**Title**

A State-of-the-Science Review of Chemical and Non-Chemical Stressors found in the Built and Natural Environments and How They May Impact American Indian/Alaska Native Children’s Health and Well-Being

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**Abstract**

Background

Children’s exposures to chemical and non-chemical stressors from their everyday environment affects their overall health and well-being. American Indian/Alaska Native (AI/AN) children may have a disproportionate burden of stressors from their built and natural environments when compared to children from other races.

Objectives

We identified chemical and non-chemical stressors from AI/AN children’s built and natural environments and evaluated linkages between stressors and health and well-being outcomes.

Methods

Library databases (e.g., PubMed) were searched to identify studies focused on stressors from the built and natural environments. References were excluded if they: did not discuss AI/AN children or they were not the primary cohort; discussed Tribes outside the U.S.; were reviews or intervention studies; or did not discuss stressors from the built or natural environments.

Results

Out of 2,539 references, 35 remained. Sample populations were mainly from rural or isolated settings. Fifteen studies shared the same cohort. All 16 studies reporting built environment stressors were from households. Primary built environment stressors were indoor use of wood for heating or cooking, lack of indoor plumbing, and presence of mold. Our analysis suggested an increase in respiratory illness from indoor use of wood for heating or cooking, or lack of indoor plumbing. More than half of the studies identified the same non-chemical (natural environment) stressor as proximity to polluted landscapes. Primary chemical stressors were PCBs, *p,pˈ*-DDE, HCB, lead, and mercury.

Conclusion

To the best of our knowledge, this is the first review to explore chemical and non-chemical stressors found in AI/AN children’s built and natural environments. Limited studies were identified, demonstrating a major research gap. Future studies need to consider stressors outside of the household and other elements of the natural environment as well as evaluate stressors from AI/AN children’s total environment (built, natural, and social). Findings can be used as a guide to promote healthy environments for AI/AN children in regards to household use of wood for heating or cooking and lack of indoor plumbing.

**Keywords**

state-of-the-science review, children, American Indian/Alaska Native, built environment, natural environment, stressors

**1. Introduction**

When compared to adults, children are more vulnerable to exposures from environmental contaminants found in their everyday environments. This vulnerability can be due to age-specific factors such as differences in physiology, developmental stages, surface-to-volume ratio, lifestage-specific activities and behaviors (e.g., object/surface-to-hand then hand-to-mouth) (Hubal et al., 2000; Faustman et al., 2000; Weiss, 2000; Goldman, 1995). Because of the way children interact with their environment, they can be exposed to the same chemical through multiple exposure routes (Faustman et al., 2000; Goldman, 1995).

Exposure to stressors during critical stages of development may lead to growth abnormalities, structural impairments, functional deficits, and altered survival (U.S. EPA, 1991; Faustman et al., 2000). Stressors are defined as any physical, chemical, social, or biological entity that can induce change in health and well-being (Tulve et al., 2016). For assessing childhood exposures, early lifestage groupings are narrow when rapid development occurs (i.e., birth to <1 month, 1 to <3 months, 3 to <6 months, 6 to <12 months, 1 to <2 years, 2 to <3 years) and broader in later childhood when the rate of development slows (i.e., 3 to <6 years, 6 to <11 years, 11 to <16 years, 16 to <21 years) (U.S. EPA, 2005).

Stressors between children’s everyday environments (built, natural, and social) may contribute to differences in children’s exposures, thereby impacting their health and well-being. The built environment represents man-made surroundings such as land use, transportation, buildings, and infrastructure. The natural environment represents naturally-occurring surroundings, living and non-living, such as the atmosphere, water bodies, forests, and mountains. The social environment may include factors related to social interactions, the economy, the community, school, safety, parental level of education, number of people in home, and access to resources (Tulve et al., 2016).

Children from some communities, such as those from American Indian/Alaska Native (AI/AN) Tribes, are disproportionately burdened with adverse health and well-being outcomes when compared to other populations in the U.S. (IHS, 2014). According to the U.S. Department of Health and Human Services’ Indian Health Service (IHS) (2014), the leading causes of post-neonatal mortality among AI/ANs from 2007 to 2009 were sudden infant death syndrome (SIDS); congenital malformations, deformations, and chromosomal abnormalities; and unintentional injuries. The mortality rate for SIDS, for example, was twice as high when compared to all races and Whites in the U.S. For AI/AN children between the ages of 1 and 4 years, the leading causes of mortality were unintentional injuries (rate was four times greater than the mortality rate among all races in the U.S.), homicide, and congenital anomalies (IHS, 2014). For children between the ages of 5 and 14 years, the leading causes of mortality were unintentional injuries, suicide, and malignant neoplasms (IHS, 2014). The leading cause of hospitalizations for children between the ages of 1 and 4 years was respiratory diseases; while the leading cause of hospitalizations for children between the ages of 5 and 14 years were respiratory system diseases, digestive system diseases, and injury and poisoning (IHS, 2014).

American Indians/Alaska Natives encounter a multitude of stressors from their built, natural, and social environments related to hazards around their communities (IHS, 2016). Disparities in stressors affecting AI/AN children need to be considered when examining their impacts on AI/AN children’s health and well-being. Previous reviews of the peer reviewed literature have focused only on stressors from AI/AN children’s social environment. These studies identified stressors related to societal, cultural, community, school, and family factors (Burnette et al., 2016); cultural implications when AI children are placed away from their communities (Green, 1983); adolescent socialization (Dinges, 1979); and the benefits of breastfeeding (Stevens, 2016). We could not find a published review of chemical and non-chemical stressors from AI/AN children’s built and natural environments.

Our objectives were to conduct a state-of-the-science review to identify chemical and non-chemical stressors from AI/AN children’s built and natural environments and to assess relationships between these stressors and any health and well-being outcomes.

1. **Methods**

This state-of-the-science review was conducted in accordance with PRISMA (Preferred

Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Moher et al., 2009).

1. *Eligibility criteria*

Studies were eligible if the title or abstract included AI/AN children in the study sample, presented findings of stressors (chemical or non-chemical entities that could impact changes in health and well-being) from the built or natural environments, were published in English, and published by December 31, 2016.

* 1. *Information sources*

Three library databases (ProQuest’s Environmental Science Collection, PubMed, and Web of Science) were searched with key words and search strings focused on AI/AN children (e.g., Alaska Native AND child). Bibliographies of relevant studies were also reviewed to locate additional relevant articles.

* 1. *Search*

The key word/search string strategy was similar across the three databases (one database’s key word/search string is listed in Figure 1). The first component of the key word/search string targeted AI/AN background (i.e., “native American” OR “american indian” OR “alaska native” OR “alaskan native”). The second component targeted children (e.g., “prenatal” OR “pre-natal” OR child\* OR youth OR adolescent OR adolescence OR preconception OR “pre-conception” OR “pre-school” OR preschool OR fet\* OR baby OR pregnancy OR toddler OR teen\*). The only difference across the databases for the key words was the fetal term. In PubMed, the fetal term was lengthened because it would have only used the first few hundred variations with a shortened term (i.e., fet\*).

These key words/search strings were searched in the title and abstract fields (ProQuest and PubMed). In Web of Science, however, there was no available field to search abstracts only so the ‘Topic’ field was selected; the ‘Abstract of Published Item’ field was bibliographic-only data for a published paper. Results from these searches were limited to: a specific end date of December 31 2016, English language articles, and scholarly journals.

* 1. *Study selection*

Titles and abstracts were screened (n=4,021) and duplicate articles removed (n=1,482) (Figure 1). References were then excluded (n=2,503) if they: 1) did not discuss AI/AN children or AI/AN children were not the primary cohort of interest; 2) discussed Tribes outside the U.S.; 3) described reviews or interventions; or 4) did not provide findings about chemical or non-chemical stressors from the built or natural environments. Full-text reviews were conducted for the remaining articles (n=36).

* 1. *Data items*

Data were collected for the study’s authors, year of publication, environment (built

or natural) of the stressor(s) described, nature of the stressor(s) (either chemical or non-chemical), outcome(s) described, number and age of children, period of study, data source(s), location of study, summary measures (e.g., mean, median, range, odds ratios, correlation and regression coefficients with indicators of statistical significance), and study’s findings. Data collection was performed for each individual stressor.

* 1. *Synthesis of results*

Results included univariate and multivariate analyses. Results were reported for the

occurrence of the chemical and non-chemical stressor(s) in the study sample by environment (built or natural), consideration of other factors in the analysis, and the impact of the stressor(s) on the outcome(s) described. A narrative review is provided for each identified stressor. Results were synthesized to compare studies with matching methodology for similar stressors and outcomes.

1. **Results** 
   1. *Study selection*

From the three library databases, 2,539 references were screened after duplicates were removed resulting in the inclusion of 35 relevant studies (Figure 1). Studies were most frequently excluded for not reporting findings on chemical or non-chemical stressors from the built or natural environments. Fourteen studies reported stressors from the built environment, 19 from the natural environment, and two from both environments. Relevant studies were published between 1986 and 2016. By journal, the greatest number of studies for stressors identified from the built environment were published in Pediatric Infectious Disease (n=3), while the greatest number of studies for stressors from the natural environment were published in Environmental Health Perspectives (n=3) (Figure 2).

