03 (−0.06 to −0.01)**	−0.04 (−0.06 to −0.02)**
	Cadmium	−0.06 (−0.09 to −0.03)***	−0.10 (−0.18 to −0.01)*	−0.05 (−0.08 to −0.02)**	−0.06 (−0.09 to −0.03)***	−0.07 (−0.11 to −0.04)***
	Caesium	No association	0.06 (0.00–0.12)*	0.03 (0.01–0.06)**	0.03 (0.01–0.04)**	0.02 (0.00–0.04)
	Lead	−0.07 (−0.09 to −0.04)***	−0.05 (−0.07 to −0.02)**	−0.04 (−0.07 to −0.01)**	−0.03 (−0.05 to −0.01)**	−0.07 (−0.09 to −0.04)***
	Mercury	0.06 (0.02–0.09)**	0.16 (0.12–0.20)***	0.09 (0.05–0.12)***	0.10 (0.07–0.14)***	0.12 (0.08–0.17)***
	Thallium	0.04 (0.01–0.06)**	0.01 (−0.01–0.03)	.03 (0.02–0.04)***	0.03 (0.01–0.04)**	0.04 (0.02–0.06)**
Serum heavy metals	Cadmium	−0.07 (−0.09 to −0.06)***	−0.09 (−0.12 to −0.07)***	−0.08 (−0.09 to −0.07)***	−0.09 (−0.11 to −0.07)***	−0.10 (−0.12 to −0.07)***
	Lead	−0.06 (−0.08 to −0.05)***	−0.05 (−0.07 to −0.04)***	−0.06 (−0.08 to −0.04)***	−0.04 (−0.06 to −0.02)**	−0.05 (−0.07 to −0.03)***
	Mercury	0.10 (0.04–0.16)**	0.13 (0.08–0.18)***	0.10 (0.08–0.13)***	0.11 (0.08–0.13)***	0.11 (0.09–0.13)***
Environmental phenols	Bisphenol A	No data	−0.06 (−0.11 to −0.01)*	−0.05 (−0.10 to −0.00)*	−0.01 (−0.05–0.04)	−0.05 (−0.07 to −0.02)**
	Benzophenone-3	No data	0.21 (0.09–0.33)**	0.24 (0.13–0.34)***	0.28 (0.20–0.36)***	0.27 (0.16–0.38)***

* Denotes statistical significance at $P < 0.05$.
** Denotes statistical significance at $P < 0.01$.
*** Denotes statistical significance at $P < 0.001$.

When these mediators were combined into one model for serum cadmium or serum iron in the 2003/4 NHANES wave they explained 75% and 63% of the model variance respectively (Fig. 1).

Diet may be a mediator for the association between PIR and urinary phthalate concentration. Total iron was identified as a mediator for both mono-n-butyl and mono-isobutyl phthalate in two NHANES waves (Table 4).

Within the NHANES data no consistent mediators were identified for antimony, bisphenol A, caesium, mono-(carboxyoctyl) phthalate, mono-benzyl phthalate and PFOA.

4. Discussion

Our results demonstrate that different toxins accumulate with different patterns according to SES. Nearly half of the toxicants robustly associated with PIR demonstrated positive associations, with increased burdens in individuals with an increased PIR. This disproved our hypothesis, which suggested, on the basis of the Environmental Justice Hypothesis, that the majority of chemical toxicants would be higher in individuals of low SES. This discrepancy may be as a result of banning the utilisation of certain chemicals in recent years.

The association between PIR and toxicant concentration was investigated for 179 chemicals. Over 15% of the chemicals investigated demonstrated significant associations with PIR in more than one NHANES wave. This is more than would be expected by chance alone supporting evidence that PIR is an important indicator of toxicant burden.

Concentrations of 28 chemicals were associated with PIR in more than one NHANES wave. There were some consistent trends across specific chemical classes. Polycyclic aromatic hydrocarbons (PAHs) demonstrated inverse associations with PIR. PAH exposure predominantly comes from air and traffic pollution and individuals of lower SES often live in poorer more industrialised neighbourhoods with higher levels of air pollution. Chemicals within the urinary heavy metals and phthalates associated both positively and negatively with PIR. This supports the current inconsistency in the literature where the toxicant burden of phthalates has been positively and negatively associated with SES (Casas et al., 2011).

Eighteen chemicals were investigated in more detail as they demonstrated significant associations with PIR in more than 2 NHANES

Table 3
Summary of the potential mediators for the toxicants robustly associated with poverty income ratio (PIR) in NHANES and the mediator variables available in NHANES.

