ABSTRACT

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The prevalence of Autism Spectrum Disorder (ASD) diagnoses in the United States has increased dramatically over the past 20 years, fueling investigations into possible environmental triggers for the disorder. Exposures to pesticides, persistent pollutants, prescription medications, and heavy metals through various routes have been examined, but very few studies have examined the potential role of chronic inhalation of hazardous air pollutants (HAPs) in the etiology of ASD. This thesis was designed to examine possible relationships between HAPs and ASD prevalence on a statewide level for the U.S., with sub-analyses on a finer, countywide level within the state of Maryland. Findings suggest consistent, positive associations between ASD prevalence and HAPs at the statewide level for the U.S. The findings do not persist at the county level in the Maryland sub-analyses. These results reinforce the concept of ASD as a spectrum of phenotypes best explained through multifactorial etiological models.

AUTISM SPECTRUM DISORDER AND HAZARDOUS AIR POLLUTANTS IN THE U.S. AND MARYLAND

By

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Table of Contents

List of Tables

List of Figures

Chapter 1: Introduction

1.1 Increased incidence and prevalence of Autism Spectrum Disorder

The prevalence and cumulative incidence of Autism Spectrum Disorder (ASD) diagnoses in the United States (U.S.) has increased dramatically over the past 20 to 30 years (Bertrand et al., 2001; Newschaffer, Falb, & Gurney, 2005; McDonald & Paul, 2010). Despite the broadened diagnostic criteria, increased awareness of the disorder, and potential for diagnostic substitution, the possibility that a true increased incidence of ASD underlies these diagnoses cannot be dismissed. Studies have shown that these diagnostic artifacts only account for a portion of the increased prevalence (Blaxill, Baskin, & Spitzer, 2003; Croen & Grether, 2003; Hertz-Picciotto & Delwiche, 2009; Newschaffer et al., 2005).

A strong genetic component of ASD has been established (Bailey et al., 1995; Le Couteur et al., 1996). However, genetic mechanisms alone cannot account for the remaining unexplained, large, and relatively rapid increase in ASD diagnoses. This suggests that exposure to exogenous agents, particularly during critical prenatal or early post-natal windows of development, may play a role in the expression of genetic susceptibility (Hertz-Picciotto et al., 2009; McDonald et al., 2010). This gene-environment model of ASD is complicated by the probable involvement of multiple genes and environmental factors.

1.2 Potential exogenous risk factors

Currently approximately 80,000 chemicals are in use or commerce in the U.S., of which about 3,000 are produced or imported in excess of 1 million pounds per year. Of these high production volume chemicals, 43% have not undergone the basic, minimum toxicity screening, and only about 7% have a full set of basic test data (U.S.Environmental Protection Agency [EPA], 1998). Thus, exposure effects, including neurodevelopmental effects on the unborn, remain unknown for the majority of these contaminants, some of which are ubiquitous in the environment, and some of which are known to cross the placenta. Prenatal exposure to many of these contaminants has been verified by examination of newborns' cord blood. The Environmental Working Group reported an average of 200 pollutants present in the umbilical cord blood of babies born in U.S. hospitals. A total of 287 chemicals were found, of which 217 are neurotoxins and 208 are teratogens or developmental toxicants to animals (Environmental Working Group, 2005). Furthermore, toxicological testing is primarily conducted on individual chemicals, and knowledge of effects of multiple exposures is lacking. Additive or synergistic effects of multiple xenobiotic agents, along with cumulative impacts of other stressors such as poverty, diet, and stress, may be instrumental in the development of complex disorders such as ASD.

Postulated biological mechanisms for environmentally-mediated ASD development include endocrine disruption, infection, and impaired metabolic and excretory functioning, which may lead to oxidative stress, immune dysregulation and inflammation, neurotransmitter imbalances, or direct neurological or neurodevelopmental toxicity effects (structural anomalies or damage) (Lawler, Croen,

Grether, & Van de Water, 2004). Metals, pesticides, organic solvents, and persistent pollutants such as polybromiated diphenyl ether (PBDE) and polychlorinated biphenyls (PCBs) have come under scrutiny with regard to their biologically plausible contributions to the risk for ASD (Lawler et al., 2004; Newschaffer et al., 2007). The following sub-section provides a brief overview of some of the existing research on a few of these contaminants with regard to the development of ASD or the symptoms often exhibited by individuals with ASD.

1.2.1 Commonly researched neurodevelopmental toxicants and suspected ASD risk factors

Heavy metals

Heavy metals, particularly lead and mercury, are known neurotoxicants, and have been researched extensively with regard to developmental delays and disabilities.

Mercury. Acute methylmercury poisoning events in Japan and Iraq resulted in severe, adverse neurodevelopmental effects to children (Harada, Akagi, Tsuda, Kizaki, & Ohno, 1999; Amin-zaki, Majeed, Clarkson, & Greenwood, 1978), and studies of exposure through diet have also indicated adverse cognitive and neurobehavioral effects (Grandjean et al., 1997; Debes, Budtz-Jorgensen, Weihe, White, & Grandjean, 2006; Oken et al., 2008). Ethylmercury exposure through routine childhood-administered thimerosal-containing vaccines has been studied extensively, and the medical and scientific communities' consensus is that no causal association with ASD has been established (Immunization Safety Review Committee, 2004; Oken et al., 2008). However, as a preventative measure, as of 2001 thimerosal has been removed as a

preservative from most routine childhood vaccines (U.S.Food and Drug Administration, 2003).

Lead. Elevated blood lead concentrations, even at levels below 10 μg/dL, the Centers for Disease Control and Prevention (CDC) recommended maximum level, reduces intelligence quotient (IQ) levels (Jusko et al., 2008), leads to cognitive and attention deficits (Chiodo, Jacobson, & Jacobson, 2004; Despres et al., 2003; Chiodo et al., 2007; Surkan et al., 2007), and has been linked to increased impulsivity and hyperactivity (Thomson et al., 1989; Silva, Hughes, Williams, & Faed, 1988; Mendelsohn et al., 1998). Many individuals with ASD present with some or all of these symptoms.

A small number of published case reports have suggested a possible association of lead exposure and ASD. Two children with severe lead poisoning were reported as having developed ASD symptoms (Lidsky & Schneider, 2005), and another case study presented one young child with ASD who was found to have elevated blood lead levels, the reduction of which corresponded with decreased severity of ASD symptoms (Eppright, Sanfacon, & Horwitz, 1996). However, environmental lead levels have decreased over the past 30 years while ASD diagnoses have increased, which is counterintuitive to a causal relationship.

Plasticizers

Plastics and associated production compounds such as plasticizers are now a ubiquitous presence in modern society, comprising a myriad of common products of everyday use (Jaakkola & Knight, 2008).

Phthalates. Exposure to phthalates from polyvinyl chloride flooring were linked with risk of ASD among a study population of young children in Sweden (Larsson, Weiss, Janson, Sundell, & Bornehag, 2009). These plasticizers acted as androgen disruptors in males in animal studies, and they have also been found to induce allergic responses in children (Jaakkola et al., 2008; Wilson, Blystsone, Hotchkiss, Rider, & Grey, Jr., 2009).

Bisphenol A. Another plasticizer and endocrine disruptor found in numerous common household products including water bottles and baby bottles is bisphenol A. Average levels of this organic compound in humans have been found to surpass corresponding harmful levels in animals in toxicological studies (vom Saal et al., 2008), and a panel of scientific experts concluded that this level of exposure was of cause for some concern with regard to adverse neurodevelopmental and neurobehavioral effects among infants (vom Saal et al., 2008).

Persistent organic pollutants

Polychlorinated biphenyls (PCBs). Polychlorinated biphenyls (PCBs) represent a group of chlorinated compounds that were once used as cooling and insulating fluids in electronics, but that were banned in the 1970s due to toxicity concerns and issues of persistence in the environment. Despite this ban, PCBs have continued to bioaccumulate in the food supply, and remain widespread in the environment. Impaired cognitive, learning, and memory skills, as well as motor skills, have been observed in association with exposure to PCBs in a number of studies worldwide (Nakajima et al., 2006; Schantz, Widholm, & Rice, 2003; Grandjean et al., 2007; Jacobson & Jacobson, 1996).

Brominated Flame Retardants. Production of brominated flame retardants such as polybrominated diphenyl ethers (PBDEs), has dramatically increased concomitantly with the increase in ASD prevalence (Birnbaum & Staskal, 2004), and studies show increasing concentrations of these chemicals in maternal and fetal blood in the U.S. (Environmental Working Group, 2005; Mazdai, Dodder, Abernathy, Hites, & Bigsby, 2003). PBDEs are similar in structure to PCBs and also bioaccumulate in adipose tissue and breast milk. PBDE disruption of thyroid-regulated brain cell growth and connectivity processes may adversely affect neurodevelopment and behavior (Legler, 2008; Costa & Giordano, 2007), and consideration of PBDEs as a potential risk factor for ASD has been postulated (Messer, 2010).

Pesticides. Prenatal pesticide exposure has also been linked with ASD and neurodevelopmental delay. A significant, approximately 2-fold increase in risk of pervasive developmental disorder for each 10-fold increase in total maternal and child urinary dialkylphosphate metabolites was observed among farm-working families in one study (Eskenazi et al., 2007). Prenatal residential proximity to agricultural application of organochlorine pesticides was found to be significantly associated with ASD among non-farm-working families. Moreover, the critical period of prenatal exposure was determined to coincide with the development of the central nervous system (Roberts et al., 2007).

Environmental tobacco smoke (prenatal exposure)

A Swedish case-control study found that daily maternal smoking during pregnancy was associated with an elevated risk for ASD (Hultman, Sparen, & Cnattingius, 2002). In addition, links between maternal smoking and slowed fetal growth and low birth weight have been well-documented (Brooke, Anderson, Bland, Peacock, &

Stewart, 1989), and an association between low birth weight and risk for ASD has been reported (Hultman et al., 2002; Schendel & Bhasin, 2008). Due to well-established adverse birth effects resulting from prenatal exposure to tobacco smoke, studies of prenatal exposures with regard to the development of ASD need to account for any confounding effects of maternal smoking.

1.2.2 Chronic inhalation exposures: Ambient air

Many of the known or suspected neurotoxicants reviewed in the preceding sub-section have been investigated in epidemiological and toxicological studies via ingestion, injection, dermal, or indoor inhalation routes of exposure. In addition, most of the limited toxicological testing of the high production volume chemicals has focused on acute, rather than chronic toxicity (Environmental Defense Fund, 1997). Yet many of these compounds are also released from mobile and stationary sources into outside ambient air, representing a source of chronic inhalation exposure to the general population.

A number of studies indicate an association of ambient criteria air pollutants, particularly particulate matter, carbon monoxide, and sulfur dioxide, with low birth weight (Wang, Ding, Ryan, & Xu, 1997; Maisonet, Bush, Correa, & Jaakkola, 2001). Low birth weight, in turn, is linked to ASD risk in a few studies (Hultman et al., 2002; Schendel et al., 2008). In addition, prenatal exposure to polycyclic aromatic hydrocarbons (PAHs), a component of particulate matter, has been linked with poor fetal growth and low birth weight (Choi et al., 2006) and with impaired cognitive functioning in young children (Perera et al., 2009).

However, few studies have examined the presence of hazardous air pollutants (HAPs) as a potential contributor to ASD development. Those studies that have

investigated this possibility have focused on just one or a select few pollutants, and have examined associations only within small geographical areas.

In one such study, Texas school districts with high levels of environmentally released mercury, as reported by the Environmental Protection Agency's (EPA's) Toxic Release Inventory, were associated with greater ASD prevalence, as recorded by the Texas Education Agency, in a cross-sectional, ecological study (Palmer, Blanchard, Stein, Mandell, & Miller, 2006). A follow-up study indicated a dose-response relationship between a school district's proximity to major sources of environmentally released mercury and ASD rates of the district's kindergarteners 5 years later (Palmer, Blanchard, & Wood, 2009).

Whereas Palmer's studies used emissions estimates to assess exposure to mercury, a case-control study of HAPs and ASD prevalence in the San Francisco Bay Area of California used average modeled estimates of ambient concentrations for the exposure assessment for 19 separate air toxics. The latter investigation documented that early childhood exposures to higher ambient concentrations of some chlorinated solvents, diesel particulate matter, and metals, particularly cadmium and mercury, were spatially associated with subsequent ASD prevalence (Windham, Zhang, Gunier, Croen, & Grether, 2006).

1.3 Study intent

For this thesis we examined the spatial relationship between ASD prevalence and all EPA-modeled HAPs concentrations ($\mu g/m^3$) at the statewide level for all U.S. states, and performed a sub-analysis at the county level within the state of Maryland, using two different study populations for each analysis. The use of two separate study populations

for both the statewide U.S. and the county level Maryland analyses allowed for consistency checks of any observed relationships. An ecological study design was employed with the hypothesis that ASD prevalence is spatially, positively correlated with prenatal distributions of HAPs with known neurotoxicity or developmental toxicant properties, in particular, solvents, heavy metals, and polycyclic organic matter or diesel particulate matter. Relevance of any correlation was further investigated with the derivation of predictive models for ASD prevalence based upon prenatal HAPs distributions.

Chapter 2: Background

2.1 Autism Spectrum Disorder

2.1.1 Definition

Autism Spectrum Disorder (ASD) represents a broad range of complex neurodevelopmental disabilities primarily characterized by impaired language, communication and social interaction skills, and by abnormally restricted and repetitive behaviors (American Psychiatric Association, 2000). Specifically, five separate diagnoses covering a broad spectrum of functioning ability are listed under the umbrella term "Pervasive Developmental Disorders" in the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM IV), and together they comprise what is referred to as Autism Spectrum Disorder. They are: Autistic Disorder or "classic autism", Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS) or "atypical autism", Asperger Syndrome, Rett Syndrome, and Childhood Disintegrative Disorder (American Psychiatric Association, 2000).

There exists some debate about whether or not the latter two diagnoses belong in this grouping due to etiological (Rett syndrome) and developmental (Childhood Disintegrative Disorder) distinctions, and they are sometimes not included in case definitions for epidemiological research purposes (Newschaffer, Fallin, & Lee, 2002). Proposed revisions for the DSM V include the removal of Rett Syndrome due to its genetic origin, and the merging of the other four diagnoses into one official Autism Spectrum Disorder diagnosis (American Psychiatric Association, 2010).

2.1.2 Demographics of ASD

Gender

Males are disproportionately affected by ASD. The CDC's Autism and Developmental Disabilities Monitoring Network (ADDM) estimated that 1 in 70 boys in the U.S. had ASD in 2006 (Centers for Disease Control and Prevention [CDC], 2009), and a study that examined data from the 2007 National Survey of Children's Health (NSCH) estimated the prevalence among boys to be as low as 1 in 58 (Kogan et al., 2009). Numerous studies have documented the prevalence among boys to be approximately 4 times higher than among girls (Kogan et al., 2009; CDC, 2009; Fombonne, 2003). This sex ratio is modified, however, by the level of cognitive impairment. A prevalence study within the metropolitan area of Atlanta, Georgia, reported that the male to female ratio among those more cognitively impaired dropped from 4.4:1 to 1.3:1 (Yeargin-Allsopp et al., 2003). Similarly, (Fombonne, 2005) reported that the male to female ASD ratio neared 2:1 among individuals with more severe intellectual disability, as opposed to 5.5:1 among those without.

Race and ethnicity

There have been mixed findings with regard to variation in ASD prevalence by race and ethnicity, although some U.S. studies report a lower prevalence among Hispanic children, as compared with non-Hispanic white and non-Hispanic black children (Schieve, Rice, Boyle, Blumberg, & Visser, 2006; CDC, 2009). Kogan et al. (2009) documented lower prevalence among non-Hispanic black and non-Hispanic multiracial children than non-Hispanic white children, whereas a California study reported a higher risk of having a child with ASD among black women (Croen, Grether, & Selvin, 2002).

Socioeconomic factors

Whereas epidemiological and surveillance studies performed prior to 1980 consistently reported decreased risk for ASD among families of lower socioeconomic status, as measured by income or level of parental education, studies thereafter have not found consistent associations when controlling for case ascertainment, case definition, and other artifacts (Bhasin & Schendel, 2007; Fombonne, 2003; Lauritsen, Pedersen, & Mortensen, 2004). Despite the mixed findings, and despite a possibly artifactual relationship with ASD, socioeconomic status remains an important potential confounder in any investigation of disease or disorder determinants (Muennig, Franks, Jia, Lubetkin, & Gold, 2005).

Rural vs. urban residence

Previous research has indicated an association of urban residence with increased risk for ASD in multiple countries (Lauritsen, Pedersen, & Mortensen, 2005; Palmer et al., 2006; Williams, Higgins, & Brayne, 2006; Hoshino, Kumashiro, Yashima, Tachibana, & Watanabe, 1982). However, the association may be attributed to higher concentrations of, and access to, specialists, and therefore, to diagnoses, in urban areas; additionally, cross-sectional studies are unable to detect post-diagnoses rural-to-urban migration. Families may move to urban areas in order to seek better treatment or access to more services and resources.

Findings from California studies that link pesticide exposure and risk for ASD among farm-working families and families living in close proximity to sites of heavy application suggest potential risks of rural residency as well (Eskenazi et al., 2007; Roberts et al., 2007).

Whether proximity to rural areas of heavy pesticide use is truly associated with increased risk for ASD, and whether increasing urbanicity is truly or artifactually associated with increased ASD prevalence, this urban vs. rural factor is a potential confounder in ASD prevalence studies (Lewandowski, 2006; Palmer et al., 2009).

2.1.3 ASD prevalence and incidence trends

There has been a ten-fold increase in the number of children with Autism Spectrum Disorder (ASD) diagnoses within the last 20 to 30 years (Blaxill, 2004). Between 5 and 10 children per 10,000 were reported as diagnosed on the spectrum of autistic disorders in the U.S. during the 1970s and 1980s (Blaxill, 2004). The CDC's ADDM 2006 surveillance study estimated that 1 in 110 U.S. children had an ASD diagnosis, for a population prevalence estimate of approximately 1% (CDC, 2009).

This estimate was based on data collected on 8-year-olds in 11 surveillance sites. The age of 8 years was selected as the index age for prevalence monitoring because by that age most cases have been diagnosed, and the diagnoses tend to be more reliable (CDC, 2009; Lord et al., 2006; Eaves & Ho, 2004; Wiggins, Baio, & Rice, 2006). In addition, numerous epidemiological studies found peak ASD prevalence among 8-year-olds in the various study populations (Yeargin-Allsopp et al., 2003; Fombonne, 2003). An ASD prevalence study that used 2007 NSCH parent-reported data on children aged 3 to 17 years documented the number of affected children as 1 in 91 (Kogan et al., 2009).

Available data on cumulative incidence trends of Autistic Disorder also reveals a steady and sizable increase by birth cohort in California, the U.S., Denmark, and Japan since the late 1980s and early 1990s (Hertz-Picciotto et al., 2009; McDonald et al., 2010).

Numerous epidemiological studies have established that some of this observed increased prevalence and cumulative incidence is due to greater public and professional awareness of the spectrum of disorders, which facilitates diagnoses made at earlier ages as well as potential detection bias, and to broadened or substituted diagnostic criteria (Fombonne, 2005; Shattuck, 2006; Lauritsen et al., 2004). However, results from several other studies indicate that the magnitude of the increase in ASD cannot be solely attributed to artifacts.

