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Unjust environments: Racial inequalities in environmental exposures and their implications for health

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Racial inequalities in environmental exposures and their implications for health

By

Lara Jennifer Cushing

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Abstract

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Some of us grow up surrounded by trees, good schools, and opportunity. Others play in the shadow of heavy industry or near abandoned brownfields, surrounded by a high concentration of poverty. Unequal – and unjust – environments shape our opportunities for good health and too often add to the hardships of socially disadvantaged groups. Research on environmental justice considers how a long history of racial discrimination in the U.S. has insured that people of color are more likely to live in neighborhoods with less desirable and less healthful environments.

In this dissertation I contribute to scholarship on environmental justice by investigating cumulative environmental hazards, chemical body burden, and the health implications of climate change from an environmental justice perspective. Chapter 1 describes my approach and how it is situated within prior research on environmental inequalities, differential vulnerability to the health impacts of pollution by socioeconomic status, and racial/ethnic disparities in health. Chapter 2 investigates social inequalities in residential proximity to cumulative environmental and social stressors to health across the state of California. It innovates upon previous work by incorporating measures of social vulnerability and geographically comparing the degree to which multiple environmental hazards are inequitably distributed in a framework that can be used to identify opportunities to reduce inequality and track progress towards environmental justice goals.

In Chapter 3 I analyze biomonitoring data to examine socio-demographic differences in chemical body burden during pregnancy, considering the number and concentrations of over 80 toxic compounds detected in blood and urine by race, ethnicity, country of origin, and educational attainment. Biomonitoring data gives an indication of possible differences in exposures to multiple toxic chemicals that can reveal inequities with implications for maternal and child health. Chapter 4 considers the potential health implications of climate change from an environmental justice perspective. Using a recent heat wave in Texas, I investigate whether extremely hot temperatures are associated with an elevated risk of preterm birth and examine the possibility that climate change could worsen existing racial and ethnic disparities in reproductive health. The research and policy implications of my findings are discussed in Chapter 5, where I stress the need to incorporate differential vulnerability and cumulative exposures into environmental regulatory policy, exercise precaution in the face of uncertainty, and focus on remedying the upstream drivers of social inequality that lead to unjust environments.

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Acknowledgments

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Staff at the Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency crafted the environmental justice screening tool I used as the basis for the research presented in Chapter 2. I thank them very much for their contributions and thoughtful feedback on both the analysis and text.

The biomonitoring data analyzed in Chapter 3 comes from the Chemicals in Our Bodies study, a joint project of Biomonitoring California, a tri-departmental state program, and the University of California at San Francisco and Berkeley. I thank staff from the California Department of Public Health (CDPH), Department of Toxic Substances Control (DTSC), OEHHA, and the UC San Francisco Program on Reproductive Health and the Environment for providing detailed comments on my analysis and interpretation of the results. Staff at the CDPH and DTSC laboratories and OEHHA also provided the description of the analytical chemistry methods given in Appendix A.

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Members of Southwest Workers Union and the Committee for Environmental Justice Action in San Antonio, Texas inspired me to work on issues of environmental justice. I am grateful to them for welcoming me into their homes and their struggle for a clean environment.

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Finally, to my sister Alina, partner Jesse, and community of friends near and far: thank you for your companionship, commiseration, and care while I wrote this, and for reminding me to have a good time along the way.

Abbreviations

ACS	American Community Survey
AT	Apparent temperature
BMI	Body mass index
CalEPA	California Environmental Protection Agency
CARB	California Air Resources Board
CDPH	California Department of Public Health
CEHTP	California Environmental Health Tracking Program
CI	Confidence interval
CI Score	Cumulative Impact Score
CIOB	Chemicals in Our Bodies
DPT	Dew point temperature
DTSC	Department of Toxic Substances Control
ED	Emergency department
GMR	Geometric mean ratio
HS	High school
LMP	Last menstrual period
MDL	Method detection limit
MI	Multiple imputation
MLE	Maximum likelihood estimation
NCDC	National Climatic Data Center
NHANES	National Health and Nutrition Examination Survey
NLCD	National Land Cover Database
NOAA	National Oceanic and Atmospheric Administration
OEHHA	Office of Environmental Health Hazard Assessment
OR	Odds ratio
PI	Pacific Islander
PM	Particulate matter
QA/QC	Quality assurance / quality control
RPD	Relative percent difference
SB	Senate bill
SES	Socioeconomic status
SPE	Solid phase extraction
SWRCB	State Water Resources Control Board
TDSHS	Texas Department of State Health Services
U.S.	United States of America
ZCTA	ZIP Code Tabulation Area

Chapter 1

Social inequality and racial disparities in environmental health

The environmental justice movement that arose in the late 1970s and early 1980s succeeded in calling national attention to the unequal distribution of hazardous land uses in the U.S. and their potential consequences for health in low income communities of color. Examples such as Warren County, North Carolina – where the decision to cite a hazardous waste dump in the county with the state's highest concentration of Black residents met protests that grabbed national headlines[1(chap1)] – and Los Angeles, California – where "white flight" to the suburbs, racially-restrictive zoning, housing covenants, and racialized forms of employment resulted in Black and Latino residents being much more likely to live near industrial hazards[2] – illustrated the extent to which discriminatory siting, as well as more subtle forms of institutionalized racism and White privilege, have contributed to unequal geographies of health risks from pollution. Environmental justice advocates critiqued traditional methods of risk assessment used in regulatory analysis for being too narrowly focused on individual pollutants and sources and failing to consider the existence of other hazardous co-exposures in toxic 'hot spots'. Advocates also called for environmental regulatory decision-making to consider the ways in which pollutant exposures might interact with social stressors such as poverty to amplify adverse health impacts in disadvantaged communities. These critiques continue to pose a significant challenge for environmental health scientists and regulators to develop new methods to characterize the cumulative impacts of both environmental and social stressors in communities where both are prevalent and are likely to contribute to ill health.[3]

In this introductory chapter I provide an overview of key concepts that inform the research included in this dissertation as well as emerging knowledge about the cumulative impacts of exposure to environmental hazards and social stressors more generally. These include 1) the existing evidence of social inequalities in environmental exposures, 2) how social stressors may exacerbate the health effects of these exposures in disadvantaged communities, and 3) the possible contribution of both factors to health disparities. In each of these cases, my primary focus is on inequality with respect to race and ethnicity and the disproportionate health burden posed by environmental hazards in communities of color. My focus on the social construct of race stems from both the long history of legal racial discrimination in the U.S. in civil rights, housing, education, and employment as well as from contemporary struggles over race-based discrimination and unequal outcomes in health, wealth, education, criminal justice, immigration policy, and other domains. Given the deeply entrenched way in which racial systems of control underpin the economic development and social history of the U.S., it is not surprising that previous research in environmental justice has found that the evidence of race-based environmental inequalities is more consistent than the evidence of inequalities with respect to economic class,[4] although race and class are of course deeply intertwined.

I use the term "unjust environments" to refer to differences in environmental conditions that disproportionately harm, or place at higher risk, the health and wellbeing of socially disadvantaged groups. Unequal conditions do not qualify as unjust and inequitable unless they are also unfair. I consider it unfair when environmental hazards that are associated with human activity are distributed in such a way as to put at greater risk those with less material resources or political power, poorer pre-existing health, or members of groups who have been subject now or

in the past to systematic interpersonal, institutional, or legal discrimination. These groups and individuals could include (but are not limited to) members of the LGBTQ community, descendants of slaves, undocumented immigrants, economic and political refugees, people with disabilities, women, low income individuals, and children. In the era of anthropogenic climate change, even the weather is influenced by human activity; for that reason, most if not all environmental hazards could result in unjust environments as I have defined them here.

The exposure-disease paradigm is illustrated in **Figure 1-1** in order to situate my work on unjust environments within the larger field of environmental health. This paradigm is useful in evaluating human exposure to chemical and physical agents and is widely employed for risk assessment in the context of environmental regulatory analysis.[5] However, the framework is typically applied in a single-pollutant or single-media context, when in the real world and especially in disproportionately impacted communities, individuals may be exposed to multiple pollutants emanating from multiple sources that result in harmful exposures via several routes at once. Individual biological differences are known to modify the effects of pollution by influencing the intake, bioavailability, elimination, accumulation, and transformation of toxicants in the body, and factors such as age, sex, and pregnancy status are often incorporated into risk assessment to try to ensure that regulatory standards protect vulnerable subpopulations. However, the potential impact of social stressors on these biological processes – including the "embodiment" of social inequalities[6] – is rarely examined. Racial residential segregation, for example, has contributed to the concentration of poverty, underemployment, poor housing quality, and disproportionate surveillance by law enforcement in communities of color that may contribute to higher levels of psychosocial stress. Stress may in turn compromise the body's ability to defend against and recover from harmful exposures to pollution.[7,8]

Within this framework, my work seeks to contribute to scholarship on environmental justice and racial disparities in environmental health in three respects. First, I characterize the distribution of multiple environmental hazards and pollutant concentrations in bodies across diverse populations. Second, my work explores the extent to which social stressors and other factors that confer greater vulnerability are prevalent in communities that also have numerous environmental hazards. In so doing I highlight the need to examine and integrate differential vulnerability and susceptibility into risk assessment practice. Finally, I contribute to the growing scholarship on climate justice by examining the extent to which extreme heat events – which are becoming more frequent and severe as a result of global warming – may lead to higher risk of preterm birth and potentially widen racial disparities in preterm birth rates.

Key concepts in environmental justice

Racial inequality in environmental exposures

Social movements for environmental justice have roots that are distinct from conservation and other environmental movements, having grown out of earlier struggles for Native American sovereignty, occupational health and safety, and civil rights.[9] Early research responding to concerns raised by environmental justice activists documented that hazardous waste sites were disproportionately located in communities of color.[10,11] Subsequent scholarly work examined residential proximity to other hazardous land uses such as major roadways[12] and industrial sites,[13] as well as disparities in exposure to air[14,15] and water[16] pollutants and cancer risk

associated with air toxics.[17] While the reasons for these inequalities are debated,[18] and there are of course exceptions to the overall pattern, the disproportionate environmental burden in communities of color is widely recognized and has resulted in federal as well state-level policies to address racial environmental inequalities.[19,20]

Research in the field of environmental justice has since expanded to consider health-promoting environmental amenities in addition to hazards and to include climate change. Work in the former realm has demonstrated inequality in access to green spaces[21,22] and recreational facilities[23,24] by race that may impact air quality, stress, mental health, and levels of physical activity.[25–28] Other work on environmental amenities has documented that Blacks and Hispanics live in neighborhoods with fewer supermarkets and less availability of fresh fruits and vegetables than do Whites,[29–33] which in turn can result in less healthful diets and increased risk of obesity.[34,35]

Scholarly work in the latter realm was catalyzed in part by Hurricane Katrina, which made painfully clear the disproportionate impact extreme weather events can have on people of color even within a wealthy country with robust emergency response systems.[36–39] International inequities with respect to anthropogenic climate change – which poses a much greater risk to life, livelihoods, and sovereignty in less industrialized countries who bear little historical responsibility for global warming in contrast to wealthy, industrialized nations – are well documented[40–42] and reflected in the United Nations Framework Convention on Climate's recognition that countries must combat climate change "on the basis of equity and in accordance with their common but differentiated responsibilities".[43(sec3)] The environmental justice perspective on climate change has added to this a focus on *within*- as well as *between*- country variations in vulnerability and impact. Research along these lines has been informed by previous studies documenting racial disparities in the impacts of natural disasters,[44,45] and includes efforts to characterize vulnerability to a range of climate-related hazards and assess neighborhood-level variation in potential impacts by race and ethnicity.[46,47]

The combined effect of environmental hazards and social stressors on health

Several studies suggest that people of low socioeconomic status (SES) have a heightened vulnerability to environmental toxicants that is not attributable to known biological risk factors. For example, several epidemiological studies find that exposure to the same amount of particulate matter has a greater effect on mortality among those with lower educational attainment,[48–50] although the findings have not always been consistent and are based on observational data.[51,52] Others have found greater effects of particulate matter on birthweight[53] and lead exposure on hypertension[54] among Blacks compared to other groups. One possible explanation for this is that lower SES confers greater co-exposure to other harmful pollutants that are not measured in these studies. Another is that predisposing health conditions, behaviors, or traits that are more prevalent among low SES populations and people of color may confer greater susceptibility, although epidemiological studies typically attempt to control for these factors. Finally, low SES may increase vulnerability directly through things like poorer nutrition, access to health care, and housing, or indirectly through less health-promoting neighborhood environments and increased psychosocial stress.[55]

This last explanation for heightened vulnerability among disadvantaged populations posits that the chronic psychosocial stress of coping with limited resources and negative life events results in a physiological "wear and tear" or "allostatic load"[a] on the body that can compromise the functioning of the immune, neuroendocrine, metabolic and cardiovascular systems.[58] Arline Geronimus proposed that the stress of living in a race-conscious society that stigmatizes and disadvantages people of color leads to physical "weathering" of the body akin to premature aging and that this may explain why the Black-White health gap widens with age.[59–62] Together, the theories of allostatic load and weathering suggest that persistent, high-effort coping with social stressors such as discrimination and poverty over the life course can take a toll on the body and reduce an individual's ability to defend against and recover from the negative effects of pollution.

Empirical research supporting this idea is limited but seems to support the hypothesis that stress can modify the relationship between environmental exposures and health.[63] In laboratory studies, chronically stressed rats have been shown to exhibit a greater adverse effect of fine particulate air pollution on respiratory function and biological markers of inflammation than less stressed rats.[64] Children exposed to violence or whose parents have high levels of stress suffer a higher risk of asthma diagnosis attributable to traffic-related pollution[65,66] and in-utero exposure to tobacco smoke.[66] In adults, elevated self-reported and biological measures of stress (allostatic load) have also been associated with a larger adverse effect of lead on cognition[67] and lead[68,69] and particulate matter[67–70] on hypertension.

Racial disparities in health

A large body of research documents pervasive and significant disparities in disease burden between racial or ethnic groups. For example, gender-specific mortality rates are markedly higher for Blacks than Whites in the U.S. up to age 84, and higher for Native Americans than Whites up to age 54 (after which Whites have higher mortality rates than Native Americans).[71] Asians and Latinos (two categories that encompass people with very different ancestry, immigration histories, cultures, and experiences of racial discrimination) have comparable or lower mortality rates than Whites; however, this is likely to be confounded by the fact that these categories include many immigrants and immigrants have lower rates of adult mortality than people born in the U.S. Blacks, Mexican Americans and Native Americans also have significantly higher rates of cardiovascular disease than Whites,[72] and several studies indicate that Blacks experience earlier onset and/or poorer prognosis of diseases such as breast cancer and depression.[71] While perinatal health outcomes have been improving over time for all groups, Blacks, Native American, and some Hispanic groups still have significantly higher rates of preterm birth and infant mortality than Whites.[73,74]Although some recent progress has been made

[a] Allostasis is the process of maintaining stability (or homeostasis) of the human body's internal environment in response to altered external conditions through physiological or behavioral changes. Bruce McEwen proposed the concept of "allostatic load" to refer to the wear and tear on the body resulting from repeated as well as inefficient cycling on and off of these responses.[56,57] While allostasis is generally adaptive in the short term, chronic activation of responses such as those of the hypothalamic-pituitary-adrenal (HPA) axis of the neuroendocrine system (which is involved in the "fight or flight" response) can be damaging.

towards shrinking racial health disparities, in general, there has been limited change or, in some cases, a worsening of inequities over time.[74–76]

This has led to scholarly and policy interest in health disparities, a term that often is used interchangeably with "health inequalities" or "health inequities" and I use here to describe "systematic, plausibly avoidable health differences adversely affecting socially disadvantaged groups", following Braveman *et al.* (2011).[77] Because they are avoidable, health disparities are a central preoccupation of public health scholars and practitioners. They are unjust because they adversely affect socially disadvantaged populations. Reducing health disparities by improving the health of disadvantaged groups has rightfully become a priority for both the World Health Organization and U.S. Department of Health and Human Services.[78,79]

A wide range of material, behavioral, psychosocial, environmental, and biological factors have been proposed to explain why race is so strongly linked to health status.[80] While some jump to genetic explanations, genes are unlikely to play more than a minor role because race and ethnicity are social constructs that poorly predict genetic variation.[81] That is, racial groupings and categories have changed through time in accordance with social convention and prejudice, and have little to do with ancestry or biological difference.[b] Social determinants of health are considered much more important than genetics in creating and sustaining racial health disparities (in addition to being something we can change). Study of the social determinants of health requires us to consider distal causes such as racism, which patterns opportunities, resources, and life experiences but is difficult to measure and complex – operating at institutional, interpersonal, and internalized levels.[83] Understanding how these distal phenomena affect more proximal material, behavioral, psychosocial, and environmental mechanisms in ways that lead to health disparities is complicated by the interrelation, interactions, and feedbacks between them over the lifespan and across generations.[84]

Given the evidence of unequal residential proximity to environmental hazards and amenities reviewed above, it is natural to wonder to what extent neighborhood environmental factors contribute to racial health disparities. Research on the effects of neighborhood context on health suggests that environments matter a great deal. For example, using five years of interview data from the National Health Interview Survey, D. Phuong Do and colleagues (2008) find that controlling for individual-level SES, body mass index and physical activity limitation, neighborhood of residence accounted for 20-26% of the Black-White difference in self-rated health for women and roughly 46% for men.[85] However, neighborhoods influence health in numerous ways, including via their physical aspects (e.g. environmental exposures, walkability, quality of housing and services) and social aspects (e.g. institutions, social cohesion,

[b] The social rather than biological basis of race is evidenced by the fact that, for example, White mothers in the U.S. are considered able to give birth to Black children but Black mothers are not considered able to give birth to White children (the "one drop rule"). I utilize racial and ethnic categories in my research as an indication of how people are perceived and treated in a race-conscious society rather than as markers of biological difference or ancestry, while acknowledging that the categories themselves are problematic in that they are key to the functioning of racism.[82]

safety/violence, norms),[86] and the extent to which any one factor contributes to disparities in particular health outcomes requires further research.

Chapter overview and novel contributions

In the following chapters, I examine environmental inequities along different points in the exposure-disease paradigm with emphasis on racial and ethnic disparities and attention towards co-exposure to multiple pollutants and differential vulnerability as illustrated in **Figure 1-1**. In Chapter 2, I present evidence of disparities in residential proximity to 11 different environmental hazards in California as well as population vulnerability due to biological and social factors. I use data from California's state-wide environmental justice screening tool CalEnviroScreen, which maps indicators of pollution and population vulnerability in an effort to identify communities high in both proximity to multiple environmental hazards and vulnerability in the form of pre-existing health conditions and low socioeconomic status that may confer greater risk of ill health. The innovation in my analysis compared to previous work in environmental justice is the incorporation of measures of vulnerability and the use of inequality metrics to characterize and compare the degree of inequity in the distribution of multiple environmental hazards in a framework that can inform regulatory policy and track progress towards environmental justice goals.

In Chapter 3, I analyze biomonitoring data from the Chemicals in Our Bodies study of pregnant women in San Francisco and pregnant women participating in the National Health and Nutrition Examination Survey between 1999 and 2012 to assess whether concentrations of environmental chemicals measured in women's blood and urine differed by race, ethnicity, nativity, and educational attainment. To my knowledge, this is the first attempt to look at socio-demographic differences in measured concentrations of over 80 potentially harmful chemicals during pregnancy. I utilize modern techniques (multiple imputation and maximum likelihood estimation) to address some of the limitations of previous studies with respect to how they have treated censored observations that were below the laboratory method's detection limit. The results of this study point to possible differences in chemical body burden during pregnancy that vary in particular by country of origin. For some chemicals I also found suggestive evidence of disproportionate exposure among women of color and women with lower levels of educational attainment.

In Chapter 4, I examine whether there are racial disparities in vulnerability to preterm birth during an extreme heat event in Texas. This work was motivated by 1) the fact that climate change is causing longer, more frequent, and more intense heat waves; 2) recent evidence suggesting heat can increase the risk of preterm birth, and 3) previous studies documenting that Blacks and Hispanics may be at increased risk of adverse health effects during period of extreme heat. The innovation in my approach over previous work is the incorporation of measures of neighborhood land cover that may contribute to localized heat-island effects. I also give more consideration than previous studies as to whether seasonal variation in the baseline risk of preterm birth arising from seasonal patterns in conception could confound the relationship between heat and preterm birth. I use survival analysis techniques to help avoid this source of bias.

Chapter 5 discusses the implications of my findings for further research and policy. I consider the challenges and opportunities for creating new knowledge about environmental inequalities by making use of cumulative impact approaches and biomonitoring data and examining the health impacts of climate change from an environmental justice perspective. I also offer thoughts on promising policy approaches to remedy unjust environments and improve community health. These include integrating input from environmental justice scholars and advocates in policy design; incorporating differential vulnerability and cumulative exposures into environmental regulatory decision-making; embracing precaution in the face of uncertainty about the health effects of synthetic chemicals; and focusing efforts on transformative social and economic policies that remedy the root causes of social inequality and environmental health inequities.

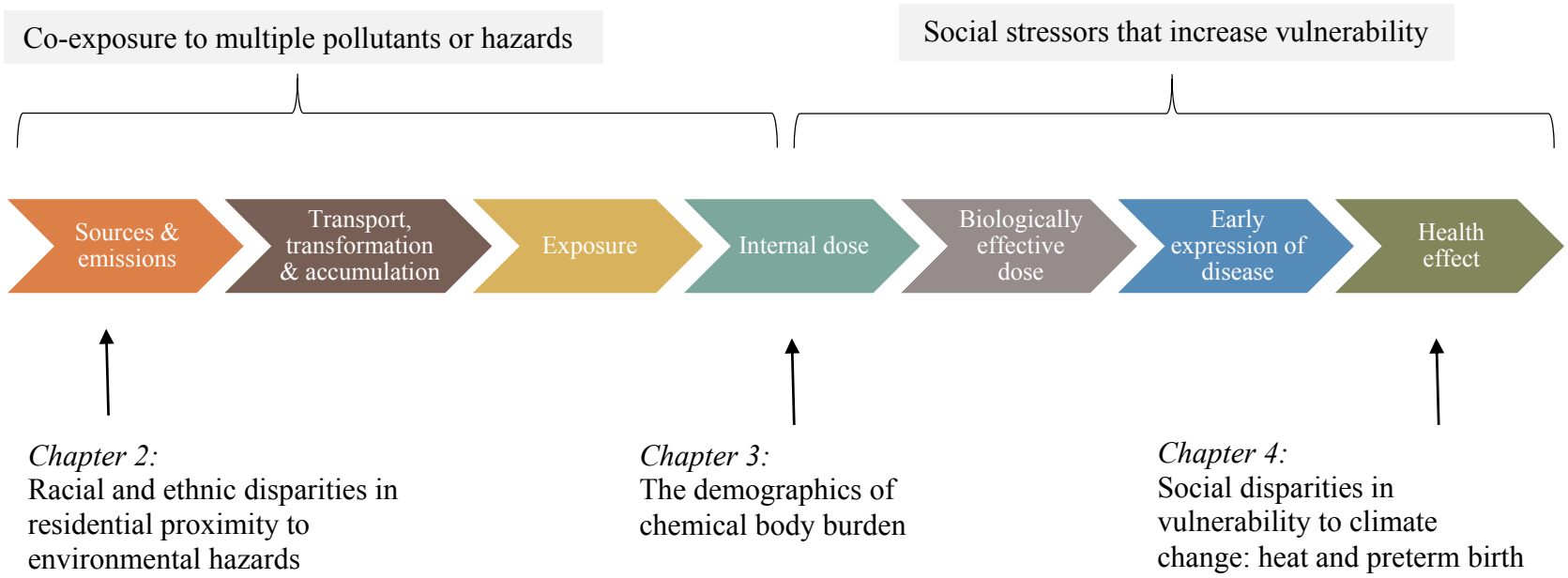


Figure 1-1 The exposure-disease paradigm, overarching dissertation themes, and chapter overview

Chapter 2

Racial/ethnic disparities in residential proximity to environmental hazards in California[a]

Abstract

In this chapter, I use an environmental justice screening tool (CalEnviroScreen 1.1) to compare the distribution of environmental hazards and vulnerable populations across California communities. CalEnviroScreen 1.1 combines 11 indicators of pollution burden and 6 indicators of population vulnerability created from publicly available data sources into a relative cumulative impact score. I compared cumulative impact scores across California ZIP codes on the basis of their location, urban or rural character, and racial/ethnic makeup. I then used a concentration index to evaluate which environmental hazards are most unequally distributed with respect to race/ethnicity and poverty. I found that, adjusting for population density, the odds of living in one of the 10% of ZIP codes with the highest (worst) cumulative impact score were 5.8 [95% CI=5.5, 6.1], 5.2 [4.7, 5.7], 1.8 [1.2, 2.6], 1.7 [1.6, 1.9] and 1.6 [1.4, 1.9] times greater for Hispanics, Blacks, Native Americans, Asian/Pacific Islanders, and other or multiracial individuals, respectively, than for non-Hispanic Whites. Environmental hazards were more regressively distributed with respect to race and ethnicity than to poverty, with pesticide use and toxic chemical releases being the most unequal. The findings suggest that environmental hazards and social stressors to health overlap geographically. They also show that many types of environmental health hazards disproportionately burden communities of color in California.

Background

Communities of color in the U.S. often reside in neighborhoods with worse air quality[17], more environmental hazards[87], and less health-promoting environmental amenities such as parks.[23] This unequal distribution of exposures may contribute to racial/ethnic health disparities in environmentally sensitive diseases such as cancer and asthma.[88] Research has shown that communities of color in California experience higher cancer risk from toxic air contaminants[89], higher average levels of nitrate contamination in their drinking water[16] and live in closer proximity to hazardous waste sites[90] and traffic[12]. However, less is known about the extent to which communities of color are simultaneously exposed to multiple sources of pollution, and the implications of such co-exposures for health.

There is thus an increasing need for analytic frameworks and decision-making tools that account for exposures to multiple environmental hazards through a variety of routes. Such frameworks should also consider differential vulnerability to the health effects of those exposures, which can vary across the population due to both individual and community-level factors.[3,91,92] For example, age and health status, including suffering from pre-existing cardiovascular disease or

[a] Portions of this chapter were published in the American Journal of Public Health as Cushing L, Faust J, August LM, Cendak R, Wieland W, Alexeeff G, "Racial/Ethnic Disparities in Cumulative Environmental Health Impacts in California: Evidence From a Statewide Environmental Justice Screening Tool (CalEnviroScreen 1.1)" *Am J Public Health* 105(11): 2341-2348. doi:10.2105/AJPH.2015.302643

asthma, have been shown to increase susceptibility to the adverse health effects of air pollution.[52,93,94] Several studies suggest that the health effects of air pollution are also modified by an individual's educational attainment, generally used as a marker for socioeconomic status, such that greater effects are observed among the less educated.[55,95] While these particular findings are limited to observational studies and possibly subject to bias due to unmeasured confounding, the idea that low socioeconomic status confers greater vulnerability makes intuitive sense. Poverty can hinder access to adequate nutrition or medical care to prevent and manage the health impacts of pollution, while at the community level, the concentration of poverty and unemployment in disadvantaged neighborhoods can lead to conditions that increase levels of chronic psychosocial stress, weakening the body's ability to defend against external challenges.[7] A cumulative impact approach that considers differential vulnerability as well as environmental hazards is particularly important for assessing racial and ethnic environmental health disparities because communities of color in the U.S. are generally more disadvantaged, with lower average education[96] and wealth[97] and, for some groups, higher rates of chronic health conditions[80] that increase their susceptibility to environmental health hazards.

Although the field is still in its infancy, several proposed methods seek to better reflect the cumulative impacts of environmental exposures and population vulnerabilities and provide assessments that can support the incorporation of equity and environmental justice goals into policy-making.[98–101] The California Environmental Protection Agency (CalEPA) first released one such method, named the California Communities Environmental Health Screening Tool or CalEnviroScreen, in April 2013, and an updated version, CalEnviroScreen 1.1, was published in September 2013.[102] CalEnviroScreen is a screening tool that considers both pollution burden and population vulnerability in assessing the potential for cumulative impacts across California ZIP codes. It was developed by the Office of Environmental Health Hazard Assessment (OEHHA) of CalEPA following consultation with government, academic, business, and nongovernmental organizations, and 12 public workshops in seven regions of the state that resulted in more than 1,000 oral and written comments on two preliminary drafts.[103] The tool employs a model that can be adapted to different applications and as new information becomes available. For example, subsequent iterations have been developed using a finer geographic resolution and the addition of new indicators.[104] It purposefully relies on publicly available datasets for transparency and relatively simple methods so that it can be understood by a general audience.

I analyzed data from CalEnviroScreen 1.1 to assess the extent of geographic and racial/ethnic disparities in the potential for cumulative environmental health impacts from multiple pollution sources in California. I employed a concentration index to examine which environmental hazards are most inequitably distributed and consider variations to CalEnviroScreen to evaluate the sensitivity of my findings to the structure of the model.

Methods

The CalEnviroScreen model

CalEnviroScreen 1.1 consists of 11 indicators related to the pollution burden and 6 indicators related to the population vulnerability of a community, which are aggregated into relative community-level Pollution Burden, Population Vulnerability, and Cumulative Impact (CI) Scores (**Figure 2-1**). Communities are defined geographically on the basis of the 2010 ZIP Code

Tabulation Area (ZCTA) of residence. ZIP codes were chosen by the creators of CalEnviroScreen as the unit of analysis because they are familiar to a general audience. ZCTAs are generalized areal representations of United States Postal Service ZIP code service areas created by the U.S. Census Bureau, and are delineated based on the most common ZIP code within each census block. ZCTAs were chosen to mitigate the issue of changing ZIP code boundaries. I hereafter refer to ZCTAs as ZIP codes for simplicity.

The goal of CalEnviroScreen is to provide a simple screening-level method to identify geographic areas that exhibit both higher relative pollution burden and higher relative vulnerability to pollution compared to other parts of the state in order to prioritize places that warrant further research and attention. A full description of data sources and the rationale for each indicator is available elsewhere.[102] Briefly, CalEnviroScreen includes 17 indicators chosen because of 1) their environmental and public health relevance; 2) the availability of state-wide data with adequate geographic resolution and variation to discern differences between ZIP codes; and 3) the accuracy, completeness, and currency of the data source and the likelihood that it will be maintained in the future. The creators of CalEnviroScreen sought to minimize the number of indicators and the potential overlap between them for parsimony and to minimize the potential for double counting.

Pollution burden was characterized by 11 indicators of pollutant sources, releases, environmental concentrations, threats to the environment, and degraded ecosystems (**Table 2-1**). These indicators were standardized by taking the percentile and averaged together to derive an overall relative Pollution Burden Score for each ZIP code. Measures of threats to the environment and degraded ecosystems were given half the weight of the other measures because the route of human exposure to these hazards was considered less immediate. This method implicitly assumes each hazard presents an equal threat to health (with the exception of the indicators that are given half weight). The creators of CalEnviroScreen chose to adopt this simplistic weighting scheme rather than employ a scheme that implied greater certainty than is warranted because of the lack of scientific evidence by which to quantify the relative importance of each hazard.

Six indicators of population vulnerability were similarly standardized and averaged to derive a Population Vulnerability Score for each ZIP code. The indicators included both biological traits and factors related to socioeconomic status that can increase susceptibility to the adverse health impacts of pollutants (**Table 2-1**).[3] Age was chosen as an indicator of biological susceptibility because the young and elderly are both known to be more sensitive to air pollution and other types of exposure. Rates of low birth weight and hospitalization for asthma were considered markers of potential vulnerability rather than indicators of the health effects of pollution. Asthmatics are more susceptible to air pollution, and low birth weight was considered a general indication of overall health. Poverty, education, and linguistic isolation were chosen as socioeconomic markers that may impact access to information, health care, nutrition, quality housing, and other resources that can help reduce the health impacts of pollution.

The Pollution Burden and Population Vulnerability Scores were then multiplied together in CalEnviroScreen to arrive at a final relative CI Score that ranged from 0-100 (**Figure 2-1**). The raw indicator values, percentiles, and Cumulative Impact Scores generated by CalEnviroScreen are publicly available in both spreadsheet and geospatial file formats.[105] A multiplicative model in which the pollution burden and population vulnerability components were multiplied together

was chosen in keeping with other risk assessment practices and epidemiological evidence of effect modification of the health impacts of air pollution by socioeconomic and disease status on a multiplicative scale (e.g., [106,107]). I compared the sensitivity of my findings to a variation of CalEnviroscreen that used an additive model in which the Pollution Burden and Population Vulnerability Scores were summed rather than multiplied to derive the CI Score.

Analytic strategy

I conducted all statistical analysis using R version 3.0.1.[108] The distribution of Pollution Burden, Population Vulnerability and CI Scores was compared across geographic regions of California and the urban/rural characteristics of communities. I defined geographic regions of the state in county groupings roughly corresponding to the extent of regional governmental bodies. Spearman's correlation coefficients were used to compare the joint distributions of individual indicators as well as their relationship to two measures of a ZIP code's urban or rural character derived from the 2010 U.S. Census: population density and the percent of the ZIP code's population that lives in an unincorporated community (Census-Designated Places, which I considered an indicator of rural communities).