*3.2 Study characteristics*

From our 35 relevant studies, sample populations were mainly from rural or isolated settings. Among studies with available information about study design, seven were case-control, five were cross-sectional, six were done at the village/community-level (two were retrospective cohort), and one was qualitative (Tables 1 and 2). Population sample sizes ranged from 22 (Petersen et al., 2003) to 10,360 (Gilbreath et al., 2006a). Village/community sample sizes ranged from 49 (Bruden et al., 2015) to 197 (Gilbreath et al., 2006a). American Indians/Alaska Natives were the only sample population in all studies except four (Goldcamp et al., 2006b; Malcoe et al., 2002; Orr et al., 2002; Xue et al., 2014). Goldcamp et al. (2006b) targeted non-fatal injuries among household youth on minority-operated farms, which were also comprised of Asian, Black, and ‘Other’ operators. Malcoe et al. (2002) examined lead exposures around a former mining region also among White children in Oklahoma. Orr et al.’s (2002) study cohort also included Black/African American, Hispanic/Latino, and Asian/Pacific Islander children of women living around hazardous waste sites in California. Xue et al.’s (2014) cohort was composed of Mexican American, Non-Hispanic White, Non-Hispanic Black, Other Hispanic, and “Asian, Pacific Islander, Native American or multiracial” participants from the National Health and Nutrition Examination Survey (NHANES) for an analysis of blood polychlorinated biphenyl (PCB) concentrations.

* 1. *Built environment*

Sixteen studies described chemical and non-chemical stressors from the built environment in early and later lifestages of childhood (Table 1). Eleven studies took place in the state of Alaska. In 12 studies, respiratory illness was the outcome of interest; medical records were the data source for eight studies. Stressors were predominantly around the household, affecting water quality (six studies), air quality (two studies), both (six studies) or were due to farm operations (two studies). There were only three studies that sampled around these environments: Singleton et al. (2016) sampled indoor air for particulate matter, carbon dioxide, and volatile organic compounds; Robin et al. (1996) sampled respirable particles in indoor air; and Surdu et al. (2006) measured mite and cat allergen concentrations in indoor dust.

*3.3.1 Household lack of plumbing/running water*

Nine studies identified the same non-chemical stressor in the home as a lack of plumbing/running water. In seven studies, an increased risk of respiratory illness was associated with a lack of plumbing/running water (Table 3). Five of these studies found an increased risk of lower respiratory tract infections (LRTIs) (Bruden et al., 2015: adjusted relative risk=1.25 (95% CI: 1.05-1.26); Hennessy et al., 2008: greatest adjusted rate ratio among those younger than one year=6.57 (95% CI: 5.58-7.72); three studies found a decreased risk of LRTIs from the presence of plumbing/running water (Bulkow et al., 2012: adjusted OR=0.29 (95% CI: 0.14-0.58); Gessner et al., 2008: adjusted outpatient LRTI beta (β) estimate from regression analyses=-0.53 (P<0.001); Morris et al., 1990: unadjusted OR=0.5 (P=0.061)). The two remaining studies observed an increased incidence of invasive pneumococcal disease (Wenger et al., 2010: 391 cases per 100,000 children per year in a region with a low proportion of households with piped water vs. 147 cases in a high-water service region (P=0.008)) or increased pneumococcal colonization (precursor for invasive disease) of the nasopharynx (Reisman et al., 2014: greatest risk among those aged less than five years, OR=1.42).

Two studies examined exposure to potential hazardous waste and waste disposal methods (Gilbreath et al., 2006a) and adverse birth outcomes (Gilbreath et al., 2006b) among mothers living near open dumpsites in Alaska Native villages who gave birth. Gilbreath et al. (2006a) found mothers from villages with high hazard dumpsite rankings were more likely to live in villages with some households or no households with piped water compared to mothers from villages with low hazard dumpsite rankings. And, a significantly greater risk of low birth weight (OR: 1.35, 95% CI: 1.06-1.72), very low birth weight (OR: 2.13, 95% CI: 1.21-3.75), and preterm birth (OR: 1.27, 95% CI: 1.07-1.51) was observed for infants from mothers who lived in villages with some households with piped water versus infants from mothers residing in villages with all households receiving piped water (Gilbreath et al., 2006b).

*3.3.2 Household use of wood for heating or cooking*

Use of wood for heating or cooking in the home was identified as a non-chemical stressor in six studies. In five studies, an increased risk of respiratory illness was observed due to a woodstove or wood-burning stove (Singleton et al., 2016: greatest adjusted OR for cough between colds=3.18 (P=0.027); Ware et al., 2014: greatest unadjusted OR for pneumonia among those aged less than five years=2.1 (95% CI: 0.6-7.2); Bulkow et al., 2012: adjusted OR for LRTIs=2.21 (95% CI: 1.20-4.10); Robin et al., 1996: unadjusted OR for acute lower respiratory infections=5.0 (95% CI: 0.6-42.8); Morris et al., 1990: adjusted OR for LRTIs=4.85 (95% CI: 1.69-12.91)). The remaining study did not find any association from household use of wood for heating (Bruden et al., 2015: unadjusted relative risk for LRTIs=1.00 (95% CI: 0.95-1.07)).

*3.3.3 Mold*

Presence of mold was identified in four studies, one of which collected information about factors contributing to chronic respiratory disease (Petersen et al., 2003). For the three studies with available effect estimates, two studies found an increased risk of respiratory illness due to mold (Ware et al., 2014: greatest unadjusted OR for flu among those aged less than five years=2.5 (95% CI: 1.0-6.1); Bulkow et al., 2012: unadjusted OR for LRTIs=1.21 (95% CI: 0.74-1.97)). The third study found a lower risk of having asthma (Surdu et al., 2006: unadjusted OR=0.83 (90% CI: 0.30-2.29)). All these associations were not statistically significant.

*3.3.4 Outdoor air quality*

Three studies identified stressors due to concerns from outdoor smoke (Ware et al., 2014), having a burn-barrel near the home (Surdue et al., 2006), and steam baths/housing sand dust (Petersen et al., 2003). Among the two studies that had available effect estimates, both observed an increased risk for respiratory illness, but were not statistically significant (Ware et al., 2014: greatest unadjusted OR for colds among those 5 to 17 years=2.0 (95% CI: 0.8-4.5); Surdu et al., 2006: unadjusted OR for asthma=1.56 (90% CI: 0.52-4.74)).

*3.3.5 Farm operations*

Two studies targeted the occurrence of non-fatal injuries among household youth on racial minority-operated farms (Goldcamp et al., 2006b) and then only among a sub-cohort of AI-operated farms (Goldcamp et al., 2006a). In the Minority Farm Operator Childhood Agricultural Injury Survey, Goldcamp et al. (2006b) found that AI household youth had almost double the rate of injuries (24.0 injuries per 1,000 household youth, 95% CI: ±4.4) compared to injury rates among other racial minority youth living on farms (Asian: 4.6, 95% CI: ±2.2; Black: 6.4, 95% CI: ±2.4; Other: 12.3, 95% CI: ±3.7). AI household youth had a greater rate of work-related injuries (17.8 per 1,000 youth, 95% CI: 12.7-22.9) compared to non-work-related injuries (13.8, 95% CI: 11.8-15.8). Goldcamp et al. (2006a) then focused on AI-operated farms and observed that more than half of AI household youth (74%) lived on livestock farms. Among AI youth that sustained injuries, 83% were due to livestock farm operations.

* 1. *Natural environment*

Twenty-one studies described chemical and non-chemical stressors from the natural environment in early and later lifestages of childhood on primarily developmental outcomes (Table 2). Fourteen of these studies shared cohorts from the same territory in the state of New York. The primary non-chemical stressor was derived from residential proximity to polluted landscapes. Chemical stressors were identified in 19 studies, including PCBs, *p,pˈ*-dichlorodiphenyldichloroethylene (*p,pˈ*-DDE), hexachlorobenzene (HCB), lead, and mercury. Thirteen studies used biomarkers to characterize exposure, with only eight studies (Ernst et al., 1986; Fitzgerald et al., 2004; Gilbreath et al., 2006a; Gilbreath et al., 2006b; Malcoe et al., 2002; Monheit et al., 2008; Orr et al., 2002; Shields et al., 1992) obtaining environmental measurements or employing other methods to characterize exposure. Apart from Gilbreath et al. (2006a, 2006b), Orr et al. (2002), and Shields et al. (1992); these studies also sampled air, food, dust, paint, soil, and water (Ernst et al., 1986; Fitzgerald et al., 2004; Malcoe et al., 2002). Monheit et al. (2008) sampled sediment, vegetation, and water. Gilbreath et al. (2006a, 2006b) and Orr et al. (2002) determined the potential for exposure of mothers from their residence and Shields et al. (1992) from their work locations.

*3.4.1 Residential proximity to polluted landscapes*

Among the 21 studies, 19 shared the same non-chemical stressor derived from residential proximity to polluted landscapes mainly contaminated by hazardous waste. For these 19 studies, investigators targeted youth (11 studies) and mothers (eight studies). Twelve of the 19 studies evaluated the impact of this stressor on developmental outcomes (cognitive function, thyroid function, sexual maturation, lung function, and birth outcomes).

*3.4.1.1* *AI* *youth*

Among the 11 studies with AI youth cohorts, ten studies examined exposures of youth from the same territory in New York adjacent to three hazardous waste sites (one National Priority Superfund site and two New York State Superfund sites) and an aluminum smelter (Ernst et al., 1986) to PCBs, *p,pˈ*-DDE, HCB, mirex, fluoride, lead, and mercury. The remaining study examined childhood lead exposures from a former uranium mining region in Oklahoma (Malcoe et al., 2002).