Researchers at the University of California-Davis, examining ASD prevalence trends with administrative records from a state services agency, documented a 600 to 700% increase in diagnosed cases of autism in California since 1990 (Hertz-Picciotto et al., 2009). Younger age at diagnosis due to increased awareness accounted for 24% of this increase, increased diagnoses of milder cases accounted for 56%, and changes in state reporting of the disorder accounted for 120%. This left 400 to 500% of the increased diagnoses unexplained. Differential migration may have played a minor role in this increase, but the possibility of a true increase in ASD prevalence could not be rejected. Another group of researchers examined the ASD prevalence trends in California between 1987 and 1994 and concluded that the observed increase was a result of diagnostic substitution (Croen, Grether, Hoogstrate, & Selvin, 2002). However, they retracted this conclusion based upon the limitations of their original data and analyses (Croen et al., 2003).

The CDC (2009) reported that the average prevalence of ASD diagnoses identified among children aged 8 years increased 57% in 10 ADDM surveillance sites between 2002 and 2006. Although improved ascertainment and younger age at diagnoses

accounted for some of the prevalence increases documented in the ADDM sites, the CDC concluded that a true increase in ASD prevalence could not be ruled out.

One examination of special education data from 1984 to 2003 concluded that the increased prevalence of ASD in the U.S. public school system was due to diagnostic shifting or substitution (Shattuck, 2006). However, a review of national special education data for years 1992 through 2001 data using different methodology found no evidence for autism diagnostic substitution for any other disabilities (Newschaffer et al., 2005).

Lastly, the examination of worldwide cumulative incidence trends for Autistic Disorder, independent of the milder phenotypes, found consistent and rapid increases in each available dataset since the late 1980s (McDonald et al., 2010). Thus, this worldwide trend also could not be attributed solely to the broadened definition of ASD. Indeed, some researchers view the phenomenon as part of an overall trend of increasing neurodevelopmental disorders among children (Atladottir et al., 2007).

2.1.4 Genetics of ASD

Such a rapid rise in ASD cases cannot be explained by sudden genetic changes in the population, and Hertz-Picciotto et al. (2009) stress the need for further research of suspect environmental causative agents. However, there is a strong and well-established genetic basis for ASD. Approximately 10% of ASD cases are accounted for by single gene disorders such as Angelman syndrome and Fragile X syndrome, although each of these known causes accounts for no more than 1-2% or less of cases (Abrahams & Geschwind, 2008). Early twin studies made a compelling case for a strong hereditary component of Autistic Disorder. One such study observed a monozygotic concordance rate of approximately 60% among the twin participants, while zero concordance was

found between dizygotic twins (Bailey et al., 1995). When the twins were reevaluated for broadened autistic phenotypes including cognitive, communicative, and/or social deficits, monozygotic concordance increased to 92% and dizygotic concordance to 10% (Bailey et al., 1995; Le Couteur et al., 1996). Family studies indicate an overall recurrence risk estimate range of 2% to 8.6% among non-twin siblings of individuals with autistic disorder (Bailey, Palferman, Heavey, & Le Couteur, 1998; Ritvo et al., 1989). The higher estimates were found by Ritvo et al., including the highest risk estimate of 14.5%, specifically for siblings of affected females. Another family study found that approximately 20% of non-twin siblings of affected individuals demonstrate some features associated with the broad autism phenotype (Piven, Palmer, Jacobi, Childress, & Arndt, 1997).

Despite these compelling findings, monozygotic concordance is less than 100%. This fact, along with the variation in the severity of impairment and range of symptoms observed among concordant siblings, is indicative of etiologic contributions from environmental factors to the development of ASD in genetically susceptible individuals. In addition, the possibility that gene-environment interactions account for some of the genetic risk component for ASD suggests that actual quantitative estimates of heritability are unknown and possibly overestimated (Newschaffer et al., 2007).

2.1.5 Challenges to epidemiological research on environmental risk factors for ASD

Evidence of a broad autism phenotype among families suggests a polygenic model of ASD heritability. While several promising candidate autism risk genes have been receiving much attention, no single gene has been consistently identified as

causatively associated with ASD etiology. The search for the most salient environmental risk factors is similarly complex, as evidenced by un-replicated or mixed findings for many putative causal agents throughout much of the literature.

Several issues prove challenging, including the lack of an animal biological model of ASD that can be generalized to fit all cases, with a definitive biologic marker for diagnosis, and the broadened definition of autism, both of which result in inconsistencies in case definition and ascertainment from study to study.

In addition, accurate exposure assessment is problematic for many environmental epidemiology investigations, and is especially so for ASD etiological research because the critical window of exposure remains unknown. Researchers have yet to discover whether environmental agents cause de novo gene mutations in children or epigenetic effects (changes in gene expression that are heritable).

Moreover, despite the increasing prevalence of ASD, it remains a relatively rare health outcome, affecting approximately 1% of the population (CDC, 2009), and thus, epidemiological studies have limited power to detect causal associations.

Further complicating ASD etiologic research is the fact that environmental risk factors for ASD may include an individual's social, emotional, and economic environments, as well as other potential factors such as birth order, parental age, and viral infections, along with exogenous chemical contaminants. It is possible that no single environmental risk factor will be identified as essential or sufficient for developing ASD.

2.2 Hazardous Air Pollutants (HAPs)

The federal Clean Air Act of 1970 (Pub. L. 91-604, 84 Stat. 1676) required the EPA to establish national health-based standards, the National Ambient Air Quality

Standards (NAAQS) for six common criteria pollutants (ozone, particulate matter, carbon monoxide, nitrogen oxides, sulfur dioxide, and lead) due to their ubiquitous presence in most communities and their ability to disperse over large areas. The EPA also regulates an additional 188 air contaminants as listed in section 112 of the 1990 Clean Air Act Amendments (Pub. L. 101-549, 104 Stat. 2468). These are pollutants associated with serious threats to human health, including known or suspected carcinogens, teratogens, and neurotoxins, and are known as hazardous air pollutants (HAPs) or "air toxics". Unlike the ubiquity of criteria air pollutants, HAPs that are present in a community tend to originate from sources within that community. EPA regulates these air toxics by requiring the maximum degree of emission reduction, known as maximum achievable control technology (MACT) that a source, such as a factory or power plant, must employ. States and local authorities may establish their own HAPs standards and may opt to regulate more than the 188 listed under the Clean Air Act, yet there are no national, health-based standards for HAPs.

Chronic exposure to neurotoxicants and developmental toxicants in ambient air is of particular concern to women of childbearing age and young children. Comprehensive monitoring of HAPs is not feasible, so in an effort to assess the spatial distribution, ambient and exposure concentrations, and potential human health risks associated with HAPs exposure, EPA developed the National-Scale Air Toxics Assessments (NATA). NATA databases provide a snapshot of potential average HAPs exposure and health risks in a given year at the census tract, county, state, and national levels, and have been generated every three years beginning in 1996.

The ongoing NATA evaluations utilize general emissions inventories from several outside stationary and mobile sources including the Toxic Release Inventory and state and local agencies' air toxics inventories. The annual ambient concentration of each HAP is then estimated by incorporating meteorological data, atmospheric decay, secondary formation, and deposition estimates into a Gaussian dispersion model, the Assessment System for Population Exposure Nationwide (ASPEN) (Rosenbaum et al., 1999). The 1996 NATA provided emissions data and modeled concentration estimates for 33 out of the Clean Air Act's list of 188 air toxics plus diesel particulate matter, and the 1999 NATA provided emissions data for 176 of the HAPs plus diesel particulate matter, and modeled concentration estimates for 80 HAPs plus diesel particulate matter (EPA, 1996c; EPA, 1999d).

Uncertainties and limitations with regard to the NATA assessments are addressed thoroughly by EPA (EPA, 1996b; EPA, 1999a; Rosenbaum et al., 1999). Comparisons of some of EPA's ASPEN estimates of HAPs concentrations with personal and monitored measurements have indicated that the modeled estimates tend to underestimate actual concentrations, but that for some volatile organic compounds, especially benzene, the modeled concentrations provide a decent surrogate for exposure (EPA, 1996a; EPA, 1999b; Rosenbaum et al., 1999; Payne-Sturges, Burke, Breysse, Diener-West, & Buckley, 2004)

Payne-Sturges et al. (2004) acknowledged the dearth of actual comprehensive monitoring data for the majority of HAPs, and especially of personal exposure data, and concluded that EPA's modeled estimates are an important tool for assessing public health risks associated with HAPs. Indeed, several studies have used the NATA modeled

estimates of air toxics in public health research (Windham et al., 2006; Apelberg, Buckley, & White, 2005; Morello-Frosch, Woodruff, Axelrad, & Caldwell, 2000).

Chapter 3: Methods

3.1 Data sources

3.1.1 Exposure assessment: HAPs

We selected median statewide concentration estimates ($\mu g/m^3$) of the 33 HAPs plus diesel particulate matter and 80 HAPs plus diesel particulate matter from the U.S. Environmental Protection Agency's 1996 and 1999 National-Scale Air Toxics Assessments (NATA), respectively, as proxies for prenatal or early childhood exposures. The HAPs modeled for each NATA assessment are shown in Tables 1 and 2. Total median concentrations were selected in order to provide more representative statewide estimates that were less influenced by extremes.

NATA estimated, countywide 1996 and 1999 HAPs concentrations were selected as proxies for prenatal or early childhood exposures for the Maryland sub-analysis. Total median concentrations were used in the sub-analysis as well.

In order to account for highly correlated compounds and to reduce data dimensions of the large number of HAPs, we used a statistical approach called principal component analyses (PCA). PCA reduced the datasets of large numbers of HAPs into a fewer number of uncorrelated components (linear combinations of the HAPs) that explained most of the variation seen in the original data. The principal components were then used in subsequent regression analyses.

Data from the two different NATA datasets were not compared for temporal trends. Rather, they provided a way to check for consistency of any associations between

prenatal HAPs exposures and subsequent ASD prevalence that were observed in both spatial analyses.

3.1.2 Outcome of interest: ASD prevalence

Our outcome variable was ASD prevalence among children aged 8 years by state (and by county for the sub-analysis) during the school years 2004-2005 and 2007-2008. The 1996 and 1999 NATA HAPs data reflects approximate prenatal and early childhood exposures for those study populations.

Statewide ASD prevalence in school years 2004-2005 and 2007-2008 among 8-year-olds were calculated using U.S. Department of Education, Office of Special Education Programs (OSEP) administrative data. Each state conducts annual counts of children receiving special education services under 13 primary disability categories as defined by the Individuals with Disabilities Education Act of 1990 (IDEA) (Pub. L. 101-476, 104 Stat. 1142). Data collection must occur on the same date sometime between October 1 and December 1 each year. This data is made publicly available through the Data Accountability Center (DAC) which is funded through a cooperative agreement with OSEP (Data Accountability Center [DAC], 2004b; DAC, 2007b).

The number of 8-year-olds served under the disability code "autism" comprised the numerators for our prevalence estimates for both school years in each state. The total number of second graders enrolled in each state for those years were used as denominators, and were derived from the National Center for Education Statistics (NCES) enrollment data (National Center for Education Statistics [NCES], 2004; NCES, 2007). NCES is part of the U.S. Department of Education's Institute of Education Sciences. Methodology for NCES data collection and limitations of use is covered in an

online Statistical Standards Program publication that was most recently updated in 2002 (NCES, 2002). The use of total enrolled second graders rather than total enrolled 8-year-olds as our prevalence denominator may introduce random bias; we felt this would not greatly affect the outcome of the study.

Numerators for the Maryland sub-analysis ASD prevalence estimates were derived from count data for 8-year-old children receiving special education services under the diagnostic code "autism" for the school years 2004-2005 and 2007-2008 by county, provided on special request by the Maryland State Department of Education (MSDE). Denominators were the total number of 8-year-olds enrolled in each of the 24 counties during both of those school years, and were also obtained from MSDE. The data sets for the sub-analysis included data disaggregated by gender, and then separately by race/ethnicity.

In order to increase the power of our analyses, we combined the calculated female ASD prevalence data with the calculated male ASD prevalence data doubling our sample sizes to 48 for both 2004 and 2007. The new dataset was named Combined data 1. Gender was then included as a dichotomous variable (0=female, 1=male) in the subsequent linear regression models using this combined data for Maryland analyses.

The original count data revealed that ASD prevalence was much higher among white 8-year-olds than those of other races/ethnicities for both 2004 and 2007 in most Maryland counties, and both case and enrollment counts for Asian/Pacific Islanders and Native Americans were extremely low. Thus, we condensed the five race/ethnicity classifications, namely, White, Black, Latino, Asian/Pacific Islander, and Native American, into two categories, White and Non-white. The resultant ASD prevalence data

derived for both White and Non-white were combined for a total sample size of 48. The new dataset was named Combined data 2. Ethnicity was then included as a dichotomous variable (0=white, 1=non-white) in the subsequent linear regression models using this combined data for a separate set of Maryland analyses.

3.1.3 Potential confounder: smoking prevalence

State-specific smoking prevalence among adults, measured as a percentage, was obtained from the CDC's Behavioral Risk Factor Surveillance System (BRFSS) for 1996 and for 1999 (CDC, 1996; CDC, 1999). The BRFSS is an annual, random-digit-dialed, telephone health survey of U.S. adults which tracks health conditions and risk behaviors. Smoking prevalence represents data on adults 18 years of age and older who reported smoking at least 100 or more cigarettes in their lifetime, and who reported smoking every day or some days at the time of the survey, defined as "current smokers", weighted according to state population.

County-specific smoking prevalence among adults in 1996 and 1999, measured as percentages, were obtained from the Maryland Behavioral Risk Factor Surveillance System (MD BRFSS), a telephone survey administered annually through the Maryland Department of Health & Mental Hygiene (Maryland Department of Health & Mental Hygiene [MDHMH], 1996; MDHMH, 1999). Smoking prevalence represents data on individuals at least 18 years of age who reported smoking 100 or more cigarettes in their lifetime, and who reported smoking every day or some days at the time of the survey, defined as "current smokers", weighted according to county population.

Smoking prevalence data for 1996 was not available for Kent and Somerset Counties, and smoking prevalence data for 1999 was not available for Dorchester, Kent,

and Somerset Counties. For these counties, smoking prevalence data from the nearest available year were substituted.

3.1.4 Potential confounder: percentage living in poverty

Socioeconomic indicators were measured as the percentage of all persons living in poverty, by state (and by county for the sub-analysis) for both 1996 and 1999. Data was obtained from the U.S. Census Bureau's Small Area Income and Poverty Estimates (SAIPE) program which provides annual estimates of income and poverty statistics for every state and county (U.S.Census Bureau, 2007a). The model-based estimates are derived from combining data from administrative records, the decennial census, intercensal population estimates, and the American Community Survey, and are regarded as more representative of current conditions than the estimates from the decennial census survey. SAIPE methodology, uncertainties, and limitations are addressed by the U.S. Census Bureau in detail (U.S.Census Bureau, 2007b).

The percentages of all persons living in poverty by county in 1996 were not available from SAIPE, so we used the 1995 poverty data for the Maryland 1996 sub-analyses. It is unlikely that county level economic circumstances had changed drastically in the span of that one year.

3.1.5 Potential confounder, Maryland sub-analyses: rural/urban designation

Each Maryland county's urban or rural status, as defined by EPA, was accounted for in our sub-analyses. This urbanicity factor was included as a dichotomous variable in the regressions (0=rural, 1=urban). EPA defined a county as "urban" if it either included a metropolitan statistical area with a population greater than 250,000 or the U.S. Census

Bureau designated more than 50 percent of the population as "urban." The 1996 National-Scale Air Toxics Assessment used 1990 census data, and the 1999 National-Scale Air Toxics Assessment used 2000 census data, for these determinations.

3.2 Statistical analysis

All HAP, outcome, and confounding variables' distributions with long right tails were log-transformed, and all variables were standardized ($\mu=0$, sd=1) prior to analyses. PCA, univariate and multiple regressions, and regression diagnostics were performed using STATA IC, version 10.0 for Windows (Stata Corp., TX), and statistical significance was set at $p<0.05$.

Chapter 4: Results

The hazardous air pollutants modeled in the 1996 and 1999 National-Scale Air Toxics Assessments and used in this study's analyses are shown in Tables 1 and 2.

Table 1-Hazardous Air Pollutants (HAPs) modeled in EPA's 1996 NATA

1996 National Air Toxics Assessment HAPs 1996	
Acetaldehyde	Formaldehyde
Acrolein	Hexachlorobenzene
Acrylonitrile	Hydrazine
Arsenic Compounds	Lead Compounds
Benzene	Manganese Compounds
Beryllium Compounds	Mercury Compounds
1,3-Butadiene	Methylene Chloride
Cadmium Compounds	Nickel Compounds
Carbon Tetrachloride	Perchloroethylene
Chloroform	Polychlorinated Biphenyls (PCBs)
Chromium Compounds	7-PAH
Coke Oven Emissions	Polycyclic Organic Matter (POM)
1,3-Dichloropropene	Propylene Dichloride
Diesel Particulate Matter	Quinoline
Ethylene Dibromide	1,1,2,2-Tetrachloroethane
Ethylene Dichloride	Trichloroethylene
Ethylene Oxide	Vinyl Chloride

Table 2-Hazardous Air Pollutants (HAPs) modeled in EPA's 1999 NATA

1999 National Air Toxics Assessment HAPs			
Acetaldehyde	Chlorine	Formaldehyde	n-Hexane
Acetonitrile	Chloroform	Glycol ethers	Nickel compounds
Acrolein	Chloroprene	Hexachlorobenzene	n-Nitrosodimethylamine
Acrylamide	Chromium VI	Hexachloroethane	o-Toluidine
Acrylic acid	Cobalt compounds	Hexamethylene-1,6-	p-Dichlorobenzene
Acrylonitrile	Coke Oven emissions	diisocyanate	p-Dimethylaminoazobenzene
Allyl chloride	Cyanide compounds	Hydrazine	Perchloroethylene
Aniline	1,2-Dibromo-3-chloropropane	Hydrochloric acid	Phosgene
Antimony compounds	Dichloroethyl ether	Hydrofluoric acid	Polychlorinated biphenyls
Arsenic compounds	1,3-Dichloropropene	Lead compounds	Polycyclic Organic Matter
(inorganic, may include	Diesel particulate matter	Maleic anhydride	Propylene dichloride
arsine)	Diethanolamine	Manganese compounds	Propylene oxide
Benzene	Dimethyl formamide	Mercury	Quinoline
Benzidine	2,4-Dinitrotoluene	Methyl bromide	1,1,2,2-Tetrachloroethane
Benzotrichloride	1,4-Dioxane	Methyl chloride	Titanium tetrachloride
Benzyl chloride	Epichlorohydrin	4,4'-Methylene bis(2-	Toluene
Beryllium compounds	Ethyl acrylate	chloroaniline)	2,4-Toluene diamine
Bis(2-ethylhexyl)phthalate	Ethyl carbamate	Methylene chloride	2,4-Toluene diisocyanate
Bis(chloromethyl)ether	Ethylene dibromide	4,4'-Methylenedianiline	1,1,2-Trichloroethane
1,3-Butadiene	Ethylene dichloride	Methylene diphenyl	Vinyl chloride
Cadmium compounds	Ethylene oxide	diisocyanate	Xylenes (isomers and mixture)
Carbon tetrachloride		Naphthalene	

4.1 United States Analyses

4.1.1 1996 HAPs distributions and 2004 ASD Prevalence

General characteristics of the data

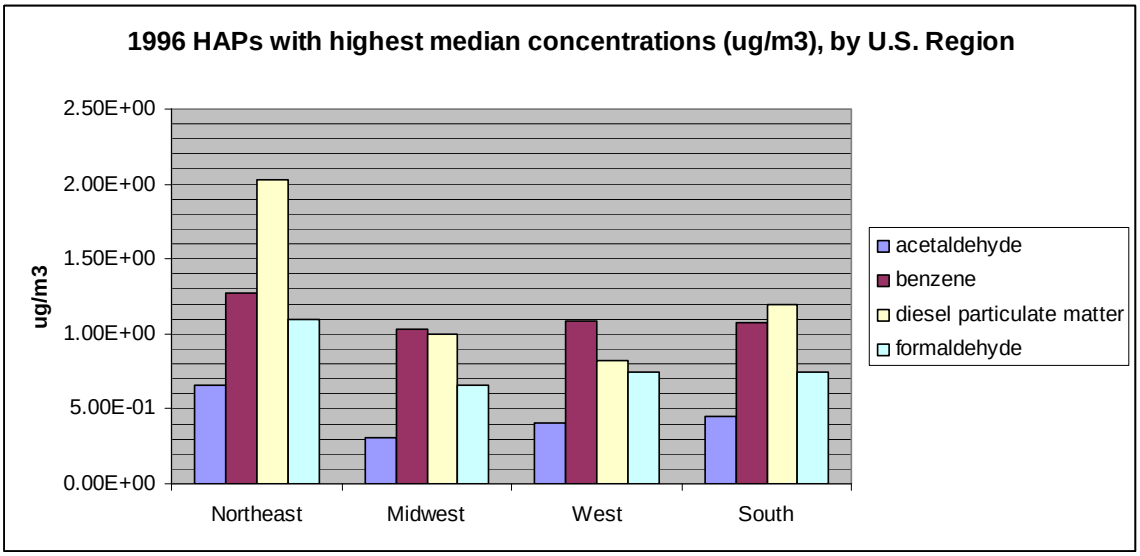
Complete data was available for 47 states and the District of Columbia. NATA did not include HAPs estimates for Alaska nor Hawaii in 1996, and special education data for the state of Wyoming had been suppressed for reasons of confidentiality. Summary statistics of ASD, poverty, and smoking distributions, including the mean, standard deviation, minima, maxima, median, and interquartile range, by geographic region, are shown in Table 3, along with the total U.S. mean. Mean ASD prevalence was highest in the Northeast and Midwest, consistent with the findings from an examination of parent-reported prevalence by region (Kogan et al., 2009). ASD prevalence among 8-year-olds in the 2004-2005 school year varied from a low of 13.7 per 10,000 in New Mexico to the highest prevalence, 104 per 10,000, in Minnesota.