Chemical	Potential mediators	Mediators available in NHANES include
Total arsenic	Water source, fish and shellfish consumption	• Dietary assessment using total protein, fat, iron and calcium in the diet
PFOA	Fish and dairy products	• Fish and shellfish consumption
PFNA	Fish and dairy products	• Frequency of consumption of milk, cheese and other dairy products
Mono-benzyl PH	Diet, occupation and medicines	• Occupation data in the 2001/2 and 2003/4 waves
Mono-isobutyl PH	Diet, occupation and medicines	• Prescription medications
Mono-n-butyl PH	Diet, occupation and medicines	• Smoking data—categorical and serum cotinine (was used in our analysis)
Mono(carboxyoctyl) PH	Diet, occupation and medicines	• Sunscreen use
Antimony	Location, occupation, smoking	
Cadmium	Occupation, smoking	
Caesium	Diet and water source	
Lead	Diet, occupation, smoking	
Mercury	Diet and water	
Thallium	Diet, occupation and smoking	
Cadmium	Occupation, smoking	
Lead	Diet, occupation, smoking	
Mercury	Diet and water	
Bisphenol A	Diet (cans and plastic containers)	
Benzophenone-3	Sunscreen	

Table 4
Summary of the indirect effect results from the structural equation model. Significant indirect effects identify potential mediators in the poverty income ratio (PIR)-toxicant association. Positive regression coefficients highlighted in bold indicate a positive association between PIR and the toxicant of interest as mediated by the relevant mediator. All others listed demonstrated significant negative associations. Results are only presented for mediators that were identified as significant in at least two NHANES waves. Statistical significance is denoted by ?, *, ** and *** representing $P < 0.1$, $P < 0.05$, $P < 0.01$ and $P < 0.001$ respectively. # represents where multiple mediators (fish and shellfish consumption) were included in one model.