**Toxicant levels.**A study by Schell et al. (2003) found youth (N=271 in New York, between 10 and 17 years of age) who were breastfed to have on average 1.3 times the levels of total PCB blood concentrations, persistent PCBs, and other toxicants (*p,pˈ*-DDE and mirex) compared to youth who were not breastfed (Table 4). Levels of another toxicant (HCB) and heavy metals (lead and mercury) were similar across both breastfed and non-breastfed youth (Schell et al., 2003). When a sample of these youth were between 17 and 20 years old (N=152), both groups (those who were breastfed and not-breastfed) had lower geometric mean concentrations of their total PCB concentrations (including concentration for PCBs detected in 50% or more of participants) than when they were sampled at a younger age (Gallo et al., 2011). Levels of other toxicants (*p,pˈ*-DDE and HCB) were similar to levels when sampled at an earlier age.

**Cognitive function.** Additional studies were conducted among the NY youth cohort to investigate relationships between PCB measures and cognitive function (Newman et al., 2006; 2009; 2014). Newman et al. (2006) observed among 271 youth, aged between 10 to 17 years, that as PCB concentrations increased, scores decreased for two measures of long-term memory (Delayed Recall Index: β=-3.6, P=0.019 and Long Term Retrieval: β=-6.9, P=0.004) and a measure of comprehension and knowledge (β=-4.6, P=0.043). Newman et al. (2009) further investigated this relationship among this cohort, specifically for PCB congeners grouped by structure (dioxin-like or non-dioxin-like) and by persistence. Newman et al. (2009) also found decreased scores for long-term memory (Delayed Recall Index and Long Term Retrieval) from increased concentrations of PCB measures (all PCB congener groups: dioxin-like, non-dioxin-like, persistence, and low-persistence). These associations were observed between PCBs grouped by structure (dioxin-like PCBs and nonverbal Ravens test scores) and persistence (persistent PCBs and Auditory Processing scores, low-persistent PCBs and scores for comprehension and knowledge). Newman et al. (2014) did not find evidence of adverse effects of persistent PCB levels on ADHD-like behavior.

**Thyroid function.** Among 232 adolescents in New York,Schell et al. (2008) observed a significant reduction in levels of thyroid function measures with higher persistent PCB concentrations (similar findings were found in a preliminary study by Schell et al. (2004) among a smaller cohort of 115 adolescents). Schell et al. (2009) found those with elevated anti-thyroid peroxidase levels (suggesting an elevated risk of autoimmune disease) among 47 adolescents who were breastfed had significantly greater levels of all PCB groupings (except non-persistent PCBs) and levels of another toxicant (*p,pˈ*-DDE).

**Other outcomes.** In a study evaluating multi-chemical exposures among adolescent girls (Denham et al., 2005), only higher lead levels were significantly associated with a delay in attaining menarche (β=-1.29, P=0.01) and a group of potentially estrogenic PCB congeners were associated with reaching menarche earlier (β=2.13, P=0.04). Another study (Ernst et al., 1986) examined lung function among 253 adolescents who lived near an aluminum smelter. Ernst et al. (1986) found significant associations between increased closing volume (may be indicative of lung abnormalities in small airways) only among boys who had lived near the smelter 60% or more of their lives, versus those who had lived farther away 60% or more of their lives (high exposure mean CV/VC%=8.25, SEE=1.02 vs. low exposure mean CV/VC%=5.36, SEE=1.07; P=0.05), and increasing levels of urinary fluoride (boys: CV/VC% slope=4.78, P=0.02; girls: CV/VC% slope=4.40, P=0.01).

*3.4.1.2 Mothers*

For the six studies targeting mothers, four studies examined maternal exposures mainly to PCBs and DDT compounds from the New York cohort. The two remaining studies investigated maternal (father and grandparents as well) exposures to radiation from residence and/or work locations in a former uranium mining region in New Mexico (Shields et al., 1992) and maternal exposures to contaminants around hazardous waste sites in California (Orr et al., 2002).

**Pregnant women**. In a study from 1992 to 1995 among 111 pregnant AI women in New York, Fitzgerald et al. (2004) observed the geometric mean of their total PCB blood concentrations to be 1.2 ppb (maximum: 7.8 ppb). The specific PCB congeners detected at the greatest concentrations were 153 (geometric mean: 0.092 ppb), 138 (0.0345 ppb), and 180 (0.0142 ppb).

**Mothers who breastfed their infants.**For AI mothers who gave birth between 1986 and 1989, the (adjusted) geometric mean of their total PCB breast milk concentration was 0.602 ppm (fat basis) (Fitzgerald et al., 1998). For AI mothers giving birth after 1989, their (adjusted) geometric mean total PCB breast milk concentration was lower (0.352 ppm in 1990 and 0.254 ppm for 1991-1992). Compared to White mothers (controls) who gave birth around the same time, their (adjusted) geometric mean total PCB breast milk concentration was lower than the geometric mean total PCB breast milk concentration among AI mothers only for the earliest period of study (between 1986 and 1989): 0.375 ppm (P<0.01). After 1989, though, the control mothers’ geometric mean total PCB breast milk concentration was slightly greater than that of the AI mothers: 0.404 ppm in 1990 and 0.318 ppm between 1991 and 1992.

The specific PCB congeners that were detected at the greatest concentrations in breast milk were identical among AI and control mothers. According to Fitzgerald et al. (1998), they were PCB congeners 138 (adjusted geometric mean: 53.5 ppb, fat basis among AI mothers vs. 29.9 ppb among control mothers), 153 (49.8 ppb vs. 32.8 ppb), and 99 (32.9 ppb vs. 14.8 ppb). Another study (Hong et al., 1994) examined the same cohort of breastfeeding mothers who gave birth between 1988 and 1990 and found specific PCB congeners to be the main contributors to the total PCB calculated toxic equivalent values. These specific congeners were 118 (25.8 pg/g lipid), 126 (25 pg/g), and 105 (10.8 pg/g).

For other toxicants that were examined among mothers who breastfed, geometric mean breast milk concentrations among AI mothers were all greater than those for White control mothers only for the earliest period of study (1986-1989): *p,pˈ*-DDE: 420 ppb (fat basis) vs. 198 ppb; HCB: 2.6 vs. 1.2 ppb; and mirex: 1.8 vs. 1.7 ppb. After 1989, the geometric mean breast milk concentration (ppb) for HCB (1990: 8.7 vs. 11.0 and 1991-1992: 12.5 vs. 14.4) and *p,pˈ*-DDE (1991-1992: 183 vs. 190) was lower than those for control mothers.

**Developmental outcomes.**Among other AI/AN study cohorts, an increased risk of adverse birth outcomes was observed when a mother lived near uranium mine dumps (tailings) in New Mexico (Shields et al., 1992), near Superfund hazardous waste site(s) in California (Orr et al., 2002), and near open dumpsites in Alaska Native villages (Gilbreath et al., 2006a, 2006b). Shields et al. (1992) found a significant increase for a group of birth outcomes (n=113) (OR: 2.71, P=0.03), including outcomes such as hip dysplasias/dislocations and mental retardation. An increased significant association for birth outcomes was also found when the mother worked at an electronics plant (OR: 2.71, P=0.03), confounding the previous association because these workers were also exposed to a variety of chemicals and solvents, including trichloroethylene and gamma emissions (Shields et al., 1992). Orr et al. (2002) found the strongest association between birth defects and potential for exposure of mothers to contaminants at hazardous waste sites among AI/ANs (OR: 1.19, 95% CI: 0.62-2.27) (vs. mothers who were not exposed) compared to associations observed among Hispanics/Latinos (OR: 1.15, 0.95-1.38), Black/African Americans (OR: 0.95, 0.70-1.28), and Asian/Pacific Islanders (OR: 1.13, 0.84-1.53). Gilbreath et al. (2006a) reported the only significant predictor for adverse birth outcomes, which included fetal/neonatal deaths and congenital anomalies, was infants born with anomalies classified as other defects from mothers who resided in Alaska Native villages containing high hazard rankings for their open dumpsite contents (compared to those with moderate rankings) (rate ratio: 4.27, 95% CI: 1.76-10.36). For other adverse birth outcomes, Gilbreath et al. (2006b) found a significantly higher proportion of infants from mothers born with low birthweight or infants born with intrauterine growth retardation who lived in villages with high hazard dumpsite rankings (OR: 2.06, 95% CI: 1.28-3.32; OR: 3.98, 95% CI: 1.93-8.21, respectively) or intermediate hazards (OR: 1.73, 95% CI: 1.06-2.84; OR: 4.38, 95% CI: 2.20-8.77, respectively) compared to low hazard dumpsites.