I visually compared the distribution of Pollution Burden, Population Vulnerability and CI Scores across categories of self-identified race/ethnicity from the American Community Survey (ACS) using box plots. I calculated the unadjusted odds of living in one of the 10% of ZIP codes with the highest CI score for each racial/ethnic group and used logistic regression to calculate the odds adjusted for population density.

In order to assess which aspects of pollution burden were most regressively distributed and whether race/ethnicity or income was more important in shaping the distribution, I plotted concentration curves and calculated a concentration index for each indicator with respect to ZIP code-level racial/ethnic makeup and the percent of the population living in poverty, similar to the method of Su et al. (2009).[109] This approach does not seek to characterize differences in exposure or risk, but rather macro-level relationships about how environmental hazards are distributed across social groups. The concentration curve is constructed by ordering all ZIP codes across the x-axis from lowest to highest in terms of the percent of the population that is 1) non-Hispanic White or 2) living above twice the federal poverty line. Multi-racial individuals and Hispanic individuals of any race were classified as non-White. The cumulative proportion of the pollution indicator is graphed on the y-axis. If an indicator is perfectly evenly distributed, the line will equal a diagonal that crosses the origin. Curves above the equality line indicate a regressive distribution (communities of color or poor communities shoulder a disproportionate amount of the environmental hazard) whereas curves below the line indicate an unequal distribution in which more advantaged (more White or wealthy) populations are more burdened.

I calculated a standard concentration index proportional to the area between the concentration curve and the diagonal line of equality as follows:

$$C = \frac{2}{n \times \mu} \sum_{i=1}^{n} x_i R_i - 1$$

where n is the sample size, x_i is the indicator of pollution burden for each ZIP code i, μ is the mean of the pollution burden indicator and R_i is the fractional rank in % white or % not poor of the ith ZIP code from least (i=1) to most disadvantaged (i=n).[110] The index ranges from -1 to 1 with zero indicating equality; negative (positive) values indicate the environmental hazard is disproportionately located in less (more) advantaged communities. The magnitude of C reflects both the strength of the relationship between ZIP code-level socioeconomic status and pollution burden and the degree of variability in the pollution variable. It does not indicate greater risk for disadvantaged groups, since it is influenced by the degree of variation rather than the absolute level of any hazard. The standard error of C also given by Kakwani et al. (1997) is used to test the null hypothesis that C = 0.[110]

Finally, I considered the sensitivity of the relative rankings produced by CalEnviroScreen to 1) the removal of any one indicator from the model, and 2) an additive model in which the Pollution Burden and Population Vulnerability Scores were summed rather than multiplied. I focused on changes within the decile of ZIP codes with the highest CI Score because I was primarily concerned with consistently identifying the most impacted communities. I used the Inverse-Rank Measure (IRM) to compare the rankings generated by the alternate models. The IRM provides a quantitative measure of the degree of similarity between ordered sets that do not necessarily share all elements.[111] It has been used to compare the results of internet search engines, and this is, to my knowledge, a novel application of this measure. The IRM considers both the elements that comprise the set and how they are ordered, and ranges from zero (no ZIP codes in set A are contained in set B), to 1 (the same ZIP codes are in both sets and they are ordered identically). Changes in rank that occur near the top of the set (e.g. the 2% highest scoring communities) are given more weight than changes in rank near the bottom of the set (e.g. the highest 8-10% of communities) in order to, again, pay particular attention to my ability to consistently identify the most impacted communities. I also compared the robustness of my findings regarding the distribution of CI Score by race/ethnicity to the model structure (multiplicative vs. additive).

Results

Ten of California's 1,769 ZIP codes did not have a resident population in the 2010 Census and were excluded from the analysis, leaving a sample size of 1,759. ZIP codes varied greatly in area (0.01 to 1,395 mi^2) and population (1 to 105,549). Data sources and descriptive statistics for the 17 indicators comprising the CalEnviroScreen model are given in **Table 2-1**. Several indicators had a highly right-skewed distribution and/or many zeroes. The percent of the population living below twice the federal poverty level exhibits a bimodal distribution (peaks near 20% and 40%, data not shown), possibly indicating residential income segregation at the ZIP code level.

I found an uneven geographic distribution of the highest Cumulative Impact Scores across the state. The San Joaquin Valley and Southern California (particularly the Greater Los Angeles area) had the greatest proportion of communities with a CI Score in the highest10% state-wide (**Figure 2-2**). Northern California, the Sacramento and San Francisco Bay areas, and San Diego are home to a smaller proportion of these communities, while no such communities were found in the Eastern Sierra and Central Coast regions.

Spearman's correlation coefficients between each pair of indicators is given in

Table 2-2. With the exception of ambient ozone concentrations, indicators of pollution burden were generally positively correlated with each other. With the exception of impaired water bodies, indicators of pollution burden were also positively correlated with indicators of vulnerable populations (proportion of children and elderly being the exception). Indicators of population vulnerability were also largely positively correlated with each other, again with the exception of age.

Spearman's correlation coefficients between each indicator and two measures of whether a ZIP code is urban or rural are given in **Table 2-3**. Nearly all indicators were positively correlated with population density and negatively correlated with the proportion of ZIP code residents living in an unincorporated community, with the exception of ambient ozone concentrations, pesticide use in agriculture, solid waste sites, the percentage of the population younger than 5 or older than 65, age-adjusted rate of emergency room visits for asthma, and the percentage of the population living in poverty, for which the correlations went in the reverse direction. The overall CI Score was also positively correlated with population density (Spearman's correlation coefficient = 0.48, p-value < 0.0001) and negatively correlated with the percent of residents living in unincorporated communities (Spearman's correlation coefficient = -0.21, p-value < 0.0001), suggesting that urban areas tend to be more highly impacted.

The median Pollution Burden Score was 15% higher for Hispanics and 10% higher for Blacks than it was for non-Hispanic Whites, for whom the average score was lowest (**Figure 2-3**). Hispanics and Blacks also had higher average Population Vulnerability and overall CI Scores than other groups. Asian/Pacific Islanders had the third highest median Pollution Burden Score, but lower median Population Vulnerability and CI Scores than Hispanics, Blacks, and Native Americans (data not shown). Native Americans had a lower median Pollution Burden Score than other groups, but the third highest median Population Vulnerability and CI Score (data not shown). Using an additive rather than a multiplicative model attenuated the percent differences in median CI Score relative to Whites by about half but did not change the ordering of racial/ethnic groups with respect to average CI Score (data not shown).

The unadjusted odds of living in one of the 10% of ZIP codes with the highest CI score was higher for all non-White groups compared to Whites (unadjusted ORs: 6.2 for Hispanics, 5.7 for Blacks, 1.9 for Native Americans, 1.8 for Asian/Pacific Islanders, and 1.6 for other/multi-racial). ORs decreased slightly when I adjusted for population density (ORs [95% CI]: 5.8 [5.5, 6.1] for Hispanics, 5.2 [4.7, 5.7] for Blacks, 1.8 [1.2, 2.6] for Native Americans, 1.7 [1.6, 1.9] for Asian/Pacific Islanders, and 1.6 [1.4, 1.9] for other/multi-racial).

Concentration curves illustrating the distribution of pollution indicators with regard to community racial/ethnic makeup and poverty are presented in **Figure 2-4**. Concentration indices and their 95% confidence intervals suggest all indicators except particulate matter (PM) 2.5 exhibit a statistically-significant regressive distribution with respect to race/ethnicity (**Table 2-4**). Pesticide use and toxic chemical releases were the most regressively distributed with respect to race/ethnicity, closely followed by clean-up sites, hazardous waste and diesel PM. Pesticide use, ozone, clean-up sites, solid waste, and diesel PM were also regressively distributed with respect to poverty. All pollution indicators with the exception of ozone were more regressively distributed with respect to race/ethnicity than they were with respect to poverty. Several indicators of population vulnerability were also regressively distributed: poverty with

respect to race/ethnicity, and asthma, low educational attainment, and linguistic isolation with respect to both race/ethnicity and poverty.

The results of the sensitivity analysis suggest that the rankings generated by CalEnviroScreen are most sensitive to the pesticide use, ozone, toxic releases, and low birth weight indicators (**Table 2-5**). Among the 176 ZIP codes originally identified as the most impacted (highest scoring) 10%, 7 to 27 fell below this benchmark when one indicator was removed from the model. Using an additive rather than a multiplicative model resulted in 11 changes with respect to the ZIP codes identified as the most impacted. All of the communities that were no longer identified as among the highest scoring 10% using the additive model were still among the highest scoring 15%.

Discussion

I have presented evidence of racial/ethnic disparities in residential proximity to multiple environmental hazards using data from an environmental justice screening tool that can be used to rank communities in California with regard to their potential for cumulative environmental health impacts. The tool does not quantify the probability of harm or health risk. Instead, it identifies communities that warrant special attention and can help policy- and decision-makers prioritize their activities to the benefit of communities that both are surrounded by many environmental hazards and exhibit high vulnerability to the impacts of pollution. It can and should be tailored to specific uses by modifying the geographic units of analysis, adding, removing, or improving specific indicators, and/or updating the indicators with subsequent years of data in order to track progress towards environmental justice goals.

I found that the potential for cumulative environmental health impacts varies across regions of California, with the Greater Los Angeles area and San Joaquin Valley being most heavily impacted. Significant inequality in the distribution of pollution and population vulnerability indicators were also observed *within* regions. While useful for state-level agencies and decision-making, the state-wide relative ranking produced by CalEnviroScreen may not be as informative about inequalities within regions, in part because some environmental indicators included in the tool are less relevant in some regions than others. Performing regional rankings may be an additional way to inform regional authorities about vulnerable areas within their jurisdiction.

The positive correlation I found in pair-wise comparisons between indicators of pollution burden and population vulnerability suggests that environmental health hazards are clustered at the ZIP-code level and that they co-occur in neighborhoods with greater vulnerability. Indicators of ambient ozone, impaired water bodies, and the proportion of young and elderly residents exhibited distinctive patterns in that they were more often negatively correlated with the other measures of pollution (in the case of ozone), population vulnerability (in the case of impaired water bodies), or both (in the case of age). This may be because ozone and water are more dispersed than the other types of environmental hazards included in CalEnviroScreen. The age indicator included elderly residents as well as children, and may have exhibited negative correlations with other indicators because the presence of older adults reflects health-promoting neighborhood conditions that result in longer life expectancy, which can vary by more than a decade across California ZIP codes.[112]

The correlation I found between the CalEnviroScreen Cumulative Impact Score and population density is consistent with the presence of many pollution sources such as vehicles in urban areas. It may also indicate that CalEnviroScreen 1.1 does not adequately capture unique exposure pathways and vulnerabilities associated with rural living. For example, Native Americans in California exhibited lower Pollution Burden Scores than other groups but may practice subsistence fishing and hunting that puts them in greater contact with contaminants in waterways and at unique risk of exposure to toxins that bioaccumulate in wildlife. The choice of indicators was limited by the availability of comprehensive, state-wide monitoring as well as by data gaps that are particularly a problem in rural areas. Disparities in water quality by ethnicity have been observed in small drinking water systems, particularly in rural California[16], and a drinking water quality indicator has been incorporated into a more recent iteration of CalEnviroScreen.[104]

I found a strong disparity in CI Score with regard to community racial/ethnic makeup that is jointly a product of the distribution of environmental hazards and population vulnerability. The fact that people of color are more likely to live in more densely populated communities did not explain the disparity: controlling for population density only slightly decreased the ORs of living in one of the most impacted 10% of communities compared to Whites. The results were also qualitatively robust to the choice of model structure. Using an additive rather than a multiplicative model changed the unadjusted ORs by less than 5% for all groups.

The concentration indices further revealed that disparities in pollution burden – with the exception of ozone – are greater with respect to race/ethnicity than they are to poverty rates. This is consistent with a meta-analysis of 49 environmental equity studies from the United States which concluded that the evidence of class-based environmental inequalities was less consistent than was the evidence of race-based inequalities.[4] Nevertheless, in my study I still found statistically-significant evidence that pesticide use, concentrations of ozone and diesel particulate matter, and clean-up and solid-waste sites in California are disproportionately located in communities with higher levels of poverty. With the exception of age and low birth weight, measures related to population vulnerability were also regressively distributed with respect to both race and poverty, although in the case of community racial/ethnic makeup, less so than were the measures of pollution burden. This is consistent with the environmental justice concept of "double jeopardy"[113(chap1)]: communities of color are disproportionately burdened both by environmental hazards and social stressors that may make them more vulnerable to the health effects of pollution.

The concentration indices also suggest that some pollution sources are more unequally distributed with regard to race/ethnicity than others, namely pesticide use, toxic releases from industry, clean-up sites, hazardous waste, and diesel particulate matter. I caution that these indices are metrics of relative difference and do not give an indication of the health risk posed by any one hazard in absolute terms. While useful as a starting point, more research on the degree of risk posed by each of the hazards is needed in order to prioritize action to reduce environmental health disparities. The percentage of each environmental indicator that would need to be linearly redistributed from the less advantaged to the more advantaged half of the ZIP codes to arrive at an equal distribution (index of zero) can be calculated by multiplying the concentration index by 75.[114] Using this property to provide another perspective on the degree of inequality, approximately a third of the most regressively distributed pollution variables would

need to be transferred from the communities with higher than average proportions of people of color to those with less in order to achieve a perfectly even distribution.

The sensitivity analysis suggested that the CalEnviroScreen model is relatively robust to changes associated with the removal of any one indicator. Nonetheless, changes to which ZIP codes were identified as the 10% most impacted communities were substantial enough to suggest that each indicator makes a unique contribution to this measure of cumulative impact. The IRM used here may be one useful way to compare the results of CalEnviroScreen with those of other environmental justice screening tools.

As with any geographic analysis utilizing discrete areas, the results are sensitive to the choice of geographic boundaries (the "modifiable areal unit problem"[115]). Other researchers have found that the strength and even direction of the association between race, income, and the location of environmental hazards can change with the geographic scale of the analysis.[116] ZIP codes vary widely in terms of area and population size, and visual examination shows that some ZIP codes encompass distinct communities that differ greatly in terms of socioeconomic status. However, preliminary analysis of a newer version of CalEnviroScreen using census tract geography[104] suggests that the strength of the associations between race, ethnicity and cumulative impact persists with the move to a smaller geography.

Together, these results provide evidence of significant inequalities between racial and ethnic groups in residential proximity to multiple environmental health hazards in California. I found that the relative prevalence of factors that may contribute to a population's vulnerability to pollution is also greater in communities of color, which could exacerbate environmental health inequities. CalEnviroScreen is one screening tool that can be used to help guide regulatory, enforcement, and other efforts to reduce cumulative environmental health burdens in disproportionately impacted communities. Specific indicators included in CalEnviroScreen may have various levels of relevance depending on the policy and jurisdictional context in which the screening method is applied, and the underlying data were made publicly available in order to allow users to tailor the tool for different applications. Future research is needed to improve methods for addressing the sensitivity of environmental justice screening tools to the geographic unit of analysis; inform the approach to scoring, including the way variables are standardized, weighted, and combined; improve the relevance to health by utilizing absolute rather than relative measures of exposure through the incorporation of threshold values or other means; and, most importantly, identify specific ways in which cumulative impact assessment can be most effectively used to reduce environmental health disparities.

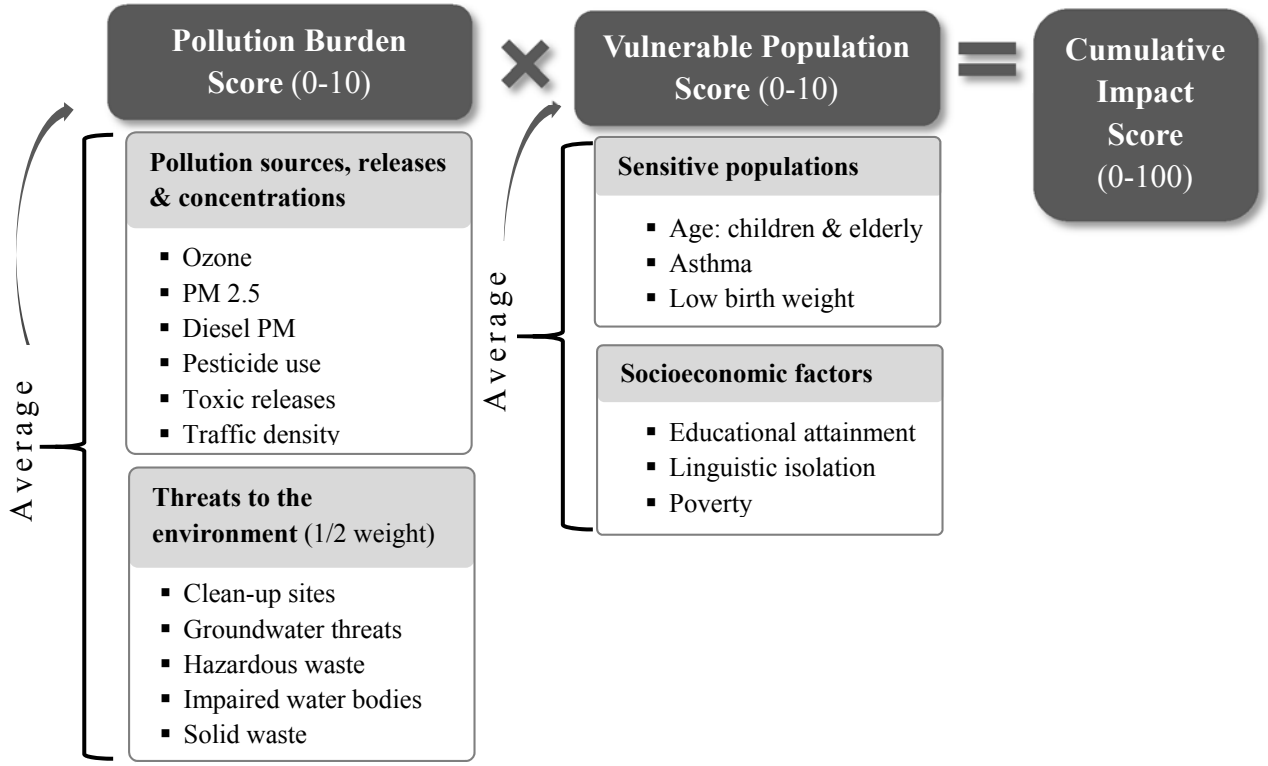


Figure 2-1 Schematic of the CalEnviroScreen 1.1 model. The model combines 11 standardized indicators of pollution burden and 6 standardized indicators of population vulnerability into a relative Cumulative Impact (CI) Score that can be used to identify communities with higher potential for cumulative environmental health impacts.

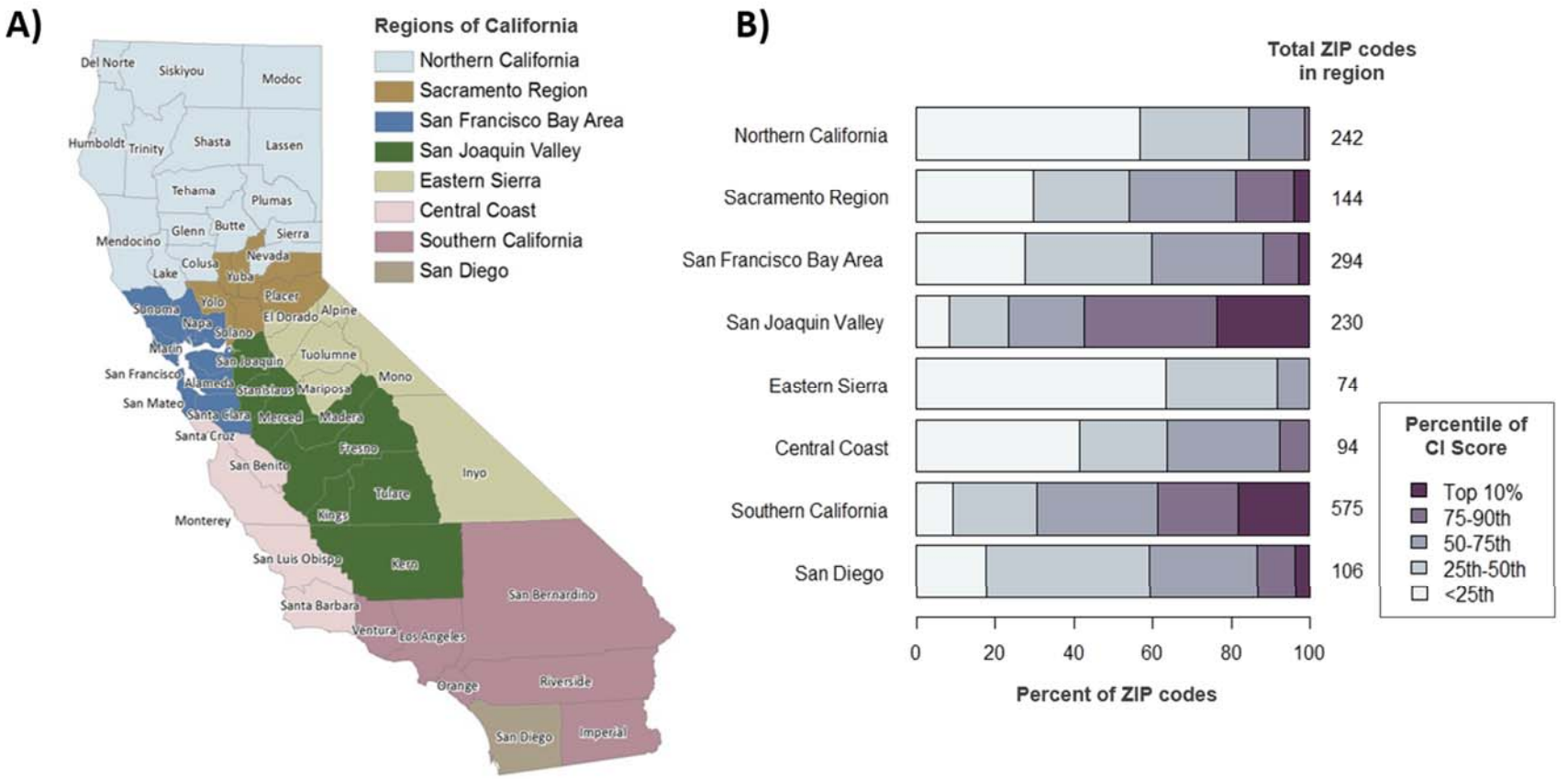


Figure 2-2 Distribution of Cumulative Impact (CI) Score across California regions. The map on the left (A) shows the 58 California counties grouped into eight regions. The bar chart on the right (B) shows the percent of ZIP codes (total n=1,759) in each category of CI Score by region and suggests greater potential for cumulative environmental health impacts in the San Joaquin Valley and Southern California regions.

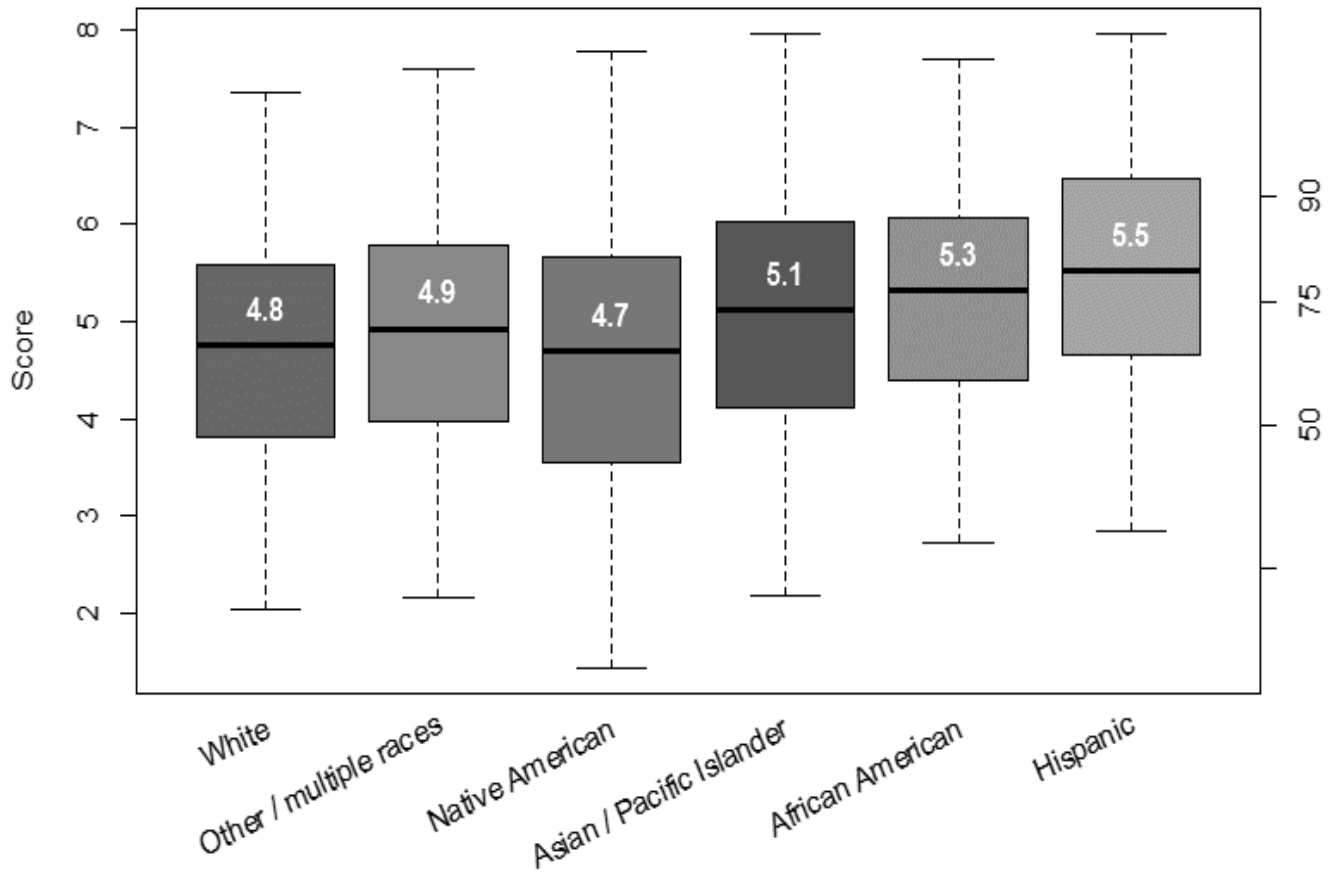


Figure 2-3 The average Pollution Burden Score for different groups indicate that Hispanic, Black and Asian/PI Californians are more likely to live in close proximity to multiple environmental hazards than are other groups (total sample population = 37,269,815). The bar indicates the median Pollution Burden Score for each group. The box delineates the interquartile range (IQR; 25th–75th percentile). The whiskers extend to the most extreme values within 1.5 · IQR of the median. Data are from ZIP codes throughout California.

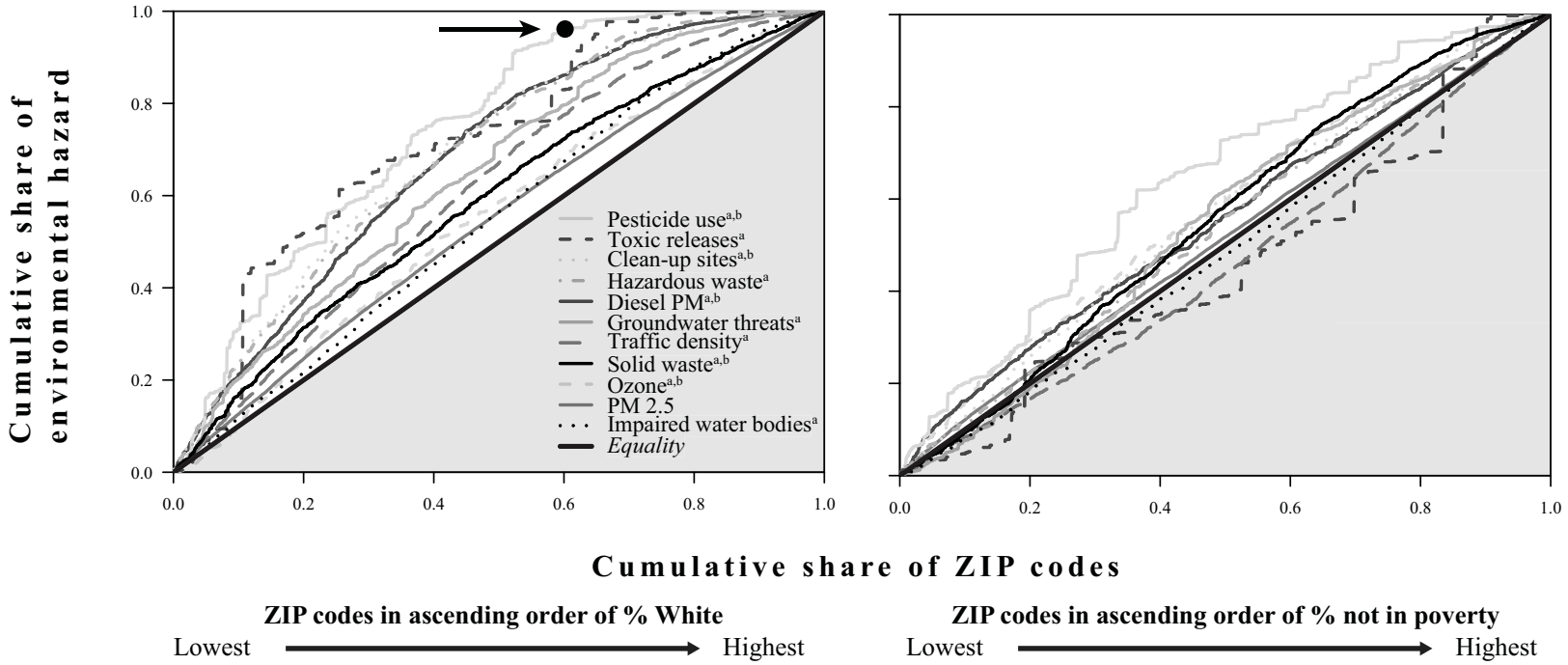


Figure 2-4 Concentration curves showing the degree of inequality in the distribution of indicators of pollution burden across California ZIP codes with respect to their racial/ethnic makeup (% non-Hispanic White) and wealth (% above twice the federal poverty line). Curves in the white area above the equality line indicate that communities of color or poor communities host a disproportionate amount of the environmental hazards. Curves in the gray area below the equality line indicate that more privileged (more White or wealthy) communities are disproportionately burdened. The point indicated by the arrow illustrates that the 60% of ZIP codes with the highest proportion of residents of color host > 95% of agricultural pesticide use in the state. No hazard disproportionately burdens ZIP codes with a higher proportion of White or wealthy residents at $P < .05$.

[a] Zip codes with a higher proportion of residents of color are disproportionately burdened ($P < .05$).

[b] Zip codes with a higher proportion of residents living in poverty are disproportionately burdened ($P < .05$).