Chemical class	Mediator(s)	2001/2	2003/4	2005/6	2007/8	2009/10
Arsenics	Total arsenic#			0.05 (0.02–0.07)***	0.01 (0.00–0.03)*	0.05 (0.03–0.06)***
	Fish consumption	No data	No association	0.02 (0.00–0.03)*	0.00 (−0.01–0.01)	0.01 (0.00–0.02)**
	Shellfish consumption			0.04 (0.03–0.05)***	0.01 (−0.01–0.02)	0.03 (0.02–0.05)***
Environmental phenols	BP3					
	Sunscreen	No data	0.14 (0.09–0.19)***	0.09 (0.05–0.13)***	Data not available on sunscreen use	
Perfluorinated compounds	PFNA					
	Shellfish consumption	No data	0.00 (−0.01–0.00)	0.01 (0.00–0.02)**	0.02 (0.01–0.02)**	0.01 (0.00–0.02)*
Urinary phthalates	Mono-n-butyl					
	Iron	0.00 (−0.01–0.00)	−0.01 (−0.01–0.00)*	−0.01 (−0.01–0.00)*	0.00 (−0.01–0.01)	0.00 (−0.01–0.00)
	Mono-iso-butyl					
	Iron	0.00 (−0.01–0.00)	−0.01 (−0.01–0.00)*	−0.01 (−0.01–0.00)?	0.00 (0.00–0.00)	0.00 (0.00–0.00)
Serum heavy metals	Cadmium					
	Smoking	−0.06 (−0.08 to −0.04)***	−0.05 (−0.06 to −0.04)***	−0.07 (−0.09 to −0.04)***	−0.07 (−0.08 to −0.05)***	−0.07 (−0.08 to −0.05)***
	Iron	−0.00 (−0.01 to −0.00)*	−0.01 (−0.01 to −0.00)*	−0.00 (−0.01–0.00)?	−0.00 (−0.01–0.00)*	−0.00 (−0.00–0.00)
	Calcium	−0.00 (−0.01–0.00)*	−0.01 (−0.02–0.00)	−0.00 (−0.00 to −0.00)*	−0.00 (−0.00–0.00)*	
	Occupation	−0.02 (−0.03 to −0.02)***	−0.03 (−0.05 to −0.02)***	No data		
	Lead					
	Smoking	−0.02 (−0.03 to −0.01)***	−0.01 (−0.02 to −0.01)***	−0.02 (−0.02 to −0.01)***	−0.02 (−0.02 to −0.01)**	−0.02 (−0.03 to −0.01)***
	Occupation	−0.02 (−0.03 to −0.01)***	−0.02 (−0.03 to −0.01)***	No data		
	Calcium	−0.00 (−0.01–0.00)**	−0.00 (−0.01–0.00)*	−0.00 (−0.00–0.00)*	−0.00 (−0.01–0.00)	0.00 (0.00–0.00)
	Iron	−0.00 (−0.01–0.00)*	−0.00 (−0.01–0.00)*	−0.00 (−0.01–0.00)*	−0.00 (−0.00–0.00)*	−0.00 (0.00–0.00)
	Mercury#	0.01 (0.00–0.03)*	0.01 (−0.03–0.04)	0.02 (0.01–0.03)**	0.02 (0.01–0.04)**	0.03 (0.02–0.04)***
	Fish consumption	0.00 (−0.02–0.02)	0.01 (−0.01–0.04)	0.01 (0.00–0.01)*	0.01 (0.01–0.02)**	0.01 (0.01–0.02)***
	Shellfish consumption	0.02 (0.01–0.03)**	0.01 (−0.01–0.02)	0.02 (0.01–0.02)***	0.02 (0.01–0.02)*	0.02 (0.01–0.03)***
Urinary heavy metals	Cadmium					
	Smoking	−0.04 (−0.06 to −0.02)***	−0.02 (−0.03 to −0.01)***	−0.03 (−0.04 to −0.01)**	−0.03 (−0.04 to −0.02)**	−0.03 (−0.04 to −0.02)***
	Lead					
	Smoking	−0.02 (−0.04–0.00)	−0.01 (−0.02–0.00)*	−0.01 (−0.02–0.00)**	−0.01 (−0.02–0.00)*	−0.01 (−0.02–0.00)*
	Occupation	−0.02 (−0.04–0.00)*	−0.02 (−0.04 to −0.01)**	No data		
	Mercury#	0.01 (0.00-0.02)*	0.00 (−0.02–0.02)	0.03 (0.01–0.05)**	0.01 (0.00–0.02)?	0.02 (0.00–0.04)*
	Fish consumption	0.00 (−0.01–0.01)	−0.01 (−0.03–0.01)	0.01 (0.00–0.02)*	0.00 (0.00–0.01)*	0.01 (0.00–0.02)*
	Shellfish consumption	0.01 (0.00–0.02)*	0.00 (−0.01–0.02)	0.01 (0.00–0.03)*	0.01 (−0.00–0.02)	0.01 (−0.00–0.03)
	Thallium					
	Shellfish consumption	0.00 (0.00–0.00)	0.00 (−0.01–0.01)	0.01 (0.00–0.01)*	0.01 (0.00–0.01)*	0.00 (−0.01–0.01)

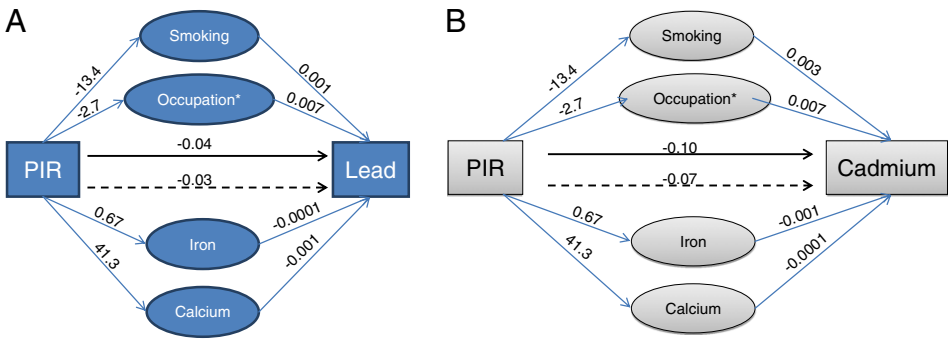

Fig. 1. Path analysis mediation models for A) serum lead and B) serum cadmium from the 2003/4 NHANES wave. The oval shapes represent specific mediators. The solid black arrow between PIR and lead/cadmium represents the regression coefficient for the association between PIR and the chemical toxicant where all individuals have all mediators measured. The dashed arrow represents the indirect effect of PIR on lead/cadmium through the 4 mediators (smoking, occupation, iron and calcium). *Occupation becomes more blue collar as it increases.

waves. Half of these chemicals were positively associated with PIR. This was unexpected, as in general, toxicant burden is considered to predominate in individuals with lower SES, as per the Environmental Justice Hypothesis.