*3.4.2 Dietary consumption*

In two studies, a non-chemical stressor was identified due to dietary consumption of aquatic vegetation (emergent tules) in California, which were applied an herbicide (Monheit et al., 2008), and of foods containing PCBs (Xue et al., 2014) (chemical stressors). Monheit et al. (2008) observed very low levels of fluridone (an herbicide) in sediment, vegetation, and water, and found the herbicide application methods posed little to no hazard of adverse effects to AI/AN children from fluridone exposure through consumption of the vegetation. Xue et al. (2014) found NHANES “Asian, Pacific Islander, Native American or multiracial” participants aged between 12 and 30 years had the highest total blood PCB concentrations (~0.6 nanograms per gram (ng/g)) when compared to total blood PCB concentrations among non-Hispanic White (>0.4 ng/g), other Hispanic (>0.4 ng/g), non-Hispanic Black (~0.4 ng/g), and Mexican American (<0.4 ng/g) participants for the study years 2001 and 2004. A linkage of these PCB blood concentrations and dietary consumption information collected for the same NHANES participants found a positive correlation between fish consumption and total PCB blood concentrations (Pearson coefficient: 0.07, P<0.01).

1. **Discussion**

To the best of our knowledge, this is the first review to focus on chemical and non-chemical stressors from AI/AN children’s built and natural environments that may impact their health and well-being. We demonstrated an information gap due to the limited number of studies that were identified. Despite a paucity of studies, this review is suggestive of a potential increase in respiratory illness from built environment stressors in the household due to use of wood for heating or cooking or lack of running water. On the other hand, for natural environment stressors, the low number of studies with matching stressors and outcomes made interpretation of the findings challenging. Among the 21 studies that identified natural environment stressors, 14 shared one cohort from the same territory in New York with all studies identifying chemical stressors from predominantly PCBs, *p,pˈ*-DDE, HCB, lead, and mercury.

From our 35 relevant studies, sample populations were mainly in rural or isolated settings. Compared to other non-urban children’s populations in the U.S., distinct chemical or non-chemical stressors were identified from these children’s built and natural environments (Loewenherz et al., 1997; Stallones, 1989; Rivara, 1985; Salmi et al., 1989; Merchant et al., 2005). For instance, Loewenherz et al. (1997) found children living in households with pesticide applicators and near pesticide-treated orchards in the state of Washington had greater organophosphorus pesticide exposures compared to children without a household pesticide applicator and a greater distance from agricultural pesticide spraying. For non-chemical stressors, the use of agricultural equipment, primarily tractors (Stallones, 1989) followed by farm wagons, combines, and forklifts posed a risk for fatal and non-fatal injuries among children living in agricultural settings (Rivara, 1985). Included in this review were two studies targeting racial minority youth living on farms (Goldcamp et al., 2006a; 2006b) where a large proportion of their non-fatal injuries were attributed to livestock farm operations. Among children up to nine years old in Wisconsin and Illinois with farm-related injury deaths between 1979 and 1985, 55% were due to moving machinery (tractors, wagons, and trucks) and 15% from drownings (Salmi et al., 1989). Other chemical and non-chemical stressors included living on farms that raise swine (asthma prevalence of 44% among rural Iowa children, P=0.01) and raising swine and adding antibiotics to feed (55.8%, P=0.013) (Merchant et al., 2005).

When compared to AI/AN children’s built environment stressors, similar stressors were identified for other children living in non-urban settings in regards to inadequate plumbing for running water and wastewater disposal services. Among 188 rural low-income households with 320 children under the age of seven years that received water from a well in two western U.S. counties, 27% of households detected at least one contaminant, including total coliforms (18%), arsenic (6%), synthetic organic chemicals (6%), nitrates (2%), fluoride (2%), and E. coli (<1%) (Postma et al., 2011). Also, in a study by Borchardt et al. (2003) among children less than 19 years old in Wisconsin, diarrhea was associated with drinking from a household well contaminated with fecal enterococci (adjusted OR=6.18, 95% CI: 1.22-31.46).

Other studies have identified stressors related to access to resources and impact of nature on life stress among children living in rural settings. According to the 2001 National Household Travel Survey, rural households traveled farther than urban residents to access health care; rural residence was associated with a trip of 30 road miles or more (OR=2.67, 95% CI: 1.39-5.15) (Probst et al., 2007). Another study found rural residence to lower levels of life stress among children in grades three to five who lived in higher levels of nearby nature (vegetation near residence) compared to children with little nearby nature (Wells et al., 2003).

* 1. *Limitations*

The main limitation of this review was the few identified relevant studies (<40). This limitation ruled out a quantitative review (i.e., meta-analysis) due to the variety of study designs, stressors, and outcomes. Few studies had matching methodology for the same stressor and the same outcome so we opted, for instance, to qualitatively compare studies for similar stressors and outcomes. We also compared effect estimates from community/village-level analyses and effect estimates from individual-level analyses for similar stressors and outcomes.

Other limitations were due to sample diversity and publication bias. A lack of diversity was noted among our studies’ sample cohorts; fourteen studies shared a cohort living around the same territory in the state of New York. These studies mainly identified the same stressor (living around hazardous waste/polluted sites and exposure to PCBs). Another limitation was that we relied on published literature, perhaps limiting us to studies that generated findings with distinctive or significant associations since non-significant associations are not as frequently published. We did not have access to unpublished literature investigating other possible stressors and outcomes.  
*4.2 Future research*

This state-of-the-science review identified an information gap concerning research outside of AI/AN children’s social environments. Almost all 35 studies from this review targeted stressors where AI/AN children lived, in mostly non-urban settings. According to Tulve et al.’s (2016) conceptual framework, a child’s total environment needs to be considered in order to examine the interrelationships between chemical and non-chemical stressors, inherent characteristics, and children’s activities and behaviors in influencing their health and well-being. The total environment includes chemical and non-chemical stressors from environments where children also learn and play (Tulve et al., 2016). Future studies need to consider chemical and non-chemical stressors for built environments outside the household (e.g., school, daycare) and in urban settings as well as other elements of the natural environment (e.g., access to open green spaces, parks). Linkages between chemical and non-chemical stressors from AI/AN children’s built, natural, and social environments can then be performed in order to evaluate the total environment and their impacts on AI/AN children’s health and well-being.

1. **Conclusion**

This state-of-the-science review provides information about the nature of chemical and non-

chemical stressors from the built and natural environments that may influence AI/AN children’s health and well-being. The findings from this review can be used as a guide to promote healthy environments for AI/AN children in regards to household use of wood for heating or cooking and access to indoor running water. This work identified a major research gap which may help direct future research initiatives to develop studies to consider stressors outside the household and other elements of the natural environment.

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**Informed consent:** Not applicable.

**References**

Borchardt, M.A., Chyou, P., DeVries, E.O., et al. 2003. Septic system density and infectious diarrhea in a defined population of children. Environ Health Perspect. 111 (5):742-748. doi:10.1289/ehp.5914.

Bruden, D.J.T, Singleton, R., Hawk, C.S. et al. 2015. Eighteen years of respiratory syncytial virus surveillance changes in seasonality and hospitalization rates in southwestern Alaska Native Children. Ped Infect Dis J. 34 (9):945-950. doi:10.1097/INF.0000000000000772.

Bulkow, L.R., Singleton, R.J., DeByle, C., et al. 2012. Risk factors for hospitalization with lower respiratory tract infections in children in rural Alaska. Pediatrics. 129 (5):E1220-E1227. doi:10.1542/peds.2011-1943.

Burnette, C.E.P., Figley, C.R.P. 2016. Risk and protective factors related to the wellness of American Indian and Alaska Native youth: a systematic review. Intl Public Health J. 8 (2):137-154.

Cohen Hubal, E.A., Sheldon, L.S., Burke, J.M., et al. 2000. Children’s exposure assessment: a review of factors influencing children’s exposure, and the data available to characterize and assess that exposure. Environ Health Perspect. 108 (6):475-486.

Denham, M., Schell, L.M., Deane, G. et al. 2005. Relationship of lead, mercury, mirex, dichlorodiphenyldichloroethylene, hexachlorobenzene, and polychlorinated biphenyls to timing of menarche among Akwesasne Mohawk girls. Pediatrics. 115 (2):e127-e134.

Dinges, N.G. 1979. American Indian adolescent socialization: a review of the literature. J Adolesc. 2 (4):259-296.

Ernst, P., Thomas, D., Becklake, M.R., et al. 1986. Respiratory survey of North American Indian children living in proximity to an aluminum smelter. Am Rev Respir Dis. 133 (2):307-312.

Faustman, E.M., Silbernagel, S.M., Fenske, R.A., et al. 2000. Mechanisms underlying children’s susceptibility to environmental toxicants. Environ Health Perspect. 108 (Supplement 1):13-21.

Fitzgerald, E.F., Hwang, S., Bush, B., et al. 1998. Fish consumption and breast milk PCB concentrations among Mohawk women at Akwesasne. Am J Epidemiol. 148 (2):164-172.

Fitzgerald, E.F., Hwang, S., Deres, D.A., et al. 2001. The association between local fish consumption and DDE, mirex, and HCB concentrations in the breast milk of Mohawk women at Akwesasne. J Expo Sci Environ Epidemiol. 11 (5):381-388. doi:10.1038/sj.jea.7500180.

Fitzgerald, E.F., Hwang, S., Langguth, K., et al. 2004. Fish consumption and other environmental exposures and their associations with serum PCB concentrations among Mohawk women at Akwesasne. Environ Res. 94 (2):160-170. https://doi.org/10.1016/S0013-9351(03)00133-6.

Gallo, M.V., Schell, L.M., DeCaprio, A.P., et al. 2011. Levels of persistent organic pollutant and their predictors among young adults. Chemosphere. 83 (10):1374-1382. https://doi.org/10.1016/j.chemosphere.2011.02.071.