Table 2-1 The 17 indicators of cumulative environmental health impact included in CalEnviroScreen 1.1

	Indicator	Description	Source	Range	Mean (SD)	Median
Pollution Burden	Ozone (ppm)	Portion of the daily maximum 8-hour ambient concentration over the federal standard (2007-9)	California Air Resources Board (CARB)	0 - 1.3	0.098 (0.18)	0.02
	PM 2.5 ($\mu g/m^3$)	Annual mean ambient concentration (2007-9)	CARB	3.6 - 21.2	10.5 (3.1)	10.2
	Diesel PM (kg/day)	Emissions from on-road and non-road sources for a 2010 summer day in July	CARB	0.0005 - 125.3	10.3 (14.3)	4.6
	Pesticide use ($lbs./mi^2$)	Selective active ingredients used in production agriculture (2009-10)	California Department of Pesticide Regulation	0 - 32,671	344 (1,975)	0.05
	Toxic releases (toxicity-weighted lbs. /yr.)	Releases to air or water (2008-10)	Toxics Release Inventory, US Environmental Protection Agency	0 - 5.1 x 108	1.73×10^6 (1.74×10^7)	0
	Traffic density (vehicle-km per hr./km)	Traffic volume by road length within 150 meters of ZIP code boundary (2004)	California Environmental Health Tracking Program (CEHTP), California Department of Public Health (CDPH)	0 - 8,417	916 (892)	665.2
	Clean-up sites (weighted sum)	Clean up sites weighted by site type and status (2013)	Department of Toxic Substances Control (DTSC) *EnviroStor* database	0 - 511	24.5 (46.6)	8.0
	Groundwater threats (weighted sum)	Potential contamination sources and monitoring wells, weighted by site type and status (2013)	State Water Resources Control Board (SWRCB) *GeoTracker* database	0 - 4,530	87.7 (231)	32.0
	Hazardous waste (weighted sum)	Permitted hazardous waste facilities and generators, weighted by waste type and volume (2013)	DTSC *EnviroStor* database	0 - 58.8	2.2 (4.0)	0.8

	Impaired water bodies (sum of pollutants)	Number of pollutants across water bodies designated as impaired (2010)	SWRCB 303(d) List of Impaired Water Bodies	0 - 32	4.0 (4.9)	2.0
	Solid waste (weighted sum)	Solid waste facilities, operations and disposal sites, weighted by site type and status (2013)	Solid Waste Information System (SWIS) and Closed Illegal, and Abandoned (CIA) Disposal Sites Program, Department of Resources, Recycling and Recovery	0 - 57	4.7 (6.4)	2.0
Vulnerable Populations	Age: children and elderly (%)	Percent of the population under age 10 or over age 65 (2010)	US Census Bureau	0 - 100	25.9 (6.5)	25.6
	Asthma (visits per 10,000/ yr.)	Spatially modeled, age-adjusted rate of emergency department visits (2007-9)	CEHTP; Office of Statewide Health Planning and Development	6.9 - 312.2	42.5 (27.0)	36.1
	Low birth weight (%)	Percent of births weighing <2,500 grams (2007-11)	CDPH Vital Statistics	1 - 14.8	6.7 (1.4)	6.6
	Educational attainment (%)	Percent of the population over age 25 with less than a high school education (2007-11)	American Community Survey (ACS) 5-year estimates, US Census Bureau	0 - 82.7	17.3 (14.8)	13.0
	Linguistic isolation (%)	Percent of households in which no one age 14 and over speaks English "very well" (2007-11)	ACS 5-year estimates	0 - 100	10.4 (10.3)	7.4
	Poverty (%)	Percent of the population living below twice the federal poverty level (2007-11)	ACS 5-year estimates	0 - 96.6	33.8 (17.8)	31.6

Table 2-2 Spearman's rank correlation coefficients between indicators of pollution burden and vulnerable populations included in CalEnviroScreen 1.1

	Ozone														
PM 2.5	0.44	PM 2.5													
Diesel PM	-0.01	0.62	Diesel PM												
Pesticide use	0.07	0.05	-0.05	Pesticide use											
Toxic releases	0.05	0.35	0.46	0.16	Toxic releases										
Traffic density	-0.08	0.42	0.81	-0.08	0.43	Traffic density									
Clean-up sites	-0.03	0.33	0.52	0.1	0.6	0.47	Clean-up sites								
Groundwater threats	-0.15	0.21	0.43	0.15	0.54	0.42	0.66	Groundwater threats							
Hazardous waste	-0.01	0.41	0.71	0.07	0.66	0.69	0.71	0.68	Hazardous waste						
Impaired water bodies	-0.31	-0.07	0.07	0.26	0.16	0.13	0.21	0.34	0.22	Impaired water bodies					
Solid waste	0.06	0.09	0.01	0.18	0.35	0.04	0.37	0.44	0.32	0.18	Solid waste				
Age: children & elderly	0.08	-0.22	-0.34	0.11	-0.22	-0.34	-0.21	-0.15	-0.29	-0.05	0.01	Age: children & elderly			
Asthma	0.14	0.07	0.06	-0.02	0.16	-0.08	0.18	0.19	0.13	-0.02	0.18	0.06	Asthma		
Low birth weight	0.08	0.27	0.26	-0.2	0.06	0.22	0.07	-0.03	0.14	-0.09	-0.06	-0.14	0.07	Low birth weight	
Educational attainment	0.21	0.31	0.21	0.28	0.25	0.05	0.25	0.24	0.22	0.02	0.26	0.00	0.49	-0.02	Educational attainment
Linguistic isolation	0.06	0.41	0.47	0.09	0.24	0.25	0.29	0.24	0.31	-0.02	0.07	-0.23	0.26	0.09	0.73	Linguistic isolation
Poverty	0.18	0.15	0.01	0.1	0.08	-0.18	0.11	0.12	0.00	-0.08	0.18	0.05	0.57	-0.03	0.74	0.59

Table 2-3 Spearman's rank correlation coefficients between indicators of pollution burden and vulnerable populations included in CalEnviroScreen 1.1 and two measures of the urban or rural character of a ZIP code.

	Population density	**% of residents living in an unincorporated community**
Ozone (ppm)	-0.09**	0.07*
PM 2.5 ($\mu g/m^3$)[a]	0.52**	-0.26**
Diesel PM (kg/day)[a]	0.86**	-0.45**
Pesticide use ($lbs./mi^2$)	-0.15**	0.11**
Toxic releases (toxicity-weighted lbs. /yr.)	0.39**	-0.24**
Traffic density (vehicle-km per hr./km)	0.76**	-0.38**
Clean-up sites (weighted sum)	0.46**	-0.28**
Groundwater threats (weighted sum)	0.38**	-0.23**
Hazardous waste (weighted sum)	0.69**	-0.39**
Impaired water bodies (sum of pollutants)	0.03	-0.09**
Solid waste (weighted sum)	-0.04	0.01
Age: children and elderly (%)	-0.36**	0.23**
Asthma (age-adjusted rate of ED visits)	0.00	0.07*
Low birth weight (%)	0.26**	-0.16**
Educational attainment (%)	0.1**	-0.02**
Linguistic isolation (%)	0.39**	-0.21**
Poverty (%)	-0.07*	0.07*

* $P < 0.001$ versus the null hypothesis of no correlation.

** $P < 0.0001$ versus the null hypothesis of no correlation.

Table 2-4 Concentration indices (C) quantify inequality in the distribution of environmental hazards and measures of population vulnerability across California ZIP codes with respect to their racial/ethnic makeup (% non-Hispanic White) and wealth (% above twice the federal poverty line). C ranges from -1 to 1 with zero indicating perfect equality. Negative values indicate a regressive distribution in which communities of color or poor communities host a disproportionate amount of the environmental hazard or vulnerability measure. Positive values indicate that non-Hispanic White or wealthy communities are disproportionately burdened. Values in brackets are 95% confidence intervals. Statistically significant results are in bold.

	Race/ ethnicity C [95% CI]			**Poverty C [95% CI]**		
Pollution Burden						
Ozone (ppm)	**-0.104**	**[-0.207,**	**-0.001]**	**-0.145**	**[-0.252,**	**-0.038]**
PM 2.5 ($\mu g/m^3$)[a]	-0.089	[-0.180,	0.002]	-0.026	[-0.120,	0.067]
Diesel PM (kg/day)[a]	**-0.369**	**[-0.464,**	**-0.275]**	**-0.106**	**[-0.207,**	**-0.006]**
Pesticide use ($lbs./mi^2$)	**-0.488**	**[-0.619,**	**-0.357]**	**-0.278**	**[-0.436,**	**-0.121]**
Toxic releases (toxicity-weighted lbs. /yr.)	**-0.439**	**[-0.654,**	**-0.223]**	0.080	[-0.225,	0.386]
Traffic density (vehicle-km per hr./km)	**-0.225**	**[-0.317,**	**-0.134]**	0.074	[-0.018,	0.165]
Clean-up sites (weighted sum)	**-0.390**	**[-0.489,**	**-0.291]**	**-0.122**	**[-0.228,**	**-0.016]**
Groundwater threats (weighted sum)	**-0.291**	**[-0.394,**	**-0.187]**	-0.091	[-0.204,	0.021]
Hazardous waste (weighted sum)	**-0.387**	**[-0.486,**	**-0.288]**	-0.076	[-0.182,	0.030]
Impaired water bodies (sum of pollutants)	**-0.097**	**[-0.188,**	**-0.005]**	0.029	[-0.066,	0.123]
Solid waste (weighted sum)	**-0.177**	**[-0.272,**	**-0.081]**	**-0.107**	**[-0.203,**	**-0.011]**
Vulnerable Populations						
Age: children and elderly	0.038	[-0.047,	0.123]	0.002	[-0.087,	0.090]
Asthma	**-0.100**	**[-0.193,**	**-0.006]**	**-0.168**	**[-0.264,**	**-0.072]**
Low birth weight	-0.019	[-0.120,	0.081]	0.002	[-0.098,	0.102]
Educational attainment	**-0.325**	**[-0.420,**	**-0.230]**	**-0.333**	**[-0.430,**	**-0.237]**
Linguistic isolation	**-0.396**	**[-0.507,**	**-0.285]**	**-0.334**	**[-0.445,**	**-0.223]**
Poverty	**-0.132**	**[-0.226,**	**-0.039]**		**--**	

[a] PM refers to particulate matter and PM 2.5 to particulate matter with diameter less than 2.5 micrometers.

Table 2-5 The degree of change that results from the deletion of a single indicator from the CalEnviroScreen 1.1 model in the ZIP codes identified as the 10% most impacted. Indicators near the top of the list are more influential in determining the relative ranking of most impacted ZIP codes.

	Changes in the 10% most impacted ZIP codes (n=176)		
Indicator removed	Number	%	IRM[a]
Pesticide use	27	15.3	0.62
Ozone	24	13.6	0.75
Toxic releases	23	13.1	0.75
Low birth weight	25	14.2	0.80
Age: children and elderly	20	11.4	0.84
PM 2.5	19	10.8	0.87
Traffic density	17	9.7	0.88
Impaired water bodies	12	6.8	0.88
Linguistic isolation	17	9.7	0.89
Diesel PM	15	8.5	0.89
Asthma	21	11.9	0.91
Solid waste	14	8.0	0.91
Poverty	12	6.8	0.92
Educational attainment	11	6.2	0.93
Hazardous waste	11	6.2	0.95
Clean-up sites	14	8.0	0.96
Groundwater threats	7	4.0	0.97

[a] The Inverse Rank Measure (IRM) is a measure of the degree of similarity between ordered sets that do not necessarily share all elements that ranges from 0 (no similarity) to 1 (perfect similarity). It considers both the elements that comprise the set and how they are ordered, with changes in rank that occur among the ZIP codes with the highest CI Scores given more weight than changes in rank closer to the bottom of the set.

Chapter 3

The demographics of chemical body burden: Education, race/ethnicity, and nativity as predictors of exposure to environmental chemicals among pregnant women fom San Francisco

Abstract

Social inequalities in prenatal chemical exposures could contribute to disparities in maternal and child health. To examine this issue, I conducted an exploratory analysis of biomonitoring data from the Chemicals in Our Bodies (CIOB) study, also known as the Maternal and Infant Environmental Exposure Project (MIEEP). CIOB measured concentrations of over 80 environmental chemicals in urine and blood samples collected at delivery from pregnant women recruited from a safety net hospital in San Francisco, CA in 2010-2011. I investigated potential exposure differences based on serum concentrations of polybrominated diethyl ethers (PBDEs), polychlorinated biphenyls (PCBs), organochlorine pesticides (OCPs), and perfluorinated compounds (PFCs); blood concentrations of metals (cadmium, lead, and mercury); and urinary concentrations of arsenic (As) and metabolites of phthalates, polycyclic aromatic hydrocarbons (PAHs), organophosphate and pyrethroid pesticides, and environmental phenols. Utilizing regression with multiple imputation to address values below the detection limit, I estimated differences in chemical concentrations based on the participants' level of educational attainment, race/ethnicity, and birth country (U.S. vs. any other), and compared my findings to the subset of pregnant women participating in the National Health and Nutrition Examination Survey (NHANES) from 1999-2012. Adjusting for age, education, and other variables, foreign-born Hispanic women in CIOB had lower average levels than White CIOB participants of BDE-153 (adjusted geometric mean ratio or GMR [95% CI]: 0.22 [0.10, 0.48]), the OCPs oxychlordane and *trans*-nonachlor (0.46 [0.26, 0.82] and 0.53 [0.32, 0.87]), perfluorooctanoic acid (PFOA) (0.60 [0.44,0.82]), perfluorooctane sulfonic acid (PFOS) (0.59 [0.35, 1.00]), cadmium (Cd) (0.71 [0.50, 1.00]) and four hydroxy-PAHs (OH-PAHS) (adjusted GMRs from 0.45-0.57). Conversely, foreign-born Hispanic women in CIOB had much higher average serum levels of 4,4′-dichlorodiphenyldichloroethylene (4,4′-DDE) than White CIOB participants (3.26 [1.28, 8.29]). No statistically-significant differences were found between U.S.-born Hispanics and Whites. Black women in CIOB had lower average urinary levels of the phthalate metabolite MECPP and higher average levels of the organophosphate pesticide metabolite diethyl phosphate (DEP) than White CIOB participants. Only some of these differences (*4,4′*-DDE, PFOA and PFOS) were also reflected in the NHANES 1999-2012 subset of pregnant women. I found additional differences in the national sample that were not reflected in the CIOB sample, including lower BDE-100 and higher lead (Pb), As, and mono-ethyl phthalate (MEP) concentrations among foreign-born Hispanics compared to U.S.-born Whites; higher levels of Cd, Pb, 4,4′-DDE, oxychlordane, *trans*-nonachlor among Blacks compared to U.S.-born Whites; higher levels of 4,4′-DDE and mono-butyl phthalate (MnBP) and lower levels of triclosan among U.S.-born Hispanics compared to U.S.-born Whites. I also found evidence of higher exposure to BDE-47, -99 and -100 and PCB-153 among more educated CIOB women, while in NHANES, average BDE-47 and -99 concentrations were lower in the most educated group of pregnant women compared to the least educated group. Geometric mean urinary levels of two OH-PAHs were higher among the least educated compared to the most educated in both the CIOB and NHANES sample. The results of my exploratory analysis of CIOB and NHANES data

point to possible differences in chemical body burden during pregnancy that vary in particular by country of origin, consistent with previous studies. My findings also provide suggestive evidence of a disproportionate exposure burden associated with SES (race, ethnicity or education) for some chemicals. Additional studies of diverse populations within the U.S. are needed to more fully assess social inequalities in chemical body burdens during pregnancy and shed light on the possible implications for children's health.

Background

Women are exposed to numerous harmful chemicals during pregnancy.[117] If exposures are high enough, they may put infants at risk of adverse effects because many chemicals are able to cross the placenta into the fetal environment.[118,119] Prenatal exposure to methylmercury, PCBs, and Pb, for example, can cause neurological and developmental effects in children.[120] Gestational chemical exposures have also been linked to adverse pregnancy outcomes such as preterm delivery and fetal growth restriction,[121] as well as increased risk of cardiovascular disease and diabetes for the child in later adulthood.[122]

Communities of color and of low socioeconomic status (SES) generally face higher potential for exposure to environmental pollutants in their neighborhoods of residence.[123] Exposures to neighborhood pollutants are increasingly recognized as potential contributors to health inequalities including disparities in maternal and child health.[8,88] While environmental justice research has primarily employed population-level studies relying on proximity to air pollutant sources and hazardous waste sites, reported pollutant emissions, or ambient air quality monitoring, biomonitoring has the potential to shed light on individual-level differences in internal dose during pregnancy resulting from indoor as well as outdoor exposures at home, at work, and in the case of pollutants that persist in the body, throughout someone's lifespan. Socioeconomic and racial/ethnic differences in internal dose may arise not only through differences in the presence of ambient neighborhood pollution but also through differences in housing, occupation, diets, activities, and the age, condition and type of consumer products used. Understanding socioeconomic and demographic patterns in chemical concentrations among pregnant women can help guide efforts to reduce exposures in high risk populations and can generate new hypotheses about sources of exposure for emerging chemicals of concern.

In the late 1990s, the U.S. government began to regularly assess exposure to a growing list of chemicals among the general, non-institutionalized population as part of the National Health and Nutrition Examination Survey (NHANES).[124] The chemicals chosen for analysis included those for which toxicity studies indicated an adverse health effect in humans as well as chemicals of concern because of their toxicity in animals, their widespread use in man-made products or agriculture, and/or their persistence in the environment. In this chapter, I use data from the NHANES and the Chemicals in Our Bodies (CIOB) study (also known as the Maternal and Infant Environmental Exposure Project), which is a collaboration between the California Environmental Contaminant Biomonitoring Program (or Biomonitoring California, www.biomonitoring.ca.gov) and the University of California (San Francisco and Berkeley). Established by legislation in 2006, Biomonitoring California is a tri-department program led by the California Department of Public Health, with the Office of Environmental Health Hazard Assessment and Department of Toxic Substances Control. Biomonitoring California's goal is to determine levels of selected environmental chemicals in Californians, measure trends in

chemical levels over time, and help assess the effectiveness of public health efforts and regulatory programs to decrease exposures to specific chemicals. CIOB was designed to study environmental chemical exposures during pregnancy among a diverse, urban population that is not well represented in the national biomonitoring program NHANES. Chemicals measured in CIOB were chosen with consideration of lab capabilities and comparability to national biomonitoring data.

Previous research on socioeconomic predictors of chemical exposure in pregnant women is limited but suggestive of some differences across social strata. Studies from the U.S.[125–127] and Spain[128,129] have found that pregnant women of higher SES (classified according to income, occupation, or education) have higher exposure to PCBs, although the differences were not always statistically significant. Greater consumption of fish and historically lower rates of breastfeeding among high SES women in previous generations have been suggested as explanations for this difference. There is somewhat contradictory evidence regarding the relationship between mother's SES and prenatal exposure to PBDEs, with one study of primarily Black women from Baltimore finding higher levels of BDE-47 and -100 in cord blood from women with less education and lower income[125] and another of majority Hispanic women from New York City finding the reverse for BDE-47, -100 and -153 in maternal serum sampled during the first trimester.[130] A third study analyzing data from the National Health and Nutrition Examination Survey (NHANES) 2003-4 found that individuals in lower income households had higher serum levels of ∑PBDEs (BDE-28, -47, -99, -100, -153, and -154.) than those in higher income households.[131] Differences in the congeners examined by these studies may explain some of the discrepancies. BDEs -47, -99 and -100 are components of commercial penta-BDE mixtures most commonly used as a flame retardant in polyurethane foam[132] whereas BDE-153 is present in both penta- and octa-BDE formulations, with the latter being used most widely in plastics and textiles.[133]

Studies of racial/ethnic disparities in chemical concentrations during pregnancy have found that country of origin is a significant predictor of PCB, mercury (Hg), DDT and other organochlorine pesticide (OCP) levels.[128,129,134] While many studies have not examined nativity, it is possible that this factor plays a role in the lower levels of PBDEs and PCBs measured in pregnant Hispanic women [127,130,135] and in cord blood samples from Asian mothers[125] in the U.S because the manufacture and use of PBDEs and PCBs was more prevalent in the U.S. than in many other countries. Several studies have documented higher exposure to lead (Pb) among pregnant Black women and women of child-bearing age[136,137] as well as the general Black population.[138,139] Low- income Blacks are more likely to live in older, dilapidated housing with elevated lead levels in soils and in paint. There is evidence that phthalate exposures vary with education as well as race and ethnicity in U.S. women of childbearing age, with studies showing that women of color have higher levels of dibutyl and diethyl phthalate metabolites in their urine and less educated women having higher levels of benzylbutyl phthalate metabolites and lower levels of di-2-ethylhexyl phthalate metabolites.[140,141]

Socioeconomic and racial/ethnic differences in exposure during pregnancy to PFCs, phenols, current use pesticides, and metals other than Pb, have to my knowledge not been studied. Analyses of NHANES data suggest higher levels of cadmium (Cd), antimony and bisphenol A (BPA) among lower SES individuals compared to higher SES individuals;[142,143] higher body burdens of Hg, arsenic (As), cesium, thallium, PFOA, PFNA and benzophenone-3 among higher

SES individuals compared to lower SES individuals;[142] higher PFC, antimony, thallium and dichlorophenol levels and higher odds of co-exposure to the neurotoxicants Pb, Hg and PCBs among Blacks versus Whites;[135,144,145] and lower PCB, Hg, BPA and PFC levels among Mexican Americans compared to other groups.[143–145]

The goal of my analysis was to examine differences in exposure to a wide range of environmental chemicals among pregnant women of differing SES, race/ethnicity and country of origin. As indicators of exposure, I used measurements of environmental chemicals in serum, whole blood, and urine from a convenience sample of pregnant women recruited from San Francisco General Hospital, a safety-net hospital serving primarily low income women, during 2010-11for the CIOB study. Utilizing regression with multiple imputation to address values below the limit of detection, I estimated differences in measured concentrations across levels of educational attainment and racial and ethnic categories adjusting for other covariates. I compared results from my analysis of CIOB data to my findings from a similar analysis of data on pregnant women from NHANES 1999-2012.

Methods

Study population and sample collection

The Chemicals in Our Bodies (CIOB) study enrolled 92 pregnant women seeking prenatal care at San Francisco General Hospital between 2010 and 2011.Women were eligible to participate if they were English- or Spanish-speaking, 18 years or older, and in their second or third trimester of pregnancy. Socioeconomic, demographic, and smoking ("Did you smoke during pregnancy?") information was collected via interview-administered questionnaire. Maternal blood and urine samples were taken at delivery. Study protocols were approved by the institutional review boards at the University of California, San Francisco (10-00861) and Berkeley (2010-05-04), as well as the California Committee for the Protection of Human Subjects under the California Health and Human Services Agency (12-08-0605).

Samples were analyzed by Biomonitoring California for over 80 chemicals at the Environmental Health Laboratory (whole blood and urine) of the California Department of Public Health and the Environmental Chemistry laboratory (serum) of the Department of Toxic Substances Control. Whole blood samples were analyzed for 3 metals (cadmium [Cd], lead [Pb], and mercury [Hg]). Serum samples were analyzed for 19 PBDEs, 4 hydroxy-BDEs (OH-BDEs), 11 PFCs, 15 PCBs, and 7 OCPs. Urine samples were analyzed for 3 metals (arsenic [As], Cd, and Hg), 6 arsenic compounds, and metabolites of 9 polycyclic aromatic hydrocarbons, 6 phthalate metabolites, 3 phenols (benzophenone-3, bisphenol A [BPA], and triclosan), and 6 pesticide metabolites. Cd and Hg were more often detected in blood than urine and I therefore limited my analysis to blood concentrations. I also omit discussion of the multiple arsenic compounds and focus on levels of total arsenic. More details on laboratory methods and a complete list of analytes measured in CIOB (including acronyms used in this chapter) are provided in Appendix A.

Statistical analysis

Participants in both CIOB and NHANES 1999-2012 were categorized according to their highest level of educational attainment (less than high school, high school graduate or equivalent, or

more than high school). I chose education as the SES measure because many women in CIOB declined to report their household income. Participants were also categorized according to their self-identified race and ethnicity as either U.S.-born White, U.S.-born Black, U.S.-born Hispanic, foreign-born Hispanic, or some other race or ethnicity. In CIOB, the other category included Asians, Pacific Islanders, and women of North African origin, approximately half of whom were foreign-born. There were not enough non-Hispanic foreign-born women in CIOB to warrant additional categories.

I examined summary statistics for each chemical for both the CIOB and NHANES samples, including the median and 95th percentile concentration and the percent of observations with concentrations above the method detection limit (MDL). I conducted further statistical analysis on chemicals that were detected in at least 60% of the CIOB samples tested. Chemicals in NHANES were additionally omitted from my analysis if 60% of NHANES samples from pregnant women were non-detects. For chemicals meeting this criterion, I calculated unadjusted geometric mean ratios (GMRs) to compare chemical concentrations across strata of education and race/ethnicity, with the most educated group and non-Hispanic White women serving as the reference group, respectively. Lipophilic compounds were examined on a lipid-adjusted basis.

I conducted linear regression on log-transformed wet-weight chemical concentrations from CIOB to assess differences across socio-demographic strata adjusting for maternal age in years, gestational age in months (for chemicals in blood and serum only, to control for possible differences due to plasma volume expansion during pregnancy), total lipids (for lipophilic compounds), creatinine (for chemicals in urine), and whether the participant reported smoking during pregnancy (for OH-PAHs and Cd). At least one previous study reports higher concentrations of arsenic in the blood of smokers;[146] I did not control for smoking in my analysis of arsenic levels because I was not aware of this study at the time. Models included both race/ethnicity (White, Black, foreign-born Hispanic, U.S.-born Hispanic, or other) and highest level of educational attainment. That is, I designed the analysis to understand racial/ethnic and education-related dimensions of SES separately, generating estimates of differences in geometric mean concentrations across levels of education that control for race/ethnicity and estimates of differences in geometric mean concentrations by race/ethnicity that control for education.

Multiple imputation with fully conditional specification was used to address censored values below the detection limit in both the CIOB and NHANES datasets.[147,148] Missing chemical concentrations were imputed 5 times and constrained to be below the MDL. Five iterations have generally been found to be sufficient with moderate amounts of missing data.[149] The imputation model assumed a log-normal distribution for chemical concentrations and included all variables in the analysis model as well as other chemicals with > 60% detected values in the same chemical class. However in some cases (for CIOB, in the case of PBDEs, PCBs, PFCs, *b*-HCH and pesticide metabolites in urine), the imputation models would not converge after 100,000,000 iterations unless the other chemicals in the chemical class were excluded from the imputation models. Effect estimates (geometric mean ratios) obtained from the five iterations of imputation were then averaged. To assess whether the assumption of a log-normality was appropriate, I examined distributions visually and using the Kolmogorov-Smirnov goodness-of-fit test, for which I considered $P < 0.10$ grounds to reject the null hypothesis that the chemical concentrations followed a log-normal distribution. To ensure that the results were not driven by

the imputation procedure, I conducted a sensitivity analysis utilizing maximum likelihood estimation to account for censored values below the detection limit.

I compared my findings from analyzing the CIOB data to biomonitoring results for the subset women aged 13-50 with a positive urine pregnancy test who participated in NHANES 1999-2012. Chemical analysis of blood and urine is conducted on a subsample of NHANES participants (generally 1/3) and the chemicals analyzed vary by survey cycle. Pooled NHANES samples were excluded from my analysis. I examined the detection frequency, median, and 95th percentile for each chemical, averaging the participant survey weights across the survey years. Percentile estimates are thus reflective of the non-institutionalized U.S. population of pregnant women aged 13-50 at the midpoint of the survey years included for each chemical.

I then utilized the same modeling and multiple imputation approach described above with slight modification to generate adjusted GMRs across socioeconomic strata and racial/ethnic groups for the NHANES women. NHANES participants with missing information on country of origin (n=55) as well as a small number of foreign-born White and Black women (n=45) were excluded from this analysis in order to make it more consistent with the CIOB sample demographics. Because my main interest was in whether the differences in exposure observed in the CIOB sample from San Francisco were also apparent in the NHANES sample, I limited the multivariate analysis to the chemicals measured in CIOB with greater than 60% detection frequencies. In order to be able to control for time trends, each NHANES participant was assigned a random sample collection date from within the 6-month interval reported in NHANES. Models of log-transformed chemical concentrations adjusted for time trend (in years since January 1, 1999), maternal age (in years), month of gestation (for chemicals in blood and serum only), creatinine (for chemicals in urine), and current smoking (based on the question "Do you now smoke?" for OH-PAHs and Cd) and incorporated the NHANES complex survey design and survey weights averaged across the survey cycles. Lipophilic compounds were modeled as wet-weight concentrations (mass per volume) with the CIOB data (with lipid concentrations as a covariate in the model); however lipophilic compounds are reported in NHANES on a per-weight rather than per-volume basis, and I therefore modeled lipid-adjusted values (mass of chemical per mass of lipid) as the outcome variable. Imputed chemical concentrations were constrained to be below the MDL (or highest lipid-adjusted MDL in the case of lipophilic chemicals), and effect estimates were averaged over 5 iterations of imputation. All analyses were conducted using SAS 9.4 (SAS Institute, Inc., Cary, NC).

Results

Chemicals in Our Bodies

Women participating in CIOB were demographically diverse, with foreign-born Hispanic women predominating (**Table 3-1**). U.S.- and foreign- born Hispanic women had less education than other racial/ethnic groups (33% and 59% with less than a high school education, respectively, compared to 11%, 14% and 18% for Blacks, Whites, and Asian/PI/Others). Smoking rates during pregnancy were highest for Blacks (67%) and Whites (43%) followed by U.S.-born Hispanics (33%), Asian/PI/Others (20%), and foreign-born Hispanics (12%).

Urine samples were successfully collected during delivery from 89 of the 92 participating women, and blood samples were successfully collected from 77 participants. Seventy-three women gave both blood and urine samples that were tested for the full panel of 84 chemicals.

MDLs and summary statistics for all chemicals are shown in **Table 3-2**. Of the 84 unique chemicals analyzed, nearly a third (27 chemicals) were detected in over 90% of women sampled. The total number of chemicals detected in a participant's blood, serum and urine ranged from 35 (42%) to 61 (73%).

The distribution of the detection frequencies by nativity are shown in **Figure 3-1.** Foreign-born women had a lower median and lower mean number of chemicals detected, but a higher maximum, compared to U.S.-born women. Foreign-born women had a higher mean detection frequency of OCPs (4.6 versus 4.0) and a lower mean detection frequency of all other chemical classes. Wilcoxon-Mann-Whitney tests suggested that the distribution of detection frequencies may have been significantly different between the two groups in the case of OCPs and OH-PAHs (two-sided $P < 0.05$), PFCs (P=0.12), pesticide metabolites and phthalates (P =0.07), phenols and the total number of chemicals detected (P =0.11), with foreign-born women having lower detection frequencies than U.S.-born women in all cases except OCPs (data not shown).

Forty-two chemicals warranted further consideration based on my criterion of at least 60% of samples having detectable levels. Geometric mean values and ratios across strata of educational attainment are shown in **Table 3-3**. Unadjusted results showed a step-wise *increase* in geometric mean concentrations of penta-BDEs and 5'-OH-BDE-47, oxychlordane, N-MeFOSAA and PFOSA, Cd and diethyl phosphate (DEP) with higher educational attainment. Concentrations of 4,4′-DDE, *b*-HCH, Pb, three OH-PAHs, and the phthalates MECPP and MEP showed a step-wise *decrease* with increasing educational attainment. However, no step-wise trends persisted after adjustment for race/ethnicity, age and other variables. Adjusted GMRs may suggest lower average BDE-47, -99 and -100 and PFOSA levels, and higher average OH-PAH (OH-2-fluo, OH-3-fluo, and OH-3-phen) levels among the least educated group compared to the most educated group; and lower average PCB-153 levels among high school graduates compared to those with more than a high school education.

Unadjusted and adjusted GMRs across categories of race/ethnicity are shown graphically in **Figure 3-2**. Unadjusted comparisons suggested that, compared to Whites, foreign-born Hispanics had lower average concentrations of most chemicals with the exception of 4,4′-DDE, *b*-HCH, PFUA, Pb, Hg, As, MnBP, MEP, benzophenone-3, triclosan and the chlorpyrifos metabolite TCPy. Blacks, on the other hand, had higher geometric mean concentrations than Whites of penta-BDEs and 5'-OH-BDE-47. Geometric mean levels of Hg, Me-PFOSA, and MBzP were also notably (>50%) higher for Blacks than Whites, while geometric mean concentrations of triclosan and MECPP were more than 50% lower. U.S.-born Hispanics had substantially (>50%) higher geometric mean levels than foreign-born Hispanics to BDE-100 and -153, 5'-OH-BDE-47, MCPP, MECPP, and benzophenone-3, and substantially (>50%) lower geometric mean concentrations of 4,4′-DDE, *b*-HCH, PFUA, and triclosan than foreign-born Hispanics.

Only some of these differences exhibited statistical significance after adjustment for age, education and other variables. Compared to Whites and independent of age and education,

foreign-born Hispanics appeared to have lower geometric mean concentrations of BDE-153 (adjusted GMR [95% CI]: 0.22 [0.10, 0.48]), oxychlordane (adjusted GMR [95% CI]: 0.46 [0.26, 0.82]), *trans*-nonachlor (adjusted GMR [95% CI]: 0.53 [0.32, 0.87]), PFOA (adjusted GMR [95% CI]: 0.56 [0.32, 0.98]), PFOS (adjusted GMR [95% CI]: 0.59 [0.35, 1.00]), Cd (adjusted GMR [95% CI]: 0.71 [0.50, 1.00]) and four OH-PAHs (adjusted GMR [95% CI]: 0.50 [0.29,0.84], 0.45 [0.25 ,0.82], 0.56 [0.32,0.97], and 0.57 [0.35,0.94] for 2-, 3- and 9- fluo and 3-phen, respectively), and higher geometric mean concentrations of 4,4′-DDE (adjusted GMR [95% CI]: 3.26 [1.28, 8.29]). Only two differences between Blacks and Whites exhibited statistical significance after adjustment: lower average concentrations of MECPP among Blacks (adjusted GMR [95% CI] compared to Whites: 0.36 [0.16, 0.83]) and higher average DEP levels among Blacks (adjusted GMR [95% CI] compared to Whites: 2.62 [1.06, 6.49]). There were no statistically significant differences in average chemical concentrations of U.S.-born Hispanics compared to Whites.

The adjusted GMRs resulting from the sensitivity analysis utilizing MLE were generally consistent with those estimated using multiple imputation. In a few instances, the estimates were in the same direction but no longer statistically significant. This included the findings of lower average concentrations of OH-PAHs in the least educated group compared to the most educated group and lower average concentrations of oxychlordane among foreign-born Hispanics compared to U.S.-born Whites.

NHANES

Chemical concentrations for pregnant women from NHANES 1999-2012 are shown in **Table 2-1**. In general, median concentrations of PBDEs, PCBs, and OCPs were higher in this national study population than in CIOB participants from San Francisco, likely reflecting the fact that concentrations of these chemicals are declining in the environment and samples were collected earlier from the NHANES participants (survey cycles 2003-4 for PBDEs and 1999-2004 for PCBs and OCPs). Median concentrations of PFCs, phthalates, and metals, most of which have been sampled nearly continuously in NHANES since 1999, were also generally higher among NHANES than CIOB participants. (PFNA is one exception.) Median OH-PAH concentrations were lower among the NHANES women possibly due to a lower prevalence of smoking in this group compared to the group of CIOB participants.