We utilised mediation analysis to attempt to understand what factors may contribute to the associations observed between specific chemical toxicants and PIR. The heavy metal mercury, measured in both serum and urine samples, was positively associated with PIR in all NHANES waves. Mercury levels were previously shown to associate with annual income in American women and this was related to increased fish consumption (Mahaffey et al., 2009). Today, the major sources of mercury exposure include, fish consumption, dental amalgams and vaccines (Clarkson and Magos, 2006). Mediation analysis suggested that both fish and shellfish consumption were crucial mediators in the association between urinary or serum mercury and PIR. This suggests that increased fish and shellfish consumption contributes to the association. However, the indirect effect was smaller than the direct effect, with shellfish consumption explaining only between 10 and 25% of the variance and fish consumption 10 and 15% of the variance. This suggests that other factors are involved in mediating the relationship between PIR and mercury concentration.

Dental amalgams may help to explain increased levels of mercury in higher SES individuals, as they contain on average 40–55% mercury (Carta et al., 2002), which was observed to increase mercury burden in children (Al-Saleh and Al-Sedairi, 2011). It is well established in the US that those of higher SES more frequently visit health care professionals (National Center for Health Statistics, 2012), hence the possibility of more dental amalgams and higher levels of mercury. Within NHANES, no data was available to investigate the role of dental amalgams on the association between mercury and PIR. It should also be noted that geographical variation across the US is associated with mercury concentration (Mahaffey et al., 2009) but this was not investigated in our study.

Several other urinary heavy metals also positively associated with PIR in at least three NHANES waves: caesium and thallium. The general population are considered to be most at risk of thallium exposure from home grown fruits and green vegetables, something that individuals of higher SES have better access to and/or desire to do. No dietary mediators were noted in this study. Thallium also concentrates in shellfish and mediation analysis suggested a significant indirect effect of shellfish consumption on the relationship between thallium and PIR in two of the five NHANES waves. The most common exposure route to caesium is from contaminated water sources. NHANES does have data on the main tap water source in an individual's home, but a role for the water source as a mediator was not noted within this data. This may be due to the low numbers of individuals who use alternative water sources. Other factors driving increased toxicant burden of these urinary heavy metals in higher SES individuals is currently unknown.

Higher burdens of the polyfluorinated compounds (PFCs) tended to be associated with increased SES as previously noted (Melzer et al., 2010a; Nelson et al., 2012). PFCs tend to be found in expensive fabrics that provide water proofing, perhaps explaining its association with higher SES. A major source of human exposure to PFCs is diet (Ericson et al., 2008), and higher SES individuals tend to consume more fresh meat, fish and vegetables, which are potential sources of PFOA and PFNA. We observed significant indirect effects for shellfish consumption in the association between PFNA and PIR. The direct effect was larger than the indirect effect suggesting other factors associated with higher SES also contribute to the association with PFC concentration. Fish consumption was not noted to be a mediator. A recent study demonstrated that serum PFC concentrations correlated with the levels of PFC in the air of offices (Fraser et al., 2011), and with higher SES individuals more likely to have white collar office jobs, this may partially explain the higher exposure. However limited occupation data was available to investigate this in more than one NHANES wave.

The environmental phenol, BP3, was also positively associated with PIR in all NHANES waves. BP3 is found in sunscreens and cosmetics, which are more likely to be used by higher SES individuals (Duquia et al., 2007). Sunscreen use had a robust indirect effect on the relationship between BP3 concentration and PIR suggesting sunscreen utilisation is an important mediator of the BP3–PIR association.

Total urinary arsenic was positively associated with PIR in 3 NHANES waves. Mediation analysis suggested the observed relationship is partially attributable to fish and shellfish consumption as previously noted (Rivera-Nunez et al., 2012). Other factors may include the primary water source, which was not noted to be a mediator in our models or the location of an individual's home, which was not considered here.