At 6.3%, New Hampshire had the lowest percentage of persons living in poverty in 1996, and the District of Columbia had the highest, at 21.9%. The percentage of adult smokers in 1996 was lowest in Utah, at 15.9%, and highest in Kentucky, at 31.6%.

Summary statistics for 31 of the 34 statewide 1996 HAPs distributions, by geographic region, are in Table 4, along with the total U.S. median concentrations. Coke oven emissions, ethylene dibromide, and polychlorinated biphenyls were dropped from analysis because of zero variance. The HAPs with the highest upper limit concentrations in each of four regions were diesel particulate matter, formaldehyde, benzene, acetaldehyde, and carbon tetrachloride. These same HAPs also had the highest median concentrations in each region. Carbon tetrachloride had near zero variance. Figure 1

compares the regional median concentrations of these HAPs, excluding carbon tetrachloride.

Figure 1.



Dimensionality reduction of 1996 U.S. HAPs

Principal component analysis generated 31 independent components, and we selected the first 4 which accounted for over 85% of the total variance in the HAPs data. Component one (pc1) accounted for approximately 69% of the variance alone. Most of the 31 HAPs in pc1 had similar component loadings. Moreover, the ten HAPs with the highest component loadings for pc1 could not be neatly defined by a single chemical family. Rather, they included 2 halogenated hydrocarbons, 4 metals, 2 aldehydes, an aromatic hydrocarbon, and diesel particulate matter. Table 9 lists the HAPs with the highest component loadings that comprised the principal components significantly associated with ASD prevalence in the U.S. 1996/2004 analysis. HAPs that were also associated with ASD prevalence in Windham et al.'s (2006) study are labeled.

None of the 4 principal components in this analysis were highly correlated with smoking or poverty prevalence.

Regression analysis

Univariate regressions, scatter plots, and diagnostics for the 4 pcs and the confounders revealed that the relationship between pc1 and ASD prevalence was significant and non-linear, and that poverty prevalence was significantly, inversely associated with ASD prevalence. A quadratic relationship between pc1 and ASD prevalence provided the best fit and improved the final multiple regression model. Figures 2 and 3 show 2004 ASD prevalence plotted against 1996 pc1 distribution and against 1996 poverty prevalence in the U.S., respectively. All other regressors did not have significant relationships with ASD prevalence in univariate analyses. The final multiple regression model, along with poverty prevalence and the quadratic function of pc1, retained pc2 and pc3. It explained approximately 48% of the variance in ASD prevalence in the U.S. in 2004. Table 10 presents the final models for each of our analyses.

Figure 2.

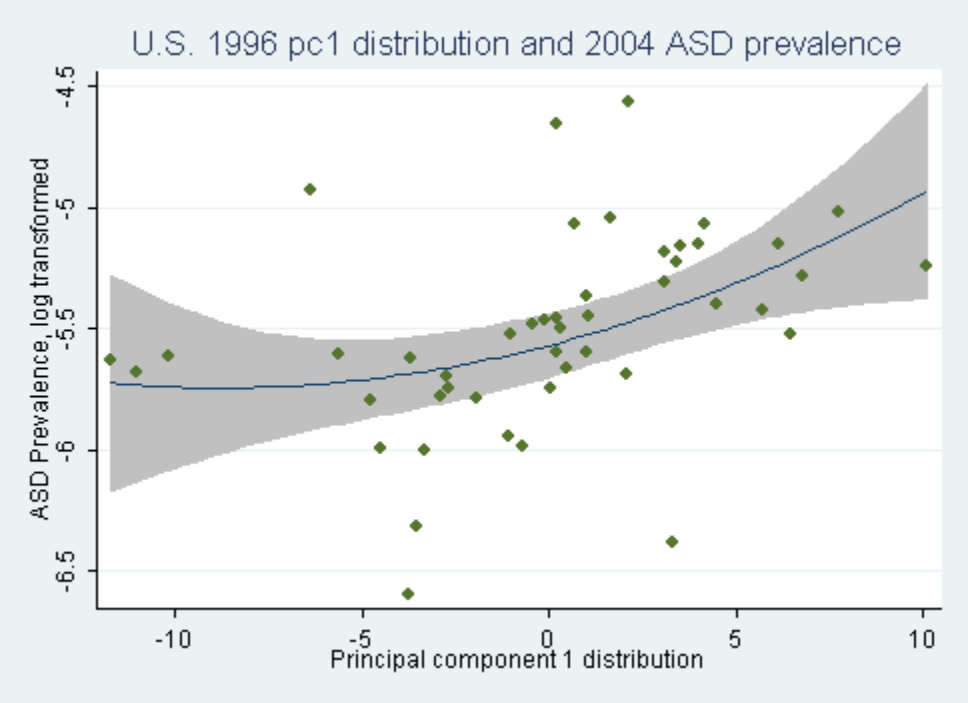
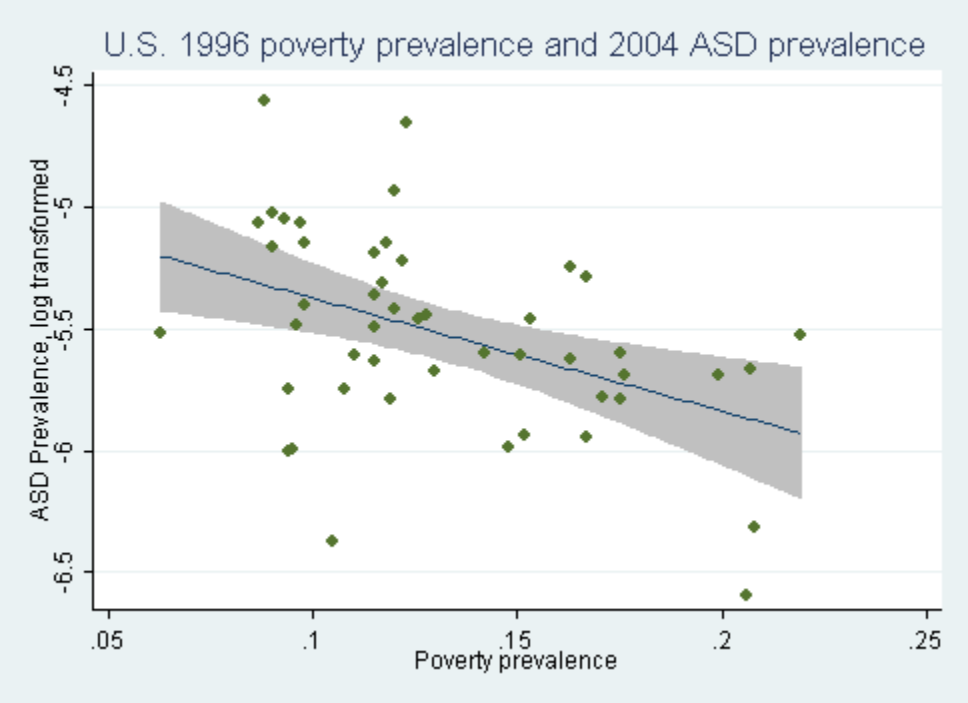


Figure 3.



4.1.2 1999 HAPs distributions and 2007 ASD Prevalence

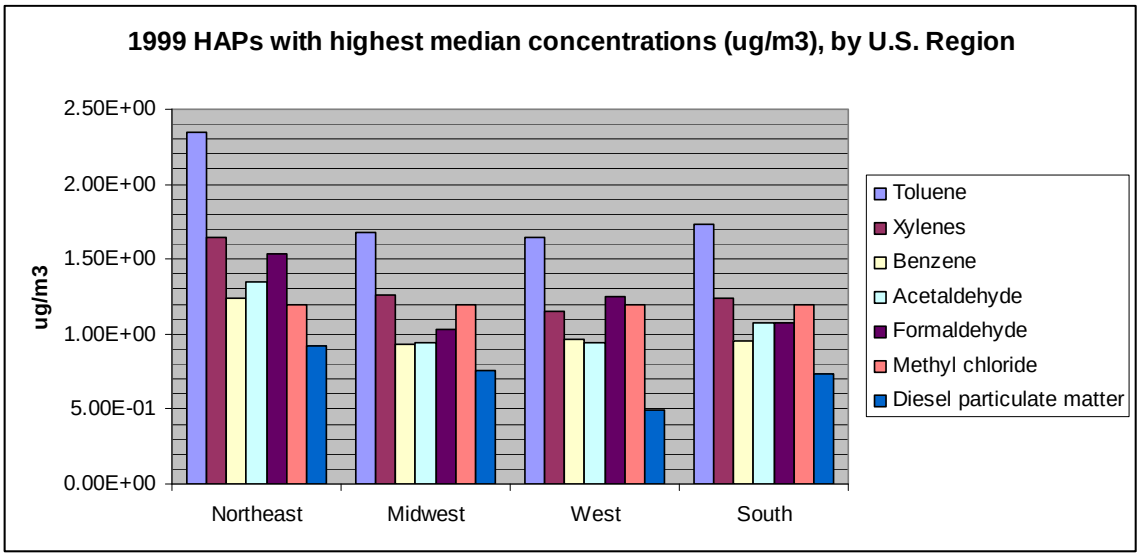
General characteristics of the data

Complete data was available for 50 states. NATA estimates were available for Alaska and Hawaii in 1999, but special education data for the District of Columbia had been suppressed for reasons of confidentiality. Refer to Table 3 for summary statistics of ASD, poverty, and smoking distributions by geographic region, along with the total U.S. mean. The Northeast and the Midwest still had the highest ASD prevalence. ASD prevalence among 8-year-olds in the 2007-2008 school year varied from a low of 19.5 per 10,000 in Iowa to the highest prevalence, 147 per 10,000 in Minnesota.

At 6.8%, Delaware had the lowest percentage of persons living in poverty in 1999, and the Arizona had the highest, at 18.2%. While the District of Columbia was not included in this analysis, the percentage of persons of all ages living in poverty in 1999 dropped to 17.3. The percentage of adult smokers in 1999 was lowest in Utah, at 13.9%, and highest in Nevada, at 31.5%.

Summary statistics for 77 of the 81 statewide 1999 HAPs distributions, by geographic region, are in Table 5, along with the total U.S. median concentrations. Bis(2-ethylhexyl)phthalate, hexachloroethane, n-nitrosodimethylamine, and p-dimethylaminoazobenzene were dropped from analysis for zero variance. For each region, the HAPs with the highest median and upper limit concentrations were toluene, xylenes, benzene, acetaldehyde, formaldehyde, methyl chloride, and diesel particulate matter. Figure 4 compares the regional median concentrations of these HAPs. Toluene, xylenes, and methyl chloride were not estimated in the 1996 NATA.

Figure 4.



Dimensionality reduction of 1999 U.S. HAPs

Principal component analysis generated 49 independent components, and we selected the first 3 which cumulatively accounted for approximately 63% of the total variance in the 1999 HAPs data. Component one (pc1) accounted for approximately 48% of the variance alone. The HAPs with the highest component loadings in pc1 represented various chemical families. Table 9 lists the HAPs with the highest component loadings of the statistically significant components for the U.S. 1999/2007 analysis that were also consistent with the 1996/2004 significant HAPs components. HAPs that were also associated with ASD prevalence in Windham et al.'s (2006) study are labeled.

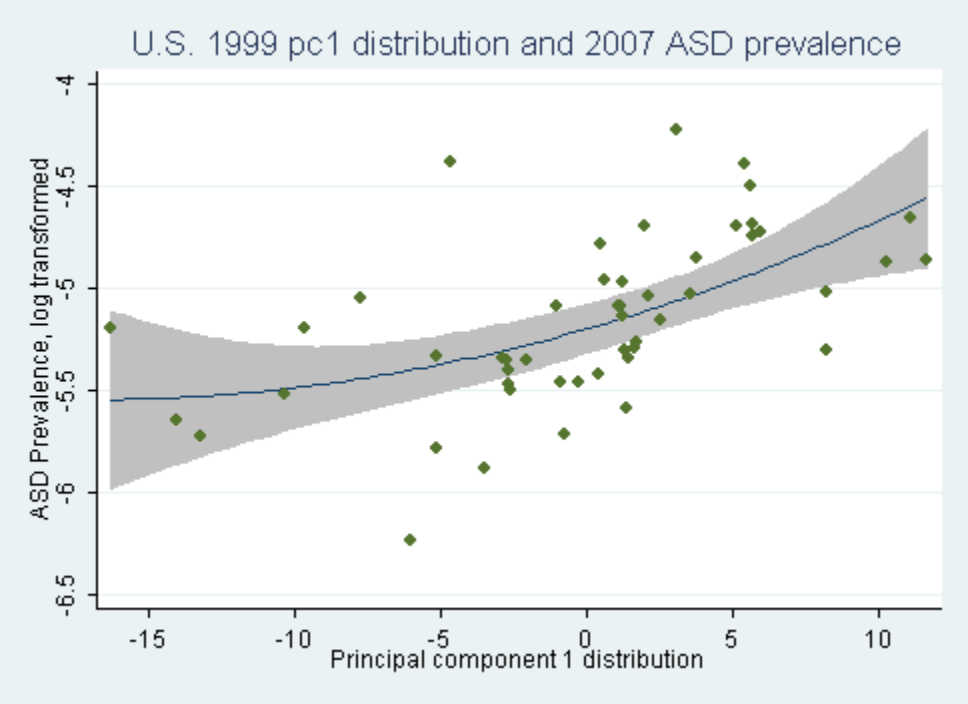
None of the 3 principal components in this analysis were highly correlated with smoking or poverty prevalence.

Regression analysis

Univariate regressions, scatter plots, and diagnostics for the 3 pcs and the confounders revealed that the relationship between pc1 and ASD prevalence was

significant and non-linear. A quadratic relationship between pc1 and ASD prevalence provided the best fit and improved the final regression model. Figure 5 shows 2007 ASD prevalence plotted against 1999 pc1 distribution in the U.S. All other regressors did not have significant relationships with ASD prevalence in univariate analyses. The final regression model contained only the quadratic function of pc1, and is presented in Table 10. This model explained approximately 29% of the variance in ASD prevalence in the U.S. in 2007.

Figure 5.



4.2 Maryland Analyses

4.2.1 1996 HAPs distributions and 2004 ASD Prevalence

General characteristics of the data

Complete data was available for all 24 Maryland counties. Summary statistics of the poverty and smoking distributions, as well as both Combined data 1 and Combined

data 2 ASD distributions, including the mean, standard deviation, minima, maxima, median, and interquartile range, are shown in Table 6.

ASD prevalence among Maryland 8-year-olds in the 2004-2005 school year was disproportionately greater among males. Ten counties had zero female ASD prevalence estimates, and two counties had zero female and male prevalence estimates. The 12 highest county ASD prevalence estimates were among males, with male ASD prevalence in Howard County ranked the highest at 2.07% or 1 in 48.

Higher ASD prevalence was observed among white Maryland 8-year-olds in the 2004-2005 school year than was observed among children in the other 4 racial/ethnic groups. However, after combining those 4 groups into one "Non-white" category, the discrepancy attenuated, and in some counties, the Non-white ASD prevalence estimates were greater than the White ASD prevalence estimates. Ten counties had zero Non-white ASD prevalence estimates, and two counties had zero Non-white and White prevalence estimates. Of the 10 highest county ASD prevalence estimates, 3 were among children of Non-white ethnicity, including the highest ASD prevalence in Howard County, at 1.35% or 1 in 74.

At 3.7%, Howard County had the lowest percentage of persons living in poverty in 1996, and Baltimore City had the highest, at 24%. The percentage of adult smokers in 1996 was lowest in Garrett County, at 13.7%, and highest in Wicomico County, at 34.2%. Fourteen counties were classified as "urban" and 10 classified as "rural".

Summary statistics for 31 of the 34 Maryland county-level 1996 HAPs distributions are in Table 7. Coke oven emissions, ethylene dibromide, and polychlorinated biphenyls were dropped from analysis for zero variance. The HAPs with

the highest upper limit concentrations were acetaldehyde, benzene, diesel particulate matter, and formaldehyde. Benzene, diesel particulate matter, and formaldehyde had the highest median concentrations.

Dimensionality reduction of 1996 Maryland County-level HAPs

Principal component analysis generated 23 independent components, and we selected the first 3 which cumulatively accounted for over 90% of the total variance in the HAPs data. Component one (pc1) accounted for approximately 78% of the variance alone. The HAPs with the highest component loadings for pc1 were varied, and consisted of 3 aldehydes, a metal, a halogenated hydrocarbon, an epoxide, an aromatic hydrocarbon, and polycyclic organic matter.

None of the 3 principal components in this analysis were highly correlated with smoking or poverty prevalence.