Gessner, B.D. 2008. Lack of piped water and sewage services is associated with pediatric lower respiratory tract infection in Alaska. J Pediatr. 152 (5):666-670. https://doi.org/10.1016/j.jpeds.2007.10.049.

Gilbreath, S. and Kass, P. 2006a. Fetal and neonatal deaths and congenital anomalies associated with open dumpsites in Alaska Native villages. Int J Circumpolar Health. 65 (2):133-147. doi: 10.3402/ijch.v65i2.18088.

Gilbreath, S. and Kass, P.H. 2006b. Adverse birth outcomes associated with open dumpsites in Alaska Native villages. Am J Epidemiol. 164 (6):518-528. https://doi.org/10.1093/aje/kwj241.

Goldcamp, E.M., Hendricks, K.J., Layne, L.A., et al. 2006a. Nonfatal injuries to household youth on Native American operated farms in the U.S., 2000. J Agromedicine. 11 (3-4):61-69. https://doi.org/10.1300/J096v11n03\_07.

Goldcamp, E.M., Hendricks, K.J., Layne, L.A., et al. 2006b. Nonfatal injuries to household youth on racial minority-operated farms in the U.S., 2000. J Agric Saf Health. 12 (4):315-324. doi:10.13031/2013.22011.

Goldman, L.R. 1995. Children-unique and vulnerable. Environmental risks facing children and recommendations for response. Environ Health Perspect. 103 (Supplement 6):13-18.

Green, H.J. 1983. Risks and attitudes associated with extra-cultural placement of American Indian children: a critical review. J Am Acad Child Psychiatry. 22 (1):63-67.

Hennessy, T.W., Ritter, T., Holman, R.C., et al. 2008. The relationship between in-home water service and the risk of respiratory tract, skin, and gastrointestinal tract infections among rural Alaska natives. Am J Pub Heal. 98 (11):2072-2078. doi:10.2105/AJPH.2007.115618.

Hong, C.S., Xiao, J., Casey, A.C., et al. 1994. Mono-ortho- and non-ortho-substituted polychlorinated biphenyls in human milk from Mohawk and control women: effects of maternal factors and previous lactation. Arch Environ Contam Toxicol. 27 (3):431-437.

IHS (Indian Health Service). United States Department of Health and Human Services. 2016. Environmental health services. Accessed on August 7, 2017. Available at https://www.ihs.gov/newsroom/factsheets/environmentalhealthservices/.

IHS (Indian Health Service). United States Department of Health and Human Services. 2014. Trends in Indian Health. 2014 edition. Accessed on June 28, 2017. Available at https://www.ihs.gov/dps/index.cfm/publications/trends2014/.

Loewenherz, C., Fenske, R.A., Simcox, N.J., et al. 1997. Biological monitoring of organophosphorus pesticide exposure among children of agricultural workers in central Washington state. Environ Health Perspect. 105 (12):1344-1353.

Malcoe, L.H., Lynch, R.A., Kegler, M.C., et al. 2002. Lead sources, behaviors, and socioeconomic factors in relation to blood lead of Native American and White children: a community-based assessment of a former mining area. Environ Health Perspect. 110 (Supplement 2):221-231.

Merchant, J.A., Naleway, A.L., Svendsen, E.R., et al. 2005. Asthma and farm exposures in a cohort of rural Iowa children. Environ Health Perpsect. 113 (3): 350-356. doi:10.1289/ehp.7240.

Moher D., Liberati A., Tetzlaff J., et al. 2009. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statement. PLoS Med. 6 (7):e1000097. doi:10.1371/

journal.pmed.1000097.

Monheit, S.G., Leavitt, R.C., Akers, P., et al. 2008. Health hazard assessment for Native Americans exposed to the herbicide fluridone via the ingestion of tules at Clear Lake, California, USA. Hum Ecol Risk Assess. 14 (5):1056-1069. doi:10.1080/10807030802387788.

Morris, K., Morganlander, M., Coulehan, J.L., et al. 1990. Wood-burning stoves and lower respiratory tract infection in American Indian children. Am J Dis Child. 144 (1):105-108.

Newman, J., Aucompaugh, A.G., Schell, L.M. et al. 2006. PCBs and cognitive functioning of Mohawk adolescents. Neurotoxicol Teratol. 28 (4):439-445. doi:10.1016/j.ntt.2006.03.001.

Newman, J., Behforooz, B., Khuzwayo, A.G., et al. 2014. PCBs and ADHD in Mohawk adolescents. Neurotoxicol Teratol. 42:25-34. http://dx.doi.org/10.1016/j.ntt.2014.01.005.

Newman, J., Gallo, M.V., Schell, L.M., et al. 2009. Analysis of PCB congeners related to cognitive functioning in adolescents. Neurotoxicology. 30(4):686-696. doi:10.1016/j.neuro.2009.05.006.

Orr, M., Bove, F., Kaye, W., et al. 2002. Elevated birth defects in racial or ethnic minority children of women living near hazardous waste sites. Int J Hyg Environ Health. 205 (1-2):19-27.

Petersen, K.M., Singleton, R.J., Leonard, L. 2003. A qualitative study of the importance and etiology of chronic respiratory disease in Alaska native children. Alaska Med. 45 (1):14-20.

Postma, J., Butterfield, P.W., Odom-Maryon, T., et al. 2011. Rural children’s exposure to well water contaminants: implications in light of the American Academy of Pediatrics’ recent policy statement. J Am Acad Nurse Pract. 23:258-265. doi:10.1111/j.1745-7599.2011.00609.x.

Reisman, J., Rudolph, K., Bruden, D., et al. 2014. Risk factors for pneumococcal colonization of the nasopharynx in Alaska Native adults and children. J Pediatric Infect Dis Soc. 3 (2):104-111. doi:10.1093/jpids/pit069.

Rivara, F.P. Fatal and nonfatal farm injuries to children and adolescents in the United States. 1985. Pediatrics. 76 (4):567-573.

Robin, L.F., Lees, P.S.J., Winget, M., et al. 1996. Wood-burning stoves and lower respiratory illnesses in Navajo children. Pediatr Infect Dis. 15 (10):859-865.

Schell, L.M., Gallo, M.V. 2010. Relationships of putative endocrine disruptors to human sexual maturation and thyroid activity in youth. Physiol Behav. 99 (2):246-253. doi:10.1016/j.physbeh.2009.09.015.

Schell, L.M., Gallo, M.V., DeCaprio, A.P. et al. 2004. Thyroid function in relation to burden of PCBs, p,pˈ-DDE, HCB, mirex and lead among Akwesasne Mohawk youth: a preliminary study. Environ Toxicol Pharmacol. 18 (2):91-99. doi:10.1016/j.etap.2004.01.010.

Schell, L.M., Gallo, M.V. Denham, M. et al. 2008. Relationship of thyroid hormone levels to levels of polychlorinated biphenyls, lead, p,pˈ-DDE, and other toxicants in Akwesasne Mohawk youth. Environ Health Perspect. 116 (6):806-813. doi:10.1289/ehp.10490.

Schell, L.M. Gallo, M.V., Ravenscroft, J., et al. 2009. Persistent organic pollutants and anti-thyroid peroxidase levels in Akwesasne Mohawk young adults. Environ Res. 109 (1):86-92. doi:10.1016/j.envres.2008.08.015.

Schell, L.M., Hubicki, L.A., DeCaprio, A.P., et al. 2003. Organochlorines, lead, and mercury in Akwesasne Mohawk youth. Environ Health Perspect. 111 (7):954-961. doi:10.1289/ehp.5990.

Shields, L.M., Wiese, W.H., Skipper, B.J., et al. 1992. Navajo birth outcomes in the Shiprock uranium mining area. Health Phys. 63 (5):542-551.

Singleton, R., Salkoski, A.J., Bulkow, L., et al. 2016. Housing characteristics and indoor air quality in households of Alaska Native children with chronic lung conditions. Indoor Air. Xx:1-9. doi: 10.1111/ina.12315.

Stallones, L. 1989. Fatal unintentional injuries among Kentucky farm children: 1979 to 1985. J Rural Health. 5 (3):246-256.

Stevens, D.C., Hanson, J.D., Prasek, J.L., et al. 2008. Breastfeeding: a review of the benefits for American Indian women. S D Med. 61 (12):448-451.

Surdu, S., Montoya, L.D., Tarbell, A., et al. 2006. Childhood asthma and indoor allergens in Native Americans in New York. Environ Health. 5:22. doi:10.1186/1476-069X-5-22.

Tulve, N.S., Ruiz, J.D.C., Lichtveld, K., et al. 2016. Development of a conceptual framework depicting a child’s total (built, natural, social) environment in order to optimize health and well-being. J Environ Health. Sci. 2 (2):1-8. doi:10.15436/2378-6841.16.1121.

U.S. EPA (United States Environmental Protection Agency). 2005. Guidance on selecting age groups for monitoring and assessing childhood exposures to environmental contaminants. Risk Assessment Forum. EPA/630/P-03/003F.

U.S. EPA (United States Environmental Protection Agency). 1991. Guidelines for developmental toxicity risk assessment. Risk Assessment Forum. EPA/600/FR-91/001.

Ware, D.N., Lewis, J., Hopkins, S. et al. 2014. Household reporting of childhood respiratory health and air pollution in rural Alaska Native communities. Int J Circumpolar Health 73:10. doi: 10.3402/ijch.v73.24324.