Adjusted GMRs across socioeconomic and racial/ethnic groups in NHANES were partially consistent with what I observed in my analysis of CIOB participants from San Francisco. I did not calculate GMRs for PCB-180, HCB, *b*-HCH, PFOSA, PFUA, and DEP because detection frequencies for these chemicals were below 60% among the NHANES participants. In both studies, pregnant women with less than high school education had higher geometric mean concentrations of the OH-PAHs OH-3-fluo and OH-3-phen compared to women with more than a high school education (NHANES GMRs [95% CI] adjusted for smoking and other variables: 2.17 [1.36, 3.46] for 3-fluo and 1.55 [1.12, 2.15] for 3-phen). However, while women in CIOB with less than a high school education had *lower* adjusted geometric mean concentrations of BDE-47, -99 and -100, these concentrations were *higher* for the less educated group in NHANES (adjusted GMRs [95% CI] compared to women with more than a high school education: 2.11 [1.25, 3.54] for BDE-47, 2.35 [1.44, 3.85] for BDE-99, and 1.09 [0.55, 2.19] for BDE-100).

As in CIOB, foreign-born Hispanic women in NHANES had lower measured concentrations of PFOA and PFOS and much higher geometric mean concentrations of 4,4′-DDE after adjustment for education and other factors (adjusted GMR [95% CI] compared to Whites: 0.59 [0.41, 0.83] for PFOA, 0.60 [0.44, 0.82] for PFOS, and 6.37 [2.95, 13.75] for 4,4′-DDE). Geometric mean levels of penta-BDEs were lower for foreign-born Hispanics than Whites in both studies, but adjusted GMRs were only statistically significant in the case of BDE-153 in CIOB (adjusted GMR [95% CI] for foreign-born Hispanics compared to Whites: 0.22 [0.10, 0.48]) and BDE-100 in NHANES (0.41 [0.17, 0.99]). Foreign-born Hispanic women also had higher geometric mean concentrations of Pb, As, and mono-ethyl phthalate (MEP) than Whites in both studies, but adjusted GMRs suggested statistically significance only in the case of NHANES (1.69 [1.47, 1.94], 1.58 [1.06, 2.34] and 1.65 [1.06, 2.55], respectively). However, unlike CIOB, foreign-born Hispanic women in NHANES had lower geometric mean concentrations of PCB-153 than Whites, adjusting for other factors (adjusted GMR [95% CI]: 0.63 [0.41, 0.95]) and did *not* have lower geometric concentrations of Cd, fluorinated OH-PAHs, nor the OCPs oxychlordane and *trans*-nonachlor compared to Whites when adjusting for other factors.

In both CIOB and NHANES, Black women had higher geometric mean concentrations of 4,4′-DDE and Cd than Whites, but adjusted GMRs suggested statistically significant differences in the NHANES sample only (GMRs [95% CI] compared to Whites: 1.63 [1.20, 2.22] and 1.23 [1.17, 1.30] respectively). Similarly, Black women had lower geometric mean concentrations of PFOA and benzophenone-3 than White women in both studies, but the differences only suggested statistically significant differences in NHANES (adjusted GMR [95% CI]: 0.58 [0.38, 0.89] for PFOA and 0.56 [0. 0.36 [0.16, 0.80] for benzophenone-3). Unlike in CIOB, Black women in NHANES had higher adjusted geometric mean levels than Whites of oxychlordane (adjusted GMR [95% CI]: 1.27 [1.00, 1.62]), *trans*-nonachlor (adjusted GMR [95% CI]: 1.43 [1.10, 1.86]), and Pb (adjusted GMR [95% CI]: 1.32 [1.11, 1.57]).

Geometric mean concentrations of 4,4′-DDE were higher for U.S.-born Hispanic women compared to Whites in both studies, with adjusted GMRs suggesting the difference might be statistically significant with the NHANES dataset only (adjusted GMRs [95% CI]: 1.93 [1.41, 2.66]). U.S.-born Hispanic women had lower geometric mean levels of BDE-99 and triclosan but again the difference were only statistically significant in NHANES after adjustment for other factors (adjusted GMR [95% CI] compared to Whites: 0.59 [0.39, 0.89] for BDE-99 and 0.38 [0.18, 0.81] for triclosan). In contrast to CIOB, U.S.-born Hispanic women in the NHANES sample had higher average concentrations of the phthalate metabolite mono-butyl phthalate (MnBP) (adjusted GMR [95% CI] compared to Whites: 1.56 [1.09, 2.24]).

Discussion

To my knowledge, this analysis of CIOB and NHANES data is the first to look at the relationship between socioeconomic status and measured concentrations of over 80 potentially harmful chemicals during pregnancy. In general, my analysis revealed more pronounced differences with respect to country of origin that with respect to race, ethnicity, or education in both the CIOB population from San Francisco and the subset of pregnant women derived from NHANES 1999-2012. I found that women born in the U.S. in the CIOB study had higher average detection frequencies for all chemical classes (PBDEs/OH-BDEs, PCBs, PFCs, metals, phthalates, PAHs, phenols and organophosphate or pyrethroid pesticides) except for

organochlorine pesticides, for which foreign-born women had a higher average detection frequency (**Figure 3-1**). Although the differences were not statistically significant in most cases, this nevertheless suggests that a larger number of chemicals are likely to be detected in infants of women born in the United States than in infants of women born in Latin America. With the exception of DDE, my examination of average concentrations of individual chemicals further suggested that infants of U.S.-born women were likely to be exposed to higher levels of several chemicals than infants of mothers born in Latin America.

In general, I found there were more pronounced socio-demographic differences in relative chemical concentrations in blood versus in urine among both the CIOB and especially the NHANES participants. Chemical concentrations of bioaccumulative chemicals in blood and serum are likely to reflect early life exposures, including those in a foreign country of origin. Urine chemical concentrations, on the other hand, reflect recent (hours to days) exposure and may fluctuate during the day and between days. Differences in urine chemical concentrations are therefore more likely to be dynamic and to reflect contemporary differences in neighborhood environments, housing, occupation, diets, and consumer product use. Single spot samples of urine, the approach used in both CIOB and NHANES, also limited my ability to detect socio-demographic differences in exposures to these chemicals.

Analysis of the CIOB data utilizing maximum likelihood estimation (MLE) rather than multiple imputation generally resulted in qualitatively consistent adjusted GMRs, although the exact estimates varied and in some cases (differences in OH-PAH concentrations with respect to education and oxychlordane concentrations among foreign-born Hispanics compared to Whites) were no longer statistically significant. This suggests my findings were generally not driven by the imputation procedure. Unlike MLE, the multiple imputation method intentionally introduces random variation in order to reflect the uncertainty inherent in the censored observations, and the exact estimates will vary every time the procedure is done.

PBDEs

I expected to find that less educated women had higher serum levels of PBDEs, given research showing PBDE exposure decreases with household income in U.S. general population[131] and is higher among children with less educated mothers and care-givers.[150,151] Others have hypothesized that the presence of older or less expensive furniture and housing size and ventilation rates may increase PBDE exposure in low-SES homes.[152] Consistent with these findings, my analysis of NHANES data suggested that average BDE-47 and -99 serum levels were lower among pregnant women in the most educated group compared to the least educated group. However, I found the opposite trend in my analysis of CIOB participants from San Francisco: higher serum levels of BDE-47, -99 and -100 among the most highly educated women compared to the least educated women. This finding is consistent with recent evidence from a study of mostly Hispanic pregnant women in New York City, in which researchers found higher levels of BDE-47 and -153 among more educated women and higher BDE-153 levels among higher income women[130]. The number of electronics in the home was predictive of concentrations of BDE-47, -99 and -100 in that study. Given the diversity of sources of exposure to PBDEs – including foam under carpeting,[153] solid cheese and processed meats,[130] in addition to electronics and furniture – the socioeconomic patterning of exposure is likely to be complex

and variable. My finding may also be the result of residual confounding due to the fact that foreign-born women had lower levels of PBDEs and education.

My analysis revealed lower serum levels of PBDEs among foreign-born Hispanic women compared to U.S.-born Whites, although the differences were only statistically significant in the case of BDE-100 (among NHANES women) and BDE-153 (among CIOB women). This agrees with previous findings of lower penta-BDE body burden among foreign-born vs. U.S.-born NHANES participants[131] and may have to do with differing lifestyles in the U.S. (e.g., spending more time indoors, using more foam-filled furniture, carpeting or electronics) and/or U.S. furniture flammability standards, including California's unique and more stringent standard, which was only recently repealed. Studies of children in California have found that those who have lived outside the U.S. have lower exposure to PBDEs[154] and that children whose mothers are foreign-born have significantly lower levels of more highly brominated PBDEs than those whose mothers are born in the U.S.[150] Other studies finding lower exposure to BDEs among Asian American infants[125] did not control for country of origin.

PCBs

A few studies have suggested PCB exposures may be higher among higher SES women. Axelrad et al. (2009) found that women of childbearing age participating in NHANES 1999-2002 with incomes above poverty level had greater serum PCB levels than lower-income women,[127] and Herbstman et al. (2007) found that levels of PCBs in cord serum from Baltimore similarly increased with the mother's income and education.[125] However, the differences were not always statistically significant. Other studies have found statistically significant evidence of increasing PCB body burden with income or education among pregnant Black women from New York City[126,155] and with social class (classified according to occupation) and educational attainment among pregnant women from Spain.[128,129] This observation may have to do with differences between socioeconomic groups in breast-feeding practices or diet, including during these women's infancy and childhoods when PCB concentrations in the environment were higher. While PCB exposure was lower among the less educated women in the CIOB study participants from San Francisco, only one difference remained statistically significant after controlling for age and other factors: women with more than a high school education had higher serum levels of PCB-153 than women with a high school education or equivalent. I did not observe any statistically significant differences in PCB levels with education in the national sample derived from NHANES.

Both Axelrad et al. (2009) and my analysis of NHANES 1999-2012 documented lower PCB-153 serum levels among foreign-born Hispanic women compared to Whites. Vrijheid et al. (2010) similarly found lower PCB levels among pregnant women in Spain who had been born in Latin America compared to those born in Spain.[128] This may be due to historical differences in the production of PCBs and timeline of phase-out across countries in the Americas. However, I did not find strong evidence of differences in PCB concentrations by country of origin among the CIOB cohort.

OCPs

Most foreign-born women participating in CIOB were born in Mexico and other Central and South American countries. I expected these women to have higher exposure to organochlorine pesticides than the U.S.-born participants because many Latin American counties banned or restricted the use of OCPs more than a decade after the U.S. began restricting their use in the 1970s and 1980s. I found significantly higher levels of 4,4′-DDE and *b*-HCH among foreign-born Hispanic women compared to U.S.-born Whites in both the CIOB and NHANES women, although only the difference for 4,4′-DDE was statistically significant independent of other factors. This is consistent with other studies documenting higher concentrations of 4,4′-DDE and *b*-HCH among women born in Latin America than the U.S..[134,155] Unexpectedly, I found lower adjusted GMRs of *trans*-nonachlor and oxychlordane (biomarkers of exposure to chlordane) among the foreign-born Hispanic women compared to U.S.-born Whites in CIOB. These differences were not reflected in the national sample and, to my knowledge, have not been found in other studies. I did not observe statistically significant differences in HCB exposure between racial/ethnic groups in either CIOB or NHANES pregnant women. In the CHAMACOS study of low income pregnant Latina women from an agricultural community in California, women born in Mexico had higher HCB levels than those born in the U.S., but the difference were less pronounced than for other OCPs. The authors noted that this may reflect the more similar timeline in the prohibition of HCB in the two countries as well as the existence of contemporary sources of exposure such as those from incineration.[134]

In my examination of pregnant women in NHANES, but not in CIOB, I found that U.S.-born Black women had significantly higher exposure to 4,4′-DDE, oxychlordane, and *trans*-nonachlor than U.S.-born Whites. This may be due to regional differences in DDT and chlordane use in agriculture and mosquito control, which appears to have been higher in the Southern U.S. than in other regions.[156,157] Non-white women in California who were pregnant during the 1960s appear to have had markedly higher exposures to DDE and DDT than did whites.[158] Most of these women were Black and born in the U.S. Southeast. U.S.-born Hispanic pregnant women in the NHANES sample had levels of 4,4′-DDE that fell between foreign-born Hispanics and Blacks. The reasons why U.S.-born Hispanic women have higher concentrations than White women are unknown but may also be associated with regional differences in historical insecticide use or occupational exposures associated with agricultural work in contaminated soils.

PFCs

Foreign-born Hispanics in both CIOB and the subset of pregnant women in NHANES had lower serum levels of PFOA and PFOS than U.S.-born Whites. PFCs are stable compounds with a long half-life in the body, and these differences may reflect lower levels of exposure to PFCs during early life spent in Latin American countries. Hispanics also consume more fresh fruits and vegetables than other groups, which may mean they are eating less prepared foods packaged in PFC-coated packaging.[159] These findings are consistent with Nelson et al. (2012), who found that foreign-born Mexican Americans participating in NHANES 2003-6 had lower concentrations of PFOA and PFOS than Whites.[143] They found that Blacks had lower levels of PFOA than Whites, which I also found in the subset of NHANES participants I analyzed. However, Nelson *et al.* found evidence that Blacks had higher levels of PFNA than Whites, which I did not observe in my analysis of pregnant women in CIOB or NHANES.

Metals

Blacks and low income individuals in the U.S. are well known to have higher exposures to Pb than other groups,[139,160] and two earlier studies have documented higher exposures among pregnant Black women than Whites.[136,137] This has been attributed to older and poorer housing quality and exposure to lead-based paint and lead contaminated soils. The findings from my analysis of pregnant women in NHANES are consistent with this, and also suggest that women with a high school education or equivalent had higher exposure than those with more than a high school education. The reason neither of these trends were observed in the CIOB study may have to do with the small number of Black participants or the overall newer housing stock in California relative to other parts of the country. I also found that foreign-born Hispanic pregnant women had higher exposure to Pb than U.S.-born Whites in NHANES. This may reflect early-life exposure in a country of origin with less stringent regulation prohibiting the use of lead in paint and other products. Decorative lead-based paints and home remedies containing lead are still sold in Mexico, for example.[161,162]

Few studies have examined variation by SES in exposure to other metals during pregnancy by SES. One study from Spain found that women of higher education and social class (classified according to occupation) had higher concentrations of Hg in cord blood samples.[128] Country of birth was a stronger predictor of Hg exposure in this study, with women from Latin American having lower exposure than those born in Spain. This is likely due to higher rates of fish consumption in Spain.[163] Two studies of the U.S. general population have similarly found that higher income individuals had higher exposure to Hg than low income individuals[142] and Mexican American women had lower exposure to Hg than high-income Whites,[145] but I did not find evidence of either trend among pregnant women in my analysis of NHANES or CIOB data. Fish consumption is a primary route of exposure to Hg and it is possible that public health advisories warning pregnant women against eating fish have been effective in eliminating elevated exposure among well educated, high SES women during pregnancy. One foreign-born Hispanic participant in CIOB had extremely high levels of Hg from use of an adulterated skin cream imported from Mexico[164], an exposure hazard that has been documented in other studies.[165–168]

I found evidence of higher Cd exposure among Blacks and lower exposure among foreign-born Hispanic pregnant women compared to White pregnant women in the NHANES sample that was not explained by smoking rates. However, smoking status is notoriously inaccurate when measured via questionnaire. I also did not have information on the presence of other smokers in the home or workplace and the higher concentrations of Cd among Black study participants could be due to exposure to environmental tobacco smoke. Foreign-born Hispanic women in the NHANES sample I analyzed also had higher arsenic concentrations in their urine than did U.S.-born Whites.

OH-PAHs

I found two trends in urinary concentrations of OH-PAHs during pregnancy. In general, pregnant women with less education had higher levels of OH-PAHs than pregnant women with more education in both the CIOB and NHANES studies, although the differences were only statistically significant for a few OH-PAHs. Foreign-born Hispanic women also had lower

measured concentrations of the three fluorinated OH-PAHs in the CIOB study. Neither of these differences were explained by self-reported recent smoking, although, this may be due to my having to rely on smoking data collected via questionnaire. As mentioned earlier, such data is notoriously inaccurate. It is possible that less educated women are exposed to more second-hand smoke in the home or in the workplace because, in the general population, people with less education are more likely to smoke.[169] Similarly, rates of current smoking are lower among Hispanics than Whites in the U.S. general population, and Hispanic women may therefore be less exposed to environmental tobacco smoke from family members. The socio-demographic differences I found could therefore possibly be the result of differential rates of exposure to environmental tobacco smoke.

Phthalate metabolites

A previous study of women of child-bearing age in NHANES 2001-8 found higher urinary levels of MECPP and lower urinary levels of MBzP with increasing education.[140] I found similar trends among pregnant women in NHANES 1999-2012, although the only statistically significant difference after adjustment for other factors was for MECPP (i.e., women with more than a high school education had higher average levels of MECPP compared to women with only a high school education). Among CIOB participants, I found a similar trend with respect to MBzP and the opposite trend in MECPP concentrations across levels of educational attainment although none of the differences were statistically significant after controlling for other factors. The conflicting trend with MECPP may reflect differences in personal care product use during pregnancy among women from San Francisco compared to other parts of the country or my limited ability to characterize differences due to the smaller sample size of CIOB relative to NHANES.

Branch et al. (2015) found racial/ethnic disparities in exposure to MEP and MnBP among women aged 20-49 participating in NHANES 2001-8, and that frequent douching accounted for some of the higher levels of MEP among Black women compared to Whites. [141] Mexican American women also had higher MEP and MnBP levels than White women, but the use of feminine hygiene products did not appear to account for the difference. I did not find that Black women had higher urinary levels of MEP in either the CIOB or NHANES 1999-2012 women. This could reflect a reduction in the use of douche and feminine sprays during pregnancy, although I did not explicitly examine this possibility. I found higher concentrations of MEP and MnBP in NHANES 1999-2012 among both foreign- and U.S.-born pregnant women who were Hispanic compared to pregnant White women. This is consistent with the higher MEP and MnBP urinary levels among Mexican Americans found by Branch et al. (2015) and suggests there may be a unique exposure pathway or pathways for phthalates among Hispanics. I also found evidence that MECPP concentrations were lower for pregnant Black women than Whites independent of other factors, suggesting a potentially unique exposure source or route for White women during pregnancy.

Phenols

I found no differences in urinary levels of benzophenone-3, triclosan, or BPA across socio-demographic groups in the CIOB study population from San Francisco. Concentrations of benzophenone-3 and triclosan in particular were highly variable between individuals, suggesting

that some unmeasured factor or factors that do not vary substantially by race, ethnicity, country of origin, or education are important in determining concentrations of these chemicals in urine. In the NHANES 1999-2012 sample, the average level of benzophenone-3 was lower among Black pregnant women than White pregnant women. This is consistent with other studies and likely reflects higher sunscreen use among White women.[170,171]

In the NHANES 1999-2012 sample, U.S.-born Hispanic pregnant women had lower average levels of triclosan compared to U.S.-born Whites. In contrast, the National Children's Study Vanguard Study found that pregnant Hispanic women had *higher* triclosan levels than other groups.[171] My analysis of pregnant women in NHANES 1999-2012 found that women with more than a high school education had higher average urinary concentrations of triclosan than those with less than a high school education. The National Children's Study Vanguard Study similarly found evidence of higher exposures among pregnant women with higher education.[171]A study of triclosan concentrations in the U.S. general population using NHANES 2003-4 found higher income individuals had higher concentrations.[172] The primary route of exposure to triclosan is thought to be personal care products, including soaps and toothpaste, and these differences might reflect differences in the types or frequency of personal care product use by socioeconomic status.

Pesticide metabolites

I found evidence of higher average urinary DEP concentrations among Black women compared to White women in the CIOB population that was not explained by differences in education or other factors. DEP is produced from the degradation or metabolism of organophosphorus insecticides such as chlorpyrifos and diazinon that are currently in wide use in agriculture; use of chlorpyrifos and diazinon in residential products has been restricted since 2001 and 2002, respectively.[173,174] Previous studies suggest that diet is the dominant pathway of exposure to dialkylphophate metabolites.[175] However, these organophosphates have a long lifetime in the household environment, and were still being applied in landscape maintenance and structural pest control applications in San Francisco in 2010.[176] Chlorpyrifos and diazinon have been found in the house dust of low income homes in nearby Oakland, CA, and researchers have proposed that low income residential environments suffer greater rates of pest infestation that can stimulate elevated pesticide use - including the application of restricted use pesticides - that may lead to harmful exposures.[177,178] Given that the median levels observed in CIOB were higher than those observed in 1999-2000 in the urine of pregnant women from a nearby agricultural community with heavy organophosphate pesticide applications and in NHANES 1999-2000, this disparity in exposure warrants more research and the investigation of potential additional exposure routes in the urban environment.

Limitations

I have presented findings from an exploratory analysis with the goal of revealing possible differences in patterns of chemical exposure across socio-demographic groups that would warrant further investigation. The fact that only spot urine samples were taken in both NHANES and CIOB limit the degree to which the chemical concentrations measured in urine were good indicators of actual differences in exposure. CIOB was a convenience sample and my findings cannot be considered representative of differences in the population of San Francisco as a whole.

Similarly, NHANES was not designed to be a representative sample of pregnant women, and although I utilized survey weights, the results of my analysis of NHANES 1999-2012 should not be considered representative of pregnant women in the U.S.

The ability to detect differences between socio-demographic groups in CIOB is limited by its small sample size. This as well as geographic or regional differences may explain why some of the differences in average chemical concentrations between groups that I found in the NHANES 1999-2012 subset of pregnant women were not reflected in the CIOB cohort (e.g., with respect to OCPs, metals and phthalates). There were also only a few number of women within each race/ethnicity category in CIOB (with the exception of foreign-born Hispanics). Small numbers can lead to large differences by chance alone. Any study that makes a large number of comparisons, as I did in this analysis, is also likely to find some statistically significant differences just by chance.

I was limited in my ability to examine differences across strata of SES by the large amount of missing data on income in the CIOB cohort. As a result, I relied on education as the sole indication of SES. A recent study of NHANES data by Nelson et al. (2012) suggests that among the general population, household income was a more consistent predictor of concentrations of BPA in urine and PFCs in serum than was education, perhaps because income better reflects immediate access to material goods and diet whereas education is a marker of longer-term socioeconomic position. Nelson and colleagues suggests this distinction may be particularly important when the primary route of chemical exposure is from consumer products or diet and chemicals are short-lived in the body, instances in which biomonitoring data reflects recent exposures likely to be influenced by recent income. The authors assert that education may be a more appropriate measure of SES for chemicals that bioaccumulate in the body because education reflects socioeconomic position on a longer time scale.

I did not control for parity in my analysis and CIOB does not include information on breast-feeding after a previous pregnancy. Breast-feeding reduces maternal body burden of persistent organic pollutants, and I cannot eliminate the possibility that the evidence I found of possible lower BDE and PCB exposures among Hispanic women in both CIOB and NHANES 1999-2010 may be the result of prior breastfeeding. I also did not control for pre-pregnancy weight or weight gain in my analysis. Higher BMI and/or weight-gain during pregnancy has been associated with a lower body burden of PBDEs, PCBs and OCP levels in pregnant women.[125,130,134,158]

I was unable to control for geographic location in the NHANES sample. Place of residence may therefore explain some of the socio-demographic trends in chemical exposure that I observed among NHANES participants, although the use of several NHANES survey cycles for most chemicals should help minimize this possibility. For example, people in California have been shown to have higher body burden of PBDEs that is likely related to California's recently repealed unique furniture flammability standard. In previous studies, accounting for residence in California explained the higher PBDE concentrations of Mexican American NHANES participants, presumably because Mexican Americans were over-sampled in California.[131]

I chose to use multiple imputation to address chemical concentrations below the MDL because the most commonly used alternatives – substituting a fixed value such as MDL/$\sqrt{2}$, or ignoring

these observations – can produce biased estimates of central tendency.[179] I chose multiple imputation over maximum likelihood estimation (MLE, another parametric approach for addressing censored observations) or non-parametric methods based on survival analysis methods because I wanted to analyze the NHANES and CIOB data utilizing the same techniques and these other options are not currently supported by the procedures for complex survey data analysis in SAS. However, MLE generally produced very similar results regarding socioeconomic differences among CIOB women.

One assumption of the multiple imputation and MLE procedures is that the chemical concentrations follow a log-normal distribution. Many of the chemicals I looked at failed the log-normality test, including BDE-47 and -99, 5'-OHBDE-47, all OCPs except HCB, all PFCs except PFOA, As, the OH-PAH 3-fluo, MCPP, MECPP, benzophenone-3, triclosan and TCPy. However, determining the data distribution is difficult with so few observations. I nevertheless chose log-normal transformations over others because environmental chemical measurements often follow log-normal distributions,[180] and cursory visual inspection suggested it was the most appropriate for much of the biomonitoring data used in this study. The chemicals with the largest number of imputed values that failed the log-normality test were BDE-99, 5'-OHBDE-47, *b*-HCH, oxychlordane and TCPy. The results for these chemicals should therefore be interpreted with more caution.

Finally, I analyzed the biomonitoring results by individual chemical; I did not combine levels of multiple chemicals that may impact similar health endpoints in the body. An interesting extension of this work would be to examine whether co-exposure to multiple chemicals with similar health endpoints may subject some groups of pregnant women in CIOB or NHANES to higher risk for particular adverse outcomes. For example, a study of women of child-bearing age in NHANES 1999-2004 found suggestive evidence that the odds of co-exposure to two or more of the neurotoxicants Pb, Hg and PCBs above median levels decreased with educational attainment and was lower among non-Hispanic White women than it was among other racial/ethnic groups.[17]

Conclusions

In conclusion, the results of my analysis provide some evidence of differences in chemical body burden during pregnancy according to country of origin, race, ethnicity, and to a lesser extent, level of educational attainment using data from two biomonitoring studies (CIOB and NHANES). In general, being born in the U.S. was associated with greater numbers and concentrations of chemicals being detected in blood and urine. For several chemicals, measured levels were higher among women with lower SES and/or women of color who participated in either of the two biomonitoring studies independent of age and other factors, raising possible environmental justice concerns. These chemicals include OH-PAHS (in relation to educational attainment), organochlorine pesticides, current use pesticide metabolites, lead, cadmium, arsenic, and phthalate metabolites (in relation to race or ethnicity). However, in some instances the findings differed by study (e.g., BDE levels in serum increased with educational attainment in CIOB study from San Francisco, but decreased with educational attainment in the subset of pregnant women in NHANES 1999-2012) or non-Hispanic White women had higher chemical levels (e.g., PFOA and the phthalate MECPP). More biomonitoring studies of diverse populations – as well as studies investigating indicators of co-exposure to chemical mixtures –

would help to further assess differences in chemical body burden during pregnancy that may hold implications for children's health and environmental justice.

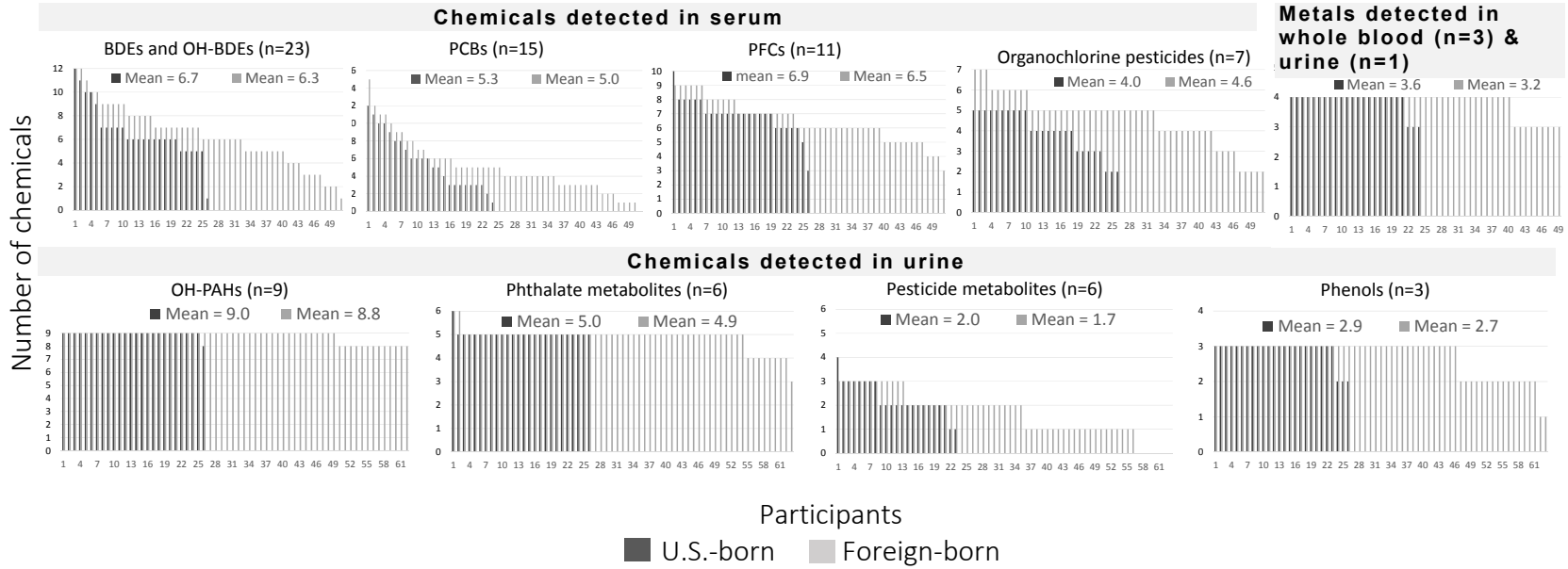
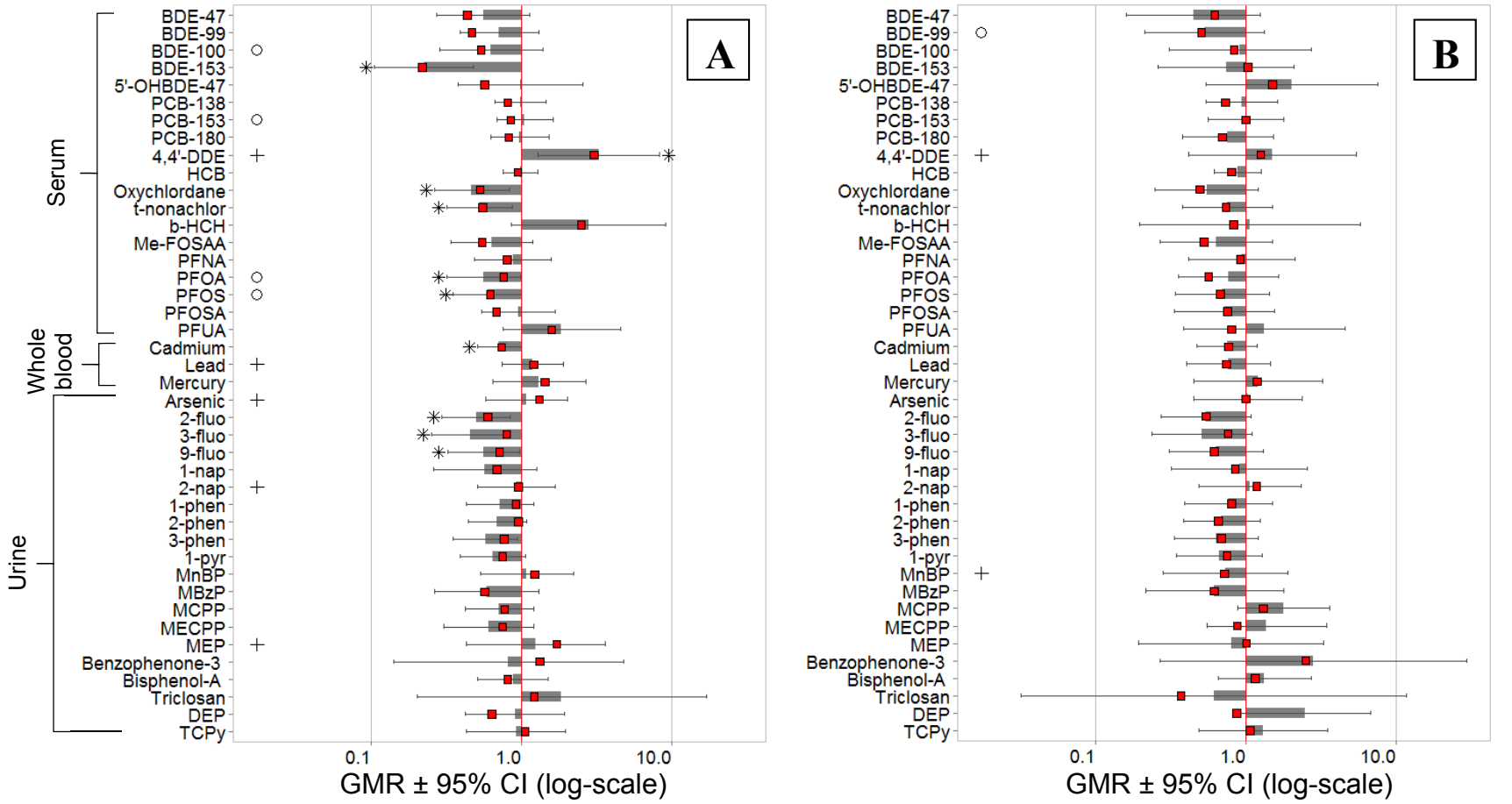


Figure 3-1 Number of chemicals detected in the blood or urine of 92 pregnant women from San Francisco by nativity.