Regression analyses

None of the 3 principal components were found to be significantly associated with ASD prevalence using Combined data 1. Univariate regressions showed that gender was significantly associated with ASD prevalence, whereas poverty prevalence, smoking prevalence, and urbanicity were not. Poverty prevalence became marginally, inversely, significant when included in the multiple regression model with gender. The best explanatory model of Maryland's 2004 ASD prevalence using Combined data 1 was thus driven mainly by gender. Table 10 presents the model results.

Using our Combined data 2, we still did not find any of the 3 principals components to be significantly associated with ASD prevalence. ASD Prevalence regressed solely on poverty prevalence yielded a significant model (p=0.0095) that

explained 15.8% of variance after adjustment, and prevalence regressed solely on smoking prevalence yielded a model (p=0.0304) that explained 10.5% of variance after adjustment. The best model retained only poverty prevalence, and the results are shown in Table 10.

4.2.2 1999 HAPs distributions and 2007 ASD Prevalence

General characteristics of the data

Complete data was available for all 24 Maryland jurisdictions. Summary statistics of the Combined data 1 and Combined data 2 ASD distributions, and the poverty and smoking distributions, including the mean, standard deviation, minima, maxima, median, and interquartile range, are shown in Table 6.

ASD prevalence among Maryland 8-year-olds in the 2007-2008 school year was disproportionately greater among males. Nine counties had zero female ASD prevalence estimates, and one county had zero female and male prevalence estimates. The 20 highest county ASD prevalence estimates were among males, with male ASD prevalence in Allegany County ranked the highest, at 2.32%.

Higher ASD prevalence was observed among white Maryland 8-year-olds in the 2007-2008 school year than was observed among children in the other 4 racial/ethnic groups. However, after combining those 4 groups into one "Non-white" category, the discrepancy attenuated, and in some counties, the Non-white ASD prevalence estimates were greater than the White ASD prevalence estimates. Six counties had zero Non-white ASD prevalence estimates, and one county had zero Non-white and White prevalence estimates. Of the 10 highest county ASD prevalence estimates, 4 were among children of

Non-white ethnicity, including the highest ASD prevalence in Worcester County, at 1.57%.

At 3.9%, Howard County had the lowest percentage of persons living in poverty in 1996, and Baltimore City had the highest, at 18.5%. The percentage of adult smokers in 1996 was lowest in Montgomery County, at 12.2%, and highest in Cecil County, at 36.1%. Fourteen counties were classified as "urban" and 10 classified as "rural".

Summary statistics for 72 of the 81 Maryland county-level 1999 HAPs distributions are in Table 8. Benzidine, bis(2-ethylhexy)phthalate, coke oven emissions, 1,2-dibromo-3-chloropropane, hexachloroethane, 4,4'-methylene bis(2-chloroaniline), n-nitrosodimethylamine, p-dimethylaminoazobenzene, and 2,4-toluene diamine were dropped from analysis for zero variance. The HAPs with the highest upper limit concentrations were acetaldehyde, benzene, diesel particulate matter, formaldehyde, methylchloride, n-hexane, toluene, and xylenes. With the exception of n-hexane, these same HAPs also had the highest median concentrations.

Dimensionality reduction of 1999 Maryland County-level HAPs

Principal component analysis generated 23 independent components, and we selected the first 4 which cumulatively accounted for over 84% of the total variance in the HAPs data. Component one (pc1) accounted for approximately 63% of the variance alone. The HAPs with the highest component loadings for pc1 consisted of 2 aldehydes, 1 metal, 4 aromatic hydrocarbons, 2 epoxides, 2 halogenated hydrocarbons, 1 halogenated aromatic hydrocarbon, and organic compounds used in the production of polyurethane and synthetic rubber.

Smoking prevalence was found to be moderately correlated with pc2 (r=0.4654). Poverty prevalence was not correlated any of the principal components.

Regression analyses

In univariate regressions, only gender was found to be a good predictor of 2007 ASD prevalence using Combined data 1. Inclusion of poverty and urbanicity in the multiple regression with gender provided the best explanatory model (p=0.0000, adjusted R-squared =0.8175), yet it is clear that most of the explanatory power is derived from gender. The model results are presented in Table 10.

None of the predictors, including the 4 HAPs components, had significant associations with Combined data 2 ASD prevalence, and no satisfactory models were constructed for 2007 ASD prevalence using this combined dataset.

Table 3-ASD, poverty, and smoking distribution statistics, by U.S. region

US 1996/2004

ASD prevalence per 10,000	Mean[1]	Std. Dev.	Min	Max	P50	IQR	US Mean[2]
Northeast	55.2	11.1	36.8	72.2	57.3	5.3	43.3
Midwest	47.8	22.1	24.7	104	43.4	25.4	
West	39.4	22.5	13.7	95.1	36.4	11	
South	36.1	10.4	18.1	63.1	34.6	11.7	
Poverty prevalence							
Northeast	10.7%	2.76%	6.3%	16.3%	11.0%	2.8%	13.2%
Midwest	10.8%	1.57%	8.7%	13.0%	11.2%	2.75%	
West	13.4%	3.65%	9.4%	20.6%	12.1%	5.8%	
South	16.1%	3.69%	9.7%	21.9%	16.7%	3.4%	
Smoking prevalence							
Northeast	23.6%	1.15%	21.9%	25.3%	23.4%	1.7%	23.8%
Midwest	24.4%	2.85%	20.6%	28.7%	24.2%	4.65%	
West	22.2%	3.28%	15.9%	28.2%	22.9%	2.3%	
South	24.3%	2.87%	20.3%	31.6%	24.2%	3.2%	

US 1999/2007

ASD prevalence per 10,000	Mean[1]	Std. Dev.	Min	Max	P50	IQR	US Mean[2]
Northeast	89.5	20.4	61.7	125	91.4	17.9	62.7
Midwest	66.8	32.8	19.5	147	65.7	36.2	
West	54.6	23.6	30.7	124	49	18.6	
South	51	15	27.8	89	47.1	19.1	
Poverty prevalence							
Northeast	9.67%	2.06%	6.8%	13.7%	9.80%	2.5%	11.4%
Midwest	9.89%	1.39%	7.5%	11.7%	10.0%	2.6%	
West	11.8%	2.77%	8.5%	18.2%	11.3%	3.8%	
South	13.4%	3.05%	8.0%	18.3%	13.2%	3.0%	
Smoking prevalence							
Northeast	22.0%	1.26%	19.4%	23.3%	22.4%	0.9%	23.1%
Midwest	23.9%	2.48%	19.5%	27.6%	23.6%	3.7%	
West	22.3%	4.33%	13.9%	31.5%	22.0%	3.9%	
South	24.0%	2.45%	20.3%	29.7%	23.6%	2.8%	

[1] Regional mean
[2] Total U.S. mean

Table 4-Regional distribution of HAPs, Statewide levels, for U.S., 1996, in μg/m^3

Northeast

HAPs	Mean	Std. Dev.	Min	Max	P50[1]	IQR	US P50[2]
acetaldehyde	7.05E-01	4.97E-01	1.30E-01	1.66E+00	6.63E-01	5.11E-01	4.30E-01
acrolein	1.07E-01	6.00E-02	4.61E-02	2.41E-01	1.00E-01	4.47E-02	6.71E-02
acrylonitrile	1.79E-03	2.03E-03	1.77E-05	6.12E-03	7.44E-04	1.66E-03	4.44E-04
arsenic compounds	6.36E-05	4.40E-05	6.67E-06	1.38E-04	6.29E-05	6.88E-05	4.92E-05
benzene	1.23E+00	3.68E-01	7.12E-01	1.84E+00	1.27E+00	4.67E-01	1.08E+00
beryllium	1.23E-05	9.10E-06	1.02E-06	2.78E-05	1.20E-05	1.15E-05	7.74E-06
1,3-butadiene	4.91E-02	2.36E-02	1.73E-02	9.30E-02	5.62E-02	2.88E-02	4.65E-02
cadmium compounds	9.52E-05	9.05E-05	4.79E-06	2.87E-04	8.05E-05	1.07E-04	3.33E-05
carbon tetrachloride	8.80E-01	7.07E-04	8.80E-01	8.82E-01	8.80E-01	0.00E+00	8.80E-01
chloroform	8.72E-02	3.99E-03	8.33E-02	9.51E-02	8.60E-02	1.10E-03	8.42E-02
chromium compounds	1.33E-03	1.04E-03	5.03E-05	2.57E-03	1.61E-03	1.84E-03	4.14E-04
1,3-dichloropropene	8.20E-02	6.36E-02	8.40E-03	2.11E-01	8.52E-02	7.08E-02	4.35E-02
diesel particulate matter	2.01E+00	1.20E+00	3.80E-01	3.90E+00	2.03E+00	1.23E+00	1.17E+00
ethylene dichloride	6.13E-02	2.69E-04	6.10E-02	6.17E-02	6.11E-02	4.00E-04	6.11E-02
ethylene oxide	1.79E-03	1.62E-03	6.47E-06	5.26E-03	1.58E-03	1.81E-03	1.05E-03
formaldehyde	1.14E+00	6.21E-01	4.77E-01	2.46E+00	1.10E+00	5.59E-01	7.42E-01
hexachlorobenzene	9.31E-05	1.72E-07	9.30E-05	9.35E-05	9.30E-05	0.00E+00	9.30E-05
hydrazine	2.63E-06	4.00E-06	7.35E-10	1.20E-05	3.78E-07	4.40E-06	1.75E-08
lead compounds	3.60E-03	4.25E-03	1.78E-04	1.32E-02	2.45E-03	2.90E-03	1.06E-03
manganese compounds	1.62E-03	1.10E-03	4.26E-04	3.75E-03	1.50E-03	1.72E-03	1.06E-03
mercury compounds	2.03E-03	5.32E-04	1.53E-03	3.21E-03	1.94E-03	4.20E-04	1.61E-03
methylene chloride	4.38E-01	2.16E-01	1.72E-01	7.84E-01	4.42E-01	3.18E-01	2.73E-01
nickel compounds	1.52E-03	1.19E-03	6.94E-05	3.18E-03	1.48E-03	1.71E-03	5.61E-04
PAH-7	3.79E-03	2.53E-03	1.01E-03	9.18E-03	3.83E-03	2.47E-03	2.02E-03
perchloroethylene	2.87E-01	1.24E-01	1.49E-01	5.20E-01	3.01E-01	1.29E-01	1.95E-01
polycyclic organic matter	6.98E-02	5.39E-02	1.04E-02	1.83E-01	6.99E-02	5.04E-02	4.25E-02
propylene dichloride	1.08E-04	1.24E-04	1.00E-06	3.68E-04	4.04E-05	9.85E-05	2.38E-05
quinoline	5.89E-07	5.41E-07	6.40E-09	1.58E-06	5.34E-07	6.23E-07	1.28E-07
1,1,2,2-tetrachloroethane	8.58E-04	1.04E-03	4.35E-06	3.24E-03	3.20E-04	7.94E-04	1.73E-04
trichloroethylene	1.66E-01	9.38E-02	8.40E-02	3.84E-01	1.56E-01	8.15E-02	1.01E-01
vinyl chloride	2.47E-03	2.74E-03	1.18E-05	8.29E-03	1.17E-03	2.66E-03	6.15E-04

Midwest

HAPs	Mean	Std. Dev.	Min	Max	P50[1]	IQR	US P50[2]
acetaldehyde	3.43E-01	2.90E-01	2.61E-02	1.04E+00	3.05E-01	3.54E-01	4.30E-01
acrolein	5.69E-02	4.54E-02	5.53E-03	1.37E-01	5.36E-02	6.30E-02	6.71E-02
acrylonitrile	6.17E-04	8.97E-04	1.79E-05	3.17E-03	2.49E-04	7.59E-04	4.44E-04
arsenic compounds	5.13E-05	3.68E-05	1.46E-06	1.06E-04	5.93E-05	5.89E-05	4.92E-05
benzene	1.03E+00	3.93E-01	5.21E-01	1.64E+00	1.03E+00	7.25E-01	1.08E+00
beryllium	7.16E-06	5.07E-06	3.16E-07	1.67E-05	7.73E-06	7.26E-06	7.74E-06
1,3-butadiene	5.00E-02	5.00E-02	3.45E-03	1.91E-01	4.58E-02	4.66E-02	4.65E-02
cadmium compounds	8.87E-05	1.24E-04	1.06E-06	4.55E-04	5.30E-05	8.49E-05	3.33E-05
carbon tetrachloride	8.80E-01	2.89E-04	8.80E-01	8.81E-01	8.80E-01	0.00E+00	8.80E-01
chloroform	8.41E-02	1.07E-03	8.30E-02	8.66E-02	8.38E-02	1.50E-03	8.42E-02
chromium compounds	1.08E-03	1.02E-03	6.38E-06	2.73E-03	9.32E-04	1.82E-03	4.14E-04
1,3-dichloropropene	3.90E-02	2.75E-02	9.52E-04	9.56E-02	4.30E-02	3.46E-02	4.35E-02
diesel particulate matter	1.13E+00	6.26E-01	2.73E-01	2.25E+00	9.93E-01	9.33E-01	1.17E+00
ethylene dichloride	6.12E-02	2.15E-04	6.10E-02	6.17E-02	6.11E-02	2.00E-04	6.11E-02
ethylene oxide	1.50E-03	2.02E-03	2.78E-05	7.54E-03	9.76E-04	1.40E-03	1.05E-03
formaldehyde	6.84E-01	3.59E-01	2.97E-01	1.60E+00	6.60E-01	4.05E-01	7.42E-01
hexachlorobenzene	9.31E-05	4.92E-08	9.30E-05	9.31E-05	9.31E-05	1.00E-07	9.30E-05
hydrazine	3.58E-08	3.90E-08	0.00E+00	1.29E-07	2.47E-08	5.17E-08	1.75E-08
lead compounds	1.74E-03	1.83E-03	3.60E-05	6.37E-03	1.27E-03	2.13E-03	1.06E-03
manganese compounds	1.42E-03	1.52E-03	4.47E-05	5.49E-03	9.65E-04	9.54E-04	1.06E-03
mercury compounds	1.63E-03	1.02E-04	1.51E-03	1.81E-03	1.62E-03	1.45E-04	1.61E-03
methylene chloride	2.91E-01	1.24E-01	1.52E-01	6.00E-01	2.75E-01	1.39E-01	2.73E-01
nickel compounds	9.82E-04	8.39E-04	1.12E-05	2.31E-03	9.72E-04	1.42E-03	5.61E-04
PAH-7	1.88E-03	1.91E-03	1.95E-04	6.94E-03	1.43E-03	1.71E-03	2.02E-03
perchloroethylene	2.31E-01	1.11E-01	1.41E-01	5.47E-01	2.06E-01	7.35E-02	1.95E-01
polycyclic organic matter	6.11E-02	7.96E-02	2.71E-03	2.99E-01	4.12E-02	4.72E-02	4.25E-02
propylene dichloride	3.18E-05	4.51E-05	1.09E-06	1.61E-04	1.34E-05	3.45E-05	2.38E-05
quinoline	2.51E-07	2.93E-07	0.00E+00	8.57E-07	1.23E-07	4.39E-07	1.28E-07
1,1,2,2-tetrachloroethane	2.48E-04	3.84E-04	9.33E-06	1.37E-03	9.46E-05	2.61E-04	1.73E-04
trichloroethylene	1.44E-01	1.02E-01	8.14E-02	4.27E-01	1.08E-01	3.71E-02	1.01E-01
vinyl chloride	8.30E-04	1.13E-03	2.30E-05	4.00E-03	3.18E-04	1.06E-03	6.15E-04

West

HAPs	Mean	Std. Dev.	Min	Max	P50[1]	IQR	US P50[2]
acetaldehyde	4.03E-01	2.97E-01	5.41E-02	1.10E+00	4.02E-01	3.34E-01	4.30E-01
acrolein	6.99E-02	3.28E-02	3.11E-02	1.44E-01	6.47E-02	3.82E-02	6.71E-02
acrylonitrile	1.20E-03	2.56E-03	9.57E-06	8.19E-03	1.80E-04	3.77E-04	4.44E-04
arsenic compounds	3.98E-05	2.50E-05	2.62E-06	8.66E-05	4.78E-05	3.47E-05	4.92E-05
benzene	1.09E+00	3.29E-01	6.01E-01	1.49E+00	1.09E+00	6.17E-01	1.08E+00
beryllium	7.54E-06	6.68E-06	3.74E-07	2.21E-05	5.79E-06	8.29E-06	7.74E-06
1,3-butadiene	4.56E-02	2.22E-02	1.19E-02	8.34E-02	4.48E-02	2.82E-02	4.65E-02
cadmium compounds	2.35E-05	2.11E-05	1.64E-06	7.27E-05	1.87E-05	1.97E-05	3.33E-05
carbon tetrachloride	8.80E-01	0.00E+00	8.80E-01	8.80E-01	8.80E-01	0.00E+00	8.80E-01
chloroform	8.40E-02	9.07E-04	8.31E-02	8.60E-02	8.37E-02	9.00E-04	8.42E-02
chromium compounds	5.68E-04	5.74E-04	1.12E-05	1.53E-03	3.58E-04	1.05E-03	4.14E-04
1,3-dichloropropene	5.02E-02	4.37E-02	1.95E-03	1.55E-01	4.58E-02	5.23E-02	4.35E-02
diesel particulate matter	8.57E-01	6.27E-01	1.34E-01	2.33E+00	8.20E-01	7.55E-01	1.17E+00
ethylene dichloride	6.12E-02	4.13E-04	6.10E-02	6.23E-02	6.10E-02	1.00E-04	6.11E-02
ethylene oxide	9.05E-04	8.68E-04	3.21E-05	2.95E-03	7.00E-04	7.67E-04	1.05E-03
formaldehyde	7.83E-01	3.22E-01	4.10E-01	1.51E+00	7.51E-01	4.47E-01	7.42E-01
hexachlorobenzene	9.30E-05	5.16E-08	9.30E-05	9.31E-05	9.30E-05	1.00E-07	9.30E-05
hydrazine	1.55E-08	2.40E-08	1.15E-10	8.10E-08	9.27E-09	1.25E-08	1.75E-08
lead compounds	1.32E-03	1.31E-03	7.00E-05	4.37E-03	8.55E-04	1.61E-03	1.06E-03
manganese compounds	1.52E-03	1.12E-03	7.46E-05	3.29E-03	1.24E-03	2.25E-03	1.06E-03
mercury compounds	1.59E-03	9.92E-05	1.51E-03	1.85E-03	1.57E-03	8.00E-05	1.61E-03
methylene chloride	2.75E-01	1.21E-01	1.55E-01	5.65E-01	2.50E-01	1.37E-01	2.73E-01
nickel compounds	6.00E-04	5.75E-04	1.83E-05	1.87E-03	4.53E-04	8.34E-04	5.61E-04
PAH-7	2.86E-03	2.11E-03	4.16E-04	7.52E-03	2.96E-03	2.47E-03	2.02E-03
perchloroethylene	2.15E-01	8.89E-02	1.42E-01	4.45E-01	1.90E-01	6.40E-02	1.95E-01
polycyclic organic matter	4.67E-02	3.79E-02	6.28E-03	1.36E-01	4.48E-02	4.36E-02	4.25E-02
propylene dichloride	7.15E-05	1.54E-04	5.74E-07	4.94E-04	1.12E-05	2.22E-05	2.38E-05
quinoline	1.17E-06	3.49E-06	1.21E-09	1.11E-05	5.41E-08	9.44E-08	1.28E-07
1,1,2,2-tetrachloroethane	6.40E-04	1.40E-03	3.96E-06	4.50E-03	8.93E-05	1.96E-04	1.73E-04
trichloroethylene	1.03E-01	2.36E-02	8.15E-02	1.47E-01	9.42E-02	2.33E-02	1.01E-01
vinyl chloride	1.68E-03	3.59E-03	1.08E-05	1.15E-02	2.59E-04	5.15E-04	6.15E-04