Weiss, B. 2000. Vulnerability of children and the developing brain to neurotoxic hazards. Environ Health Perspect. 108 (Supplement 3):375-381.

Wells, N.M., Evans, G.W. 2003. Nearby nature: a buffer of life stress among rural children. Environ Behav. 35:311-330. doi:10.1177/0013916503035003001.

Wenger, J.D., Zulz, T., Bruden, D., et al. 2010. Invasive pneumococcal disease in Alaskan children impact of the seven-valent pneumococcal conjugate vaccine and the role of water supply. Pediatr Infect Dis J. 29 (3):251-256. doi:10.1097/INF.0b013e3181bdbed5.

Xue, J., Liu, S.V., Zartarian, V.G., et al. 2014. Analysis of NHANES measured blood PCBs in the general US population and application of SHEDS model to identify key exposure factors. J Expo Sci Environ Epidemiol. 24 (6):615-621. doi:10.1038/jes.2013.91.

Figure 1. State-of-the-science review study selection (reporting of items adapted from Moher et al., 2009).

Example of a search string:

(“native american” OR “american indian” OR “alaska native” OR “alaskan native”)

AND

(prenatal OR “pre-natal” OR child\* OR youth OR adolescent OR adolescence OR preconception OR “pre-conception” OR “pre-school” OR preschool OR fet\* OR fetus OR baby OR pregnancy OR toddler OR teen\*)

**Identification**

Records identified through database searching

(n = 4,008)

Records identified through other sources

(n = 13)

**Screening**

Total records collected & screened

(n = 4,021)

Records after duplicates removed (n = 2,539)

Records excluded

(n = 2,503)\*

Records screened

(n = 2,539)

**Eligibility**

Record excluded (review)

(n=1)

Full-text articles assessed for eligibility

(n = 36)

Studies included in review

(n = 35)

**Included**

\*~1,200 discussed stressors in social environments; ~1,300 discussed only outcomes, did not discuss AI/AN children or not primary cohort, were interventions or reviews, or did not discuss stressors from built or natural environments.

Figure 2. Number of relevant studies published by journal and environment.





Table 1. Characteristics from 16 studies by stressors from the built environment.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |
| **Study** | **Health outcome(s)** | **Lifestage group1** | **Location (U.S. state)/period of observation** | **Sample size/design** | **Data source(s)** |
|  |  |  |  |  |  |
| **INDOOR WATER QUALITY** | |  |  |  |  |
| *Lack of piped/running water* |  |  |  |  |  |
| Bruden et al., 2015 | LRTI RSV | <12 mos | AK 1995-2012 | N=49 villages village-level analysis | ACS, Census, med. records |
| Bulkow et al., 2012 | hMPV hPIV LRTI RSV | <12 mos 1-<2 yrs 2-<3 yrs | AK 2006-2007 | n=128 cases n=186 controls case-control | Med. records, questionnaires |
| Gessner et al., 2008 | LRTI | <12 mos 1-<2 yrs | AK 1998-2003 | N=108 villages community-level analysis | Census, med. assistance/water service records, provider billing |
| Hennesy et al., 2008 | PNA and flu RSV | <12 mos 1-<2 yrs 2-<3 yrs 3-<6 yrs 11-<16 yrs 16-21 yrs | AK 2000-2004 | N=128 villages, 12,480 homes in 6 regions village-level analysis | Med. records, outbreak investigation, sanitation inventory, surveillance |
| Morris et al., 1990 | LRTI (PNA, bronchiolitis) | <12 mos 1-<2 yrs | AZ 1988 | n=58 cases n=58 controls case-control | Interviews, med. records |
| Reisman et al., 2014 | Pneumococcal colonization of nasopharynx | <12 mos 1-<2 yrs 2-<3 yrs 3-<6 yrs 11-<16 yrs 16-21 yrs | AK 2008-2011 | N=6,080 cross-sectional | Interviews, med. records, nasopharyngeal swabs for *Streptococcus pneumoniae* |
| Wenger et al., 2010 | IPD | <12 mos 1-<2 yrs 2-<3 yrs 3-<6 yrs | AK 2001-2007 | N=50 villages village/city-level analysis | CDC's Arctic Investigations Program, sanitation inventory |
| Gilbreath et al., 2006a | Adverse birth outcomes | <12 mos | AK 1997-2001 | N=10,073 from 197 villages  retrospective cohort | Birth certificates, open dumpsite hazard rankings |
| Gilbreath et al., 2006b | - | <12 mos | AK 1997-2001 | N=10,360 from 197 villages  retrospective cohort | Birth certificates, open dumpsite hazard rankings |
| **INDOOR AIR QUALITY** | |  |  |  |  |
| *Use of wood for heating or cooking* | |  |  |  |  |
| Bruden et al., 2015 | LRTI RSV | <12 mos | AK 1994-2012 | N=49 villages village-level analysis | ACS, Census, med. records |
| Bulkow et al., 2012 | LRTI | <12 mos 1-<2 yrs 2-<3 yrs | AK 2006-2007 | n=128 cases n=186 controls case-control | Med. records, questionnaires |
| Morris et al., 1990 | LRTI (PNA, bronchiolitis) | <12 mos 1-<2 yrs | AZ 1988 | n=58 cases n=58 controls case-control | Interviews, med. records |
| Ware et al., 2014 | Asthma LRTI | <12 mos 1-<2 yrs 2-<3 yrs 3-<6 yrs 6-<11 yrs 11-<16 yrs 16-21 yrs | AK 2011-2012 | N=475 in 241 households cross-sectional | Questionnaires |
| Robin et al., 1996 | ALRI | <12 mos 1-<2 yrs | AZ 1992-1993 | n=45 cases n=45 controls case-control | Interviews, med. records |
| Singleton et al., 2016 | Severe/chronic lung disease | 1-<2 yrs 2-<3 yrs 3-<6 yrs 6-<11 yrs 11-<16 yrs | AK 2012-2015 | N=63 households analyses between indoor air pollutants and respiratory symptoms/diagnoses | Air monitoring, interviews |
| *Dirt floor* |  |  |  |  |  |
| Morris et al., 1990 | LRTI (PNA, bronchiolitis) | <12 mos 1-<2 yrs | AZ 1988 | n=58 cases n=58 controls case-control | Interviews, med. records |
| *Garage attached to home* | |  |  |  |  |
| Surdu et al., 2006 | Asthma | 2-<3 yrs 3-<6 yrs 6-<11 yrs 11-<16 yrs | NY - | n=25 cases n=25 controls case-control | Air/dust samples, interviews, med. records |
| *House built before 1985* | |  |  |  |  |
| Ware et al., 2014 | Respiratory disease | <12 mos 1-<2 yrs 2-<3 yrs 3-<6 yrs 6-<11 yrs 11-<16 yrs 16-21 yrs | AK 2011-2012 | N=475 in 241 households cross-sectional | Questionnaires |
| **INDOOR WATER/AIR QUALITY** | |  |  |  |  |
| *Mold* |  |  |  |  |  |
| Bulkow et al., 2012 | LRTI | <12 mos 1-<2 yrs 2-<3 yrs | AK 2006-2007 | n=128 cases n=186 controls case-control | Med. records, questionnaires |
| Surdu et al., 2006 | Asthma | 2-<3 yrs 3-<6 yrs 6-<11 yrs 11-<16 yrs | NY - | n=25 cases n=25 controls case-control | Air/dust samples, interviews, med. records |
| Ware et al., 2014 | Respiratory disease | <12 mos 1-<2 yrs 2-<3 yrs 3-<6 yrs 6-<11 yrs 11-<16 yrs 16-21 yrs | AK 2011-2012 | N=475 in 241 households cross-sectional | Questionnaires |
| Petersen et al., 2003 | CRD | <12 mos >12 mos | AK - | N=22 community members (parents, healthcare providers) qualitative | Interviews |
| **OUTDOOR AIR QUALITY** | |  |  |  |  |
| *Outdoor air pollution* |  |  |  |  |  |
| Surdu et al., 2006 | Asthma | 2-<3 yrs 3-<6 yrs 6-<11 yrs 11-<16 yrs | NY - | n=25 cases n=25 controls case-control | Air/dust samples, interviews, med. records |
| Ware et al., 2014 | Respiratory disease | <12 mos 1-<2 yrs 2-<3 yrs 3-<6 yrs 6-<11 yrs 11-<16 yrs 16-21 yrs | AK 2011-2012 | N=475 in 241 households cross-sectional | Questionnaires |
| *Steam baths/housing sand dust/poor sanitation* | | |  |  |  |
| Petersen et al., 2003 | CRD | <12 mos >12 mos | AK - | N=22 community members (parents, healthcare providers) qualitative | Interviews |
| **FARM OPERATIONS** |  |  |  |  |  |
| Goldcamp et al., 2006a | Non-fatal injury | 6-<11 yrs  11-<16 yrs 16-21 yrs | Nationwide 2000 | N=7,381 AI youth living on racial minority-operated farms | USDA survey for NIOSH, Census of Agriculture |
| Goldcamp et al., 2006b | Non-fatal injury | 6-<11 yrs  11-<16 yrs 16-21 yrs | Nationwide 2000 | N=7,381 youth living on 9,556 AI-operated farms | USDA survey for NIOSH, Census of Agriculture |
| 1U.S. Environmental Protection Agency. Guidance on selecting age groups for monitoring and assessing childhood exposures to environmental | | | | | |
| contaminants. Risk Assessment Forum. November 2005. EPA/630/P-03/003F. | | | | | |
|  | | | | | |
| ACS - American Community Survey; AI – American Indian; AK - Alaska; ALRI - acute lower respiratory illness; AZ - Arizona; CA - California; CDC - Centers for Disease Control and Prevention; CRD - chronic respiratory disease; hMPV - human metapneumovirus; hPIV - | | | | | |
| human parainfluenza virus; IPD - invasive pneumococcal disease; LRTI - lower respiratory tract infection; NIOSH – National Institute for | | | | | |
| Occupational Safety and Health; NY- New York; PNA – pneumonia; RSV - respiratory syncytial virus; USDA – United States Department of Agriculture. | | | | | |
|  | | | | | |