A
B
Serum
Whole blood
Urine
BDE-47
BDE-99
BDE-100
BDE-153
5'-OHBDE-47
PCB-138
PCB-153
PCB-180
4,4'-DDE
HCB
Oxychlordane
t-nonachlor
b-HCH
Me-FOSAA
PFNA
PFOA
PFOS
PFOSA
PFUA
Cadmium
Lead
Mercury
Arsenic
2-fluo
3-fluo
9-fluo
1-nap
2-nap
1-phen
2-phen
3-phen
1-pyr
MnBP
MBzP
MCPP
MECPP
MEP
Benzophenone-3
Bisphenol-A
Triclosan
DEP
TCPy
0.1
1.0
10.0
GMR ± 95% CI (log-scale)

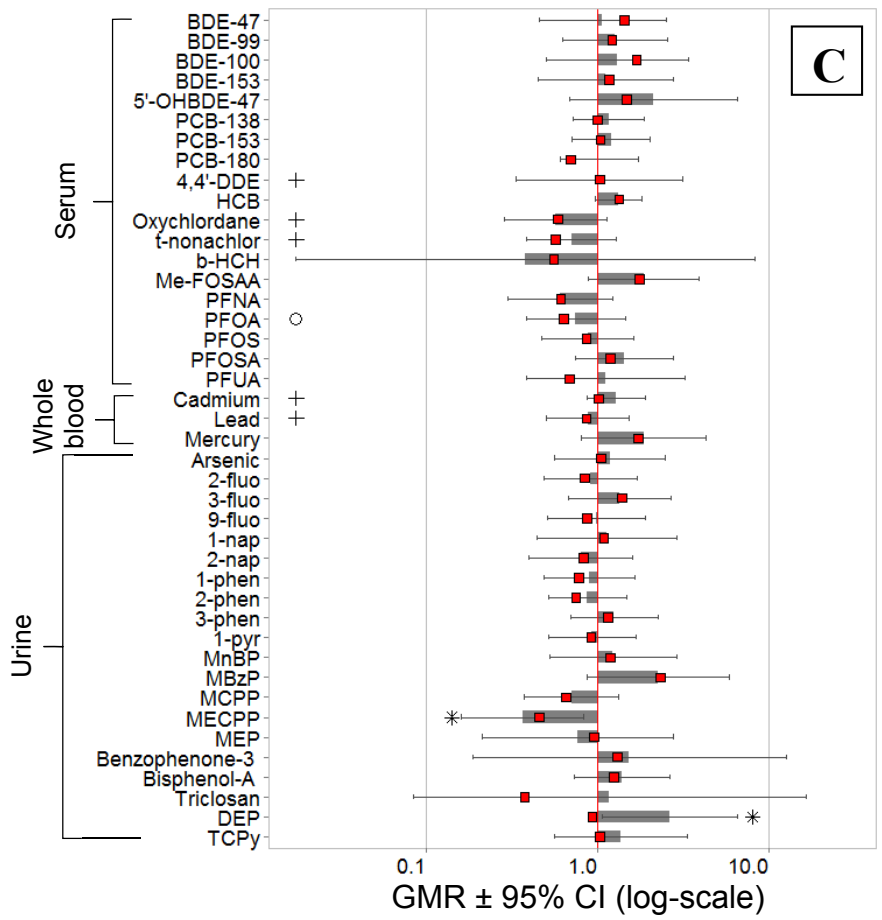


Figure 3-2 Ratios of geometric mean chemical concentrations among foreign-born Hispanic (A), U.S.-born Hispanic (B), and Black (C) pregnant women from San Francisco, as compared to White women. Bars are adjusted geometric mean ratios (GMRs)[a] with 95% confidence intervals. Red boxes indicate unadjusted GMRs. A GMR of 1 suggests no difference between geometric mean concentrations in comparison to non-Hispanic, U.S.-born White women. Adjusted GMRs that were different from 1 at $P < 0.05$ are denoted by "*". Chemicals for which adjusted GMRs suggested a statistically significantly difference between groups at $P < 0.05$ among NHANES 1999-2012 pregnant women are denoted by "+" (GMR > 1) and "o" (GMR <1). Total sample size is 77 for serum and blood chemicals and 89[b] for urine chemicals.

[a] Adjusted estimates of GMRs were derived using multiple imputation to account for observations < MDL and control for maternal age (in years), education (< HS, HS or equivalent, or > HS), gestational age in months (for chemicals in blood and serum only), total lipid concentration (chemicals in serum only), creatinine (chemicals in urine only) and smoking during pregnancy (Cd and OH-PAHs only).

[b] N=88 for OH-PAHs due to limited sample quantity.

Table 3-1 Characteristics of pregnant women participating in the Chemicals in Our Bodies (CIOB) study and women aged 13-50 with a positive pregnancy test and biomonitoring data from the National Health and Nutrition Examination Survey 1999-2012[a]

	CIOB (n=92)		**NHANES** (n=1,434)	
	N	*(%)*	*N*	*(%)*
RACE/ETHNICITY				
Foreign-born Hispanic	59	(64)	304	(21)
U.S.-born Hispanic	6	(7)	183	(13)
U.S.-born Black	9	(10)	203	(14)
U.S.-born White	7	(8)	562	(39)
Asian / PI	7	(8)	*NA*	--
Other / Unknown	4	(4)	182	(13)
COUNTRY OF ORIGIN				
U.S.	28	(30)	982	(68)
Mexico	31	(34)	263	(18)
Other	33	(36)	134	(9)
Unknown	0	(0)	55	(4)
EDUCATIONAL ATTAINMENT				
Not a high school graduate	41	(45)	450	(31)
High school graduate or equivalent	24	(26)	309	(22)
More than high school	23	(25)	674	(47)
Missing	4	(4)	1	(0.1)
HOUSEHOLD INCOME				
Under $20,000	32	(35)	301	(21)
$20,000 +	27	(29)	968	(68)
Missing	33	(36)	165	(12)
CURRENT SMOKER				
Yes	20	(22)	119	(8)
No	70	(76)	1141	(80)
Missing	2	(2)	174	(12)

[a] Pooled samples and women over age 50 with a positive pregnancy test were excluded from the NHANES dataset. Smokers in NHANES were defined based on response to the question "Do you now smoke?"

Table 3-2 Chemical concentrations in the blood and urine of pregnant women from San Francisco, California

	Wet-weight MDL (µg/L)	No. detected	% detected	Wet-weight		Adjusted	
				Median	95th percentile	Median	95th percentile
Chemicals in blood and serum (N=77)							
PBDEs				*(µg/L)*		*(ng/g lipid)*	
BDE-17	0.005	0	0	<MDL	<MDL	<MDL	<MDL
BDE-28	0.005	28	36	<MDL	0.02	<MDL	2.73
BDE-47	0.023	71	92	0.07	0.60	8.34	104.00
BDE-66	0.005	3	4	<MDL	<MDL	<MDL	<MDL
BDE-85	0.005	5	6	<MDL	0.02	<MDL	1.83
BDE-99	0.019	47	61	0.02	0.20	2.74	24.40
BDE-100	0.005	69	90	0.02	0.11	1.96	15.60
BDE-153	0.005	69	90	0.02	0.13	1.94	19.40
BDE-154	0.007	7	9	<MDL	0.01	<MDL	1.16
BDE-183	0.007	3	4	<MDL	<MDL	<MDL	<MDL
BDE-196	0.007	2	3	<MDL	<MDL	<MDL	<MDL
BDE-197	0.007	28	36	<MDL	0.02	<MDL	2.01
BDE-201	0.007	2	3	<MDL	<MDL	<MDL	<MDL
BDE-202	0.007	0	0	<MDL	<MDL	<MDL	<MDL
BDE-203	0.007	1	1	<MDL	<MDL	<MDL	<MDL
BDE-206	0.009	3	4	<MDL	<MDL	<MDL	<MDL
BDE-207	0.009	18	23	<MDL	0.02	<MDL	3.02
BDE-208	0.009	7	9	<MDL	0.01	<MDL	1.45
BDE-209	0.045	41	53	0.05	0.14	5.15	16.00
OH-BDEs							

2′-OH-BDE-68	0.008	5	6	<MDL	0.01	--	--
4′-OH-BDE-049	0.008	31	40	<MDL	0.04	--	--
5′-OH-BDE-047	0.006	55	71	0.01	0.09	--	--
OH-BDE-099	0.012	0	0	<MDL	<MDL	--	--
PCBs							
PCB-66	0.009	4	5	<MDL	0.01	<MDL	1.02
PCB-74	0.008	8	10	<MDL	0.01	<MDL	1.59
PCB-99	0.014	14	18	<MDL	0.02	<MDL	2.98
PCB-101	0.016	15	19	<MDL	0.02	<MDL	3.25
PCB-105	0.010	5	6	<MDL	0.01	<MDL	1.06
PCB-118	0.014	24	31	<MDL	0.03	<MDL	3.70
PCB-138	0.006	72	94	0.02	0.05	1.90	5.11
PCB-153	0.011	67	87	0.03	0.07	3.02	7.85
PCB-156	0.005	19	25	<MDL	0.01	<MDL	1.13
PCB-170	0.005	42	55	0.01	0.02	0.61	1.95
PCB-180	0.007	67	87	0.02	0.06	1.79	5.75
PCB-183	0.012	2	3	<MDL	<MDL	<MDL	<MDL
PCB-187	0.009	22	29	<MDL	0.02	<MDL	2.25
PCB-194	0.007	12	16	<MDL	0.01	<MDL	1.42
PCB-203	0.007	20	26	<MDL	0.02	<MDL	2.98
OCPs							
2,4′-DDT	0.005	5	6	<MDL	0.01	<MDL	1.52
4,4′-DDE	0.005	77	100	0.77	15.11	94.30	1520.00
4,4′-DDT	0.005	19	25	<MDL	0.27	<MDL	35.20
HCB	0.034	77	100	0.07	0.13	8.43	16.90
b-HCH (Lindane)	0.005	49	64	0.01	0.17	1.59	20.60
Oxychlordane	0.005	51	66	0.01	0.03	0.93	5.02
trans-nonachlor	0.006	60	78	0.01	0.06	1.80	6.68

PFCs							
N-EtFOSAA	0.011	40	52	0.01	0.03	--	--
N-MeFOSAA	0.013	75	97	0.06	0.39	--	--
PFBS	0.022	4	5	<MDL	0.02	--	--
PFDeA	0.032	20	26	<MDL	0.78	--	--
PFDoA	0.036	3	4	<MDL	<MDL	--	--
PFHpA	0.059	25	32	<MDL	0.20	--	--
PFNA	0.075	76	99	0.79	2.14	--	--
PFOA	0.301	49	64	0.47	2.11	--	--
PFOS	0.083	77	100	2.43	7.25	--	--
PFOSA	0.009	69	90	0.02	0.07	--	--
PFUA	0.010	71	92	0.17	0.60	--	--
Metals							
Cd	0.140	64	83	0.22	0.49	--	--
Pb (µg/dL)	0.27	77	100	0.60	2.14	--	--
Hg	0.064	77	100	0.46	1.62	--	--
Chemicals in urine (N=89)							
Metals				*(µg/L)*		*(µg/g creatinine)*	
Total arsenic	0.158	89	100	8.15	40.00	8.03	44.60
OH-PAHs [a]							
OH-2-fluo	0.0200	88	100	0.19	1.07	0.23	0.65
OH-3-fluo	0.0200	75	85	0.05	0.35	0.05	0.30
OH-9-fluo	0.0370	88	100	0.54	2.17	0.59	2.08
OH-1-nap	0.0250	88	100	0.86	9.15	1.11	7.33
OH-2-nap	0.0200	88	100	6.78	38.50	7.52	28.30

[a] N=88 for OH-PAHs due to limited sample quantity.

OH-1-phen	0.0100	88	100	0.20	0.82	0.22	0.61
OH-2-phen	0.0100	88	100	0.09	0.30	0.12	0.31
OH-3-phen	0.0100	88	100	0.07	0.24	0.08	0.20
OH-1-pyr	0.0200	87	99	0.21	0.79	0.23	0.60
Phthalate metabolites							
MBzP	0.25	89	100	6.54	110.00	8.81	72.30
MCHP	0.50	3	3	<MDL	<MDL	<MDL	<MDL
MCPP	0.13	89	100	0.75	5.58	1.00	3.36
MECPP	0.50	89	100	14.60	125.00	18.90	101.00
MEP	8.00	81	91	103.00	996.00	98.70	800.00
MnBP	2.00	87	98	16.20	93.90	19.10	113.00
Phenols							
Benzophenone-3	0.50	83	93	25.45	2250.00	26.60	3500.00
Bisphenol-A	0.20	84	94	1.26	6.75	1.41	5.57
Triclosan	1.0	78	88	11.10	970.00	10.90	1210.00
Pesticide metabolites							
DEDTP	0.10	2	2	<MDL	<MDL	<MDL	<MDL
DEP	0.50	60	67	1.76	8.56	1.72	7.59
DMDTP	1.0	2	2	<MDL	<MDL	<MDL	<MDL
DMTP	0.50	7	8	<MDL	8.09	<MDL	8.80
3-PBA	0.40	23	26	<MDL	3.14	<MDL	3.55
TCPy	0.20	63	71	0.53	3.38	0.50	3.14

Table 3-3 Average chemical concentrations across strata of educational attainment in the blood (N=77), serum (N=77), and urine (N=89[b]) of pregnant women from San Francisco. Geometric mean ratios (GMRs) are in comparison to the most educated group. Differences that were statistically significant at $P < 0.05$ are shown in bold. Color coding reflects whether adjusted GMRs among the subset of pregnant participants in NHANES 1999-2012 qualitatively agreed or disagreed with those from the CIOB participants. For example, results from both studies suggested higher concentrations of PFOS with increasing educational attainment (adjusted GMRs > 1 for those with less education compared to most educated group). These were considered qualitatively similar and are colored blue. In contrast, analysis of the CIOB results suggests lower concentrations of BDEs -44, -99, and -100 among the less educated compared to those with more education (adjusted GMRs < 1). Because my analysis of the NHANES results suggested the opposite trend (adjusted GMRs > 1 for less educated women compared to women with more education), there findings were considered qualitatively different and these cells in the table are colored brown.

Same direction & statistically significant in NHANES
Same direction & not statistically significant in NHANES
Opposite direction & statistically significant in NHANES
Opposite direction & not statistically significant in NHANES

	Geometric mean concentrations			Unadjusted GMRs		Adjusted GMRs [95% CI][c]	
	< HS	HS or GED	> HS	< HS	HS or GED	< HS	HS or GED
Chemicals in serum (ng/g lipid)							
BDE-47	7.5	10.3	19.9	0.38	0.52	**0.47 [0.27 , 0.83]**	0.57 [0.32 , 1.01]
BDE-99	3.2	6.0	8.6	0.37	0.70	**0.53 [0.32 , 0.89]**	0.71 [0.44 , 1.14]
BDE-100	1.9	2.6	4.6	0.40	0.55	**0.50 [0.26 , 0.94]**	0.63 [0.33 , 1.20]
BDE-153	2.1	3.0	6.9	0.31	0.43	0.70 [0.39 , 1.28]	0.77 [0.42 , 1.43]
PCB-138	1.9	1.9	2.8	0.67	0.67	0.85 [0.63 , 1.15]	0.76 [0.55 , 1.03]
PCB-153	3.3	2.7	4.9	0.67	0.56	0.79 [0.57 , 1.10]	**0.69 [0.49 , 0.96]**

[b] *N*=88 for OH-PAHs due to limited sample quantity.

[c] GMRs are adjusted for maternal age (in years), month of gestation (chemicals in blood and serum only), race/ethnicity (U.S.-born White, U.S.-born Black, U.S.-born Hispanic, foreign-born Hispanic, and Other), total lipid content (lipophilic chemicals only, which were modeled as wet-weight concentrations), creatinine (chemicals in urine only), and smoking during pregnancy (Cd and OH-PAHs only). Adjusted estimates were calculated utilizing multiple imputation to account for observations < MDL.

PCB-180	2.2	1.9	3.2	0.69	0.61	0.73 [0.51 , 1.06]	0.71 [0.50 , 1.01]
4,4′-DDE	137.1	93.9	92.1	1.49	1.02	0.92 [0.45 , 1.89]	0.75 [0.36 , 1.57]
HCB	7.6	9.1	9.0	0.84	1.01	0.96 [0.78 , 1.17]	1.05 [0.86 , 1.30]
Oxychlordane	1.3	1.7	2.2	0.58	0.77	0.95 [0.60 , 1.52]	1.14 [0.72 , 1.81]
t-nonachlor	2.1	2.7	2.5	0.83	1.08	1.03 [0.70 , 1.51]	1.35 [0.91 , 2.01]
b-HCH (lindane)	5.8	3.2	2.9	2.01	1.12	1.19 [0.49 , 2.88]	1.01 [0.41 , 2.49]
5'-OH-BDE-047	0.02	0.026	0.03	0.52	0.79	0.51 [0.25 , 1.07]	0.77 [0.37 , 1.61]
N-MeFOSAA	0.05	0.08	0.12	0.44	0.66	0.63 [0.39 , 1.02]	0.74 [0.45 , 1.21]
PFNA	0.74	0.71	0.85	0.87	0.84	0.73 [0.46 , 1.15]	0.78 [0.49 , 1.24]
PFOA	0.73	0.58	0.87	0.84	0.66	0.92 [0.59 , 1.44]	0.76 [0.49 , 1.18]
PFOS	2.5	2.4	2.8	0.87	0.85	1.13 [0.75 , 1.69]	1.01 [0.67 , 1.54]
PFOSA	0.02	0.02	0.03	0.68	0.82	0.64 [0.41 , 0.99]	0.70 [0.45 , 1.08]
PFUA	0.22	0.13	0.15	1.47	0.86	0.81 [0.40 , 1.62]	0.69 [0.34 , 1.42]
Chemicals in blood (µg/L)							
Cadmium	0.24	0.25	0.27	0.88	0.92	1.14 [0.88 , 1.47]	1.03 [0.79 , 1.34]
Lead	0.71	0.62	0.61	1.17	1.02	1.05 [0.73 , 1.52]	0.96 [0.66 , 1.38]
Mercury	0.48	0.39	0.43	1.11	0.91	1.21 [0.70 , 2.09]	0.96 [0.55 , 1.68]
Chemicals in urine (µg/g creatinine)							
Total arsenic	9.6	10.7	8.7	1.11	1.23	1.15 [0.73 , 1.79]	1.14 [0.73 , 1.78]
OH-2-fluo	0.25	0.24	0.22	1.13	1.07	**1.53 [1.06 , 2.22]**	1.13 [0.78 , 1.64]
OH-3-fluo	0.06	0.08	0.08	0.84	1.05	**1.57 [1.03 , 2.41]**	1.22 [0.81 , 1.84]
OH-9-fluo	0.76	0.55	0.63	1.20	0.87	**1.47 [1.00 , 2.17]**	0.87 [0.59 , 1.28]
OH-1-nap	1.24	1.42	1.15	1.08	1.24	1.48 [0.85 , 2.58]	1.36 [0.78 , 2.37]
OH-2-nap	8.38	9.94	6.23	1.34	1.60	1.19 [0.78 , 1.80]	1.25 [0.82 , 1.89]
OH-1-phen	0.27	0.22	0.22	1.21	1.00	1.23 [0.86 , 1.77]	0.86 [0.60 , 1.24]
OH-2-phen	0.13	0.12	0.10	1.28	1.18	**1.36 [1.00 , 1.87]**	1.12 [0.82 , 1.54]
OH-3-phen	0.09	0.08	0.08	1.15	1.05	**1.58 [1.12 , 2.23]**	1.10 [0.78 , 1.56]
OH-1-pyr	0.23	0.25	0.23	1.01	1.07	1.25 [0.88 , 1.77]	1.07 [0.75 , 1.52]
MnBP	23.5	17.6	19.5	1.21	0.90	1.10 [0.66 , 1.84]	0.86 [0.51 , 1.43]

MBzP	8.5	7.1	15.8	0.54	0.45	0.82 [0.46 , 1.46]	0.58 [0.33 , 1.02]
MCPP	1.08	1.11	1.00	1.07	1.10	1.05 [0.72 , 1.53]	1.07 [0.73 , 1.56]
MECPP	23.5	21.5	16.9	1.39	1.27	1.27 [0.78 , 2.08]	1.19 [0.73 , 1.94]
MEP	187.0	151.5	104.5	1.79	1.45	0.91 [0.42 , 1.94]	0.92 [0.43 , 1.96]
Benzophenone-3	67.1	39.6	49.5	1.36	0.80	1.37 [0.39 , 4.86]	0.64 [0.18 , 2.23]
Bisphenol-A	1.3	1.9	1.8	0.72	1.04	0.89 [0.60 , 1.33]	1.11 [0.75 , 1.65]
Triclosan	24.4	49.3	27.2	0.90	1.82	0.40 [0.07 , 2.30]	1.43 [0.26 , 8.01]
DEP	2.3	3.0	3.4	0.67	0.87	0.78 [0.45 , 1.34]	0.76 [0.43 , 1.33]
TCPy	0.7	1.1	0.8	0.86	1.28	1.00 [0.58 , 1.73]	1.50 [0.86 , 2.64]

Table 3-4 Chemical concentrations in the blood, serum and urine of pregnant women aged 13-50 in NHANES 1999-2012.[d]

		Sample years	Sample size	MDL[e]	% detected	Median[c]	95th percentile[f]
Chemicals in blood or serum							
PBDEs (ng/g lipid)							
	BDE-17	2003-4	74	1.0	5	<MDL	0.4
	BDE-28	2003-4	75	0.8	92	1.3	3.8
	BDE-47	2003-4	75	4.2	99	23.7	100.0
	BDE-66	2003-4	72	1.0	26	<MDL	0.7
	BDE-85	2003-4	73	2.4	34	<MDL	2.2
	BDE-99	2003-4	75	5.0	84	5.1	21.8
	BDE-100	2003-4	75	1.4	97	6.6	23.2
	BDE-153	2003-4	75	2.2	100	7.8	127.0
	BDE-154	2003-4	75	0.8	67	0.5	2.3
	BDE-183	2003-4	74	1.7	19	<MDL	1.0
PCBs (ng/g lipid)							
	PCB-66	1999-2004	262	12.4	32	<MDL	7.8
	PCB-74	1999-2004	264	12.4	50	<MDL	7.9
	PCB-99	1999-2004	261	12.5	44	<MDL	9.5
	PCB-101	1999-2004	262	25.7	31	<MDL	9.9
	PCB-105	1999-2004	262	12.4	32	<MDL	4.9

[d] Includes all women under age 50 with a positive urine pregnancy test and who were tested for at least one of the chemicals in the Chemicals in Our Bodies study. Pooled samples were excluded. Total N = 1,434.

[e] For lipophilic compounds (PBDEs, PCBs and OCPs), the MDL varies by individual and the highest lipid-adjusted MDL is reported. This is why, for some chemicals, the median or 95th percentile is below the reported MDL.

[f] Percentile point estimates make use of survey weights averaged across the survey years.

	PCB-118	1999-2004	264	12.5	56	4.2	13.4
	PCB-138	1999-2004	264	41.4	64	9.2	25.5
	PCB-153	1999-2004	263	55.6	70	12.7	31.8
	PCB-156	1999-2004	261	12.5	30	<MDL	5.4
	PCB-170	1999-2004	255	17.2	46	<MDL	9.5
	PCB-180	1999-2004	263	28.2	59	6.8	23.5
	PCB-183	1999-2004	261	12.4	27	<MDL	4.9
	PCB-187	1999-2004	264	12.4	40	<MDL	9.2
	PCB-194	2001-4	178	10.5	37	<MDL	6.5
OCPs (ng/g lipid)							
	2,4'-DDT	1999-2004	241	20.7	2	<MDL	<MDL
	4,4′-DDE	1999-2004	257	18.6	100	117.0	1340.0
	4,4′-DDT	1999-2004	243	20.7	39	<MDL	5.2
	HCB	1999-2004	247	118	30	<MDL	44.5
	b-HCH (lindane)	1999-2004	256	9.36	55	3.2	31.2
	Oxychlordane	1999-2004	237	14.5	63	4.9	11.4
	trans-nonachlor	1999-2004	255	14.5	82	8.0	19.9
PFCs (µg/L)							
	N-EtFOSAA	1999-2000;2003-12	299	0.4	25	<MDL	0.5
	N-MeFOSAA	1999-2000;2003-12	299	0.523	64	0.3	1.0
	PFBS	2003-12	220	0.4	2	<MDL	<MDL
	PFDeA	1999-2000;2003-12	299	0.3	47	<MDL	0.8
	PFDoA	1999-2000;2003-12	299	1	3	<MDL	<MDL
	PFHpA	1999-2000;2003-12	299	0.4	7	<MDL	0.4
	PFNA	1999-2000;2003-12	299	0.1	97	0.7	1.9
	PFOA	1999-2000;2003-12	299	0.2	99	2.2	5.7
	PFOS	1999-2000;2003-12	299	0.4	100	7.8	23.8
	PFOSA	1999-2000;2003-12	299	0.1	32	<MDL	0.3
	PFUA	1999-2000;2003-12	299	0.3	20	<MDL	0.4

Metals						
Cd *(µg/L)*	1999-2012	1069	0.3	67	0.3	0.8
Pb *(µg/dL)*	1999-2012	1069	0.3	97	0.6	1.5
Hg *(µg/L)*	2003-2012	769	0.33	84	0.7	2.9
Chemicals in urine						
Metals (µg/L)						
Total arsenic	2003-12	252	1.25	99	8.9	66.6
OH-PAHs (µg/L)						
OH-2-fluo	2003-8; 2011-12	249	0.01	100	0.2	1.0
OH-3-fluo	2001-8; 2011-12	352	0.01	97	0.0	0.3
OH-9-fluo	2003-8; 2011-12	244	0.01	100	0.2	1.3
OH-1-nap	2001-8; 2011-12	357	0.048	100	1.0	27.8
OH-2-nap	2001-8; 2011-12	360	0.042	100	2.4	18.3
OH-1-phen	2001-8; 2011-12	358	0.01	100	0.1	0.6
OH-2-phen	2001-8; 2011-12	354	0.01	97	0.1	0.2
OH-3-phen	2001-8; 2011-12	353	0.01	99	0.0	0.3
OH-1-pyr	2003-8; 2011-12	244	0.01	100	0.1	0.4
Phthalate metabolites (µg/L)						
MBzP	1999-2012	503	0.576	99	10.7	28.4
MCHP	1999-2010	485	1.81	6	0.4	1.3
MCPP	2001-12	396	0.4	93	2.1	10.1
MECPP	2003-12	285	0.6	100	19.2	265.3
MEP	1999-2012	503	0.792	100	89.2	1541.3
MnBP	1999-2012	503	1.1	99	18.3	150.3
Phenols (µg/L)						
benzophenone-3	2003-12	281	0.4	98	26.2	2070.0
bisphenol-A	2003-12	281	0.4	92	1.5	11.2
triclosan	2003-12	281	2.3	81	16.5	597.0

Pesticide metabolites (µg/L)						
DEDTP	1999-2008	419	0.39	18	<MDL	0.4
DEP	1999-2008	431	0.37	49	<MDL	11.4
DMDTP	1999-2008	428	0.51	40	<MDL	9.1
DMTP	1999-2008	431	0.55	69	2.0	36.8
3-PBA	1999-2002; 2007-10	232	0.1	68	0.2	2.5
TCPy	1999-2002; 2007-10	234	0.4	81	1.4	8.2

Chapter 4

Social disparities in vulnerability to climate change: heat and preterm birth

Abstract

Climate change is predicted to increase the frequency, duration and intensity of extreme heat events, and there is some evidence that acute exposure to high ambient temperatures increases the risk of preterm birth. Previous studies of heat waves have found that people of color suffer greater heat-related mortality and morbidity. This raises the possibility that climate change could worsen existing racial and ethnic disparities in preterm birth rates. I examined this possibility using five years of birth records from Harris County, TX, during a time period (2007-2011) that encompasses an unusually hot summer. I used survival analysis methods to model the risk of being born preterm (<37 completed weeks) up to a week after unusually hot days defined three different ways: daily maximum apparent temperature (AT_{max}) ≥ 40 °C, both maximum (T_{max}) and minimum (T_{min}) dry-bulb temperatures above the 90th percentile of historical (1971-2000) summer months (JJA), and the second or more consecutive day meeting the previous criteria of T_{max} and T_{min} above the JJA 90th percentile ("heat wave day"). I found an elevated but statistically insignificant risk of preterm birth immediately following hot days. Controlling for secular trend and individual risk factors, hot days were associated with a 3-8% increase in the risk of premature birth the following day, depending on the definition used (hazard ratios [95% CI]: 1.08 [0.96, 1.20] for AT_{max} ≥ 40°C vs. < 20°C; 1.03 [0.96, 1.11] for T_{max} and T_{min} above the JJA 90th percentile; and 1.04 [0.94, 1.14] for heat wave days). Although Black, Hispanic, and Asian/Pacific Islander mothers were more likely to live in neighborhoods with heat-trapping land cover and few trees, I found no evidence that such land cover characteristics increased the effect of heat on preterm birth. The lack of strong evidence of a heat effect may be due to acclimation and behavioral and infrastructural adaptation to hot weather on the part of Harris County residents. This study demonstrates one approach for investigating climate change health impacts from an environmental justice perspective that can inform adaptation planning.