The other consistent associations we observed between chemical burden and SES were negative associations. Negative associations are predicted by the Environment Justice Hypothesis (Brown, 1995). Serum and urinary concentrations of lead and cadmium were negatively associated with PIR in all NHANES waves investigated. This was consistent with previous findings (McKelvey et al., 2007; Pirkle et al., 1998). Lead exposure can occur through a variety of sources, including air, home remedies, drinking water, diet, smoking and toy jewellery (Pirkle et al., 1998). Mediation analysis in the NHANES data suggested smoking may in part, drive the association between PIR and lead concentration, explaining between 25 and 50% of the variance. Occupation also mediated the association between lead and PIR. Individuals in lower income jobs are more likely to have workplace exposure to lead, as they are more likely to have industrial jobs (Tong et al., 2000). Other mediators identified included a diet low in calcium and iron, although the indirect effect of these factors was minimal. Diet tends to be poorer in individuals with a lower SES and therefore it is unsurprising that these dietary factors are

potential mediators in this relationship. In the 2003/4 wave we noted that when these mediators were combined 63% of the model variance was explained, suggesting we have identified some of the key mediators in this relationship.

The principle sources of cadmium exposure include cigarette smoke and diet in the US. We investigated the role of cigarette smoking in our mediation models. Smoking status as determined by serum cotinine levels was an important mediator of the inverse association noted between either serum or urinary cadmium and PIR. The indirect effect of smoking on the relationship between serum cadmium and PIR explained over 50% of the variance in four NHANES waves, highlighting the importance of smoking in this relationship. Higher cadmium levels are observed if the diet is low in calcium, protein, or iron, or is high in fat (Mijal and Holzman, 2010) and both dietary calcium and iron levels were identified as mediators in at least two NHANES waves. Occupation may influence an individual's cadmium levels and their socio-economic status, and here occupation was noted to be a mediator in the association between serum and urinary cadmium burden and PIR.

For cadmium, lead and mercury we observed associations in both serum and urinary measures. This strengthens the validity of our findings. Urinary measures of heavy metals tend to be the biomarker of choice for chronic exposure. There is growing concern that lifelong accumulation of low level chemicals will have a substantial impact on human health. Urinary measures therefore provide a more accurate reflection of toxicant accumulation over the life course.

Our results were consistent with several recent studies which have demonstrated that low SES does not always associate with increased chemical burdens (Morrens et al., 2012; Nelson et al., 2012). Our study significantly extends this work investigating a much broader range of toxicants and considering the factors which link SES to toxicant burden.

4.1. Strengths and limitations

We investigated the relationship of 179 chemicals with PIR in a representative sample of the US population using 5 NHANES waves. To our knowledge no other study has investigated this number of chemicals in 5 independent samples. To reduce the possibility of chance findings we only carried out a detailed investigation of chemicals where significant association with PIR was noted in at least two waves of NHANES. The individual waves of NHANES allowed independent replication of our findings in entirely new population samples. This increases the confidence that associations we have reported are not the products of chance. We also investigated the associations using continuous data, ensuring we did not limit the power of our analysis.

There are several limitations with this work. We cannot exclude 'false' negative associations. These may arise because of small effect sizes, limited population exposures, or misclassification of exposure. The demographic data for the NHANES waves investigated demonstrated significant increases in BMI, age and the proportion of individuals living below the poverty threshold over the decade of study from 2001/2 to 2009/10. These factors may have influenced our results. However, in the subset of chemicals robustly associated with PIR, whilst fluctuations were observed in the regression coefficients obtained over the decade of study, no clear trends were observed. This suggests that whilst the demographic alters significantly across the decade, the association between PIR and toxicant burden is not altered in robustly associated. It should be noted that changes in the demographic may have resulted in missing some chemicals which are associated with SES.

Our findings may be limited by the size of each NHANES wave only (~4300 individuals with PIR), with smaller subsets having chemical toxicant data. We did not pool our data as we wanted to investigate associations in multiple discrete waves. Confirmatory analysis is now required in larger cohorts. Another limitation of the NHANES dataset is lack of geographical data freely available. Location will influence potential environmental exposures. However this was considered to be beyond the scope of this study which focused on classic markers of SES. Future work will consider this variable.

SES is a multidimensional construct normally based on education, income and occupation. However, our analyses focused on PIR. Future work should consider the role of SES on toxicant burden in another cohort, possibly using principal component analysis to create a single variable from several different SES markers. In larger studies it would also be possible to stratify analyses by race/ethnicity.

5. Conclusions

Overall these findings provide a comprehensive overview of the extent to which overall burden of toxicant exposure in the US general population is determined by SES. We have demonstrated that higher SES groups are not always protected from increased levels of environmental toxicants. In fact over a third of the associations observed involved increased risk of toxicant burdens for higher SES individuals. This suggests that efforts to reduce exposure inequalities need to be group specific, and that public health messages may be targeted more effectively. A better understanding of environmental inequalities and their determinants are essential in order to address them.

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