Table 2. Characteristics from 22 studies by stressors from the natural environment.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Chemical(s) of interest** | **Health outcome(s)** | **Lifestage group1** | **Location (U.S. state)/ period** | | **Sample size/design** | **Data source(s)** |
|  |  |  |  |  | |  |  |
| **RESIDENTIAL PROXIMITY TO POLLUTED LANDSCAPES** | | | | |  | |  |
| *Youth (cohort from same territory)* | |  |  |  | |  |  |
| Schell et al., 2004 | *p,p'*-DDE, HCB, mirex, PCBs | Thyroid function | 6-<11 yrs 11-<16 yrs 16-21 yrs | NY - | | N=115 - | Blood samples |
| Schell et al., 2008 | *p,p'*-DDE, HCB, PCBs, lead | Thyroid hormone levels | 6-<11 yrs 11-<16 yrs 16-21 yrs | NY 1995-2000 | | N=232 - | Blood samples, interviews |
| Schell et al., 2009 | *p,p'*-DDE, HCB, PCBs | Thyroid function | 6-<11 yrs 11-<16 yrs 16-21 yrs | NY 1995-2000 | | N=115 - | Blood samples, interviews, questionnaires |
| Newman et al., 2006 | PCBs | Cognitive function | 6-<11 yrs 11-<16 yrs 16-21 yrs | NY - | | N=271 - | Blood samples, cognitive tests, interviews |
| Newman et al., 2009 | PCBs | Cognitive function | 6-<11 yrs 11-<16 yrs 16-21 yrs | NY - | | N=271 - | Blood samples, cognitive tests, interviews |
| Newman et al., 2014 | PCBs | ADHD | 6-<11 yrs 11-<16 yrs 16-21 yrs | NY - | | N=271 cross-sectional | Behavioral ratings, blood samples |
| Denham et al., 2005 | *p,p'*-DDE, HCB, PCBs, mirex, lead, mercury | Timing of menarche | 6-<11 yrs 11-<16 yrs 16-21 yrs | NY - | | N=138 cross-sectional | Blood samples, interviews |
| Ernst et al., 1986 | Fluoride from aluminum smelter | Lung function | 11-<16 yrs 16-21 yrs | NY 1981 | | N=253 children analyses btw. community air pollution and individual lung function | Air and urine sampling, interviews, lung function tests, plant fluoride content |
| Gallo et al., 2011 | *p,p'*-DDE, HCB, PCBs | - | 16-21 yrs | NY - | | N=152 - | Blood samples, questionnaires |
| Schell et al., 2003 | *p,p'*-DDE, HCB, mirex, PCBs, lead, mercury | - | 6-<11 yrs 11-<16 yrs 16-21 yrs | NY 1996-2000 | | N=271 - | Blood samples, interviews |
| *Youth (other AI cohort)* | |  |  |  | |  |  |
| Malcoe et al., 2002 | Lead from a former uranium mining region | - | 1-<2 yrs 2-<3 yrs 3-<6 yrs 6-<11 yrs | OK - | | n=95 AI n=129 White n=26 cases n=198 controls case-control | Blood, dust, paint, soil, water samples; interviews |
| *Mothers/infants (cohort from same territory)* | | |  |  | |  |  |
| Fitzgerald et al., 1998 | PCBs | - | <12 mos >12 mos | NY 1986-1992 | | n=97 AI (cases) who gave birth 1969-1992, n=154 White (controls) in counties relatively free of PCB contamination who gave birth during same period cross-sectional | Breast milk samples, interviews |
| Fitzgerald et al., 2004 | PCBs | - | <12 mos | NY 1992-1995 | | N=111 pregnant AI women  - | Air, blood, food, soil samples; interviews |
| Hong et al., 1994 | PCBs | - | <12 mos | NY 1988-1990 | | n=20 AI (cases), n=30 controls from WIC clinics in 2 NY counties who gave birth 1988-1990 - | Breast milk samples, interviews |
| Fitzgerald et al., 2001 | *p,p'*-DDE, HCB, mirex | - | <12 mos >12 mos | NY 1986-1992 | | n=97 AI (cases), n=154 White (controls) from other rural areas in NY - | Breast milk samples, interviews |
| *Mothers/infants (Other AI/AN cohorts)* | | |  |  | |  |  |
| Gilbreath et al., 2006a | Potential exposure to hazardous waste and waste disposal methods | Fetal/neonatal deaths, congenital anomalies | <12 mos | AK  1997-2001 | | N=10,360 from 197 villages  retrospective cohort | Birth certificates, open dumpsite hazard rankings |
| Gilbreath et al., 2006b | Potential exposure to hazardous waste and waste disposal methods | Adverse birth outcomes | <12 mos | AK  1997-2001 | | N=10,073 from 197 villages  retrospective cohort | Birth certificates, open dumpsite hazard rankings |
| Orr et al., 2002 | COIs, inorganic compounds, nitrates/ nitrites, pesticides, VOCs | Birth defect | <12 mos | CA 1983-1988 | | n=431 cases n=392 controls case-control | Birth defects program, residence |
| Shields et al., 1992 | Radiation from a former uranium mining region | Adverse birth outcomes | <12 mos | NM 1964-1981 | | N=266 pairs of cases/controls case-control | Interviews, med. records, NIOSH |
| **DIETARY CONSUMPTION** | | |  |  | |  |  |
| Monheit et al., 2008 | Fluridone (herbicide) | - | <12 mos >12 mos | CA 2005 | | N=60 environmental samples human health hazard assessment | Aquatic tule vegetation, sediment, water samples |
| Xue et al., 2014 | PCBs | - | 11-<16 yrs 16-21 yrs | Nationwide 2001-2004 blood PCB levels; 1999-2006 dietary consumption | | 3.9% of Asian/Pacific Islander, Native American, or multiracial (A/P/N/M) participants among 12-≤30 yrs of study sample for blood PCB levels, n=321 for A/P/N/M 12-20 years for consumption data - | NHANES, NYC Asian Market Survey, U.S. EPA's Food Consumption Intake Database |
| 1U.S. Environmental Protection Agency. 2005. Guidance on selecting age groups for monitoring and assessing childhood exposures to | | | | | | | |
| environmental contaminants. Risk Assessment Forum. EPA/630/P-03/003F. | | | | | | | |
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| *p,p'*-DDE - dichlorodiphenyldichloroethylene; AI/AN – American Indian/Alaska Native; ACS - American Community Survey; ADHD - attention deficit hyperactivity disorder; CA - California; COI - cytochrome oxidase inhibitor; HCB - hexachlorobenzene; NHANES - National Health and Nutrition Examination Survey; NIOSH - National Institute for Occupational Safety and Health; NM – New Mexico; NY – New | | | | | | | |
| York; OK – Oklahoma; PCB – polychlorinated biphenyl; U.S. EPA - United States Environmental Protection Agency; VOC – volatile | | | | | | | |
| organic compound; WIC - Women, Infants, and Children. | | | | | | | |
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Table 3. Study findings for stressors from the built environment.