Introduction

Preterm births remain a major public health concern in the U.S., where nearly half a million babies are born prematurely each year.[73] In contrast, rates of prematurity among other high income countries are less than 10% and as low as 5.5%, with the U.S. preterm birth rate surpassing that estimated for lower income countries such as Rwanda (9.5%), Vietnam (9.4%), Lebanon (7.9%), Mexico (7.3%), Morocco (6.7%) and Cuba (6.4%).[181] Prematurity is a primary cause of infant mortality[182] and can lead to later health problems including asthma,[183,184] cognitive and behavioral outcomes in children,[185] and cardiovascular and other chronic medical conditions into adulthood.[186,187] Infants are generally considered preterm if born before completing 37 weeks of gestation, extremely premature if born before completing 27 weeks of gestation, and low birth weight if they weigh less than 2,500 grams at birth (about 5.5 pounds). Maternal risk factors for preterm delivery include chronic infections, hypertension, stress, smoking, poor nutritional status, lack of prenatal care, low body mass index (BMI)[188] as well as exposure to air pollution[189,190] and pesticides.[191]

Racial disparities in preterm birth rates are large and troublingly persistent.[192] While all groups have experienced a decline in preterm birth rates since 2007, the rate remains 60% higher for Black infants than White infants (17.1% vs. 10.8%).[73] Native American (13.6%) and Hispanic (11.8%) infants are also at higher risk than Whites and Asian/Pacific Islanders (PI). The rate of early preterm births (<34 completed weeks) among Black infants is more than double that of Whites (6.1% vs. 2.9%).[73] These racial disparities do not appear to be explained entirely by differences in the mothers' preconceptual health or prenatal care.[193] Several studies demonstrate that individual experiences of racism contribute to racial disparities in preterm birth and very low birth weigth.[194,195]

Studies from the Gambia, Germany, Greece, Israel, Japan, the U.S. and Zimbabwe suggest preterm birth rates tend to peak in summer, winter, or both, suggesting that temperature extremes may also be a cause.[196,197] However the mechanisms by which extreme temperatures could lead to preterm birth remain poorly understood. Laboratory studies with ewes and pregnant women suggest that acute heat stress can cause uterine contractility and the release of hormones that induce labor.[198,199] Pregnant women may also be at greater risk of heat stress.[200] Weight gain and fetal growth raise a woman's basal metabolic rate during pregnancy.[201] At the same time, pregnant women are less able to dissipate body heat via evaporative cooling (sweating) because of the decrease in their surface-area-to-body-mass ratio. The fat deposition associated with pregnancy also increases the specific heat of the body, resulting in a greater sensitivity of core temperature to thermal stress.[202] The fetus also contributes to maternal heat stress directly through its metabolism.[203] Dehydration may also induce uterine contractions.[189] Eclampsia and preeclampsia, risk factors for preterm birth, also exhibit seasonality, although most studies indicate higher risks for women delivering during colder months.[197]

Several epidemiological studies suggest that acute exposure to high ambient temperature may increase the risk of preterm birth, which is worrisome given that climate change is causing extreme heat events to become more frequent, longer, and more intense.[204] Lajinian and colleagues (1997) found an association between heat-humidity index and preterm labor among births at a Brooklyn, NY hospital.[205] The risk of preterm births was also associated with higher temperatures in a study from Israel[206] and a study from Greece found that the mean temperature during the month of birth was negatively correlated with gestational age.[207] In a study of almost 60,000 births in California during the warm (May-September) months of 1999-2006, Basu and colleagues (2010) found an 8.6% increase in preterm delivery per 10°F increase in average apparent temperature (AT) during the week prior to birth.[208] Risks were elevated for mothers under the age of 20, Black, and Asian mothers. Strand and colleagues (2011) looked at preterm birth and stillbirth among over 100,000 births in Brisbane, Australia during 2005-9 and found an association between higher-than-average mean temperature during the last week of pregnancy and delivering preterm for pregnancies with gestational ages greater than 28 weeks.[209] The pattern was similar when the average temperature over the last four weeks of pregnancy was considered, while reduced risk was observed at the most extreme temperatures, possibly because of precautionary behavior on the part of expectant mothers at these highest temperatures. Wang and colleagues (2013) also looked at births in Brisbane in relation to several different definitions of short-term exposure to heat waves and found a 13 to 100% increase in the risk of preterm birth depending on the definition used.[210] Schifano and colleagues (2013) found a 1.9% increase in preterm births per 1°C increase in maximum AT the 2 days preceding delivery during 2001-2010 warm season births in Rome, with younger mothers (< 20 years of age) again being at higher

risk. The authors also found a 19% increase in preterm births associated with heat waves, defined as at least two consecutive days with maximum AT above the monthly 90th percentile or the daily minimum temperature above the monthly 90th percentile and maximum AT above the median monthly value of the 1987–2010 period, excluding 2003.[211] At least one study also suggests exposure to high temperatures over the duration of the pregnancy may increase the risk of preterm birth.[212] Other epidemiological time series analyses have found no association between ambient temperature and preterm birth.[213–215]

Two studies of preterm birth and heat suggest that Black, Asian,[208] and Indigenous Australian[210] mothers are at increased risk compared to other groups. Elevated vulnerability to heat-related mortality and morbidity among Blacks is well documented,[216–223] although not all studies have found this and, in at least one instance, Whites were more adversely affected than other groups.[224] Several studies suggest Hispanics are also at greater risk of heat-related morbidity than other groups.[225–228] Possible explanations for racial/ethnic differences in vulnerability to heat include occupation and the ability to control one's work environment (e.g. take breaks and seek shade) and housing characteristics (e.g. ventilation and whether air conditioning is present). Another possible explanation is higher prevalence of pre-existing diseases that increase susceptibility to heat-related illness and/or require the use of medications that reduce perceptions of heat or suppress thermoregulatory responses such as thirst.[229] Finally, racial residential segregation has resulted in differences in physical and social neighborhood environments that may change neighborhood microclimates and behavior during extreme heat events. In his ethnography of the Chicago heat wave of 1995, Eric Klinenberg concluded that social isolation of seniors living alone in poor, institutionally abandoned neighborhoods led to higher death rates among older Blacks than other groups.[230] People of color also live in neighborhoods with a lower prevalence of trees, which provide shade and evapotransporative cooling, and a higher prevalence of heat-trapping impervious surfaces such as asphalt and concrete, which may contribute to greater localized heat-island effects.[22]

Methods

Study site

I investigated the possibility of racial/ethnic differences in the effect of high ambient temperatures on preterm birth using five years of birth records (2007-11) from Harris County, Texas. Texas is a diverse state with some of the largest disparities in health and income in the nation.[231] Prior to the Affordable Care Act, Texas had the lowest health insurance coverage in the country with more than half of Hispanics lacking coverage, and it exhibits greater racial disparities in access to care than other states.[232] Racial disparities in preterm birth mirror those of the nation, with Black and Hispanic infants having higher rates than White or Asian/PI infants (16.6% and 12.5% vs. 11.1% and 10.7%, respectively).[233]

In 2011, Texas experienced its hottest summer since record keeping began in 1895. June, July, August average temperatures across the state were roughly 2.5 °F warmer than any previous summer and over 5 °F above the long-term average. An unusually high number of days reached or exceeded 100 °F.[234] The event was associated with La Niña and exacerbated by the lack of rainfall prior to and during the summer, which reduced evapotransporative cooling.[235] An extended drought also contributed to widespread wildfires that burned over 4 million acres

statewide in what is considered one of the worst fire seasons in history.[236] Research on extreme events and the probability of summertime temperatures of this intensity suggest that the 2011 heat wave would have been very unlikely without anthropogenic global warming.[237]

Given this context, Texas has the potential for large disparities in health vulnerability to extreme heat events and climate change more generally, although until recently the region has received little scholarly attention in this regard.[47,238,239] One study of Houston found increased emergency department visits during the 2011 heat wave, particularly among those 65 years and older, but no excess deaths.[240] Provisional data from the Texas Department of State Health Services suggested that statewide, 159 people died from exposure to excessive natural heat (Marc Montrose, personal communication). By comparison, Texas typically averages slightly more than 30 heat-related deaths during the summer months.[241] Neither of these figures include deaths related to cardiovascular or respiratory illness, rates of which are often also elevated during heat waves.

Study objectives and design

In this study I linked 2007-2011 birth records from Harris County (where Houston is located, and where approximately one fifth of births in the state of Texas occurred during this period) to daily temperature and humidity data from 10 nearby weather stations. Using visual examination of time series and survival analysis methods, I attempted to establish whether acute exposure to high ambient temperatures during the week prior to birth was associated with a greater risk of preterm delivery independent of known individual-level risk factors. I also examined whether particular groups were at higher risk depending on their race/ethnicity and health status, and whether neighborhood land cover characteristics modified the risk. Study protocols were approved by the institutional review boards at Texas Department of State Health Services (#13-047) and the University of California, Berkeley (#2013-07-5481).

Many studies of the relationship between temperature and health control for ozone and particulate matter (PM) air pollution as potential confounders because both are correlated with temperature in many locations. I considered PM and ozone as causal intermediates on the pathway between heat exposure and preterm birth because sunlight and high temperatures promote their formation from precursor molecules in the atmosphere.[242,243] I treated ozone and PM as mediators rather than confounders and sought to estimate the combined direct and indirect effect of heat on preterm birth via increased air pollution (**Figure 4-1**).[244]

Birth data

I obtained geo-coded birth records from the Texas Department of State Health Services (TDSHS) for the years 2007-11. Births were eligible for inclusion if they were not an induced labor (78% of all births) and contained a valid date of last menstrual period (LMP) (95.8% of all births). If a month and/or year but no day of LMP was reported, LMP was considered missing. Gestational age was measured in days from the date of LMP.

The birth records were geo-coded by TDSHS using Centrus Desktop produced by Pitney Bowes (Stamford, CT) (personal communication with Leon Kincy, TDSHS). To assess geo-coding accuracy, I geo-coded the records for the entire state using an alternative method, the NA Streets Composite US geocoder in ArcGIS 10.2 (ESRI, Redlands, CA) with default settings. Overall,

street- and zip code- level match rates for the two methods were 95.0%, 91.8% and 3.2% (Centrus) and 99.5%, 88.3% and 11.2% (ArcGIS), respectively. Among records geo-coded to street level by both methods, differences ranged from 0.0001 to 338 km with 99% of records being located within 155 meters of each other by the two methods. Given its higher street-level match rate, I used the results of the Centrus geo-coding and included only births matched to the street level (center of road segment, intersection, or address).

Exclusion criteria and the construction of the sample population are illustrated in **Figure 4-2**. Births prior to 20 or more than 42 completed weeks, multiple births, birth anomalies, and births with an improbable combinations of gestational age and birth weight (following Alexander 1996)[245] were excluded. An additional 1.6% of births were excluded because the mother's residential addresses could not be successfully geo-coded to the street level. The success of geo-coding was not differential with respect to induction of labor, the distribution of maternal or gestational ages, preeclampsia, or other variables considered in the analysis. Of these geo-coded births, a further 12.5% were excluded because they were not within 20km of a weather station.

Births conceived prior to August 14, 2006 (19 weeks, 6 days prior to the beginning of the study period) or after March 6, 2011 (42 weeks, 6 days prior to the end of the study period) were excluded in order to control for "truncation" or "fixed cohort" bias. Truncation bias arises in retrospective observational studies that restrict on the date of birth because longer pregnancies are over-represented at the beginning of the study period and shorter pregnancies are over-represented at the end of the study (see **Figure 4-3**).[246] This could be problematic in my study because 2011 was an unusually hot year, which could lead to a spurious association between hotter temperatures and shorter gestation. Restricting on conception date ensures that all women who were pregnant at the same time as women who delivered during the study period are included in the study.

Pregnancies with one or more of the following, mutually exclusive risk factors were designated as high risk: diabetes (gestational or pre-pregnancy diagnosis), hypertension (including pre-pregnancy and pregnancy-induced), preeclampsia or eclampsia. Adequacy of prenatal care was characterized using an index which contains two dimensions, following Kotelchuck (1994) (**Table 4-1**): the month prenatal care and the fraction of recommended visits, adjusted by gestation length and initiation of care.[247] Current guidelines are a visit every 4 weeks for the first 28 weeks starting week 8-10, every 2-3 weeks until 36 weeks, and every week thereafter (e.g., 14 visits for a 40 week pregnancy).[248] No prenatal care (index=0) was assumed if a) the month of prenatal care initiation was zero and the number of visits was missing or zero or b) if the number of visits was zero and the month care was initiated was missing or zero.

Temperature

Sub-hourly weather data from the Global Historical Climatology Network (GHCN) were downloaded for the entire State of Texas from the NOAA's Climate Data Online portal (http://www.ncdc.noaa.gov/cdo-web/). Air temperature observations flagged as suspect or erroneous were removed (<3% of observations). Daily maximum apparent temperature (AT)

were estimated using the day's maximum dry-bulb temperature and mean vapor pressure using the formula given in Steadman (1984):

$$\text{Vapor pressure: } E\ (kPA) = 0.611 \times 10^{(7.5 \times DPT)/(237.3+DPT)} \quad \text{[Eq 1]}$$

$$\text{Apparent temperature: } AT\ (°C) = -1.3 + 0.92T + 2.2E \quad \text{[Eq 2]}$$

Where *T* is the dry-bulb air temperature in °C, *DPT* is the dew point temperature in °C, and *E* is the actual vapor pressure in kPa. In instances where DPT was missing or flagged as suspect or erroneous, the DPT from the nearest station was substituted. Daily temperature records were also excluded if they were derived from observations spanning less than 8 consecutive hours of the day (< 1% of station-days). The resulting dataset was narrowed to 10 weather stations within 20km of a Harris County mother's residence, some of which lay outside the county and some of which were only operational during portions of the study period.

NOAA's GHCN-daily product was used to obtain June, July and August (JJA) daily extremes of dry-bulb air temperature from 1971-2000 from the two locations in the county operational throughout the thirty years: George W. Bush International Airport and Hobby Airport. These records were used to calculate historical averages for summertime minimum and maximum air temperatures after removing observations that failed quality assurance check. Unusually hot days during the study period were defined as those with both minimum and maximum air temperatures over their respective historical summertime 90th percentiles. A "heat wave day" was defined as the second or more consecutive day in a row meeting this criterion.

Neighborhood variables

Census tracts were used as an estimate of each mother's neighborhood of residence at the time of birth and served as the basis for assigning neighborhood-level variables using 2011 vintage TIGER/Line files[l] for the census tract boundaries. The percent of a census tract that is covered by impervious surfaces and tree canopy were estimated from 2011 National Land Cover Database (NLCD) products. The NLCD is a remote sensing product derived from Landsat satellite imagery that estimates the percent of land area that is covered in impervious surfaces and tree canopy at 30 x 30m resolution.[249] From this, the percent cover for each land cover type was estimated as the mean of the grid cells with some portion falling within the tract using the Zonal Statistics tool in ArcMap 10.3 (ESRI, Redlands, CA) after projecting census tract boundaries to match the projection of the NLCD products. These NLCD products do not distinguish water bodies, and the percent of each census tract covered in water was obtained separately from the TIGER/Line files.

Land cover was characterized as low or high heat risk using a two-part index similar to Jesdale *et al.* (2013). High heat risk tracts were defined as those with none of their area covered in water, less than 5% of their area covered in tree canopy, and more than 60% of their area covered in impervious surfaces. These cutoffs corresponded roughly to the 20th and 75th percentile of the

[l] Available at https://www.census.gov/geo/maps-data/data/tiger-line.html (accessed December 15, 2015)

observed range of canopy and impervious surface cover among tracts in Harris County, respectively.

Analytic strategy

I examined descriptive statistics for all variables and compared crude preterm birth rates by risk factors defined *a priori* based on previous studies. The relationship between temperature and preterm birth rate was examined graphically by plotting a time series of temperature at one weather station (George W. Bush International airport) and the daily preterm birth rate across all geo-coded births in the county.

I then examined the risk of preterm birth using a series of Cox proportional hazards models with gestational age (in days) rather than calendar time as the time axes. This accounts for the fact that the likelihood of giving birth increases with gestational age and ensures that the model estimates the likelihood of preterm birth versus staying pregnant among pregnancies at the same stage of pregnancy.[250] It also helps address the fact that seasonal patterns in conception result in changes in the underlying distribution of gestational ages and baseline risk of birth through time.[251] This as well as the ability to incorporate time-varying confounders is a strength of this study design over others. Pregnancies entered the study at 20 completed weeks (140 days) and were censored at 37 completed weeks (259 days) when they were no longer at risk of preterm birth. The Efron method was used to handle ties because it has been shown to be the least biased.[252]

The first set of models included only two independent variables: one temperature variable and the number of days since January 1, 2007, which was included to control for any secular decrease in preterm birth rates. I considered the following temperature measures in separate models: the day's maximum apparent temperature (AT_{max} in 5°C increments), whether the daytime high (T_{max}) and nighttime low (T_{min}) of dry-bulb temperatures both exceeded the historical (1971-2000) summertime (JJA) 90th percentile (indicator variable), and whether the day qualified as a "heat wave day" (indicator variable). Heat wave days were defined as the second or more consecutive day with T_{max} and T_{min} above the historical JJA 90th percentiles. Lagged variables up to a week prior week (lag_1-lag_7) were considered for each of these variables. I also examined average AT_{max} over the three days (lag_1-lag_3) and seven days (lag_1-lag_7) prior to birth.

The second set of models included time-invariant individual risk factors for preterm birth as covariates. The third set of models added separate interaction terms for race/ethnicity, high risk pregnancies (women with diabetes or hypertension), and neighborhood land cover in order to assess any potentially vulnerable subgroups. Finally, I conducted a sensitivity analysis excluding women with no risk of exposure to extreme heat during the period they were at risk of preterm birth (weeks 19-36). In this case, approximately 1/3 of pregnancies were excluded because they were conceived between April 20th and September 16th, which meant weeks 19-36 of their pregnancy did not overlap with the months of June, July or August when the highest temperatures were observed.

Results

The final sample population included 189,420 births, 12.3% of which were preterm. The majority (56%) of mothers identified as Hispanic/Hispanic, 20% as non-Hispanic White, 18% as non-Hispanic Black, and 6% as Asian/Pacific-Islander (PI). Nearly half were foreign-born, with Hispanic, Asian/PI, and multiracial women or women of other ethnicities predominating in the foreign-born group. Other characteristics of the sample population are given in **Table 4-2**.

Crude rates of preterm birth were higher for several risk factors identified *a priori* (**Table 4-3**, all $P < 0.0001$, Chi-square test): male infants, nativity (lower rate for foreign-born), smoking during pregnancy or the three months prior, maternal age (higher rates under age 20 and over age 35), underweight or overweight/obese, inadequate or more than adequate prenatal care, and Black race or Hispanic ethnicity. Women whose primary expected source of payment was private insurance had a higher crude rate of preterm birth than those with Medicaid or who planned to self-pay. Women in the highest education category (at least some college) had a lower crude rate of preterm birth than those with a high school education or less. 8.5% of women had pre-pregnancy or gestational diabetes or hypertension (including eclampsia). This group had a much higher overall crude risk of preterm delivery (22% vs. 11%). Parity and receipt of WIC were not strong predictors and were therefore excluded from the multivariate proportional hazards models.

The study population exhibited pronounced seasonality in conception that increased steadily from July (6.6% of conceptions) to December (10.3% of conceptions) and then decreased steadily again (**Figure 4-4**). Birth rates mirrored this, with the most births occurring in August or September and the least during March, April and May.

Maximum apparent temperatures during the study period ranged from -0.9 to 44.9°C and averaged 34.1°C during the summer months (JJA). A graphical time series of summertime apparent temperatures at George W. Bush International Airport and the preterm birth rate across Harris County is given in **Figure 4-5**. Heat wave days (indicated in red) are apparent in all five summers, with 2011 having a particularly large number in August (20 versus 1-3 in previous years). Preterm birth rates sometimes increased in the days immediately following a heat wave day (e.g. during the first hot period of June, 2009) and sometimes decreased (e.g. following hot days in August, 2009). Volatility in the day-to-day rates makes patterns difficult to discern. 49,368 (26%) women were exposed to at least one day with $AT_{max} \geq 40$°C during the period they were at risk of preterm delivery (weeks 19-36 of their pregnancy). 43% were exposed to at least one day with T_{max} and T_{min} > JJA 90^{th} percentile, and 34% were exposed to at least one heat wave day.

Census tracts in Harris County varied widely in their land cover characteristics, with the percent of area covered in tree canopy ranging from 0-73% and the percent of area covered in impervious surface from 3-93%. The average neighborhood area covered in tree canopy for Non-Hispanic White mothers in the study population was 20.6% versus 13.8%, 15.6% and 15.1% for Hispanic, Black, and Asian/PI mothers, respectively. The average area covered in impervious surfaces for Whites was 44.5% versus 52.2%, 48.8%, and 51.5% for Hispanic, Black, and Asian/PI mothers, respectively. 4.6% of White mothers lived in tracts qualifying as high heat risk (0% water, <5% trees and > 60% impervious surface) versus 11.5%, 9.6% and 10.1% for Hispanic, Black, and Asian/PI mothers, respectively.

Hazards ratios for preterm birth following high temperatures for lags from 1 to 7 days prior to birth are shown graphically in **Figure 4-6**. All estimates control for secular trends by including a term for the number of days since January 1, 2007 in the model. No effect estimates were statistically significant at $P < 0.05$. A one-day lag suggested the highest possible adverse effect on preterm birth and for that reason, one-day lags were the focus of the subsequent models. Controlling for secular trends, high temperatures the day prior suggested an increase in the risk of preterm birth < 37 completed weeks from 6-8%, depending on the definition used (HR [95% CI]: 1.08 [0.97, 1.20] for $AT_{max} \geq 40°C$; 1.06 [0.99,1.14] for T_{max} and T_{min} > JJA 90^{th} percentile; 1.07 [0.97, 1.17] for heat wave day). Controlling for individual risk factors reduced this to an increase of 3-8%, and the effect estimates were again not statistically significant at $P < 0.05$ (HR [95% CI]: 1.08 [0.96, 1.20], 1.03 [0.96, 1.11], and 1.04 [0.94, 1.14], respectively) (**Table 4-4**,**Table 4-5** and **Table 4-6**). When pregnancies at no risk of exposure during weeks 19-36 were excluded, effect estimates of one-day lagged temperature variables changed by less than 1%.

Other variables included in the multivariate models exhibited statistically significant relationships with preterm birth in the expected direction: underweight and less educated mothers, those under age 20 or over age 40, those with diabetes or hypertension, U.S.-born as opposed to foreign-born, smokers, and male infants were at higher risk of a preterm birth. The only variable that did not exhibit the expected relationship with preterm birth was insurance status. Women with private insurance exhibited higher risk than Medicaid/self-pay patients controlling for age, education, nativity and other factors.

Including interaction terms for race suggested a larger effect of temperature among non-Hispanic Blacks and Asians and a smaller effect among non-Hispanics, however none of the effects were statistically significant (HRs [95% CI] for $AT_{max} \geq 40°C$ vs. < 20°C: 1.12 [0.90, 1.40] for Blacks; 1.24 [0.80, 1.92] for Asians; 1.08 [0.84, 1.40] for Whites; and 1.03 [0.88, 1.20] for Hispanics). Interactions between temperature and land cover, and temperature and diabetes/hypertension were in the opposite direction than expected (suggesting less effect in high-heat risk neighborhoods and among high risk pregnancies), but also never statistically significant (data not shown).

Discussion

I found elevated but statistically insignificant effects of extreme heat on the risk of preterm birth despite the fact that maximum temperatures in my study were higher than in other recent studies from California, Brisbane, and Rome that found stronger evidence of an adverse effect of heat.[208,210,211] The upper bounds of the confidence intervals on the hazards ratios I obtained suggest that unusually hot temperatures are unlikely to cause more than an 11-20% increase in risk, depending on the way hot temperatures are defined. This may be explained by the fact that residents of Houston are accustomed to hot weather and most households have air conditioning. Regression-based modeling of appliance ownership data from the Residence Energy Consumption Survey suggests that over 95% of Harris County housing units have air conditioning (unpublished data described in [253] and obtained from Zeke Hausfather). Pregnant women may also have heeded public health warnings and undertaken precautionary behavior during the heat wave of 2011, which accounted for three quarters of the days during the five year study period with apparent temepratures above 40°C.

I also found limited evidence of effect modification to suggest particular groups were at increased risk of preterm birth following extreme ambient temperatures. The groups with the highest preterm birth rates overall, based on unadjusted rates as well as covariate effect estimates from the multivariate models, were women with diabetes or hypertension, women receiving inadequate or more than adequate levels of prenatal care, and Black women. Hispanic and Asian/PI women also had higher rates of preterm birth when controlling for nativity and other factors. These striking racial disparities are consistent with other studies and require further research.

I found large differences in neighborhood land cover characteristics by race and ethnicity. Compared to White women, women of color were more than twice as likely to live in a "high heat risk" neighborhood with few trees and many heat-trapping surfaces. Although living in such a neighborhood did not seem to increase preterm birth risk due to heat, disparities in neighborhood green-ness may be a concern for other reasons. Several recent studies suggest that a lack of neighborhood green space is associated with poorer birth outcomes.[254–256] Crude preterm birth rates were 3% higher in high heat-risk neighborhoods, and effect estimates from my multivariate models suggested that living in a high heat risk neighborhood was associated with small albeit statistically insignificant increases in the risk of preterm birth at most temperature ranges and independent of individual risk factors. However, my study was not designed to answer this question and the relationship between land cover characteristics and preterm birth would need to be investigated further.

It is estimated that less than half of conceptions result in live birth,[257,258] and one limitation of my study was the lack of information on stillbirths or miscarriages. At least one study suggests that higher ambient temperature during the last four weeks of the pregnancy increases the risk of stillbirth.[209] Several studies have also found evidence that exposure to social and environmental stresses – including unexpectedly cold temperatures[259] – leads to differential miscarriage of male and weaker fetuses. This is thought to happen via unknown, heritable biological mechanisms that are conserved by natural selection because they maximize the likelihood of grandchildren. I am not aware of any studies to date that have examined whether heat stress may similarly alter the sex ratio of live births via an increase in miscarriages. If this were the case, it could mean that more heat-stressed or heat-sensitive women may have been culled from my sample population.

Seasonality in conception creates a challenge for studying the effect of time-varying exposures like temperature. The fact that conception rates in this study population of live births were highest in December and lowest in July means that both the number of pregnant women and the average gestational age of all pregnancies in my sample increased over the summer months. Because the risk of preterm birth increases exponentially with gestational age, this also results in an increase in the underlying risk of preterm birth precisely during the time when temperatures are also rising. Cross-sectional and ecological study designs would be limited in their ability to separate a causal effect of temperature from the baseline effect of seasonal variation in the population at risk due to multicollinearity between season and temperature. The survival analysis methods I used help eliminate this potential source of confounding by comparing women at the same stage of pregnancy regardless of when they conceived. Differences between my findings and those of studies that found stronger evidence of an effect of heat may be partly attributable to differences in study design, including control for truncation bias and seasonal variation in conception.

A limitation of this study was my reliance on distant weather stations to assign exposure. Women in my sample lived as close as 200m and as far as 20km from the nearest weather station, with the majority living more than 10km away. Observations at these stations of course also fail to capture true exposure, which depends on housing characteristics, physical activity levels, clothing, actual air conditioning use, and other factors. This is likely to have led to significant exposure misclassification.

Finally, this study was designed to investigate differential vulnerability to climate change with the hopes of informing future public health planning and climate adaptation measures. Although I did not find a strong evidence of an effect of heat on preterm birth, higher temperatures than those observed in this study are expected because of anthropogenic climate change. Beyond a certain threshold temperature and barring radical adaptation measures, impacts are inevitable because of thermodynamic limits to the body's ability to cool itself.[260] Inequity in the impacts of rising temperatures also warrant further investigation and precautionary action. In particular, the existing literature suggests that socioeconomically disadvantaged groups are at increased vulnerability to heat-related health impacts, including Blacks[216–223] and farm workers,[261] many of whom are undocumented and paid piecemeal, which may lead them not to take breaks during hot weather for fear of reprisal or lost income. Thoughtful assessment and adaptation planning can help prevent climate-related increases in extreme heat events from exacerbating already large and unjust racial disparities in health.

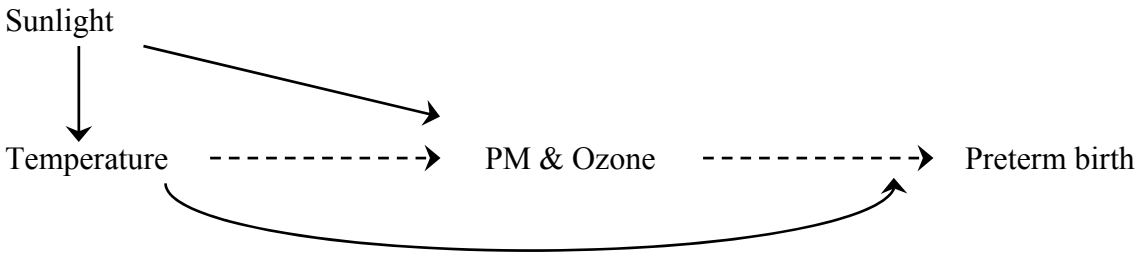


Figure 4-1 Directed acyclic graph illustrating the causal model between ambient temperature and preterm birth showing both direct and indirect (dashed line) effects mediated by air pollution. PM = particulate matter.

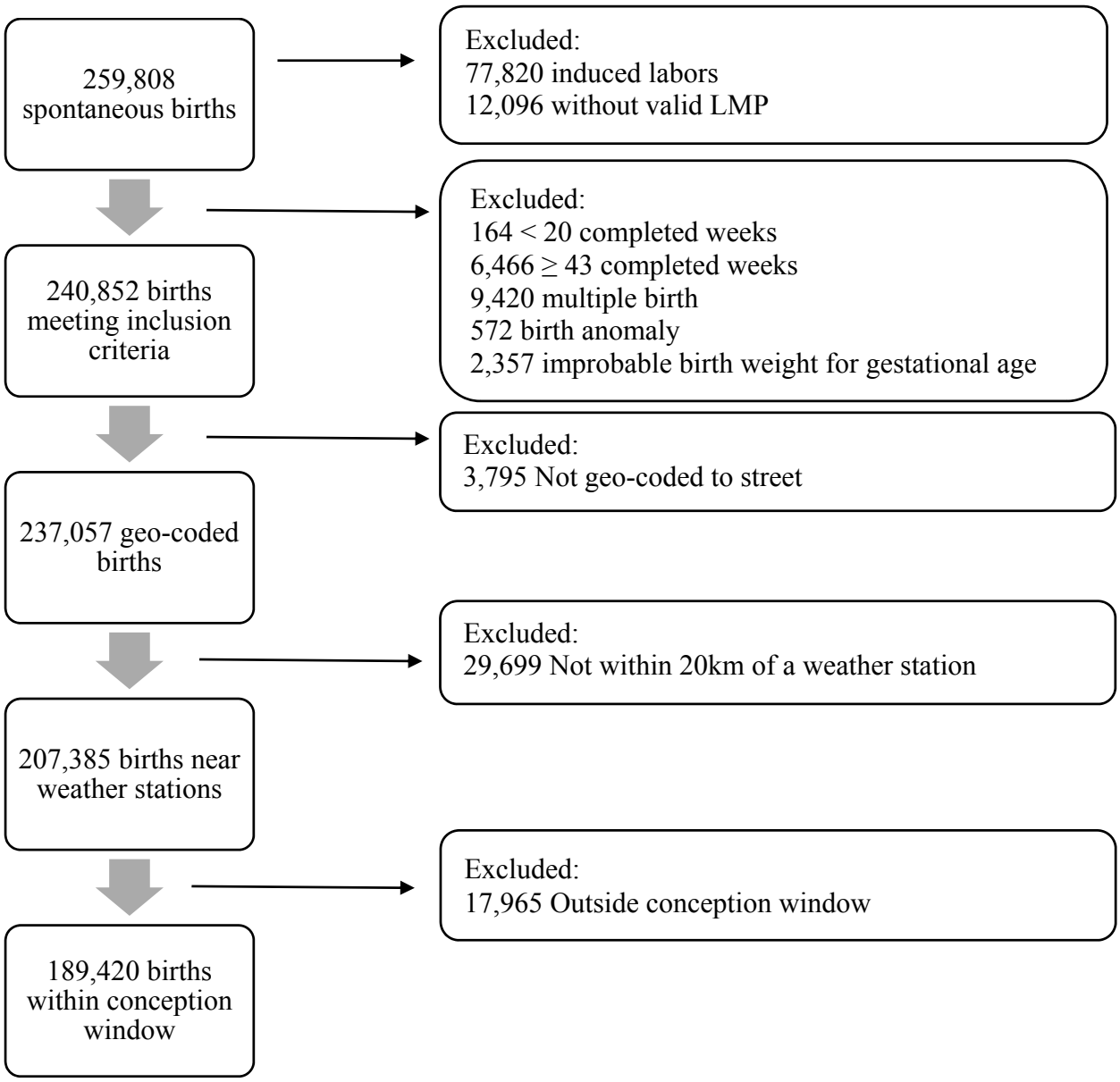


Figure 4-2 Flow diagram of study population assembly from 2007-2011 Harris County, TX birth records. Exclusion criteria are not mutually exclusive. Because some weather stations were not operational during the entire study period, 492 women of the final 189,420 were missing all temperature observations.

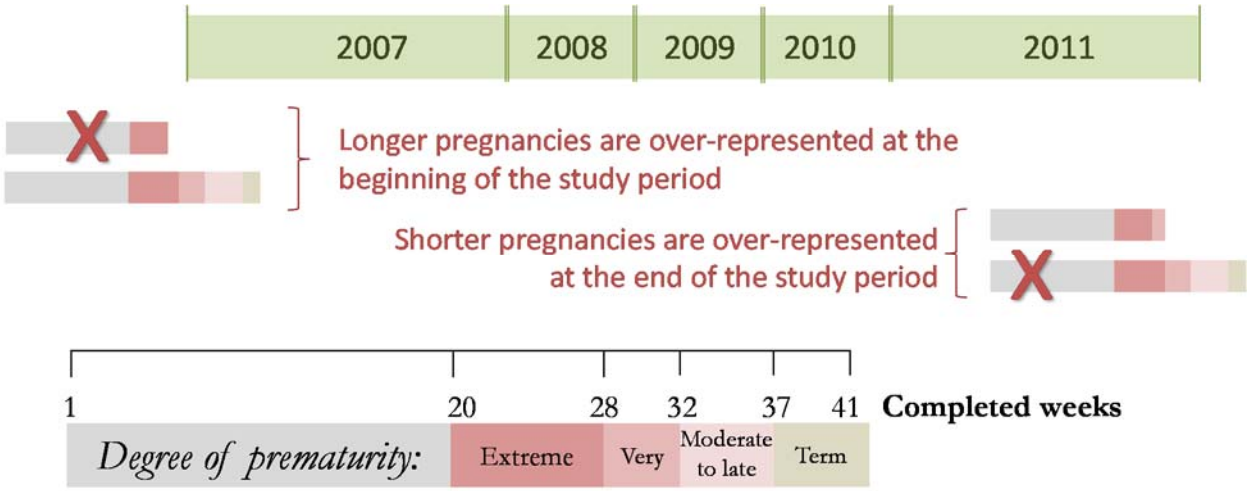


Figure 4-3 Restricting on the date of birth can introduce bias. The over-representation of shorter pregnancies during the latter part of the study period could introduce a spurious association between heat and preterm birth because 2011 was a particularly hot year.