South

HAPs	Mean	Std. Dev.	Min	Max	P50[1]	IQR	US P50[2]
acetaldehyde	5.23E-01	2.58E-01	2.32E-01	1.10E+00	4.52E-01	3.27E-01	4.30E-01
acrolein	8.14E-02	3.17E-02	4.11E-02	1.60E-01	8.00E-02	3.04E-02	6.71E-02
acrylonitrile	5.19E-04	2.86E-04	1.03E-04	1.17E-03	4.72E-04	3.47E-04	4.44E-04
arsenic compounds	6.60E-05	4.44E-05	1.64E-05	1.66E-04	4.90E-05	2.60E-05	4.92E-05
benzene	1.10E+00	2.95E-01	7.54E-01	1.82E+00	1.07E+00	2.97E-01	1.08E+00
beryllium	9.96E-06	7.94E-06	2.76E-06	3.11E-05	7.18E-06	8.41E-06	7.74E-06
1,3-butadiene	4.86E-02	1.98E-02	2.05E-02	9.85E-02	4.75E-02	1.96E-02	4.65E-02
cadmium compounds	4.61E-05	4.74E-05	9.47E-06	1.87E-04	3.29E-05	2.08E-05	3.33E-05
carbon tetrachloride	8.80E-01	3.32E-04	8.80E-01	8.81E-01	8.80E-01	0.00E+00	8.80E-01
chloroform	8.47E-02	1.44E-03	8.34E-02	8.83E-02	8.44E-02	1.40E-03	8.42E-02
chromium compounds	4.56E-04	4.12E-04	8.66E-05	1.68E-03	3.11E-04	2.14E-04	4.14E-04
1,3-dichloropropene	5.43E-02	4.03E-02	1.73E-02	1.70E-01	3.68E-02	4.15E-02	4.35E-02
diesel particulate matter	1.40E+00	6.60E-01	6.45E-01	2.85E+00	1.20E+00	2.90E-01	1.17E+00
ethylene dichloride	6.11E-02	1.06E-04	6.10E-02	6.14E-02	6.11E-02	1.00E-04	6.11E-02
ethylene oxide	1.82E-03	2.04E-03	5.05E-04	8.46E-03	1.26E-03	8.34E-04	1.05E-03
formaldehyde	8.58E-01	3.19E-01	5.39E-01	1.72E+00	7.47E-01	2.34E-01	7.42E-01
hexachlorobenzene	9.30E-05	5.88E-08	9.30E-05	9.32E-05	9.30E-05	0.00E+00	9.30E-05
hydrazine	4.49E-08	8.37E-08	2.57E-09	3.52E-07	1.84E-08	2.34E-08	1.75E-08
lead compounds	1.52E-03	1.54E-03	2.56E-04	6.34E-03	9.53E-04	1.00E-03	1.06E-03
manganese compounds	1.19E-03	5.64E-04	5.18E-04	2.49E-03	1.03E-03	5.28E-04	1.06E-03
mercury compounds	1.72E-03	2.64E-04	1.53E-03	2.49E-03	1.61E-03	6.00E-05	1.61E-03
methylene chloride	2.89E-01	8.52E-02	1.89E-01	5.41E-01	2.71E-01	6.50E-02	2.73E-01
nickel compounds	7.39E-04	8.39E-04	1.53E-04	3.75E-03	4.87E-04	2.96E-04	5.61E-04
PAH-7	2.44E-03	1.42E-03	1.25E-03	6.00E-03	2.10E-03	9.90E-04	2.02E-03
perchloroethylene	2.22E-01	6.79E-02	1.60E-01	4.24E-01	1.91E-01	5.60E-02	1.95E-01
polycyclic organic matter	4.50E-02	2.53E-02	1.89E-02	1.14E-01	4.12E-02	2.04E-02	4.25E-02
propylene dichloride	2.93E-05	1.71E-05	6.28E-06	6.42E-05	2.41E-05	2.36E-05	2.38E-05
quinoline	1.93E-07	1.69E-07	2.61E-08	7.10E-07	1.38E-07	8.90E-08	1.28E-07
1,1,2,2-tetrachloroethane	2.12E-04	1.31E-04	3.76E-05	5.04E-04	1.79E-04	1.69E-04	1.73E-04
trichloroethylene	1.06E-01	2.29E-02	8.58E-02	1.86E-01	1.01E-01	9.00E-03	1.01E-01
vinyl chloride	1.90E-03	5.16E-03	1.32E-04	2.19E-02	6.48E-04	4.88E-04	6.15E-04

[1] Regional median concentration
[2] Total U.S. median concentration

Table 5- Regional distribution of HAPs, Statewide levels, for U.S., 1999, in µg/m^3

Northeast

HAPs	Mean	Std. Dev.	Min	Max	P50[1]	IQR	P50[2]
acetaldehyde	1.31E+00	4.56E-01	6.51E-01	1.89E+00	1.35E+00	6.27E-01	1.05E+00
acetonitrile	3.51E-04	3.56E-04	1.62E-05	9.93E-04	2.26E-04	3.41E-04	6.48E-05
acrolein	9.64E-02	7.54E-02	1.69E-02	2.71E-01	8.01E-02	6.24E-02	5.07E-02
acrylamide	1.71E-07	1.98E-07	4.25E-09	5.56E-07	9.69E-08	1.93E-07	2.44E-08
acrylic acid	2.94E-05	4.74E-05	2.74E-07	1.49E-04	1.26E-05	2.91E-05	2.47E-06
acrylonitrile	1.07E-03	1.19E-03	4.53E-05	4.02E-03	7.55E-04	7.69E-04	4.31E-04
allyl chloride	1.41E-05	1.91E-05	6.99E-07	4.94E-05	5.36E-06	4.97E-06	2.86E-06
aniline	1.80E-04	4.88E-04	1.49E-07	1.48E-03	6.10E-06	3.73E-05	1.56E-06
antimony compounds	3.59E-05	4.63E-05	1.22E-07	1.42E-04	3.11E-05	4.79E-05	5.25E-06
arsenic compounds	6.59E-05	3.59E-05	8.48E-06	1.16E-04	6.75E-05	2.79E-05	3.04E-05
benzene	1.16E+00	4.25E-01	5.69E-01	1.91E+00	1.24E+00	4.81E-01	9.58E-01
benzidine	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
benzotrichloride	5.72E-08	7.21E-08	1.65E-09	2.21E-07	3.12E-08	5.16E-08	7.37E-09
benzyl chloride	9.43E-06	1.55E-05	3.05E-07	4.98E-05	4.66E-06	6.23E-06	1.69E-06
beryllium	5.79E-05	6.64E-05	3.12E-06	1.73E-04	3.08E-05	1.72E-05	4.40E-06
bis(chloromethyl)ether	7.36E-09	7.63E-09	2.49E-10	2.02E-08	5.11E-09	8.46E-09	1.10E-09
1,3-butadiene	1.29E-01	1.22E-01	1.23E-02	4.27E-01	1.23E-01	8.54E-02	6.53E-02
cadmium compounds	5.03E-05	2.68E-05	6.71E-06	8.54E-05	6.15E-05	2.91E-05	1.62E-05
carbon tetrachloride	2.71E-01	7.07E-04	2.70E-01	2.72E-01	2.71E-01	1.00E-03	2.70E-01
chlorine	4.45E-04	3.70E-04	3.13E-06	8.97E-04	3.19E-04	7.19E-04	4.16E-04
chloroform	7.84E-02	2.76E-02	3.97E-02	1.21E-01	7.91E-02	4.16E-02	5.75E-02
chloroprene	1.36E-05	1.05E-05	1.09E-06	3.07E-05	1.37E-05	9.53E-06	5.09E-06
chromium IV	8.82E-05	4.76E-05	5.04E-06	1.81E-04	9.48E-05	3.68E-05	5.38E-05
cobalt compounds	3.12E-05	4.16E-05	1.89E-07	1.08E-04	1.44E-05	1.50E-05	1.23E-05
coke oven emissions	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
cyanide compounds	5.88E-02	3.35E-02	7.19E-03	1.17E-01	6.06E-02	4.06E-02	3.71E-02
1,2-dibromo-3-chloropropane	1.36E-06	2.70E-06	0.00E+00	6.60E-06	0.00E+00	0.00E+00	0.00E+00
dichloroethyl ether	6.87E-07	2.03E-06	2.07E-10	6.11E-06	4.36E-09	7.54E-09	1.10E-09
1,3-dichloropropene	8.38E-02	4.99E-02	9.24E-03	1.53E-01	7.90E-02	4.25E-02	5.00E-02
diesel particulate matter	9.13E-01	6.08E-01	1.09E-01	1.80E+00	9.24E-01	9.88E-01	7.23E-01
diethanolamine	6.81E-06	1.47E-05	1.13E-08	4.51E-05	5.90E-07	3.57E-06	5.91E-07
dimethyl formamide	4.12E-03	4.06E-03	2.72E-04	1.33E-02	3.27E-03	3.48E-03	1.59E-03
2,4-dinitrotoluene	1.37E-05	1.02E-05	1.76E-06	3.27E-05	1.07E-05	1.26E-05	5.90E-06
1,4-dioxane	6.42E-05	9.84E-05	1.42E-06	2.63E-04	1.58E-05	3.51E-05	1.01E-05
epichlorohydrin	2.19E-05	3.43E-05	2.24E-07	9.94E-05	3.73E-06	3.07E-05	1.40E-06
ethyl acrylate	2.46E-05	3.56E-05	1.64E-07	9.73E-05	4.14E-06	3.82E-05	1.12E-06
ethyl carbamate	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
ethylene dibromide	2.45E-02	9.98E-03	5.34E-03	3.49E-02	2.95E-02	1.36E-02	1.82E-02
ethylene dichloride	3.90E-02	1.08E-02	1.83E-02	5.00E-02	4.45E-02	1.49E-02	3.29E-02
ethylene oxide	2.87E-03	3.12E-03	1.94E-05	8.09E-03	1.39E-03	3.14E-03	6.65E-04
formaldehyde	1.43E+00	5.04E-01	6.45E-01	2.14E+00	1.53E+00	7.40E-01	1.13E+00
glycol ethers	7.12E-02	6.72E-02	5.09E-03	2.33E-01	5.27E-02	4.15E-02	3.36E-02
hexachlorobenzene	2.44E-07	2.01E-07	5.12E-08	6.18E-07	1.75E-07	2.33E-07	1.66E-07
hexamethylene-1,6-diisocyanate	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
hydrazine	1.04E-05	2.90E-05	8.51E-10	8.76E-05	2.70E-07	1.08E-06	7.35E-09
hydrochloric acid	7.72E-02	5.09E-02	5.86E-03	1.73E-01	6.66E-02	5.45E-02	6.72E-02
hydrofluoric acid	5.28E-03	5.23E-03	1.75E-04	1.54E-02	3.39E-03	4.38E-03	4.83E-03
lead compounds	1.83E-03	1.37E-03	1.42E-04	4.44E-03	1.60E-03	1.88E-03	1.10E-03
maleic anhydride	1.72E-03	5.09E-03	1.57E-07	1.53E-02	5.63E-06	1.58E-05	1.36E-06
manganese compounds	5.52E-04	4.46E-04	1.44E-04	1.34E-03	5.57E-04	4.69E-04	4.49E-04
mercury	1.58E-03	5.29E-05	1.51E-03	1.65E-03	1.59E-03	9.00E-05	1.52E-03
methyl bromide	1.61E-01	7.27E-02	5.23E-02	2.69E-01	1.52E-01	6.40E-02	1.02E-01
methyl chloride	1.20E+00	5.27E-03	1.20E+00	1.21E+00	1.20E+00	1.00E-02	1.20E+00
4,4'-methylene bis(2-chloroaniline)	3.07E-07	6.74E-07	0.00E+00	1.96E-06	0.00E+00	0.00E+00	0.00E+00
methylene chloride	4.91E-01	1.98E-01	1.59E-01	7.58E-01	5.16E-01	2.23E-01	3.80E-01
4,4'-methylenedianiline	4.42E-06	1.32E-05	1.48E-09	3.95E-05	2.81E-08	9.46E-08	1.19E-08
methylene diphenyl diisocyanate	9.06E-06	8.10E-06	8.37E-08	2.62E-05	1.00E-05	1.00E-05	5.95E-06
naphthalene	6.28E-02	4.99E-02	8.96E-03	1.81E-01	5.61E-02	1.57E-02	3.23E-02
n-hexane	5.39E-01	4.57E-01	8.60E-02	1.60E+00	4.98E-01	3.47E-01	3.72E-01
nickel compounds	2.33E-03	3.86E-03	1.03E-04	1.25E-02	9.06E-04	9.09E-04	3.32E-04
o-toluidine	1.93E-07	2.59E-07	1.61E-08	8.16E-07	7.71E-08	2.55E-07	5.75E-08
p-dichlorobenzene	3.98E-02	2.35E-02	4.69E-03	7.84E-02	4.00E-02	3.14E-02	2.21E-02
perchloroethylene	2.03E-01	1.45E-01	3.89E-02	5.43E-01	1.99E-01	9.30E-02	1.27E-01
phosgene	6.54E-08	9.83E-08	1.57E-09	3.08E-07	3.00E-08	5.02E-08	1.08E-08
polychlorinated biphenyls	4.03E-04	2.24E-05	3.80E-04	4.54E-04	3.99E-04	2.60E-05	3.95E-04
polycyclic organic matter	1.96E-02	1.30E-02	6.91E-03	4.74E-02	1.49E-02	5.40E-03	9.39E-03
propylene dichloride	2.13E-02	6.08E-03	9.65E-03	2.76E-02	2.42E-02	8.30E-03	1.73E-02
propylene oxide	1.13E-03	1.39E-03	1.43E-04	3.99E-03	4.57E-04	3.22E-04	4.01E-04
quinoline	3.42E-07	3.24E-07	1.19E-08	8.86E-07	2.93E-07	3.90E-07	6.70E-08
1,1,2,2-tetrachloroethane	5.95E-02	1.83E-02	2.44E-02	7.80E-02	7.10E-02	2.49E-02	4.78E-02
titanium tetrachloride	9.42E-06	2.80E-05	4.21E-09	8.41E-05	7.97E-08	1.32E-07	2.18E-08
toluene	2.27E+00	1.22E+00	5.93E-01	4.34E+00	2.35E+00	1.42E+00	1.72E+00
2,4-toluene diamine	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
2,4-toluene diisocyanate	4.04E-03	3.67E-03	8.09E-04	1.01E-02	1.81E-03	6.15E-03	7.73E-04
1,1,2-trichloroethane	5.24E-06	7.64E-06	1.20E-07	2.21E-05	2.65E-06	2.25E-06	8.28E-07
vinyl chloride	5.75E-02	2.50E-02	1.16E-02	8.87E-02	6.95E-02	3.41E-02	4.10E-02
xylenes	1.65E+00	9.40E-01	4.89E-01	3.55E+00	1.65E+00	7.60E-01	1.25E+00

Midwest

HAPs	Mean	Std. Dev.	Min	Max	P50[1]	IQR	P50[2]
acetaldehyde	9.40E-01	3.25E-01	5.25E-01	1.63E+00	9.39E-01	4.66E-01	1.05E+00
acetonitrile	7.31E-05	6.97E-05	2.04E-06	2.54E-04	5.37E-05	7.40E-05	6.48E-05
acrolein	3.81E-02	2.83E-02	3.57E-03	9.91E-02	3.85E-02	3.76E-02	5.07E-02
acrylamide	5.48E-08	6.45E-08	0.00E+00	1.67E-07	2.82E-08	1.03E-07	2.44E-08
acrylic acid	2.37E-05	6.54E-05	7.60E-10	2.30E-04	2.26E-06	8.40E-06	2.47E-06
acrylonitrile	5.27E-04	7.17E-04	1.26E-05	2.59E-03	2.98E-04	5.49E-04	4.31E-04
allyl chloride	2.59E-06	1.50E-06	9.41E-08	4.64E-06	2.75E-06	2.06E-06	2.86E-06
aniline	3.31E-06	4.42E-06	0.00E+00	1.51E-05	1.51E-06	3.85E-06	1.56E-06
antimony compounds	2.69E-05	3.72E-05	2.44E-09	1.24E-04	9.64E-06	3.69E-05	5.25E-06
arsenic compounds	3.15E-05	2.76E-05	4.51E-07	8.26E-05	2.71E-05	3.63E-05	3.04E-05
benzene	8.46E-01	3.47E-01	2.81E-01	1.36E+00	9.34E-01	4.83E-01	9.58E-01
benzidine	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
benzotrichloride	1.35E-08	1.67E-08	0.00E+00	5.86E-08	8.20E-09	1.78E-08	7.37E-09
benzyl chloride	1.72E-05	2.83E-05	4.81E-08	8.23E-05	3.23E-06	1.57E-05	1.69E-06
beryllium	4.55E-06	2.94E-06	2.21E-07	9.50E-06	4.89E-06	4.24E-06	4.40E-06
bis(chloromethyl)ether	2.13E-09	2.49E-09	0.00E+00	8.54E-09	1.34E-09	2.92E-09	1.10E-09
1,3-butadiene	6.03E-02	4.06E-02	2.06E-03	1.35E-01	6.45E-02	5.85E-02	6.53E-02
cadmium compounds	6.79E-05	1.25E-04	3.59E-07	4.43E-04	2.11E-05	7.54E-05	1.62E-05
carbon tetrachloride	2.70E-01	0.00E+00	2.70E-01	2.70E-01	2.70E-01	0.00E+00	2.70E-01
chlorine	2.24E-03	3.12E-03	7.94E-08	8.97E-03	6.28E-04	3.00E-03	4.16E-04
chloroform	5.64E-02	1.71E-02	3.24E-02	9.47E-02	5.57E-02	2.03E-02	5.75E-02
chloroprene	4.73E-06	3.38E-06	1.54E-07	1.23E-05	4.57E-06	4.12E-06	5.09E-06
chromium IV	7.81E-05	7.03E-05	6.74E-07	2.18E-04	7.43E-05	1.12E-04	5.38E-05
cobalt compounds	3.02E-05	3.18E-05	1.03E-08	9.65E-05	2.44E-05	3.99E-05	1.23E-05
coke oven emissions	4.62E-04	1.60E-03	0.00E+00	5.54E-03	0.00E+00	0.00E+00	0.00E+00
cyanide compounds	3.00E-02	2.01E-02	1.24E-03	6.64E-02	2.88E-02	2.77E-02	3.71E-02
1,2-dibromo-3-chloropropane	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
dichloroethyl ether	1.73E-09	2.42E-09	0.00E+00	8.58E-09	7.84E-10	1.75E-09	1.10E-09
1,3-dichloropropene	4.94E-02	3.80E-02	1.13E-03	1.20E-01	4.26E-02	6.18E-02	5.00E-02
diesel particulate matter	7.66E-01	3.28E-01	2.80E-01	1.36E+00	7.59E-01	4.71E-01	7.23E-01
diethanolamine	6.13E-06	1.37E-05	1.32E-10	4.86E-05	1.38E-06	3.73E-06	5.91E-07
dimethyl formamide	1.53E-03	1.10E-03	3.45E-05	4.00E-03	1.59E-03	1.20E-03	1.59E-03
2,4-dinitrotoluene	5.34E-06	3.26E-06	1.98E-07	1.10E-05	5.67E-06	4.10E-06	5.90E-06
1,4-dioxane	3.54E-05	8.48E-05	2.01E-07	3.03E-04	1.10E-05	1.60E-05	1.01E-05
epichlorohydrin	1.16E-04	3.95E-04	3.18E-08	1.37E-03	1.46E-06	2.15E-06	1.40E-06
ethyl acrylate	1.59E-05	4.49E-05	1.65E-08	1.57E-04	9.59E-07	2.76E-06	1.12E-06
ethyl carbamate	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
ethylene dibromide	1.62E-02	8.94E-03	2.09E-08	2.85E-02	1.77E-02	1.22E-02	1.82E-02
ethylene dichloride	2.91E-02	1.15E-02	2.65E-03	4.30E-02	3.15E-02	1.32E-02	3.29E-02
ethylene oxide	1.96E-03	2.53E-03	2.16E-05	6.63E-03	4.27E-04	3.87E-03	6.65E-04
formaldehyde	9.83E-01	3.85E-01	3.12E-01	1.70E+00	1.04E+00	4.81E-01	1.13E+00
glycol ethers	6.52E-02	5.86E-02	9.53E-04	1.65E-01	5.55E-02	9.12E-02	3.36E-02
hexachlorobenzene	1.22E-07	8.50E-08	2.85E-08	2.63E-07	1.04E-07	1.49E-07	1.66E-07
hexamethylene-1,6-diisocyanate	7.35E-06	1.88E-05	0.00E+00	6.23E-05	0.00E+00	2.78E-07	0.00E+00
hydrazine	2.30E-08	4.04E-08	0.00E+00	1.36E-07	7.35E-09	1.80E-08	7.35E-09
hydrochloric acid	9.40E-02	1.03E-01	1.21E-03	3.54E-01	6.65E-02	1.01E-01	6.72E-02
hydrofluoric acid	7.20E-03	5.80E-03	8.54E-06	1.77E-02	5.73E-03	6.06E-03	4.83E-03
lead compounds	1.69E-03	1.58E-03	3.11E-05	5.97E-03	1.66E-03	1.52E-03	1.10E-03
maleic anhydride	1.70E-03	5.86E-03	0.00E+00	2.03E-02	1.41E-06	8.39E-06	1.36E-06
manganese compounds	8.76E-04	1.02E-03	8.38E-06	3.35E-03	5.70E-04	1.12E-03	4.49E-04
mercury	1.55E-03	5.96E-05	1.50E-03	1.72E-03	1.53E-03	4.50E-05	1.52E-03
methyl bromide	1.00E-01	5.00E-02	4.07E-02	2.11E-01	9.74E-02	4.46E-02	1.02E-01
methyl chloride	1.20E+00	2.89E-03	1.20E+00	1.21E+00	1.20E+00	0.00E+00	1.20E+00
4,4'-methylene bis(2-chloroaniline)	3.07E-07	1.06E-06	0.00E+00	3.68E-06	0.00E+00	0.00E+00	0.00E+00
methylene chloride	3.35E-01	1.78E-01	8.54E-03	6.53E-01	3.65E-01	2.00E-01	3.80E-01
4,4'-methylenedianiline	1.30E-06	3.63E-06	0.00E+00	1.25E-05	1.59E-08	3.29E-08	1.19E-08
methylene diphenyl diisocyanate	1.73E-05	2.61E-05	0.00E+00	9.39E-05	1.03E-05	1.68E-05	5.95E-06
naphthalene	3.06E-02	2.08E-02	1.37E-03	6.04E-02	3.29E-02	3.34E-02	3.23E-02
n-hexane	3.14E-01	1.95E-01	1.38E-02	6.84E-01	3.24E-01	2.15E-01	3.72E-01
nickel compounds	4.75E-04	4.01E-04	4.25E-06	1.14E-03	4.82E-04	6.81E-04	3.32E-04
o-toluidine	8.01E-08	9.42E-08	2.87E-09	3.52E-07	5.71E-08	6.41E-08	5.75E-08
p-dichlorobenzene	2.17E-02	1.78E-02	5.64E-04	6.07E-02	2.05E-02	1.53E-02	2.21E-02
perchloroethylene	1.22E-01	8.50E-02	1.63E-03	3.05E-01	1.20E-01	7.27E-02	1.27E-01
phosgene	1.65E-08	1.95E-08	0.00E+00	6.52E-08	9.37E-09	2.19E-08	1.08E-08
polychlorinated biphenyls	3.93E-04	1.09E-05	3.82E-04	4.17E-04	3.92E-04	1.60E-05	3.95E-04
polycyclic organic matter	8.55E-03	6.19E-03	9.50E-04	1.95E-02	8.88E-03	1.05E-02	9.39E-03
propylene dichloride	1.57E-02	6.37E-03	9.52E-04	2.34E-02	1.70E-02	7.30E-03	1.73E-02
propylene oxide	4.05E-04	4.70E-04	3.12E-05	1.54E-03	2.06E-04	3.11E-04	4.01E-04
quinoline	3.82E-07	7.87E-07	0.00E+00	2.80E-06	6.15E-08	4.11E-07	6.70E-08
1,1,2,2-tetrachloroethane	4.30E-02	1.91E-02	1.54E-05	6.65E-02	4.72E-02	2.24E-02	4.78E-02
titanium tetrachloride	3.21E-08	4.56E-08	0.00E+00	1.62E-07	1.40E-08	3.30E-08	2.18E-08
toluene	1.43E+00	9.38E-01	7.84E-02	2.95E+00	1.68E+00	1.18E+00	1.72E+00
2,4-toluene diamine	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
2,4-toluene diisocyanate	1.41E-03	1.74E-03	4.74E-05	5.60E-03	5.06E-04	2.32E-03	7.73E-04
1,1,2-trichloroethane	1.28E-06	1.23E-06	1.12E-08	3.45E-06	8.20E-07	2.34E-06	8.28E-07
vinyl chloride	3.65E-02	2.06E-02	2.07E-05	6.45E-02	4.03E-02	2.79E-02	4.10E-02
xylenes	1.09E+00	5.95E-01	2.24E-01	1.97E+00	1.27E+00	8.13E-01	1.25E+00

West

HAPs	Mean	Std. Dev.	Min	Max	P50[1]	IQR	P50[2]
acetaldehyde	9.66E-01	3.52E-01	5.62E-01	1.80E+00	9.47E-01	4.97E-01	1.05E+00
acetonitrile	1.06E-04	2.17E-04	2.81E-06	8.42E-04	3.87E-05	6.40E-05	6.48E-05
acrolein	6.69E-02	5.68E-02	9.21E-03	2.02E-01	5.15E-02	6.09E-02	5.07E-02
acrylamide	1.68E-08	1.79E-08	0.00E+00	4.62E-08	6.41E-09	3.26E-08	2.44E-08
acrylic acid	1.14E-06	1.18E-06	1.12E-09	2.80E-06	7.48E-07	2.35E-06	2.47E-06
acrylonitrile	1.57E-03	3.44E-03	1.49E-05	1.29E-02	3.14E-04	5.61E-04	4.31E-04
allyl chloride	2.09E-06	2.16E-06	0.00E+00	7.28E-06	1.66E-06	1.62E-06	2.86E-06
aniline	7.46E-07	8.67E-07	0.00E+00	2.82E-06	3.91E-07	1.42E-06	1.56E-06
antimony compounds	3.11E-05	6.98E-05	4.51E-09	2.42E-04	7.15E-07	2.67E-05	5.25E-06
arsenic compounds	5.95E-05	1.05E-04	1.31E-06	3.66E-04	1.25E-05	6.16E-05	3.04E-05
benzene	9.10E-01	4.01E-01	3.55E-01	1.62E+00	9.61E-01	4.76E-01	9.58E-01
benzidine	9.07E-12	3.39E-11	0.00E+00	1.27E-10	0.00E+00	0.00E+00	0.00E+00
benzotrichloride	7.81E-09	8.79E-09	0.00E+00	2.39E-08	4.36E-09	1.53E-08	7.37E-09
benzyl chloride	4.26E-06	8.38E-06	6.60E-08	2.52E-05	8.28E-07	9.36E-07	1.69E-06
beryllium	3.00E-06	2.57E-06	7.51E-07	9.11E-06	2.01E-06	3.37E-06	4.40E-06
bis(chloromethyl)ether	1.05E-09	1.31E-09	0.00E+00	3.93E-09	3.79E-10	1.96E-09	1.10E-09
1,3-butadiene	7.93E-02	5.29E-02	7.61E-03	1.84E-01	8.45E-02	9.75E-02	6.53E-02
cadmium compounds	4.65E-05	1.07E-04	1.55E-06	4.08E-04	8.00E-06	3.08E-05	1.62E-05
carbon tetrachloride	2.70E-01	1.34E-03	2.70E-01	2.75E-01	2.70E-01	0.00E+00	2.70E-01
chlorine	7.57E-03	2.42E-02	2.78E-08	9.12E-02	2.42E-04	8.09E-04	4.16E-04
chloroform	6.29E-02	2.38E-02	3.80E-02	1.17E-01	5.95E-02	2.83E-02	5.75E-02
chloroprene	4.77E-06	4.73E-06	2.37E-07	1.47E-05	3.02E-06	7.90E-06	5.09E-06
chromium IV	8.90E-05	1.07E-04	1.21E-06	3.03E-04	4.71E-05	1.60E-04	5.38E-05
cobalt compounds	1.03E-04	3.17E-04	1.00E-08	1.19E-03	1.32E-06	2.26E-05	1.23E-05
coke oven emissions	1.31E-04	4.92E-04	0.00E+00	1.84E-03	0.00E+00	0.00E+00	0.00E+00
cyanide compounds	4.94E-02	7.52E-02	3.21E-03	2.93E-01	2.67E-02	2.85E-02	3.71E-02
1,2-dibromo-3-chloropropane	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
dichloroethyl ether	9.34E-10	1.15E-09	0.00E+00	3.48E-09	3.37E-10	1.71E-09	1.10E-09
1,3-dichloropropene	5.98E-02	4.66E-02	2.97E-03	1.55E-01	5.52E-02	8.37E-02	5.00E-02
diesel particulate matter	5.03E-01	3.38E-01	7.26E-02	1.17E+00	4.92E-01	5.29E-01	7.23E-01
diethanolamine	3.00E-06	7.73E-06	1.72E-10	2.72E-05	5.07E-08	6.94E-07	5.91E-07
dimethyl formamide	1.63E-03	1.73E-03	3.57E-05	6.48E-03	1.31E-03	1.76E-03	1.59E-03
2,4-dinitrotoluene	4.30E-06	4.93E-06	0.00E+00	1.55E-05	2.75E-06	4.77E-06	5.90E-06
1,4-dioxane	7.39E-05	2.23E-04	4.44E-07	8.41E-04	4.96E-06	9.33E-06	1.01E-05
epichlorohydrin	2.05E-06	3.44E-06	4.61E-08	1.01E-05	6.27E-07	1.36E-06	1.40E-06
ethyl acrylate	9.52E-07	1.64E-06	0.00E+00	6.28E-06	3.60E-07	1.05E-06	1.12E-06
ethyl carbamate	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
ethylene dibromide	2.10E-02	1.36E-02	1.72E-03	4.07E-02	2.42E-02	2.85E-02	1.82E-02
ethylene dichloride	3.51E-02	1.47E-02	1.44E-02	5.58E-02	3.84E-02	3.04E-02	3.29E-02
ethylene oxide	7.69E-04	9.84E-04	2.48E-05	2.94E-03	2.14E-04	8.85E-04	6.65E-04
formaldehyde	1.21E+00	4.95E-01	5.10E-01	2.39E+00	1.25E+00	6.55E-01	1.13E+00
glycol ethers	6.40E-02	1.36E-01	1.36E-03	5.28E-01	2.41E-02	2.62E-02	3.36E-02
hexachlorobenzene	1.95E-07	3.85E-07	2.48E-10	1.25E-06	2.96E-08	1.31E-07	1.66E-07
hexamethylene-1,6-diisocyanate	1.75E-06	5.12E-06	0.00E+00	1.87E-05	0.00E+00	0.00E+00	0.00E+00
hydrazine	2.27E-08	5.96E-08	0.00E+00	2.28E-07	3.01E-09	1.53E-08	7.35E-09
hydrochloric acid	4.59E-02	5.48E-02	4.28E-03	2.11E-01	2.62E-02	6.02E-02	6.72E-02
hydrofluoric acid	3.07E-03	3.57E-03	4.33E-06	1.11E-02	2.26E-03	4.20E-03	4.83E-03
lead compounds	1.60E-03	2.30E-03	1.02E-04	8.81E-03	7.69E-04	2.04E-03	1.10E-03
maleic anhydride	1.55E-06	2.83E-06	0.00E+00	1.08E-05	5.25E-07	1.79E-06	1.36E-06
manganese compounds	1.63E-03	3.18E-03	7.59E-06	1.14E-02	1.54E-04	1.19E-03	4.49E-04
mercury	1.55E-03	8.84E-05	1.50E-03	1.76E-03	1.51E-03	1.00E-05	1.52E-03
methyl bromide	1.12E-01	6.61E-02	4.32E-02	2.95E-01	1.08E-01	7.70E-02	1.02E-01
methyl chloride	1.25E+00	1.62E-01	1.20E+00	1.81E+00	1.20E+00	1.00E-02	1.20E+00
4,4'-methylene bis(2-chloroaniline)	9.36E-13	3.50E-12	0.00E+00	1.31E-11	0.00E+00	0.00E+00	0.00E+00
methylene chloride	3.82E-01	2.42E-01	9.54E-02	1.03E+00	4.07E-01	3.06E-01	3.80E-01
4,4'-methylenedianiline	1.11E-08	1.78E-08	0.00E+00	6.72E-08	4.23E-09	1.42E-08	1.19E-08
methylene diphenyl diisocyanate	3.01E-05	9.65E-05	2.85E-12	3.64E-04	9.05E-07	7.08E-06	5.95E-06
naphthalene	3.30E-02	2.92E-02	3.03E-03	1.01E-01	2.67E-02	3.15E-02	3.23E-02
n-hexane	3.33E-01	3.24E-01	2.48E-02	1.30E+00	2.79E-01	3.22E-01	3.72E-01
nickel compounds	3.19E-04	5.67E-04	8.06E-06	2.21E-03	1.44E-04	1.72E-04	3.32E-04
o-toluidine	3.82E-08	3.80E-08	0.00E+00	1.18E-07	2.35E-08	5.20E-08	5.75E-08
p-dichlorobenzene	3.02E-02	3.68E-02	1.50E-03	1.49E-01	2.46E-02	2.74E-02	2.21E-02
perchloroethylene	1.91E-01	1.94E-01	1.49E-02	7.81E-01	1.74E-01	1.70E-01	1.27E-01
phosgene	3.58E-07	1.28E-06	1.48E-12	4.80E-06	6.97E-09	2.20E-08	1.08E-08
polychlorinated biphenyls	4.02E-04	4.22E-05	3.80E-04	5.14E-04	3.82E-04	1.80E-05	3.95E-04
polycyclic organic matter	2.81E-02	7.18E-02	2.09E-03	2.75E-01	4.40E-03	9.47E-03	9.39E-03
propylene dichloride	1.90E-02	8.22E-03	7.48E-03	3.06E-02	2.11E-02	1.72E-02	1.73E-02
propylene oxide	4.10E-04	3.77E-04	3.81E-05	1.34E-03	3.01E-04	2.35E-04	4.01E-04
quinoline	5.50E-08	6.05E-08	0.00E+00	1.80E-07	3.21E-08	9.35E-08	6.70E-08
1,1,2,2-tetrachloroethane	5.33E-02	2.56E-02	1.77E-02	8.82E-02	5.85E-02	5.23E-02	4.78E-02
titanium tetrachloride	3.40E-06	1.02E-05	0.00E+00	3.79E-05	2.05E-08	6.06E-08	2.18E-08
toluene	1.85E+00	1.64E+00	1.32E-01	5.35E+00	1.64E+00	1.52E+00	1.72E+00
2,4-toluene diamine	4.24E-11	1.59E-10	0.00E+00	5.94E-10	0.00E+00	0.00E+00	0.00E+00
2,4-toluene diisocyanate	4.57E-04	5.42E-04	2.65E-06	1.85E-03	2.12E-04	4.73E-04	7.73E-04
1,1,2-trichloroethane	3.22E-06	6.86E-06	1.85E-08	2.11E-05	3.20E-07	1.20E-06	8.28E-07
vinyl chloride	4.84E-02	3.26E-02	3.26E-03	9.84E-02	5.41E-02	6.43E-02	4.10E-02
xylenes	1.54E+00	1.71E+00	2.54E-01	6.79E+00	1.16E+00	9.65E-01	1.25E+00