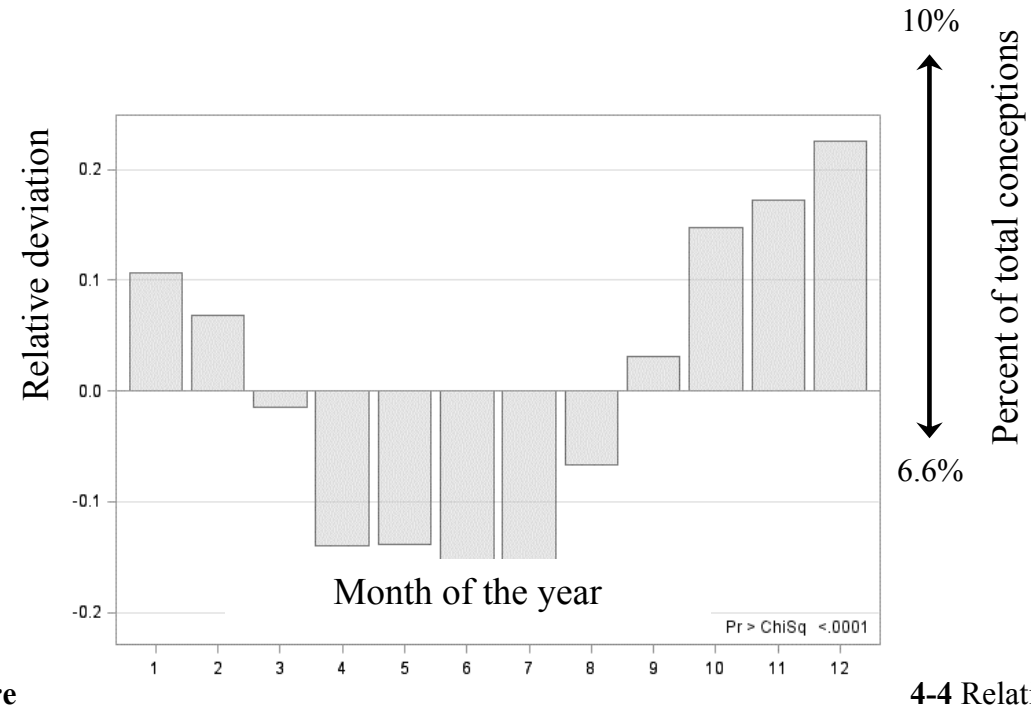


Figure 4-4 Relative deviation from expected average percent of conceptions resulting in live birth per calendar month (8.3%), Harris County, TX 2005-11 birth records (N=189,420)

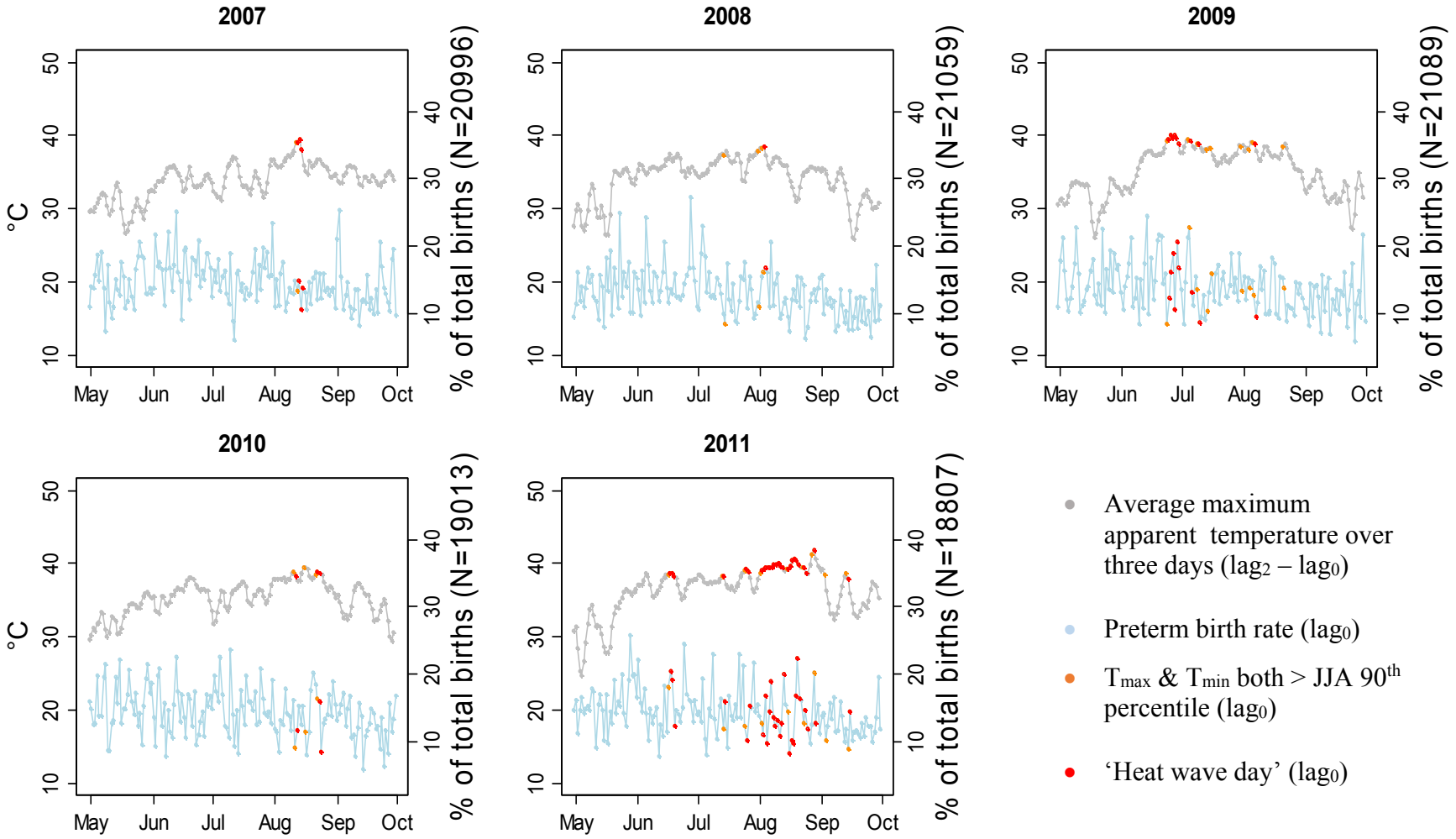


Figure 4-5 Warm season temperatures at George W. Bush International airport, Houston, TX, and the preterm birth rate among geo-coded births 20-42 weeks, Harris County, TX (total N=100,964)

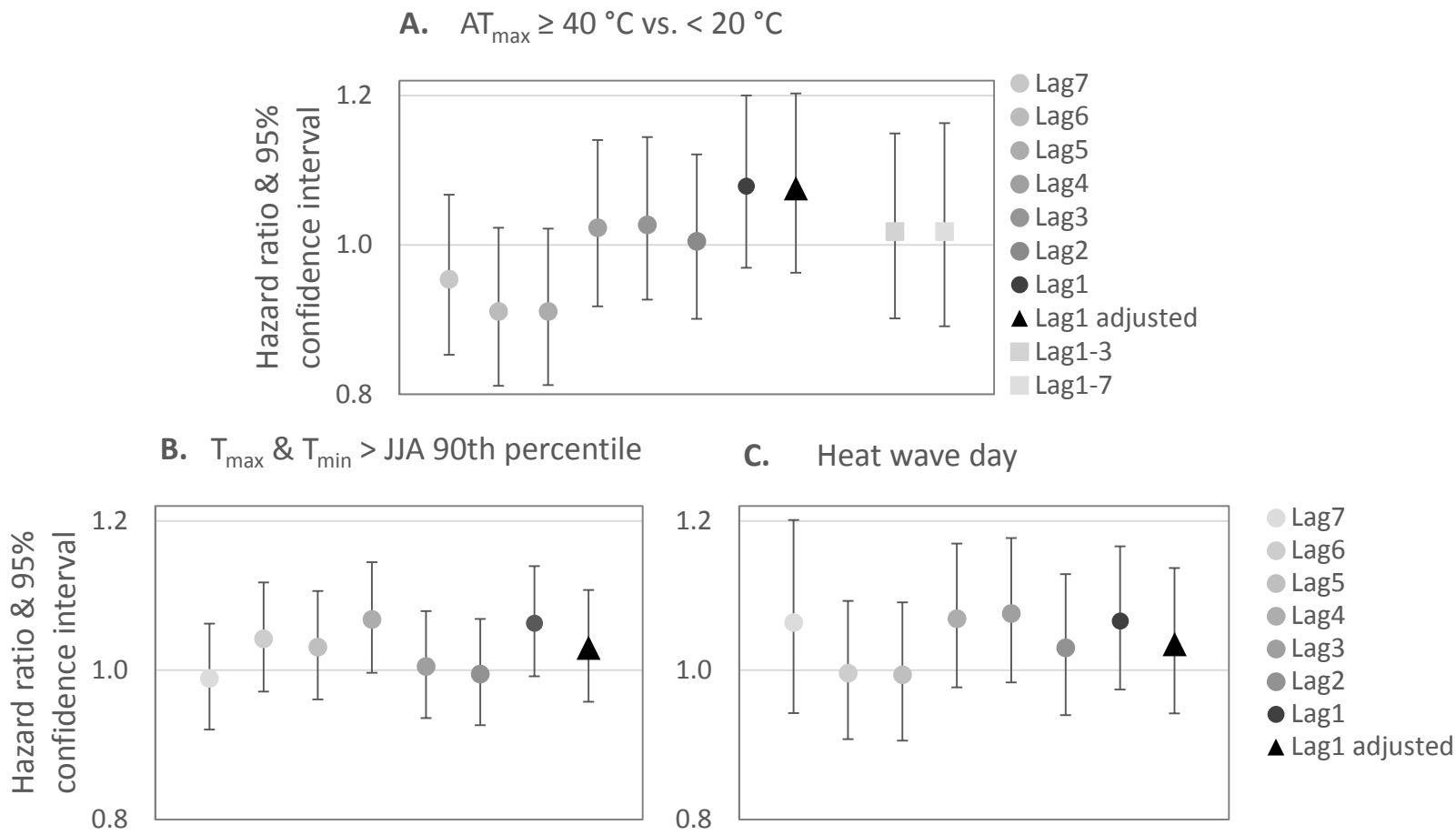


Figure 4-6 Hazard ratios and 95% confidence intervals for the effect of heat on preterm birth using three different definitions of heat. A "heat wave day" (C) is the second or more consecutive day meeting the definition in (B) of daytime highs and nighttime lows above the 90th percentile of historical (1971-2000) summertime (JJA) dry bulb air temperatures. Lag_1 indicates one day prior to birth, lag_2 two days prior, etc. Lag_{1-3} and lag_{1-7} are averages over the three and seven days prior to birth, respectively. All models control for secular trend. Adjusted models additionally control for infant sex and maternal age, BMI, diabetes/hypertension, race/ethnicity, nativity, education, insurance, prenatal care, and smoking. AT = apparent temperature.

Table 4-1 Kotelchuck index of adequacy of prenatal care utilization

Initiation of Care	Under 50%	50-79%	80-109%	110%+
Month 7-9, or no care	Inadequate (1)	Inadequate (1)	Inadequate (1)	Inadequate (1)
Month 5-6	Inadequate (1)	Inadequate (1)	Inadequate (1)	Inadequate (1)
Month 3-4	Inadequate (1)	Intermediate (2)	Adequate (3)	Adequate plus (4)
Month 1-2	Inadequate (1)	Intermediate (2)	Adequate (3)	Adequate plus (4)

Number of recommended visits

Table 4-2 Characteristics of the study population of Harris County, TX births, 2007-11 (N=189,420)

	N	(%)
Race/ethnicity		
White	37,097	(19.6)
Hispanic/Hispanic	105,120	(55.5)
Black	33,865	(17.9)
Asian/Pacific Islander	11,692	(6.2)
Native American	203	(0.1)
Other/multiple/missing	1,443	(0.8)
Foreign-born	86,114	(45.5)
Mother's education		
< H.S.	70,266	(37.1)
H.S. graduate or equivalent	42,556	(22.5)
> H.S.	76,433	(40.4)
Expected principle form of payment		
Medicaid	90,334	(47.7)
Private insurance	58,660	(31.0)
Self-pay	15,733	(8.3)
Other/unknown	24,693	(13.0)
Adequacy of prenatal care		
Inadequate	55,849	(29.5)
Intermediate	22,992	(12.1)
Adequate	57,304	(30.3)
Adequate plus	42,996	(22.7)
None or missing	10,279	(5.4)
BMI		
Normal or healthy weight	89,776	(47.4)
Underweight	9,677	(5.1)
Overweight/obese	89,967	(47.5)
Smoked during or within 3 months prior to pregnancy		
Yes	6,324	(3.3)
No	182,851	(96.5)
Gestational age (completed weeks)		
Extremely preterm (20 - 27)	803	(0.4)
Very preterm (28 - 31)	1,905	(1.0)
Moderately preterm (32 - 36)	20,639	(10.9)
Early term (37 - 38)	61,700	(32.6)
Term (39 - 41)	104,373	(55.1)
Birthweight (grams)		
Very low (<1,500)	2,142	(1.1)
Low (1,500-2,500)	11,398	(6.0)
Not low (≥2,500)	175,880	(92.9)

Table 4-3 Crude preterm birth rates by risk factor (N=189,420). Overall rate was 12.3%.

	Preterm birth rate per 100	P-value (Chi-square)
Diabetes or hypertension (pre-pregnancy, gestational, or eclampsia)		
Yes	22.2	<0.0001
No	11.4	
Infant sex		
Male	12.8	<0.0001
Female	11.8	
BMI		
Normal or healthy weight	11.8	
Underweight	14.4	<0.0001
Overweight/Obese	12.6	
Maternal age		
< 20	13.9	
20-25	12.5	
25-30	11.4	<0.0001
30-35	11.5	
35-40	13.3	
≥ 40	16.3	
Smoked during or within 3 months prior to pregnancy		
Yes	15.9	<0.0001
No	12.2	
Race/ethnicity		
White	11.0	
Hispanic/Latina	11.7	
Black	16.8	<0.0001
Asian/PI	9.8	
Other/multiple/unknown	10.4	
Country of origin		
Not U.S.	10.8	<0.0001
U.S.	13.6	
Mother's education		
<H.S.	12.7	
H.S. graduate or equivalent	13.2	<0.0001
>H.S.	11.5	
Expected principle form of payment		
Private insurance	12.8	<0.0001
Medicaid/Self-pay/Other	11.3	
Adequacy of prenatal care		
Inadequate	12.2	
Intermediate	4.3	<0.0001
Adequate	4.3	
Adequate plus	26.0	

Table 4-4 Cox proportional hazards model results of the risk of preterm birth (<37 completed weeks) associated with the prior day's maximum apparent temperature (AT_{max}) (N=188,928). SE = standard error.

Parameter		Effect estimate	SE	P-value	Hazard ratio	95% CI
AT_{max} (lag1) (*reference:* <20°C)	≥40°C	0.07	0.06	0.20	1.08	[0.96 , 1.20]
	35-40°C	-0.03	0.02	0.16	0.97	[0.93 , 1.01]
	30-35°C	-0.02	0.02	0.28	0.98	[0.93 , 1.02]
	25-30°C	-0.01	0.02	0.78	0.99	[0.95 , 1.04]
	20-25°C	-0.02	0.02	0.46	0.98	[0.94 , 1.03]
Year (day since Jan 1, 1960)		-0.0001	0.00001	<.0001	1.00	[1.00 , 1.00]
Age (*reference:* < 20)	≥40	0.24	0.04	<.0001	1.27	[1.16 , 1.38]
	35-40	0.05	0.03	0.08	1.05	[0.99 , 1.12]
	30-35	-0.07	0.03	0.01	0.93	[0.88 , 0.98]
	25-30	-0.11	0.03	<.0001	0.90	[0.85 , 0.94]
	20-25	-0.06	0.02	0.02	0.95	[0.90 , 0.99]
Sex (*reference:* Female)	Male	0.08	0.01	<.0001	1.08	[1.05 , 1.11]
Prenatal care (*reference:* Adequate)	Intermediate	-0.02	0.04	0.62	0.98	[0.91 , 1.06]
	Inadequate	0.98	0.02	<.0001	2.66	[2.53 , 2.79]
	Adequate Plus	1.86	0.02	<.0001	6.44	[6.16 , 6.73]
Diabetes or hypertension (*reference:* No)		0.58	0.02	<.0001	1.79	[1.72 , 1.86]
Race/ethnicity (*reference:* N-H White)	Hispanic/Latina	0.09	0.02	0.0002	1.09	[1.04 , 1.15]
	N-H Black	0.40	0.02	<.0001	1.50	[1.43 , 1.57]
	N-H Asian/PI	0.08	0.04	0.04	1.08	[1.01 , 1.17]
	Other/multiple/unknown	-0.0008	0.09	0.99	1.00	[0.84 , 1.19]
Nativity (*reference:* U.S.-born)	Foreign-born	-0.22	0.02	<.0001	0.80	[0.77 , 0.83]
Education (*reference:* HS graduate)	> HS	-0.13	0.02	<.0001	0.88	[0.85 , 0.92]
	< HS	0.10	0.02	<.0001	1.11	[1.06 , 1.15]
BMI (*reference:* Normal)	Underweight	0.20	0.03	<.0001	1.22	[1.15 , 1.29]
	Overweight/Obese	-0.05	0.01	0.00	0.95	[0.92 , 0.98]
Smoking (*reference:* Non-smoker)	Smoker	0.18	0.03	<.0001	1.20	[1.12 , 1.28]

Expected primary source of payment (*reference:* Medicaid/self pay/other)	Private insurance	0.07	0.02	0.00	1.08	[	1.03	,	1.12	]

Table 4-5 Cox proportional hazards model results of the risk of preterm birth (<37 completed weeks) following a day with daytime high and nighttime low temperatures above the 90th percentile of historical (1971-2000) summer months (JJA) (N=188,928). SE = standard error.

Parameter		Effect estimate	SE	P-value	Hazard Ratio	95% CI
T_{min} & T_{max} > JJA 90th percentile (lag_1) (*reference:* No)		0.03	0.04	0.43	1.03	[0.96 , 1.11]
Year (day since Jan 1, 1960)		-0.0001	0.00001	<.0001	1.00	[1.00 , 1.00]
Age (*reference:* < 20)	≥40	0.24	0.04	<.0001	1.27	[1.16 , 1.38]
	35-40	0.054	0.03	0.083	1.05	[0.99 , 1.12]
	30-35	-0.074	0.03	0.01	0.93	[0.88 , 0.98]
	25-30	-0.18	0.03	<.0001	0.90	[0.85 , 0.94]
	20-25	-0.06	0.02	0.02	0.95	[0.90 , 0.99]
Sex (*reference:* Female)	Male	0.08	0.01	<.0001	1.08	[1.05 , 1.11]
Prenatal care (*reference:* Adequate)	Intermediate	-0.02	0.04	0.62	0.98	[0.91 , 1.06]
	Inadequate	0.98	0.024	<.0001	2.66	[2.53 , 2.79]
	Adequate Plus	1.86	0.02	<.0001	6.44	[6.16 , 6.73]
Diabetes or hypertension (*reference:* No)		0.58	0.02	<.0001	1.79	[1.72 , 1.86]
Race/ethnicity (*reference:* N-H White)	Hispanic/Latina	0.09	0.02	0.0002	1.09	[1.04 , 1.15]
	N-H Black	0.40	0.02	<.0001	1.50	[1.43 , 1.57]
	N-H Asian/PI	0.08	0.04	0.04	1.08	[1.01 , 1.17]
	Other/multiple/unknown	-0.0008	0.09	0.99	1.00	[0.84 , 1.19]
Nativity (*reference:* U.S.-born)	Foreign-born	-0.22	0.02	<.0001	0.80	[0.77 , 0.83]
Education (*reference:* HS graduate)	> HS	-0.13	0.022	<.0001	0.88	[0.85 , 0.92]
	< HS	0.10	0.02	<.0001	1.11	[1.06 , 1.15]
BMI (*reference:* Normal)	Underweight	0.20	0.03	<.0001	1.22	[1.14 , 1.29]
	Overweight/Obese	-0.05	0.01	0.0003	0.95	[0.92 , 0.98]
Smoking (*reference:* Non-smoker)	Smoker	0.18	0.04	<.0001	1.19	[1.12 , 1.28]
Expected primary source of payment (*reference:* Medicaid/self pay/other)	Private insurance	0.07	0.02	0.0003	1.08	[1.03 , 1.12]

Table 4-6 Cox proportional hazards model results of the risk of preterm birth (<37 completed weeks) following a day "heat wave day", defined as the second or more consecutive day with daytime high and nighttime low temperatures > JJA 90th percentile (1971-2000) (N=188,928). SE = standard error.

Parameter		Effect estimate	SE	P-value	Hazard Ratio	95% CI
Heat wave day (*reference:* No)		0.03	0.05	0.47	1.04	[0.94 , 1.14]
Year (day since Jan 1, 1960)		-0.0001	0.00001	<.0001	1.00	[1.00 , 1.00]
Age (*reference:* < 20)	≥40	0.24	0.04	<.0001	1.27	[1.16 , 1.38]
	35-40	0.05	0.03	0.08	1.05	[0.99 , 1.12]
	30-35	-0.07	0.03	0.01	0.93	[0.88 , 0.98]
	25-30	-0.11	0.03	<.0001	0.90	[0.85 , 0.94]
	20-25	-0.06	0.02	0.02	0.95	[0.90 , 0.99]
Sex (*reference:* Female)	Male	0.08	0.01	<.0001	1.08	[1.05 , 1.11]
Prenatal care (*reference:* Adequate)	Intermediate	-0.02	0.04	0.62	0.98	[0.91 , 1.06]
	Inadequate	0.98	0.02	<.0001	2.66	[2.53 , 2.79]
	Adequate Plus	1.86	0.02	<.0001	6.44	[6.16 , 6.73]
Diabetes or hypertension (*reference:* No)		0.58	0.02	<.0001	1.79	[1.72 , 1.86]
	Hispanic/Latina	0.09	0.02	0.0002	1.09	[1.04 , 1.15]
	N-H Black	0.40	0.02	<.0001	1.50	[1.43 , 1.57]
	N-H Asian/PI	0.08	0.04	0.04	1.08	[1.01 , 1.17]
	Other/multiple/unknown	0.00	0.09	0.99	1.00	[0.84 , 1.19]
Nativity (*reference:* U.S.-born)	Foreign-born	-0.22	0.02	<.0001	0.80	[0.77 , 0.83]
Education (*reference:* HS graduate)	> HS	-0.13	0.02	<.0001	0.88	[0.85 , 0.92]
	< HS	0.10	0.02	<.0001	1.11	[1.06 , 1.15]
BMI (*reference:* Normal)	Underweight	0.20	0.03	<.0001	1.22	[1.14 , 1.29]
	Overweight/Obese	-0.05	0.01	0.0003	0.95	[0.92 , 0.98]
Smoking (*reference:* Non-smoker)	Smoker	0.18	0.03	<.0001	1.19	[1.12 , 1.28]
Expected primary source of payment (*reference:* Medicaid/self pay/other)	Private insurance	0.07	0.02	0.0003	1.08	[1.03 , 1.12]

Chapter 5

Towards environmental justice: implications for research and policy

Addressing environmental health inequities requires multifaceted, interdisciplinary approaches in both the creation of new knowledge and its translation into effective policies and analytic tools to advance regulatory decision-making. In this dissertation I have drawn on the disciplines of epidemiology, geography and environmental health to investigate environmental justice concerns. Historical, ethnographic, experimental, experiential and other types of knowledge all have and will continue to provide valuable insight into the causes and consequences of environmental exposures that disproportionately burden disadvantaged communities. In **Figure 5-1** I illustrate the ways in which differing scientific disciplines contribute to our understanding of environmental justice and the ways in which different types of public policy can help remedy inequities. Although there is much to learn, we also have enough evidence to warrant changes in policy to reduce disparities in environmental hazards in order to advance community health. Social movements have and will continue to provide the political and persuasive power to leverage existing and emerging scientific knowledge about the health implications of environmental inequalities into policy and regulatory change.

Unfortunately, even well intentioned policies to improve public health have had unintended negative consequences for the very communities they aimed to help. For example, from the 1950s to 1970s, the U.S. federal government funded urban renewal projects that were ostensibly designed to improve housing and economic conditions in poor neighborhoods but ultimately led to the displacement of more than four million low income and minority residents.[262] Efforts by environmentalists to clean up brownfields, create green space, and replace heavy industry with less polluting businesses can drive increases in housing prices and job losses that similarly displace long-term residents and low income families. In the case of climate change mitigation policy, economists have pointed out that greenhouse gas emissions trading schemes allow for the persistence of toxic 'hot spots' in areas with high pollution abatement costs, potentially undermining local air quality and health goals.[263]

Some of these pitfalls are more likely to be avoided if policies and programs incorporate input from environmental justice scholars and advocates, including members of the disproportionately impacted communities they are intended to help. One example of this may be the recent adoption of new legislation in California (Senate Bill, or SB, 535) that directs the state to invest a significant share of the proceeds of greenhouse gas emissions trading in climate change mitigation projects that are located in – and that bring benefits to – environmentally or socioeconomically disadvantaged communities. These communities are being identified in part geographically using the environmental justice screening tool CalEnviroScreen discussed in Chapter 2. California's cap-and-trade program is seen as the means by which to achieve large portions of the greenhouse gas reduction goals spelled out in the State's 2006 Global Warming Solutions Act (Assembly Bill 32). SB 535 was championed by environmental justice advocates shortly after the implementation of the cap-and-trade program. Many of these advocates were skeptical of market-based mitigation strategies like cap-and-trade and were concerned that emissions trading would allow large, dirtier facilities in the State – which are disproportionately located in low income communities and communities of color – to stay open and even expand. SB 535 innovatively leveraged existing climate change policy to advance environmental and

economic equity goals through the direction of State funding towards disadvantaged communities. Future analyses will be needed to assess the extent to which this approach succeeds in achieving both greenhouse gas mitigation goals and environmental or economic benefits to environmental justice communities.

In previous chapters I presented research findings from three projects that sought to advance our understanding of social disparities in exposure to environmental health hazards. My goal was to generate new knowledge that would inform action to improve health in disadvantaged communities. My investigation of racial and ethnic inequalities in spatial measures of cumulative environmental and socioeconomic disadvantage (Chapter 2), chemical body burden (Chapter 3), and the risk of preterm birth during an extreme heat event in the larger context of climate change (Chapter 4) offer fresh perspectives and analytic frameworks for identifying environmental inequities with implications for health. In this chapter, I discuss the lessons I learned along the way and their implications for future research and policy related to environmental justice.

Implications for research

Residential proximity to hazards and cumulative impact approaches

Maps are powerful in their ability to reveal spatial patterns of inequality, and Chapter 2 is one of many examples of the utility of geographic approaches in environmental justice research. One innovation in my approach over previous efforts that look at geographic proximity to environmental hazards is the assessment of overlapping geographies of risk via the combination of information on many types of environmental hazards and the integration of measures of population vulnerability. I did this in an effort to respond to calls to assess the potential for cumulative health impacts from both environmental and social stressors in socioeconomically disadvantaged communities.[3] Combining measures of very different environmental hazards is difficult because significant assumptions have to be made about the relative importance of each factor and the ways they interact with each other to impact health. Future work is needed to inform these choices. Nevertheless, the fact that environmental and social stressors to health overlap in space as documented in Chapter 2 suggests that future research on environmental justice should more explicitly examine cumulative exposures as well as social and biological sources of differential vulnerability that may lead to greater health impacts from pollution.

The concentration index I used in Chapter 2 to quantify inequity is common in economics but less often encountered in the field of environmental health. It and other similar inequality metrics can be useful in comparing the degree of inequality across different measures of environmental quality or health and for measuring change over time. However, the choice of metric is important and it is worth looking at several because different metrics can lead to differing conclusions about the degree and even direction of inequality (i.e., how disproportionate the burden is, and who in society is burdened most).[264,265] Applying metrics on an absolute rather than a relative scale and incorporating regulatory benchmarks, when available, could make these approaches to spatial cumulative impacts screening more interpretable with respect to potential health implications and more relevant for regulatory decision-making.

Finally, one limitation of quantitative geographic research on environmental justice is the fact that studies typically rely on imperfect secondary data sources, including emissions inventories

that are self-reported by industry and linked to company mailing addresses rather than the physical location of an emission source or regulated activity. Analyses are typically temporally static and often exclusively focus on neighborhood of residence, as is true of my work in Chapter 2. Because of this, we are limited in our knowledge about cumulative exposures from hazards encountered away from home as well as other types of sources. Hazards in the workplace as well as those associated with diet and consumer products are all likely to differ by race and socioeconomic status, among other factors. Moreover, for convenience we usually rely on census or ZIP code boundaries that do not necessarily match local conceptions of neighborhood boundaries, producing results that are both sensitive to the geographic unit of analysis and potentially inaccurate for a given location. When used to produce a map, these hard boundaries misleadingly suggest abrupt transitions between adjacent neighborhoods. Some potential improvements to address these limitations include spatial-temporal approaches that look longitudinally and integrate activity patterns and residential mobility; fuzzy logic and other methods for incorporating uncertainty; and geospatial techniques that get away from area-based measures and move toward, for example, continuous gridded surfaces that are better able to represent gradual transitions.

Socioeconomic differences in chemical body burden

Biomonitoring can add to the study of environmental justice by revealing whether socioeconomically disadvantaged groups have higher concentrations of harmful chemicals in their bodies than others, which may reflect disproportionate exposures. In the case of chemicals with long persistence in the body, biomonitoring data can give an indication of exposure histories that may be useful in moving toward longitudinal perspectives on inequalities in exposure over the course of a lifetime. At the same time, because we lack analytic techniques to measure many of the synthetic chemicals in commerce today, the choice of chemicals to measure is limited and somewhat arbitrary. Interpretation is difficult because for the vast majority of chemicals, we lack more than very basic health and safety information and have limited knowledge of their main sources or how to reduce exposures. The use of a single spot sample can also miss exposures that lead to rapid changes in chemical concentrations in the body over time and limit our ability to document differences in chemical body burden because of chance.

In addition to these drawbacks, the utility of biomonitoring studies for environmental justice research is limited by small sample sizes and legitimate confidentiality concerns that make it difficult to assess disparities across population subgroups and geographic areas. The race and ethnicity categories used in health research are crude and any one category includes people with very diverse life histories, genealogies, and experiences of discrimination or privilege. Crude socio-demographic information and small cell counts both limit the utility of biomonitoring for environmental justice research and the ability to infer larger population-level patterns. More narrowly focused studies of unique subpopulations including workers and communities living on the fence-lines of polluting industries would help in this respect.

Despite these limitations, biomonitoring results provide detailed, individual data that often triggers stronger personal and public reactions than other forms of human exposure evidence. Biomonitoring data can serve as a vehicle to inform and empower study participants to take steps to reduce their exposure and engage in policy debates about the regulation of air and water quality or synthetic chemical use in commerce.[124,266] Environmental justice analyses of

biomonitoring data can provide new evidence of how unjust environments get "under the skin". When making comparisons between sub-populations, across study populations, or through time, careful attention must be paid to differences in the method detection limit. Modern techniques for handling censored data – including non-parametric approaches adopted from survival analysis methods and the parametric techniques I utilize in Chapter 3 – are useful in this respect and should be more widely adopted.[179] Assessment of concentrations of multiple chemicals that affect similar health endpoints, as well as the integration of measurement of bio-markers of effect and stress are all promising arenas for future research on the health and environmental justice implications of biomonitoring data.

Environmental justice perspectives on climate change

Studies of the health impacts of climate change are difficult because of the complex direct and indirect relationships between climate and health. Most diseases are climate-sensitive, but local context, natural systems such as those affecting disease vector ecology, and social factors all play a pivotal role in determining the degree to which climate change will impact human health.[267] Because of this, two heat waves of similar duration and intensity would result in very different health impacts depending on the population's pre-existing health and socioeconomic status, the population's degree of acclimatization, housing conditions, and the robustness of existing public health systems. This makes predicting the severity of impact and potential differences across socio-demographic groups more difficult.

To date, most research on climate change from an environmental justice perspective has been of two types. One looks at the question of equity through the lens of historical responsibility for greenhouse gas emissions, the distribution and human rights implications of present and future impacts, and/or the capacity to mitigate emissions and adapt to the impacts of climate change, typically on the scale of nation states.[40,41,268,269] A second approach employs spatial measures of climate-related hazards, population susceptibility and adaptive capacity to map differences in vulnerability to climate change in relation to community socio-demographics.[46,47] Epidemiological research of effect measure modification like that described in Chapter 4 is another approach that can shed light on whether the health of particular members of society is likely to be disproportionately impacted during the type of extreme weather events that will become more frequent with climate change. Although they are less common in the environmental justice literature, studies employing this approach such as those documenting that people of color can be more vulnerable to heat-related mortality and morbidity[208,219] provide useful evidence for understanding potential inequitable outcomes related to climate change.

Studies of the impact of heat on health are likely to suffer from significant exposure misclassification when relying on existing weather stations that are often located in outlying areas such as airports. A "heat island effect" can arise in urban areas because of the prevalence of heat-trapping surfaces such as asphalt and concrete that prevent evapotransporative cooling, the concentration of buildings and vehicles that give off heat, and changes in wind patterns. These and other factors can create small-scale variations in temperature within cities that are not captured by the existing network of weather stations. Remote sensing products can be used to estimate land cover characteristics as a proxy for local variation in temperature, as I do in Chapter 4. Understanding the extent to which land cover characteristics contribute to heat exposure risks is useful because land cover types can be changed. However, neither weather

stations nor remote sensing will capture differences in building characteristics (e.g. ventilation rates, presence of air conditioning) or behavioral adaptations (e.g. clothing, physical activity, use of cooling technologies). These factors significantly change the temperature an individual experiences and are best measured using personal monitors. Research on heat and health thus faces an inherent tradeoff between the accuracy of exposure assessment on the one hand and on the other, the large sample size and representativeness facilitated by the analysis of existing secondary data. Going forward, methods that integrate weather station, remote sensing and personal monitoring could improve our understanding of heat-related health impacts.

Much work remains to be done in order to understand the mechanisms by which – and threshold temperatures at which – heat can lead to increased risk of preterm birth or other adverse reproductive health outcomes. My findings in Chapter 4 suggest either that apparent temperatures up to 45 °C have little impact on preterm birth or that the population of Houston, Texas is well adapted to heat, exhibiting little adverse effects even during prolonged periods of unusually high temperatures. Nevertheless, it is clear that beyond certain temperatures, adverse birth and other health impacts are inevitable because the body has limits to its ability to maintain normal core body temperatures as ambient temperatures rise.[260] When taken together with the fact that people of color are over-represented in outdoor occupations, have lower air conditioning ownership rates (at least in other U.S. cities), often suffer from higher rates of illness that pre-dispose one to heat-related illness, and have suffered larger impacts in other studies of extreme heat (e.g.,[208,219]), my finding of large racial disparities in neighborhood heat-trapping land cover characteristics in Harris County, Texas, indicates that more frequent heat waves are an environmental justice concern worthy of further research.