South

HAPs	Mean	Std. Dev.	Min	Max	P50[1]	IQR	P50[2]
acetaldehyde	1.07E+00	2.15E-01	7.57E-01	1.57E+00	1.07E+00	3.32E-01	1.05E+00
acetonitrile	9.28E-04	2.25E-03	2.30E-05	8.32E-03	7.14E-05	1.44E-04	6.48E-05
acrolein	6.05E-02	3.18E-02	2.42E-02	1.49E-01	5.24E-02	3.54E-02	5.07E-02
acrylamide	8.08E-08	1.24E-07	7.27E-10	4.50E-07	2.68E-08	8.74E-08	2.44E-08
acrylic acid	4.84E-05	1.48E-04	9.08E-07	5.82E-04	5.89E-06	2.02E-05	2.47E-06
acrylonitrile	3.93E-04	1.87E-04	1.00E-04	7.39E-04	4.24E-04	2.22E-04	4.31E-04
allyl chloride	6.37E-06	9.28E-06	1.39E-06	3.91E-05	4.19E-06	3.66E-06	2.86E-06
aniline	1.84E-05	3.79E-05	2.94E-07	1.37E-04	1.98E-06	1.13E-05	1.56E-06
antimony compounds	2.67E-05	4.33E-05	3.46E-07	1.60E-04	7.67E-06	3.03E-05	5.25E-06
arsenic compounds	4.47E-05	3.08E-05	8.70E-06	1.35E-04	3.91E-05	4.00E-05	3.04E-05
benzene	9.47E-01	2.16E-01	6.35E-01	1.35E+00	9.54E-01	2.84E-01	9.58E-01
benzidine	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
benzotrichloride	2.63E-08	6.31E-08	1.35E-09	2.52E-07	7.84E-09	1.45E-08	7.37E-09
benzyl chloride	9.02E-05	3.40E-04	7.81E-07	1.32E-03	1.91E-06	1.38E-06	1.69E-06
beryllium	7.42E-06	7.19E-06	2.11E-06	2.92E-05	4.37E-06	3.94E-06	4.40E-06
bis(chloromethyl)ether	2.34E-09	3.16E-09	2.22E-10	1.26E-08	1.29E-09	1.90E-09	1.10E-09
1,3-butadiene	6.46E-02	3.43E-02	1.86E-02	1.24E-01	5.62E-02	5.52E-02	6.53E-02
cadmium compounds	2.18E-05	2.01E-05	4.92E-06	7.62E-05	1.34E-05	1.20E-05	1.62E-05
carbon tetrachloride	2.70E-01	4.58E-04	2.70E-01	2.71E-01	2.70E-01	1.00E-03	2.70E-01
chlorine	1.33E-03	2.25E-03	2.38E-05	8.34E-03	3.17E-04	1.56E-03	4.16E-04
chloroform	5.80E-02	1.30E-02	4.35E-02	9.31E-02	5.54E-02	1.97E-02	5.75E-02
chloroprene	7.06E-06	3.53E-06	2.56E-06	1.42E-05	6.90E-06	6.43E-06	5.09E-06
chromium IV	6.73E-05	6.83E-05	2.42E-05	2.83E-04	4.49E-05	2.17E-05	5.38E-05
cobalt compounds	1.71E-05	1.81E-05	1.37E-06	7.72E-05	1.31E-05	1.33E-05	1.23E-05
coke oven emissions	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
cyanide compounds	4.22E-02	1.84E-02	2.22E-02	7.80E-02	4.09E-02	2.11E-02	3.71E-02
1,2-dibromo-3-chloropropane	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
dichloroethyl ether	1.97E-07	7.13E-07	3.76E-10	2.77E-06	1.42E-09	1.91E-09	1.10E-09
1,3-dichloropropene	4.25E-02	2.10E-02	1.80E-02	9.58E-02	4.24E-02	2.99E-02	5.00E-02
diesel particulate matter	7.92E-01	2.89E-01	4.73E-01	1.49E+00	7.38E-01	2.44E-01	7.23E-01
diethanolamine	2.20E-06	3.61E-06	1.82E-08	1.26E-05	6.46E-07	3.60E-06	5.91E-07
dimethyl formamide	1.70E-03	1.02E-03	5.87E-04	4.06E-03	1.50E-03	1.25E-03	1.59E-03
2,4-dinitrotoluene	6.90E-06	2.95E-06	2.35E-06	1.34E-05	6.81E-06	4.75E-06	5.90E-06
1,4-dioxane	8.87E-05	2.09E-04	4.80E-06	8.08E-04	1.31E-05	2.76E-05	1.01E-05
epichlorohydrin	4.93E-06	1.26E-05	6.13E-07	5.04E-05	1.75E-06	1.25E-06	1.40E-06
ethyl acrylate	8.76E-06	1.39E-05	4.68E-07	4.65E-05	1.39E-06	1.87E-05	1.12E-06
ethyl carbamate	9.73E-08	3.77E-07	0.00E+00	1.46E-06	0.00E+00	0.00E+00	0.00E+00
ethylene dibromide	1.70E-02	7.94E-03	5.50E-03	3.08E-02	1.45E-02	1.24E-02	1.82E-02
ethylene dichloride	3.17E-02	9.29E-03	1.85E-02	4.90E-02	2.86E-02	1.48E-02	3.29E-02
ethylene oxide	2.05E-03	2.77E-03	2.75E-04	9.44E-03	7.04E-04	1.92E-03	6.65E-04
formaldehyde	1.13E+00	2.90E-01	7.57E-01	1.67E+00	1.08E+00	4.37E-01	1.13E+00
glycol ethers	3.73E-02	1.51E-02	1.83E-02	6.85E-02	3.22E-02	2.23E-02	3.36E-02
hexachlorobenzene	3.76E-07	1.98E-07	7.67E-08	7.38E-07	3.58E-07	2.36E-07	1.66E-07
hexamethylene-1,6-diisocyanate	1.63E-05	4.61E-05	0.00E+00	1.70E-04	0.00E+00	2.18E-06	0.00E+00
hydrazine	2.92E-08	8.16E-08	3.68E-10	3.23E-07	5.90E-09	1.69E-08	7.35E-09
hydrochloric acid	1.28E-01	1.29E-01	3.09E-02	5.59E-01	1.00E-01	9.14E-02	6.72E-02
hydrofluoric acid	1.45E-02	1.55E-02	1.12E-03	6.56E-02	1.37E-02	1.22E-02	4.83E-03
lead compounds	1.14E-03	4.79E-04	6.05E-04	2.18E-03	1.00E-03	8.49E-04	1.10E-03
maleic anhydride	6.26E-06	9.12E-06	3.33E-07	3.30E-05	1.40E-06	1.16E-05	1.36E-06
manganese compounds	5.99E-04	3.79E-04	1.31E-04	1.65E-03	4.59E-04	2.90E-04	4.49E-04
mercury	1.55E-03	7.76E-05	1.51E-03	1.80E-03	1.52E-03	3.00E-05	1.52E-03
methyl bromide	1.05E-01	3.49E-02	6.47E-02	1.77E-01	9.99E-02	4.00E-02	1.02E-01
methyl chloride	1.20E+00	8.28E-03	1.20E+00	1.23E+00	1.20E+00	1.00E-02	1.20E+00
4,4'-methylene bis(2-chloroaniline)	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
methylene chloride	3.55E-01	1.04E-01	2.06E-01	5.75E-01	3.44E-01	1.49E-01	3.80E-01
4,4'-methylenedianiline	1.43E-08	1.77E-08	2.20E-09	7.24E-08	7.24E-09	1.14E-08	1.19E-08
methylene diphenyl diisocyanate	1.90E-04	6.95E-04	4.22E-07	2.70E-03	6.52E-06	7.53E-06	5.95E-06
naphthalene	2.81E-02	8.47E-03	1.32E-02	4.01E-02	3.01E-02	1.18E-02	3.23E-02
n-hexane	3.76E-01	1.27E-01	1.70E-01	5.55E-01	3.87E-01	2.00E-01	3.72E-01
nickel compounds	4.33E-04	2.99E-04	1.37E-04	1.40E-03	3.37E-04	2.58E-04	3.32E-04
o-toluidine	7.91E-08	4.93E-08	1.48E-08	2.02E-07	7.90E-08	6.29E-08	5.75E-08
p-dichlorobenzene	2.24E-02	1.19E-02	9.05E-03	5.16E-02	2.12E-02	1.50E-02	2.21E-02
perchloroethylene	1.16E-01	4.87E-02	5.19E-02	2.21E-01	1.00E-01	7.40E-02	1.27E-01
phosgene	1.06E-05	4.11E-05	2.10E-09	1.59E-04	9.85E-09	9.24E-09	1.08E-08
polychlorinated biphenyls	4.09E-04	1.94E-05	3.83E-04	4.47E-04	4.02E-04	3.70E-05	3.95E-04
polycyclic organic matter	1.02E-02	4.56E-03	3.53E-03	1.85E-02	9.69E-03	5.51E-03	9.39E-03
propylene dichloride	1.66E-02	4.66E-03	9.75E-03	2.47E-02	1.51E-02	7.40E-03	1.73E-02
propylene oxide	6.75E-04	5.31E-04	1.89E-04	2.11E-03	5.04E-04	4.71E-04	4.01E-04
quinoline	1.17E-07	1.41E-07	1.74E-08	5.83E-07	7.37E-08	8.10E-08	6.70E-08
1,1,2,2-tetrachloroethane	4.56E-02	1.43E-02	2.48E-02	7.05E-02	4.12E-02	2.22E-02	4.78E-02
titanium tetrachloride	1.66E-06	4.59E-06	6.45E-09	1.64E-05	2.02E-08	3.21E-08	2.18E-08
toluene	1.65E+00	5.46E-01	8.07E-01	2.77E+00	1.73E+00	6.90E-01	1.72E+00
2,4-toluene diamine	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00	0.00E+00
2,4-toluene diisocyanate	1.61E-03	1.94E-03	1.31E-04	7.84E-03	1.10E-03	1.53E-03	7.73E-04
1,1,2-trichloroethane	3.64E-06	7.54E-06	3.97E-07	3.04E-05	8.22E-07	2.45E-06	8.28E-07
vinyl chloride	4.03E-02	2.19E-02	1.27E-02	9.45E-02	3.23E-02	2.69E-02	4.10E-02
xylenes	1.23E+00	3.36E-01	6.95E-01	1.94E+00	1.24E+00	5.17E-01	1.25E+00

[1] Regional median concentration

[2] Total U.S. median concentration

Table 6-ASD, poverty, and smoking distribution statistics, for Maryland

MD 1996/2004	**Mean**	**Std. Dev.**	**Min**	**Max**	**P50**	**IQR**
ASD prevalence per 10,000						
Combined data 1	51.9	51.9	0	207	36.9	74.8
Combined data 2	50.7	43.2	0	135	44.5	81.2
Poverty prevalence	10.0%	5.29%	3.7%	24.0%	8.65%	6.75%
Smoking prevalence	22.4%	5.57%	13.7%	34.2%	22.1%	8.2%

MD 1999/2007	**Mean**	**Std. Dev.**	**Min**	**Max**	**P50**	**IQR**
ASD prevalence per 10,000						
Combined data 1	73.8	70.9	0	232	41.5	122
Combined data 2	73.9	43.2	0	157	81.9	66.6
Poverty prevalence	8.82%	4.02%	3.9%	18.5%	7.6%	5.35%
Smoking prevalence	23.3%	5.03%	12.2%	36.1%	22.7%	6.05%

Table 7-Distribution of HAPs, county level, for MD, 1996, in $\mu g/m^3$

HAPS	Mean	Std. Dev.	Min	Max	P50	IQR
acetaldehyde	5.09E-01	3.89E-01	8.90E-02	1.61E+00	4.61E-01	5.59E-01
acrolein	7.88E-02	5.39E-02	2.10E-02	2.36E-01	6.40E-02	7.18E-02
acrylonitrile	5.90E-04	5.43E-04	4.64E-05	1.89E-03	4.19E-04	4.67E-04
arsenic compounds	1.39E-04	3.29E-04	6.13E-06	1.54E-03	3.76E-05	6.43E-05
benzene	1.08E+00	5.35E-01	5.95E-01	2.96E+00	8.95E-01	6.21E-01
beryllium	7.61E-06	7.53E-06	6.99E-07	3.38E-05	5.33E-06	7.34E-06
1,3-butadiene	3.98E-02	4.05E-02	1.01E-02	2.00E-01	2.64E-02	4.00E-02
cadmium compounds	4.93E-05	5.49E-05	2.24E-06	2.12E-04	2.27E-05	7.86E-05
carbon tetrachloride	8.80E-01	3.77E-04	8.80E-01	8.81E-01	8.80E-01	0.00E+00
chloroform	8.49E-02	1.57E-03	8.32E-02	8.93E-02	8.45E-02	2.25E-03
chromium compounds	2.63E-04	2.94E-04	2.52E-05	1.38E-03	1.58E-04	3.42E-04
1,3-dichloropropene	5.41E-02	5.79E-02	4.47E-03	2.62E-01	3.48E-02	6.54E-02
diesel particulate matter	1.88E+00	6.49E-01	8.11E-01	3.45E+00	1.79E+00	9.00E-01
ethylene dichloride	6.11E-02	7.43E-05	6.10E-02	6.12E-02	6.11E-02	1.00E-04
ethylene oxide	1.36E-03	2.37E-03	4.98E-05	1.17E-02	7.38E-04	1.21E-03
formaldehyde	9.23E-01	5.10E-01	4.03E-01	2.49E+00	8.06E-01	6.96E-01
hexachlorobenzene	9.31E-05	5.05E-08	9.30E-05	9.31E-05	9.31E-05	1.00E-07
hydrazine	3.84E-08	8.13E-08	2.34E-11	3.78E-07	4.98E-09	2.79E-08
lead compounds	1.63E-03	1.95E-03	6.06E-05	6.44E-03	8.28E-04	2.37E-03
manganese compounds	1.18E-03	1.33E-03	8.10E-05	4.76E-03	6.29E-04	1.32E-03
mercury compounds	1.80E-03	3.06E-04	1.51E-03	2.77E-03	1.75E-03	4.45E-04
methylene chloride	2.81E-01	1.22E-01	1.61E-01	6.84E-01	2.57E-01	1.74E-01
nickel compounds	6.65E-04	8.75E-04	4.80E-05	4.08E-03	3.05E-04	8.78E-04
PAH-7	2.26E-03	1.80E-03	5.77E-04	8.46E-03	1.91E-03	2.19E-03
perchloroethylene	2.11E-01	8.17E-02	1.44E-01	5.04E-01	1.82E-01	7.80E-02
polycyclic organic matter	3.94E-02	3.72E-02	6.38E-03	1.70E-01	2.94E-02	4.40E-02
propylene dichloride	3.41E-05	3.31E-05	2.92E-06	1.12E-04	2.20E-05	2.92E-05
quinoline	2.03E-07	3.18E-07	5.27E-10	1.49E-06	7.56E-08	2.50E-07
1,1,2,2-tetrachloroethane	2.65E-04	2.74E-04	2.09E-05	9.76E-04	1.53E-04	2.21E-04
trichloroethylene	1.00E-01	2.18E-02	8.18E-02	1.70E-01	9.12E-02	2.57E-02
vinyl chloride	1.27E-03	2.61E-03	8.87E-05	1.32E-02	5.69E-04	7.57E-04

Table 8-Distribution of HAPs, county level, for MD, 1999, in $\mu g/m^3$

HAPs	Mean	Std. Dev.	Min	Max	P50	IQR
acetaldehyde	1.09E+00	4.60E-01	6.29E-01	2.46E+00	9.73E-01	6.83E-01
acetonitrile	1.71E-04	3.79E-04	1.02E-05	1.93E-03	7.49E-05	1.32E-04
acrolein	5.35E-02	4.23E-02	1.17E-02	1.81E-01	4.10E-02	6.36E-02
acrylamide	4.65E-07	1.38E-06	2.64E-11	6.16E-06	2.85E-08	8.06E-08
acrylic acid	1.36E-05	1.96E-05	5.51E-09	6.95E-05	2.72E-06	1.88E-05
acrylonitrile	4.89E-04	3.54E-04	7.31E-05	1.23E-03	3.62E-04	5.91E-04
allyl chloride	4.17E-06	3.73E-06	3.35E-07	1.75E-05	3.28E-06	4.56E-06
aniline	1.91E-06	3.44E-06	2.87E-09	1.65E-05	8.24E-07	1.64E-06
antimony compounds	7.83E-05	1.38E-04	5.49E-09	5.06E-04	1.52E-05	7.13E-05
arsenic compounds	6.27E-05	1.23E-04	3.20E-06	6.29E-04	3.03E-05	3.70E-05
benzene	8.96E-01	4.36E-01	4.07E-01	2.23E+00	8.20E-01	6.13E-01
benzotrichloride	1.47E-08	1.71E-08	4.19E-11	5.73E-08	9.32E-09	1.44E-08
benzyl chloride	1.57E-05	6.90E-05	1.37E-07	3.43E-04	1.39E-06	2.03E-06
beryllium	1.02E-05	1.03E-05	1.59E-06	5.22E-05	8.50E-06	9.06E-06
bis(chloromethyl)ether	2.41E-09	2.81E-09	6.87E-12	9.40E-09	1.53E-09	2.36E-09
1,3-butadiene	5.40E-02	5.59E-02	4.68E-03	2.16E-01	3.45E-02	6.89E-02
cadmium compounds	6.32E-05	8.26E-05	2.25E-06	3.80E-04	4.43E-05	8.50E-05
carbon tetrachloride	2.70E-01	4.59E-04	2.70E-01	2.71E-01	2.70E-01	1.00E-03
chlorine	4.91E-04	9.78E-04	1.87E-08	4.85E-03	1.91E-04	5.96E-04
chloroform	6.30E-02	2.80E-02	3.51E-02	1.35E-01	5.78E-02	3.56E-02
chloroprene	6.14E-06	4.62E-06	6.49E-07	1.60E-05	5.02E-06	7.50E-06
chromium IV	5.31E-05	8.09E-05	2.21E-06	3.66E-04	3.14E-05	4.14E-05
cobalt compounds	1.29E-05	1.79E-05	3.23E-08	8.57E-05	6.39E-06	1.32E-05
cyanide compounds	4.35E-02	3.31E-02	8.58E-03	1.54E-01	3.35E-02	3.89E-02
dichloroethyl ether	4.35E-08	2.01E-07	5.21E-12	9.98E-07	1.31E-09	2.56E-09
1,3-dichloropropene	4.80E-02	4.99E-02	5.60E-03	2.21E-01	3.28E-02	5.44E-02
diesel particulate matter	1.03E+00	3.88E-01	4.42E-01	2.06E+00	9.51E-01	5.76E-01
diethanolamine	7.14E-07	1.16E-06	6.06E-11	3.65E-06	9.80E-08	1.26E-06
dimethyl formamide	1.64E-03	1.98E-03	1.54E-04	8.92E-03	9.56E-04	1.73E-03
2,4-dinitrotoluene	8.32E-06	5.83E-06	7.39E-07	2.12E-05	7.47E-06	1.01E-05
1,4-dioxane	2.01E-05	5.85E-05	8.41E-07	2.96E-04	6.19E-06	1.23E-05
epichlorohydrin	1.25E-06	9.05E-07	1.34E-07	3.10E-06	1.07E-06	1.47E-06
ethyl acrylate	2.65E-06	4.82E-06	7.25E-08	1.94E-05	8.47E-07	1.56E-06
ethyl carbamate	1.86E-06	3.95E-06	0.00E+00	1.78E-05	0.00E+00	2.02E-06
ethylene dibromide	1.39E-02	1.09E-02	4.41E-08	3.63E-02	1.30E-02	1.29E-02
ethylene dichloride	2.68E-02	1.24E-02	5.28E-03	5.12E-02	2.64E-02	1.38E-02
ethylene oxide	4.99E-03	5.88E-03	5.59E-04	2.74E-02	2.85E-03	6.10E-03
formaldehyde	1.05E+00	5.09E-01	4.72E-01	2.41E+00	9.26E-01	7.99E-01
glycol ethers	2.48E-02	2.88E-02	1.51E-03	1.13E-01	1.60E-02	2.89E-02
hexachlorobenzene	8.47E-07	8.30E-07	4.52E-08	3.23E-06	5.06E-07	7.66E-07
hexamethylene-1,6-diisocyanate	3.84E-05	6.47E-05	0.00E+00	3.04E-04	1.30E-05	5.56E-05
hydrazine	1.64E-08	2.66E-08	1.24E-11	1.13E-07	5.18E-09	1.45E-08
hydrochloric acid	1.36E-01	1.03E-01	9.32E-03	3.76E-01	1.03E-01	1.59E-01
hydrofluoric acid	1.21E-02	1.10E-02	3.17E-05	4.03E-02	1.03E-02	1.51E-02
lead compounds	1.79E-03	1.32E-03	3.33E-04	6.88E-03	1.68E-03	1.54E-03
maleic anhydride	4.73E-06	6.45E-06	3.38E-09	2.60E-05	1.14E-06	6.91E-06
manganese compounds	1.51E-03	2.16E-03	1.70E-05	8.30E-03	3.71E-04	2.51E-03
mercury	1.64E-03	2.14E-04	1.50E-03	2.53E-03	1.57E-03	1.65E-04
methyl bromide	1.09E-01	7.14E-02	4.71E-02	3.53E-01	8.63E-02	8.05E-02
methyl chloride	1.20E+00	3.77E-03	1.20E+00	1.21E+00	1.20E+00	0.00E+00
methylene chloride	3.20E-01	2.16E-01	3.58E-02	9.29E-01	2.89E-01	3.09E-01
4,4'-methylenedianiline	1.35E-08	1.58E-08	3.35E-11	5.32E-08	8.46E-09	1.30E-08
methylene diphenyl diisocyanate	4.64E-05	1.69E-04	2.09E-09	8.46E-04	5.38E-06	1.72E-05
naphthalene	1.85E-02	1.36E-02	2.72E-03	5.75E-02	1.62E-02	2.01E-02
n-hexane	3.15E-01	2.44E-01	6.44E-02	1.12E+00	2.52E-01	3.36E-01
nickel compounds	3.73E-04	3.11E-04	3.91E-05	1.33E-03	2.98E-04	4.46E-04
o-toluidine	8.32E-08	7.56E-08	3.35E-09	3.25E-07	6.47E-08	1.01E-07
p-dichlorobenzene	2.61E-02	2.69E-02	3.03E-03	1.19E-01	1.82E-02	3.02E-02
perchloroethylene	1.09E-01	9.12E-02	4.82E-03	3.74E-01	9.13E-02	1.11E-01
phosgene	2.46E-06	1.19E-05	3.84E-11	5.87E-05	8.99E-09	1.38E-08
polychlorinated biphenyls	4.28E-04	3.84E-05	3.85E-04	5.35E-04	4.16E-04	4.50E-05
polycyclic organic matter	2.40E-02	4.01E-02	2.57E-03	1.94E-01	1.22E-02	1.30E-02
propylene dichloride	1.44E-02	6.94E-03	2.38E-03	2.80E-02	1.42E-02	7.70E-03
propylene oxide	7.79E-04	7.37E-04	9.66E-05	3.06E-03	4.96E-04	1.10E-03
quinoline	1.08E-07	1.28E-07	2.70E-10	4.29E-07	6.80E-08	1.05E-07
1,1,2,2-tetrachloroethane	3.88E-02	2.12E-02	2.22E-03	8.04E-02	3.83E-02	2.35E-02
titanium tetrachloride	6.78E-06	1.09E-05	1.07E-10	3.83E-05	3.17E-08	1.22E-05
toluene	1.56E+00	1.23E+00	3.51E-01	5.70E+00	1.22E+00	1.54E+00
2,4-toluene diisocyanate	4.01E-03	3.71E-03	2.22E-04	1.53E-02	2.92E-03	4.33E-03
1,1,2-trichloroethane	7.79E-05	2.51E-04	1.09E-07	1.25E-03	3.81E-06	4.66E-05
vinyl chloride	3.14E-02	2.42E-02	9.78E-05	8.18E-02	2.99E-02	2.94E-02
xylenes	1.21E+00	7.64E-01	4.11E-01	3.76E+00	9.37E-01	9.81E-01