Implications for policy

Protect vulnerable and disproportionately exposed groups

In Chapter 2, I demonstrated that environmental and social stressors to health are spatially correlated across California neighborhoods in such a way that people of color are at greater risk of cumulative health impacts. My findings suggest that neighborhoods with more environmental hazards are also more socioeconomically disadvantaged. These overlapping geographies of risk – a phenomenon others have called "double jeopardy"[113] – holds implications for regulatory pollution standards. Because they rarely factor in cumulative exposures or social stressors that may influence susceptibility to the adverse health effects of pollution, regulatory standards may not adequately protect vulnerable subgroups and those who experience disproportionate exposures to multiple pollutants.

Increasingly, new laws require attention to social equity in the regulation and implementation of environmental laws and programs. For example, as mentioned earlier, California passed legislation in 2012 that requires a quarter of greenhouse gas mitigation funding from the State's cap-and-trade program to benefit disadvantaged communities "disproportionately affected by environmental pollution" and/or socioeconomic disadvantage.[270] Environmental justice screening tools that integrate metrics of pollution burden and socioeconomic disadvantage can be useful for decision-makers in complying with such laws by identifying places where pollution reductions can bring benefits to disadvantaged groups. As regulators grapple with ways to reduce inequity in addition to overall exposure, inequality metrics such as the concentration index I employ in

Chapter 2 can help characterize the degree of inequity and measure progress towards policy goals over time. Climate change adaptation strategies that protect vulnerable subpopulations also need to be identified in order to prevent inequitable outcomes.

Precaution in the face of uncertainty

The biomonitoring data presented in Chapter 3 reveals that the ubiquitous presence of several man-made chemicals in the environment and consumer products expose women and the developing fetus to potential adverse health risks during pregnancy. It is difficult to evaluate whether the concentrations measured in biomonitoring studies warrant concern because current policy in the U.S. requires little health and safety testing of the synthetic chemicals used in industry (pharmaceuticals and pesticides require more). We therefore know very little about the possible health effects of the vast majority of the tens of thousands of chemicals available for use today, including whether they produce additive, antagonistic or synergistic effects when present in combination. (We do know that many chemicals can cross the placenta, exposing the fetus.[119]) The burden of proof rests with regulators to prove harm rather than manufacturers to provide evidence of a chemical's safety. This has led many environmental health advocates to suggest we need a comprehensive shift in chemicals policy towards precaution in the face of uncertainty. The growing evidence that early life exposures influence disease rates in adulthood[271] and even across generations through changes in epigenetics[272] only makes the case for precaution to prevent prenatal exposures stronger.

Focus on upstream drivers

Larger social forces influence both the distribution of environmental hazards and social determinants of health across populations (**Figure 5-1**). For example, as a result of red-lining and other discriminatory federal and local housing policies that enforced racial residential segregation and lead to the concentration of poverty, Black and Hispanic households typically live in neighborhoods with median incomes similar to those of very poor White households.[273] Living in a poorer neighborhood may result in poorer health independent of one's own income.[274] At the same time, in a society where wealth confers power and political influence, the concentration of poverty in communities of color also means less political power to resist the siting of undesirable land uses and industries, demand more stringent environmental regulation, or secure public resources to remove environmental hazards. While researchers continue to untangle the complex ways in which pollution and neighborhood environments contribute to environmental health disparities, we should not lose sight of the importance of the larger, upstream drivers that help determine where people live, work and play and sustain unjust environmental and economic conditions. Changing the larger forces that create and sustain social inequality is likely to bring multiple benefits to the health of disadvantaged communities by improving environmental quality as well as the material and social conditions that can make people sick.

There is also evidence that policies to reduce social inequality may bring health benefits to socially advantaged groups as well as disadvantaged groups. Several studies have found that unequal societies tend to have poorer overall health and more polluted environments than more equal societies.[275–279] The relationship between inequality and detriments to population health has been attributed to psychosocial stress resulting from perceptions of relative disadvantage and

the erosion of social cohesion or social capital, including divestment in public goods.[280,281] Hypotheses as to why social inequality may lead societies to pollute more include the vested interest of wealthy groups in dirty industries and their political power to protect those interests from environmental regulation; the ways in which perceived relative social disadvantage drives people to work and consume more; and the erosion of social cohesion and willingness to cooperate to protect common resources.[282] Policies that seek to redistribute power, wealth and opportunity in more egalitarian ways may therefore indirectly bring environmental and health benefits to advantaged and disadvantaged members of society alike. In other words, progressive social and economic policy is also good health and environmental policy.

This last point begs the question of whether narrowly focused environmental advocacy misses larger opportunities to protect the environment by failing to attack root causes of inequality in power. Social movements for environmental justice – including the forging of international and "blue-green" alliances that link worker rights and sustainability – hold promise in this respect. By linking social justice and the environment, such movements can help usher in larger societal transformations that advance global sustainability and wellbeing.

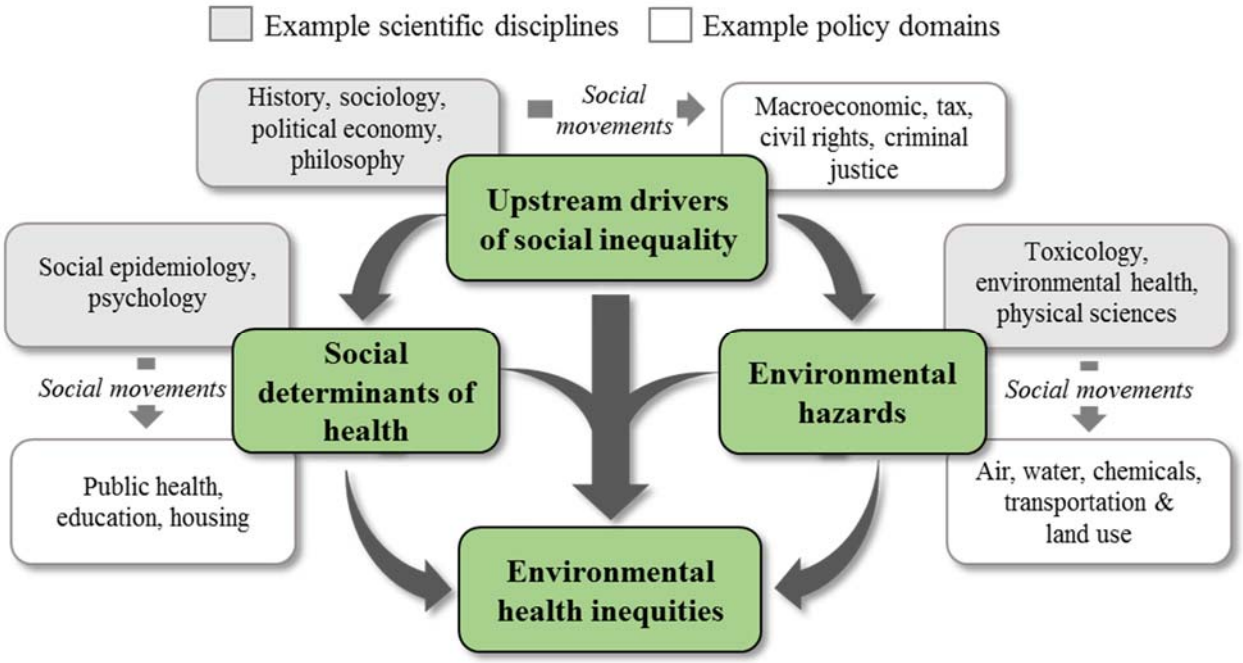


Figure 5-1 Diverse research and policy approaches are needed to address environmental health inequities. Social movements leverage current and emerging scientific knowledge to promote policy change that advances environmental equity goals.

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APPENDIX A

Description of laboratory methods and list of analytes: Chemicals in Our Bodies study[a]

Sample collection and storage

Blood was collected in EDTA-coated tubes and stored at -20°C until it was analyzed for metals. For serum preparation, approximately 40 mL of blood was collected in tubes without additives or anticoagulants and, within 24 hours, serum was separated by allowing blood to clot at room temperature, then centrifuging the sample twice at 2000 rpm. Serum was then transferred to amber glass vials for storage at -20°C until analysis for persistent organic pollutants (PBDEs, PCBs and OCPs), PFCs and hydroxylated PBDE metabolites (OH-BDEs).

Urine sample collection procedures are described in Dobraca et al. (2015).[1] Participants were asked to wash their hands prior to providing urine specimens into polypropylene containers. A set of urine collection, sample aliquoting and storage containers were tested for the targeted analytes to rule out background contamination prior to use. Spot urine samples were stored frozen at -20°C at the clinic until delivery to the Environmental Health Laboratory (EHL) of the California Department of Public health in Richmond, CA. Upon arrival at EHL, samples were thawed, split into smaller containers, and re-frozen and stored at -70°C until analyses. Gavin et al. (2013) verified that phenols in urine samples were not degraded because of the freeze-thaw cycles.[2]

Laboratory methods

Chemical analyses were conducted at two Biomonitoring California laboratories. The Environmental Chemistry Laboratory of the Department of Toxic Substances Control in Berkeley, California analyzed serum and EHL analyzed urine and whole blood.

Cholesterol and triglycerides in blood were enzymatically determined at Boston Children′s Hospital (Boston, MA). The total serum lipid content was calculated as follows:[3]

$$TL = 2.27TC + TG + 0.623$$

where TL denotes total lipids, TC stands for total cholesterol and TG for triglycerides. Creatinine in urine was measured using applications of a colorimetric method known as the Jaffe reaction,

[a] Chemicals in Our Bodies is a joint project of Biomonitoring California, a tri-departmental state program, and the University of California at San Francisco and Berkeley. The descriptions of analytical chemistry methods included in this appendix were provided by staff at the laboratories of the California Department of Public Health and Department of Toxic Substances Control, with additional contributions from staff at the Office of Environmental Health Hazard Assessment of the California Environmental Protection Agency. Further documentation of the methods used in Biomonitoring California have been published previously in the *International Journal of Environmental Analytical Chemistry*, *Environmental Science & Technology*, *Chemosphere*, the *Journal of Chromatography*, *Analytical Methods*, and the *Journal of Occupational and Environmental Medicine* in the references given at the end of this text.

and based in part on a commercially available method (BioAssay Systems QuantiChrom Creatinine Assay Kit DICT-500).

PBDEs, PCBs & OCPs in serum

The extraction method and instrumentation for the determination of these persistent organic pollutants in serum using gas chromatography/high resolution mass spectrometry (GC-HRMS) have been published elsewhere[4,5] and were used in the current study with slight modifications. Thawed serum samples (2 mL) were spiked with carbon-labeled surrogate standards: nine ^{13}C-labeled PBDEs ($^{13}C_{12}$-BDE-28, -47, -99, -153, -154, -183, -197, -207, and -209); nine ^{13}C-labeled PCBs ($^{13}C_{12}$-PCB-101, -105, 118, -138, -153, -156, -170, -180, and -194); seven ^{13}C-labeled OCPs ($^{13}C_{12}$-2,4′-DDT, $^{13}C_{12}$-4,4′-DDE, $^{13}C_{12}$-4,4′-DDT, $^{13}C_6$-hexachlorobenzene, $^{13}C_{10}$-oxychlordane, $^{13}C_{10}$-trans-nonachlor, and $^{13}C_6$-β-BHC). Equal volumes (4 mL) of formic acid and water were added to each sample before loading on the solid phase extraction (SPE) modules (RapidTrace, Biotage®, USA). Oasis HLB cartridges (3 cc, 500 mg, Waters, Inc. USA) and acidified silica (500° C pre-baked, manually packed, 3 cc) were used for the sample extraction and clean-up, respectively. The collected final eluates were concentrated and spiked with recovery standard ($^{13}C_{12}$-PCB-209). NIST standard reference material 1589a and bovine serum pre-spiked with known amounts of target analytes were used as quality assurance/quality control (QA/QC) samples.

Gas chromatography/high-resolution mass spectrometry (GC-HRMS) using the Thermo Scientific™ DFS™ Magnetic Sector GC-HRMS system (ThermoFisher, Bremen, Germany) was used to measure PBDEs and PCBs/OCPs in two separate injections. For OCP and PCB analyses, 2 μL of extract were injected in splitless mode and separated using a HT8-PCB column (60 m × 0.25 mm I.D., 0.25 μm film thickness, SGE International Pty Ltd., Australia & Pacific Region) with helium as carrier gas. For PBDE analysis, 2 μL of extract were injected and separated using a DB-5 MS column (J&W Scientific, USA) (15 m × 0.25 mm I.D., 0.10 μm film thickness) with helium as carrier gas. The MS was operated in electron impact ionization mode using multiple ion detection. For both analyte groups, the source temperature was set to 260° C, ionization energy was set to 42 V, and electron current was typically 0.7 mA, with a mass resolution power of 10,000. Perfluorokerosene (PFK) was used as the mass reference.

PBDE metabolites (OH-BDEs) in serum

The analysis of OH-PBDEs in serum was carried out on a Prominence Ultra-Fast liquid chromatography system (UFLC) (Shimadzu Corporation, Columbia, MD, USA) interfaced with an AB Sciex 5500 Qtrap System (Applied Bioscience, Foster City, CA, USA) in triple quadrupole MS/MS mode. An off-line SPE sample cleanup was implemented including a 3-hr enzymatic hydrolysis prior to extraction of the analytes from 250 μL of serum.[6] The SPE was performed using OASIS™ HLB, 60 mg, 3 cc (Waters Inc., MA, USA) and the chromatographic separation was achieved on a mixed-mode column (Acclaim Surfactant Plus, 3 μm, 2.1 mm x 250 mm; Thermo Scientific, Madison, WI, USA). An aliquot of 10 μL of the reconstituted sample diluted four times was used for analysis. QC materials (low, medium and high) were processed with each batch of samples. Blank samples were also processed with each batch and no OH-PBDEs were detected.

PFCs in serum

PFC concentrations in serum were determined using an online solid phase extraction high-performance liquid chromatography tandem mass spectrometry (SPE-HPLC-MS/MS) method.[7] Briefly, 100 μL of serum were mixed with 0.1M formic acid, and internal standards were added ($^{13}C_2$-PFOA and $^{13}C_4$-PFOS), then injected by the online Symbiosis™ SPE-HPLC system (Symbiosis TM Pharma system with Mistral CS Cool, IChrom Inc.) to a C18 cartridge (HySphere C18 HD, 7 μm, 10 mm × 2 mm). After washing, the target analytes were eluted to a C8 HPLC column (BETASIL C8 column, Thermo Fisher Scientific) for separation. The eluate was then introduced to the MS/MS (API 4000 QTrap, ABSciex) for multiple-reaction-monitoring (MRM) analysis. Analytes were quantified using a calibration curve constructed for each batch: regression coefficients of 0.98 to 0.99 were generally obtained. Standard reference materials (SRM 1958) from the National Institute of Standards and Technology (NIST, Gaithersburg, MD), as well as PFC-spiked samples of known concentration from the U.S. Centers for Disease Control and Prevention (CDC) were used as reference materials. Blank samples (bovine serum) were processed with each batch of samples, and no PFCs were detected above their respective MDLs.

Metals in blood

Whole blood specimens were analyzed for total mercury (Hg), cadmium (Cd) and lead (Pb), using an Agilent 7500cx inductively coupled plasma-mass spectrometry system with a helium collision cell (Agilent Technologies, Inc., Folsom, CA).[8] Blood specimens were diluted 1:50 prior to analysis with a diluent comprised of 4% w/v of n-butanol, 2% w/v of NH_4OH, 0.1% w/v Triton X-100 and 0.1% w/v of H_4EDTA to minimize blood matrix effects. The diluent was used for calibration standards and blood specimen preparation. Each specimen was analyzed in duplicate and the final result was calculated by averaging the two. Acceptance criteria were based on the relative percent difference (RPD) between the two specimens. The average result was deemed acceptable if the RPD was ≤20%. Fewer than1% of the reported samples had RPDs >20% due to issues with sample clotting, especially with cord blood specimens. RPDs for these exceptions were <35%, and the average RPDs for Cd, Pb and Hg were 11.3%, 3.7% and 6.4%, respectively. RPDs were not considered when analytical values were below the MDL.

QC reference materials and intermediate calibration standards were prepared from stock standard solutions traceable to the NIST. QC reference materials were prepared by spiking defibrinated sheep blood obtained from Hemostat Laboratories (Dixon, CA, USA) with stock standard solutions at three concentrations (low, medium and high). All reference materials were analyzed at both the beginning and end of each batch analysis. Four concentrations of NIST Standard Reference Material 955c were periodically analyzed throughout the study to assure independent confirmation.

Total arsenic in urine [b]

Urine specimens were analyzed for total arsenic (As) using an Agilent 7500 inductively coupled plasma mass spectrometry (ICP-MS) system. The ICP-MS was configured with a helium mode collision cell to reduce polyatomic interferences. Matrix-matched calibration standards were prepared with 1% NaCl to minimize any potential bias caused by matrix effects. Both urine specimens and calibration standards were diluted 1:20 with a diluent containing 2% (w/v) ethanol (200 proof), 2% (w/v) nitric acid, 0.05% (w/v) Triton X-100, 1 mg/L gold and internal standards (Ge, Rh and Re), and then aspirated into the ICP-MS using an integrated sample introduction system (ISIS) as a flow injection technique. Each urine specimen was analyzed in duplicate. Analytical precision, or relative percent difference (RPD), was better than 20% when an analyte level was greater than 10 times the method detection limit.

OH-PAHs in urine

Sample preparation was accomplished by liquid-liquid extraction with a Gilson Quad-Z 215 Liquid Handler (Gilson, Middleton, WI, USA). Urine samples were extracted twice with 5 mL of 20% toluene/80% pentane after the addition of 2 mL of MilliQ water. Samples were mixed and centrifuged to separate the aqueous and organic phases. 1 mL of 1 M silver nitrate was added to 10 mL of purified extract, mixed, and transfers the 10 mL of the washed extract to a new product tube. The sample extract was spiked with 10 µL dodecane, transferred to a 15 mL conical bottom centrifuge tube, and evaporated to approximately 2 mL in 15 minutes under a gentle stream of N_2 around 5 psi using a Caliper LifeSciences TurboVap LV evaporator (Biotage AB, Box 8, 751 03 Uppsala, Sweden) at 40°C water bath. Samples were then moved to a second TurboVap LV evaporator at 80°C water bath and evaporated to approximately 10 µL in 10 to 15 min under a gentle stream of N_2. After the evaporation, 20 µL toluene, 5 µL of recovery spike standard of $^{13}C_{12}$-PCB -105L, and 10 µL of N-methyl-N-(trimethylsilyl)-trifluoroacetamide (MSTFA) were added to each tube. The contents were transferred to a 0.3 mL glass autosampler insert with spring in an amber autosampler vial that was capped after displacing the air in the vial with a gentle stream of Argon. The vials were then placed in a 60°C oven for 30 min for derivatization.

The concentrations of OH-PAHs were determined by Double Focusing System (DFS) Gas Chromatography High Resolution Mass Spectrometer (GC-HRMS) (Thermo Scientific, Waltham, MA, USA) coupled with Trace GC Ultra and TriPlus XT autosampler. The mass spectrometer was operated in Electron Impact (EI) ionization mode, with 1 mA of emission current, 45 eV of electron energy. Ion source temperature was set to 260°C, and FC43 was used for lock and calibration of the accuracy of mass during analysis. Before injecting each batch of samples and standards for analysis, the resolution of the DFS GC-HRMS was tuned to 10,000 ± 500.

Multiple ions detection (MID) mode was used to achieve the maximum sensitivity and selectivity. 1 µL of each sample was injected into the GC system in splitless mode. The temperature of the injector was set at 260°C and the transfer line temperature was set at 260°C.

[b] Chemicals in Our Bodies also measured 6 arsenic compounds and two additional metals (Cd and Hg) in urine. A description of laboratory methods for these analytes is omitted here because they were not included in the analysis presented in Chapter 3.

A column with dimension 0.25 mm inner diameter, 30 m length, 0.25 μm film thickness (DB-5 MS, J&W Scientific, Folsom, CA, USA) was used for the separation and analysis. Ultra High Purity helium (99.999%) was used as the carrier gas at a constant flow of 0.8 mL min^{-1}. The initial oven temperature 90°C was equilibrated for 2 min. After equilibrium, the temperature was increased to 155°C at 15°C min^{-1}, then increased to 225°C at 3.9°C min^{-1}, then finally increased to 310°C at 28.3°C min^{-1} and held for 5 min. OH-PAHs were quantified by isotopic dilution by using labeled OH-PAH internal standards. Laboratory blank and three levels of internal QC samples were included with each run to assess background contamination and method precision and accuracy.

Phthalate metabolites in urine

Phthalate laboratory methods were adapted from Kato *et al.* (2005).[9] Urine samples were spiked with a mixture of stable isotope-labeled internal standards (Cambridge Isotope) and enzymatically digested with glucuronidase at 37ºC for 90 min. Five hundred microliters of digested sample solution were injected into an on-line SPE column and analyzed using a high-performance liquid chromatography/tandem mass spectrometer (HPLC-MS/MS) system (API 5000, AB Sciex). Target analytes were chromatographically separated on a Betasil™ phenyl column in a mobile phase consisting of acetonitrile and 0.1% acetic acid in gradient elution mode. Ionization of analytes was carried out with an electrospray ionization (ESI) source operating in negative mode. To enhance sensitivity, the mass spectrometer data was acquired using multi-period mode during chromatographic elution time.

The correlation coefficients (r^2) of calibration curves for all target analytes were ≥ 0.99. Randomly selected samples (approximately 5%) were analyzed in duplicate and the relative percent differences (RPD) between duplicate results were ≤20%. Quality control samples were included in every analytical run and the recoveries were all within 30% of the respective target values. Precision for each quality control level was good, with coefficients of variation (CV) for all analytes ≤15%.

Phenols in urine

The simultaneous determination of phenols in urine was accomplished with off-line SPE sample cleanup and HPLC/MS-MS analysis with a QTRAP 5500 (AM Sciex, Foster City, CA) in a method that has been described elsewhere.[2] Briefly, samples were enzymatically hydrolyzed by overnight incubation at 37°C of a 1.0 mL aliquot of urine with the addition of 100 μL of internal standard mixture and, immediately prior to the incubation, 500 μL of freshly prepared enzyme mixture containing β-glucuronidase/sulfatase. The reaction was terminated by addition of 0.5 mL of 1 M formic acid. Samples were then purified by SPE procedure using a VBond Elut-C18 column (100 mg 3 ml, Varian, Inc.) on a vacuum manifold (Supelco Visiprep 24™ DL). SPE cartridges were preconditioned with 2.0 mL of methanol and 1.0 mL of water. 2.1 mL of samples were applied to the columns and the compounds were eluted with 2.0mL of methanol after cartridges were washed with 1.0 mL of 10% methanol in water. Eluates were evaporated to dryness under a stream of dry nitrogen (10–12 psi, UHP grade) with a Turbo Vap LV evaporator from Caliper Life Sciences (Hopkinton, MA) at 40°C for about 30 minutes. The phenol residues were then reconstituted with 200 μL of methanol:water (1:1, v:v) and transferred to inserts in auto sampler vials.

Chromatographic separation was performed using a Shimadzu Prominence LC system (LC-20AD, Columbia, MD) with water as solvent A and methanol as solvent B. An injection volume of 10 µL was used on an ACE Excel C18-PFP (4.6 × 100 mm, 3.0 µm, Chadds Ford, PA) column using a gradient elution program with a total flow rate of 500 µL/min. Gradient programming was 0.0–2.0 min, 60% B; 2–10 min, 60% to100% B; 10–15 min, 100% B; 15–15.1 min, 100% to 60% B; and 15.1 min –20 min, 60% B.

The QTRAP 5500 mass spectrometer with the Analyst 1.5.1 software was used for data acquisition and processing. Negative ion atmospheric pressure chemical ionization (APCI) was used for acquisition and quantification with the following settings: curtain gas (N_2) 20 psi, heated ion source gas 30 psi, heated gas temperature 450°C, nebulizer current –3.5 µA. Declustering potential, entrance potential, and collision energy were optimized for each analyte. All channels were monitored with a different dwell time adding up to 1.4-s cycle time.

Quantification was performed using up to a 12-point calibration curve prepared in pooled diluted human urine with phenol concentrations ranging from 0.1 ng/mL to 1000 ng/mL. The correlation coefficients (r^2) of calibration curves for all target analytes were ≥ 0.99.

Quality control material consisted of anonymously collected human urine from multiple volunteers that was pooled, filtered through a 0.45 µm SuperCap-100 Capsule (Pall Corp., Ann Arbor, MI) and spiked with spiking solution containing D_3 and 13-C-labelled phenols to yield concentrations of 5.0 ng/mL (Low Quality Control or LQC), 20 ng/mL (Medium Quality Control or MQC), and 50 ng/mL (High Quality Control or HQC) with the exception of BPA having a concentration of 1.0 ng/mL, 4.0 ng/mL, and 10 ng/mL. One aliquot from each of the LQC, MQC, and HQC was analyzed along with the real urine samples. The relative recoveries were between 90.1% and 104% at all spike levels. Coefficients of variation between 5.24% and 14.3% reflect low variability or excellent precision of the method.

Organophosphate and pyrethroid pesticide metabolites in urine

The analysis of specific metabolites of organophosphate and pyrethroids metabolites in urine was carried out on a Shimadzu LC system composed of a micro-volume pump, inline membrane degasser, and mixer which is attached to thermostated PAL- HTC auto sampler with cooled rack (Shimadzu Corporation, Columbia, MD, USA) interfaced with an AB Sciex 5500 QQQ System (Sciex, Foster City, CA, USA) . An off-line SPE sample cleanup was implemented including overnight enzymatic hydrolysis prior to extraction of the analytes from 1.0 mL urine sample. The SPE was performed using OASIS® HLB, 60 mg, 3 cc (Waters Inc., MA, USA) and the chromatographic separation was achieved on a narrow bore 2.1 x 100-mm, 3.0 µm ACE Excel C18-PFP column mm; (MAC-MOD Analytical, Inc., PA, USA). The binary pumps were configured to run a gradient elution program with a flow rate of 350µL/min. An aliquot of 10 µL of the reconstituted sample was used for analysis. In house prepared QC materials (low, medium and high) and method blanks were processed with each batch of samples.

The 5500 triple quad mass spectrometer with the Analyst 1.6.1 software program (Sciex, Foster City, CA) was used for acquisition and quantitation of these compounds. Quantification was performed using 8 point calibration curve prepared in diluted urine and extracted with every batch. The calibration range was selected to cover the lowest level seen on the instrument with a

good signal-to-noise ratio of 3:1 or better. 3-PBA was analyzed by using the continuous polarity switching feature of the instrument.

Table A-1 Complete list of analytes measured in Chemicals in Our Bodies

Serum	
PBDEs	**Acronym**
2,2′,4′-tri-bromodiphenyl ether	BDE-17
2,4,4′-tri-bromodiphenyl ether	BDE-28
2,2′,4,4′-tetra-bromodiphenyl ether	BDE-47
2,3′,4,4′-tetra-bromodiphenyl ether	BDE-66
2,2′,3,4,4′-penta-bromodiphenyl ether	BDE-85
2,2′,4,4′,5-penta-bromodiphenyl ether	BDE-99
2,2′,4,4′,6-penta-bromodiphenyl ether	BDE-100
2,2′,4,4′,5,5′-hexa-bromodiphenyl ether	BDE-153
2,2′,4,4′,5,6′-hexa-bromodiphenyl ether	BDE-154
2,2′,3,4,4′,5′,6-hepta-bromodiphenyl ether	BDE-183
2,2′,3,3′,4,4′,5,6′-octa-bromodiphenyl ether	BDE-196
2,2′,3,3′,4,4′,6,6′-octa-bromodiphenyl ether	BDE-197
2,2′,3,3′,4,5′,6,6′-octa-bromodiphenyl ether	BDE-201
2,2′,3,3′,5,5′,6,6′-octa-bromodiphenyl ether	BDE-202
2,2′,3,4,4′,5,5′,6-octa-bromodiphenyl ether	BDE-203
2,2′,3,3′,4,4′,5,5′,6-nona-bromodiphenyl ether	BDE-206
2,2′,3,3′,4,4′,5,6,6′-nona-bromodiphenyl ether	BDE-207
2,2′,3,3′,4,5,5′,6,6′-nona-bromodiphenyl ether	BDE-208
2,2′,3,3′,4,4′,5,5′,6,6′-deca-bromodiphenyl ether	BDE-209
OH-BDEs	
2′-OH-BDE-068	2′-OH-BDE-068
6′-OH-BDE-099	6′-OH-BDE-099
5′-OH-BDE-047	5′-OH-BDE-047
4′-OH-BDE-049	4′-OH-BDE-049
PCBs	
2,3′,4,4′-tetrachlorobiphenyl	PCB-66
2,4,4′,5-tetrachlorobiphenyl	PCB-74
2,2′,4,4′,5-pentachlorobiphenyl	PCB-99
2,2′,4,5,5′-pentachlorobiphenyl	PCB-101
2,3,3′,4,4′-pentachlorobiphenyl	PCB-105
2,3′,4,4′,5-pentachlorobiphenyl	PCB-118
2,2′,3,4,4′,5′-hexachlorobiphenyl	PCB-138
2,2′,4,4′,5,5′-hexachlorobiphenyl	PCB-153
2,3,3′,4,4′,5-hexachlorobiphenyl	PCB-156
2,2′,3,3′,4,4′,5-heptachlorobiphenyl	PCB-170
2,2′,3,4,4′,5,5′-heptachlorobiphenyl	PCB-180

2,2′,3,4,4′,5′,6-heptachlorobiphenyl	PCB-183
2,2′,3,4′,5,5′,6-heptachlorobiphenyl	PCB-187
2,2′,3,3′,4,4′,5,5′-octachlorobiphenyl	PCB-194
2,2′,3,4,4′,5,5′,6-octachlorobiphenyl	PCB-203
PFCs	
2-(N-Ethyl-perfluorooctane sulfonamido) acetic acid	N-Et-FOSAA
2-(N-Methyl-perfluorooctane sulfonamido) acetic acid	N-Me-FOSAA
Perfluorobutane sulfonic acid	PFBS
Perfluorodecanoic acid	PFDeA
Perfluorododecanoic acid	PFDoA
Perfluoroheptanoic acid	PFHpA
Perfluorononanoic acid	PFNA
Perfluorooctanoic acid	PFOA
Perflucorooctane sulfonic acid	PFOS
Perfluorooctane sulfonamide	PFOSA
Perfluoroundecanoic acid	PFUA
Organochlorine pesticides (OCPs)	
2,4′-Dichlorodiphenyltrichloroethane	2,4′-DDT
4,4′-Dichlorodiphenyltrichloroethane	4,4′-DDT
4,4′-Dichlorodiphenyldichloroethylene	4,4′-DDE
Lindane (*gamma*-hexachlorocyclohexane)	*b*-HCH
Hexachlorobenzene	HCB
Oxychlordane	oxychlordane
trans-nonachlor	*t*-nonachlor
Whole blood	
Metals	
Cadmium	Cd
Lead	Pb
Mercury	Hg
Urine	
Metals	
Cadmium	Cd
Mercury	Hg
Total arsenic	As
Speciated arsenic	
Arsenobetaine	AB
Arsenocholine	AC
Arsenous (III) acid	AsIII
Arsenic (V) acid	AsV
Dimethylarsinic acid	DMA
Monomethylarsonic acid	MMA
OH-PAHs	
2-Hydroxyfluorene	OH-2-fluo
3-Hydroxyfluorene	OH-3-fluo

9-Hydroxyfluorene	OH-9-fluo
1-Hydroxynapthalene	OH-1-nap
2-Hydroxynapthalene	OH-2-nap
1-Hydroxyphenanthrene	OH-1-phen
2-Hydroxyphenanthrene	OH-2-phen
3-Hydroxyphenanthrene	OH-3-phen
1-Hydroxypyrene	OH-1-pyr
Phthalate metabolites	
Mono-butyl phthalate	MBP
Mono-benzyl phthalate	MBzP
Mono-(3-carboxypropyl) phthalate	MCPP
Mono-(2-ethyl-5-carboxypentyl) phthalate	MECPP
Mono-ethyl phthalate	MEP
Mono-cyclohexyl phthalate	MCHP
Phenols	
2-hydroxy-4-methoxybenzophenone	benzophenone-3
4,4′-(propane-2,2-diyl)diphenol	Bisphenol-A or BPA
2,4,4′ –trichloro-2′-hydroxydiphenyl ether	triclosan
Organophosphate and pyrethroid pesticide metabolites	
Diethyl phosphate	DEP
Diethyldithiophosphate	DEDTP
Dimethyldithiophosphate	DMDTP
Dimethylthiophosphate	DMTP
3-Phenoxybenzoic acid	3-PBA
3,5,6-Trichloro-2-pyridinol	TCPy
Other	
Creatinine	

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