Table 9-HAPs with highest component loadings in principal components significantly associated with ASD prevalence

U.S. 1996	
pc1 (69% of HAPs variance)	
HAP	*Chemical Family*
acetaldehyde	aldehyde
formaldehyde	aldehyde
benzene	aromatic hydrocarbon
beryllium	metal
cadmium compounds*	metal
lead compounds†	metal
nickel compounds*	metal
methylene chloride*	halogenated hydrocarbon
1,3-dichloropropene	halogenated hydrocarbon
diesel particulate matter†	hydrocarbon mixture

U.S. 1999	
pc1 (48% of HAPs variance)	
HAP^	*Chemical Family*
acetaldehyde	aldehyde
benzene	aromatic hydrocarbon
cadmium compounds*	metal
lead compounds†	metal
1,3-dichloropropene	halogenated hydrocarbon

* Statistically significant in Windham et al. (2006)
† Moderately significant in Windham et al. (2006)
^ Consistent with HAPs with high component loadings in pc1 for 1996.

Table 10-Results of regression models for ASD prevalence

Variable	Coef.	Standard error	p-value	Sequential R^2_{adj}
Model for US 2004 ASD prev.			0.0000	0.4791
HAPs pc1	0.126	0.027	0.000	
HAPs pc2	-0.315	0.131	0.021	0.2661
HAPs pc3	-0.419	0.107	0.000	
HAPs pc1^2	0.024	0.007	0.002	
Poverty prevalence	-0.459	0.106	0.000	0.1747
Constant	-0.498	0.184	0.010	-
Model for US 2007 ASD prev.			0.0001	0.2885
HAPs pc1	0.099	0.021	0.000	0.2885
HAPs pc1^2	0.003	0.002	0.204	
Constant	-0.106	0.145	0.469	-
MD 2004 ASD prev. combined data 1			0.0000	0.5197
Gender	1.534	0.243	0.000	0.4862
Poverty prevalence	-0.223	0.122	0.076	-0.0271
Constant	-0.995	0.196	0.000	-
MD 2004 ASD prev. combined data 2			0.0095	0.1577
Poverty prevalence	-0.434	0.158	0.010	0.1577
Constant	-0.080	0.156	0.609	-
MD 2007 ASD prev. combined data 1			0.0000	0.8175
Gender	1.779	0.143	0.000	0.7933
Poverty prevalence	-0.208	0.088	0.023	-0.0201
Urbanicity	-0.448	0.191	0.025	0.0484
Constant	-0.770	0.175	0.000	-
MD 2007 ASD prev. combined data 2				
No satisfactory models				

Chapter 5: Discussion

5.1 U.S. Analyses

We observed a significant, positive association between hazardous air pollutants and U.S. ASD prevalence on a statewide level for the two separate study populations examined. The significant principal components in our two U.S. analyses both had quadratic relationships with ASD prevalence. This may indicate that there is a certain exposure threshold among those who are genetically susceptible to ASD with regard to HAPs.

There is a dearth of research on HAPs and ASD prevalence with which to compare our results. Our findings did not support Palmer et al.'s (2006 & 2009) findings with regard to ambient mercury and ASD prevalence. Cadmium, lead, methylene chloride, and nickel featured prominently in both the Windham et al. (2006) study and our study, although cadmium was the only one with statistical significance in both.

The HAPs that were most effectively captured by our principal components, and that featured significantly in our regression models for both the 1996/2004 and the 1999/2007 analyses, were acetaldehyde, benzene, cadmium compounds, lead compounds, and 1,3-dichloropropene. Brief overviews of some of the health-related data available on these five HAPs are provided in the following subsections. It should be noted that many more HAPs were estimated in the 1999 NATA than were in the 1996 NATA, and thus, there is a possibility that additional HAPs would have been found significant in both of our two study populations had 1996 estimates been available.

5.1.1 Health-related data for prominent, consistent HAPs

Acetaldehyde

The largest sources of emitted acetaldehyde, as used in the NATA estimations, were from the combustion of fuels from mobile sources (EPA, 1996c; EPA, 1999d). EPA has classified it has a Group B2 probable human carcinogen (EPA, 1999c), and chronic exposure effects include symptoms similar to those associated with alcoholism (The Merck Index, 1989). Studies have investigated health effects of acetaldehyde, particularly as an intermediate metabolite of ethanol, and have found that chronic exposure to acetaldehyde is associated with the inhibition of cell growth, and may also affect proper regulation of cell division and apoptosis (Zimmerman, Crawford, Dahl, Simon, & Mapoles, 1995). Other studies indicated that acetaldehyde stimulates the production of auto-antibodies, leading to adverse immune responses (Pietrzak, Shanley, & Kroon, 1995), and autoimmune responses have been postulated as possible mechanisms for the development of ASD (Lawler et al., 2004). Acetaldehyde has also been shown to have teratogenic effects. Neural tube closure abnormalities and developmental delay were observed in mice following prenatal acetaldehyde exposure (O'Shea & Kaufman, 1979; O'Shea & Kaufman, 1981).

However, peer-reviewed studies linking acetaldehyde to ASD are scarce, and propose various indirect mechanisms of effect. One such postulated mechanism involves the cholinergic system of the basal forebrain, which is associated with learning and cognitive development, and with the ability to focus and respond appropriately to the environment (Lam, Aman, & Arnold, 2005). Reports of neuropathological abnormalities of cholinergic neurons in some individuals with autism have led to speculation the

possible role of the reduced release of the neurotransmitter acetylcholine, which is critical to proper functioning of the cholinergic system, in the development of ASD (Lam et al., 2005). Decreased release of acetylcholine, has in turn, been linked with higher acetaldehyde concentrations in the body (Jamal et al., 2007).

Benzene

The largest emitted sources of benzene, as used in the NATA estimates, were from mobile sources (EPA, 1996c; EPA, 1999d). Benzene is an EPA classified Group A carcinogen and causes blood disorders and chromosomal aberrations in humans (EPA, 2000b). Research on developmental effects on humans has been inconclusive, but animal studies have observed low birth weight among the offspring of maternal animals exposed to benzene. The offspring of women occupationally exposed to solvents during pregnancy showed cognitive, motor, and behavioral impairment as compared with unexposed children in the study by Laslo-Baker et al. (2004), although benzene was not specifically listed as one of the common exposure solvents in the study. Xylenes and hexane were listed as common occupational solvent exposures in the study, however, and, although not modeled for ambient concentrations in the 1996 NATA, they were in 1999. Both were observed to be associated with our 2007 ASD prevalence by way of pc1.

Only very indirect associations between ASD and benzene exposure have been reported. Researchers investigating possible impairment of detoxification capabilities in children with ASD have found elevated body burdens of a number of solvents, including benzene and xylene, in diagnosed children (Edelson & Cantor, 1998). A cross-sectional Minnesota study found increased prevalence of ASD in school districts with at least one National Priority List (NPL) Superfund site within a 10-mile radius, as compared with

districts with no such sites within that radius (DeSoto, 2009). The most frequently found toxins at NPL sites include benzene, as well as cadmium and lead, two other contaminants which featured significantly in our analyses (Agency for Toxic Substances and Disease Registry, 2007).

Lead

Lead, as addressed in Chapter 1, has been well-established as a neurotoxicant. However, environmental lead has decreased dramatically over the fast few decades while ASD diagnoses have increased. It is likely that in any observed spatial association of ambient lead with ASD prevalence, lead would be a proxy for other highly correlated and potentially causal contaminants.

Cadmium

Cadmium, another heavy metal, has been found associated with impaired learning ability and aberrant behavior in animals prenatally exposed (Agency for Toxic Substances & Disease Registry, 2008). Findings with regard to human neurodevelopmental effects have been mixed. However, a dose-dependent relationship between urinary cadmium levels and the impairment of certain neurobehavioral functions such as concentration, equilibrium, and psychomotor functions, and increased signs of peripheral neuropathy, were reported among workers in a cadmium production plant as compared with a control group. The findings persisted after adjustment for age, exposure to other neurotoxicants, and existing renal impairment (Viaene et al., 2000). Cadmium exposure has also been associated with impaired fetal growth and low birth weight (Kuhnert, Kuhnert, Debanne, & Williams, 1987), and is a suspected endocrine disruptor.

1,3-Dichloropropene

No studies have been performed to observe human developmental or neurodevelopmental effects of 1,3-dichloropropene exposure. However, exposure has been linked to low birth weight and fewer offspring in rats (EPA, 2000a). Its primary use is as a nematocide, and EPA has classified it as a Group B2 probable carcinogen.

5.2 Maryland analyses

Our findings for the U.S. analyses were not supported by the findings from our Maryland sub-analyses. Poverty prevalence and especially gender were the prominent predictors of variance of ASD prevalence throughout the state. Increased risk associated with the male gender and with higher social class unadjusted for artifacts are findings that are consistent with the existing literature. However, unlike in the U.S. analyses, none of the principal components of HAPs were associated with ASD prevalence.

One reason for this may be that the NATA methods for long-term estimates allow for broad geographic coverage, but do not capture peak spatial and temporal concentrations which may have more effect on smaller geographic areas (EPA, 1996b; EPA, 1999a). Another possibility is that there may be less variance in HAPs distribution across Maryland counties as compared with distributions across states. Also, mobility between counties may often be greater than between most states, and many children may be enrolled in schools in counties that they do not reside in. The possibility that our U.S. analyses findings are spurious must also be considered.

Had significant associations been observed between certain HAPs and ASD prevalence in the sub-analyses, interpretive caution would be warranted due to the small sample sizes of theses analyses, especially with regard to the disaggregated data.

5.3 Study Limitations

The mobility factor, and thus, possible misclassification of exposure, is one of the primary limitations of this study. The location of the school of attendance does not necessarily equate to the location of prenatal residence or birth. According to the U.S. Census Bureau, approximately 16% of the entire U.S. population moves in a given year, but most moves are within-county. However, approximately one-third of 20 to 29 year olds moved (U.S.Census Bureau, 2001). Another study in Texas that found about one-third of mothers moved between conception and delivery (Canfield, Ramadhani, Langlois, & Waller, 2006).

Families with children with ASD may also move post-diagnosis, to counties or cities with better access to therapeutic services or schools with better resources for special needs students. These counties may be in areas with higher ambient concentrations of HAPs, such as many urban areas. However, we did not observe any statistically significant association of ASD prevalence with urbanicity in our Maryland sub-analyses.

Counties with better access to service resources, and with better schools, may also define areas with lower prevalence of poverty. For example, this may explain the relatively high prevalence of ASD in Howard County. The percentage of people of all ages in Maryland living in poverty were not only lowest in Howard County in 1996 and 1999, but also in 2004 and 2007 (U.S.Census Bureau, 2007a). The observed association between ASD prevalence and poverty prevalence might also be explained as an artifact of case ascertainment.

Case ascertainment presents another area of potential misclassification in this study. Case ascertainment, as derived from educational administrative data, was not standardized across states. Under IDEA there are 13 different diagnostic eligibility codes available for states' use in administering services to students. Depending on the state and on the year, children with ASD and co-morbid disorders may be classified under the "multiple disabilities" code, or under another diagnostic code (DAC, 2004a; DAC, 2007a). Even those without co-morbid disorders may be served under different categories, or not served at all, depending on the eligibility criteria used by the particular state (Yeargin-Allsopp et al., 2003). Within-state discrepancies have also been reported on a county level, district level, and even on a school level basis, attributed to available resources (Palmer, Blanchard, Jean, & Mandell, 2005). However, despite the potential for state-discretion misclassification errors, some research suggests that, overall, ASD diagnoses have been made with reliability and specificity in the field (Jick, Kaye, & Black, 2003; Hill et al., 2001; Mahoney et al., 1998).

"Autism" was introduced as a separate eligibility code under the IDEA in 1990. Several studies since have indicated that diagnostic substitution ensued. Shattuck (2006), in a review of state-by-state data trends between 1984 and 2003, reported concomitant decreases in the number of children coded under "mental retardation" and "specific learning disability" as those coded under "autism" increased. However, a study that used nationally aggregated cohort data trends reported no concomitant decrease in classifications of "mental retardation" and "speech/language impairment" (Newschaffer et al., 2005). Shattuck (2006) also acknowledged that any discovery of diagnostic shift

with regard to the autism category does not necessarily preclude the role of environmental risk factors in ASD etiology.

Any diagnostic shifting that has indeed occurred may also be attributed to another relatively new category, "developmental delay", which has been experiencing dramatic growth as well (Shattuck, 2006). In fact, federal law in 1997 allowed states the option to extend eligibility under the "developmental delay" category to include children ages 6-9 years, whereas it was previously limited to children under 6 years of age (Pub. L. No. 105-17, 111 Stat. 37). This extension may have contributed to an underestimation of 8-year-olds with ASD in our study (DAC, 2004a; DAC, 2007a; Yeargin-Allsopp et al., 2003).

Underestimation of ASD prevalence must also be attributed to the fact that our data excludes counts from private and charter schools, as well as children in residential placements and other institutions. Lastly, the child count data is measured at a point-in-time, and does not represent a cumulative count of all students served throughout the school year. It is possible that more children are served throughout the year than are collected from count reports.

Underestimation of exposure is another limitation of this study. Comparison of some NATA estimates with monitored data and with personal exposure measurements have consistently found that the NATA models underestimate the majority of the HAPs' actual ambient concentrations as well as actual personal exposure (Payne-Sturges et al., 2004; Rosenbaum et al., 1999; EPA, 1996a; EPA, 1999b). NATA reports a "level of confidence" for each HAP's ASPEN-modeled estimates. Benzene receives a high level of confidence, while most of the heavy metals, including cadmium, lead, and beryllium, are

rated at low levels. Acetaldehyde and formaldehyde receive medium levels of confidence (EPA, 1996b).

It is important to note that NATA estimated HAPs reflect only inhalation exposures from ambient air, and thus do not represent total possible exposures to these contaminants. Dermal, ingestion, and injection exposures are not accounted for, as well as inhalation of indoor exposures. Indoor sources factor heavily into personal exposures, especially occupational sources and smoking and environmental tobacco smoke (ETS). Much of the general population's exposures to benzene, acetaldehyde, cadmium, lead, and many other contaminants featured significantly in our regression models come from smoking and ETS. However, smoking prevalence was not observed to be significantly associated with ASD prevalence at an ecological level in our analyses.

Due to the ecological design of our analyses, no causal associations between HAPs and ASD prevalence can be made.

Lastly, other study limitations include those specific to the data sources we used, which are addressed in detail by those particular sources, and to which we have provided references to throughout this study.

5.4 Study Strengths

Strengths of this study include the examination of two separate study populations for both the U.S. and the Maryland analyses in order to seek consistency in findings. We also sought to validate any findings from the U.S. analyses on a finer scale with our Maryland sub-analyses.

In addition, we strived to improve exposure assessment estimates by using the NATA's ASPEN modeled estimates as surrogates of exposure, which incorporate

meteorological, decay, deposition, secondary formation, and other data, into the models, along with emissions from not only major and area point sources, but also on-road and non-road mobile sources, and background contributions. To further improve exposure assessment, we selected median, rather than average, ambient concentrations to best represent statewide and county-level estimates with reduced influence from outliers.

Principal component analysis is an excellent tool for exploratory research which provides a scientifically rigorous method of data dimensionality reduction that reflects both the common and unique variability of the data. In our study, using principal component analysis provided a more realistic assessment of HAPs exposure than the mere selection of individual or a small assortment of HAPs would have, because it reflected the highly correlative nature of the air toxics.

Lastly, we accounted for any potential confounding effects of poverty prevalence, smoking prevalence, and, in our sub-analyses, urbanicity, gender, and ethnicity.

Chapter 6: Conclusion

This study provides the first ecological examination of HAPs distribution in relation to ASD prevalence, by state, for the U.S. We observed a significant, positive association, but it did not endure at the county-level for the Maryland sub-analysis.

The likelihood that development of ASD results from a web of interactions between multiple genes and environmental factors specific to each individual child, presents challenges to the investigation of those potential environmental risk factors, especially through ecological analyses.

Large, comprehensive case-control studies such as U.C. Davis's Childhood Autism Risks from Genetics and the Environment (CHARGE) study, or longitudinal studies such as the National Children's Study are better suited to determine potential causative factors. Individual exposure and case ascertainment data, along with biomonitoring data, and other physical, genetic, and modifying factors, can be obtained from these types of studies. The National Children's Study, funded by Congress and a consortium of federal agencies, will follow more than 100,000 children from before birth through age 21. Assuming an ASD prevalence of 1 in 100 children, there may be approximately 1,000 children in the study cohort expected to receive an ASD diagnosis, and a nested case-control study could be efficiently designed.

It is possible that prenatal exposure to air toxics may contribute to an individual's overall risk of ASD. Future research should continue to include this exposure as part of a comprehensive assessment of environmental risks for development of ASD.

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Trousdale, K., Martin, J., Abulafia, L., Barnett, C., & Westinghouse, C. (2010). Children's environmental health: The school environment. *Perspectives. Intellectual and Developmental Disabilities, 48,* 135-144. doi: 10.1352/1934-9556-48.2.135.

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