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| **Study** | **Variable of interest** | **Health outcome(s)** | **Effect estimate/ measure of association/ summary measure** | **Other variables considered** | **Association(s) between stressor and health outcome(s)** |
|  |  |  |  |  |  |
| **INDOOR WATER QUALITY** | |  |  |  |  |
| *Lack of piped/running water* | |  |  |  |  |
| Bruden et al., 2015 | Lack of plumbed water | LRTI, RSV | (UNADJUSTED) LRTI RR: 1.65 (95% CI: 1.49-1.83); RSV RR: 1.85 (95% CI: 1.57-2.17) (ADJUSTED) LRTI RR: 1.25 (95% CI: 1.05-1.26); RSV RR: 1.45 (95% CI: 1.19-1.78) | Coastal community, community size, healthcare access, household crowding, period, poverty, wood heating | Higher hospitalization rates for LRTIs and RSV in communities with higher proportion of households that lack plumbed water |
| Bulkow et al., 2012 | Sinks in 2 or more rooms in house | hMPV, hPIV, LRTI, RSV | (UNADJUSTED) hMPV OR: 0.58 (P=0.350); hPIV OR: 0.10 (P=0.030); LRTI OR: 0.41 (95% CI: 0.23-0.73); RSV OR: 0.30 (P=0.081) (ADJUSTED) LRTI OR: 0.29 (95% CI: 0.14-0.58) | Bottle fed, medically high-risk, regularly vomiting after feeding, wood stove in house | Decreased risk of hospitalizations for hMPV, hPIV, LRTIs, and RSV for households with sinks in 2 or more rooms |
| Gessner et al., 2008 | Modern water service (in-home piped water/ septic system or water delivered by closed haul truck) | LRTI | (ADJUSTED) Outpatient LRTI β: -0.53 (P<0.001) inpatient LRTI β: -0.15 (P=0.088) | Adult education, Alaska Native resident, young children in household, cigarette use, employment, household crowding, poverty, wood stove use | Higher incidence of LRTIs among households lacking modern water service |
| Hennessy et al., 2008 | Low in-home water service by region | Pneumonia and influenza, RSV | (ADJUSTED) Pneumonia and influenza <1 yr rate ratio: 6.57 (95% CI: 5.58-7.72); pneumonia and influenza 1-4 yrs rate ratio: 2.96 (95% CI: 2.51-3.50); pneumonia and influenza 5-19 yrs rate ratio: 1.80 (95% CI: 1.39-2.33); RSV <5 yrs rate ratio: 3.4 (95% CI: 3.0-3.8) | Household crowding | Higher hospitalization rates for pneumonia and influenza and RSV in regions with lower proportion of home water service |
| Morris et al., 1990 | Presence of running water | LRTI (bronchiolitis or pneumonia) | (UNADJUSTED) OR=0.5 (P=0.061) | Asthma history, respiratory illness exposure, wood-burning stove | Children in households with running water tended to have fewer LRTIs |
| Reisman et al., 2014 | Lack of in-home running water | Pneumococcal colonization of nasopharynx | (UNADJUSTED) <10 yrs OR: 1.25 (P=0.001); 10-17 yrs OR: 1.09 (P=0.26) (ADJUSTED) <10 yrs OR: 1.35 (95% CI: 1.08-1.69) (P=0.01); <5 yrs OR: 1.42 (P-value not available) | Antibiotic use, household crowding, no. of young children, otitus media, pneumonia, respiratory infection, strep throat, village | Increased prevalence of pneumococcal colonization significantly associated with lack of in-home running water among children less than 10 years |
| Wenger et al., 2010 | Lack of in-home piped water | IPD | (UNADJUSTED) IPD rate for low water service (<10% of households served in region): 391 cases/100,000 children/yr (P=0.008); IPD rate for midlevel water service (10-80%): 263 cases/100,000/yr; IPD rate for high water service (80%+): 147 cases/100,000/yr (ADJUSTED) IPR rate and water service (P<0.02) | Household crowding, poverty, wood for heating | Higher IPD rates associated with lack of in-home piped water |
| Gilbreath et al., 2006a | Some or no piped water to households in village | Adverse birth outcomes | (UNADJUSTED) low birth weight: some households plumbed OR: 1.35 (95% CI: 1.06-1.72) no households plumbed OR: 1.32 (1.00-1.74) vs. all households plumbed; preterm birth: some households plumbed OR: 1.27 (1.07-1.51) no households plumbed OR: 1.41 (1.17-1.71); intrauterine growth retardation: some households plumbed OR: 0.92 (0.58-1.5) no households plumbed OR: 1.118 (0.71-2.0) | Birth weight, gender, healthcare options, interpregnancy interval, maternal age/education, missing values, parity, prenatal care, race, tobacco/alcohol use, year of birth | Among mothers living near open dumpsites, a significantly higher risk of low birth weight, and preterm birth was associated with maternal residence in villages with some households receiving piped water compared to villages with all households receiving piped water. |
| Gilbreath et al., 2006b | Some or no piped water to households in village | - | (UNADJUSTED) Villages with high hazard dumpsite rankings: no households plumbed 36%, some households plumbed 39%, all households plumbed 25% vs. villages with low hazard dumpsite rankings: no households plumbed 30%, some households plumbed 57%, all households plumbed 13% | Birth weight, gender, healthcare options, interpregnancy interval, maternal age/education, missing values, parity, prenatal care, race, tobacco/alcohol use, year of birth | Mothers from villages containing high hazard open dumpsite rankings were more likely to be in villages with some or no households with piped water compared to mothers from villages with low hazard ranked dumpsites. |
| **INDOOR AIR QUALITY** | | |  |  |  |
| *Use of wood for heating or cooking* | |  |  |  |  |
| Bruden et al., 2015 | Use of wood for heating | LRTI, RSV | (UNADJUSTED) LRTI RR: 1.00 (95% CI: 0.95-1.07); RSV RR: 1.02 (95% CI: 0.93-1.15) | Coastal community, community size, healthcare access, household crowding, period, poverty, lack plumbing | Hospitalizations for LRTIs and RSV not significantly associated with proportion of households using wood for heating |
| Bulkow et al., 2012 | Woodstove for heating and/or cooking in house | hMPV, hPIV, LRTI, RSV | (UNADJUSTED) hMPV OR: 1.61 (P=0.351); hPIV OR: 1.43 (P=0.624); RSV OR: 1.22 (P=0.686); unknown viral pathogen OR:3.43 (P=0.01) (ADJUSTED) LRTI OR: 2.21 (95% CI: 1.20-4.10); unknown viral pathogen OR: 6.23 (P=0.01) | Bottle fed, medically high-risk, regularly vomiting after feeding, 2 or more rooms with sinks in house | Increased risk of hospitalizations for LRTIs associated with woodstove use in homes |
| Morris et al., 1990 | Wood-burning stove for heat | LRTI (bronchiolitis or pneumonia) | (UNADJUSTED) OR: 4.2 (P=0.001) (ADJUSTED) OR: 4.85 (95% CI: 1.69-12.91) (P=0.003) | Asthma history, respiratory illness exposure, running water | Higher risk of LRTIs associated with children living in homes with a wood-burning stove |
| Ware et al., 2014 | Woodstove for heating | Bronchitis, cold, flu, middle-ear infection, pneumonia, throat infection | (UNADJUSTED) <5 yrs pneumonia OR: 2.1 (95% CI: 0.6-7.2), bronchitis OR: 2.0 (0.7-6.3), flu OR: 1.0 (0.3-3.1), cold OR: 1.8 (0.5-6.3), throat infection OR: 1.9 (0.6-6.1), middle-ear infection OR: 1.7 (0.7-4.4); 5-17 yrs pneumonia OR: 1.5 (0.6-4.0), bronchitis OR: 1.5 (0.7-3.3), flu OR: 1.0 (0.5-2.3), cold OR: 1.0 (0.5-2.0), throat infection OR: 1.5 (0.8-3.0), middle-ear infection OR: 1.2 (0.6-2.3) | Age of house, ventilation/purification, crowding, heating, household smoker, mold | Increased risk for respiratory infection among children living in homes heated exclusively with wood stoves compared to homes heated exclusively with fuel oil, but associations not statistically significant |
| Robin et al., 1996 | Cooked with wood-burning stove, measured respirable particle concentration ≥65 µg/m3 | ALRI | (UNADJUSTED) OR any wood vs. gas/electricity alone OR: 5.0 (95% CI: 0.6-42.8); respirable particle concentration ≥65 µg/m3 vs. lower concentration of respirable particles OR: 7.0 (95% CI: 0.9-56.9) | Access to clinic/hospital, no. of rooms, no. of children in home, indoor air respirable particles ≥65 µg/m3, primary caretaker other than mother, running water, smoker in household, smoking of ceremonial herbs, type of home | Increased risk of ALRI was associated (although CI was wide) with cooking with wood-burning stoves and higher indoor air concentrations of respirable particles |
| Singleton et al., 2016 | Woodstove for primary heat source, measured pollutants (VOCs - BTEX > 100 µg/m3, CO2 > 1000 ppm, PM2.5 > 25 µg/m3) | Cough between colds, health provider ever said child had asthma, wheeze between colds, | (ADJUSTED) Cough between colds: woodstove for primary heat source OR: 3.18 (P=0.027), BTEX>100 µg/m3 OR: 4.42 (P<0.001), PM2.5 > 25 µg/m3 OR: 2.18 (P=0.026); wheezing between colds OR: 1.88 (P=0.068) for BTEX>100 µg/m3; ever said child had asthma OR: 3.02 (P=0.031) for BTEX>100 µg/m3, OR=0.38 (P=0.112) for CO2>1000 ppm | Average PM2.5 > 25 µg/m3, BTEX > 100 µg/m3, CO2 > 1500 ppm; household crowding, mold in child's bedroom, piped water/sewer system, RH, smoker in household | Higher risk for cough between colds associated with primary wood heat, VOCs > 100 µg/m3, and PM2.5 > 25 µg/m3; higher risk of wheezing between colds and asthma diagnosis associated with VOCs > 100 µg/m3 |
| *Other* |  |  |  |  |  |
| Morris et al., 1990 | Dirt floor | LRTI (bronchiolitis or pneumonia) | Too few controls with a dirt floor for OR | Family history of asthma, respiratory illness exposure, running water, wood-burning stove | - |
| Surdu et al., 2006 | Garage attached to home | Asthma | (UNADJUSTED) OR: 1.31 (90% CI: 0.39-4.43) | Asthma history; smoking in house; born before due date; breastfed; burn-barrel near home; insects in house; day-care first 2 years of life; moist walls, ceilings, carpets, furniture; mold in house; pets; smoking during pregnancy | Non-significant increased risk of asthma associated with families with a garage attached to house |
| Ware et al., 2014 | House built before 1985 | Bronchitis, cold, flu, middle-ear infection, pneumonia, throat infection | (UNADJUSTED) <5 yrs bronchitis OR: 0.2 (0.1-0.6), cold OR: 0.2 (0.1-0.7), flu OR: 1.2 (0.5-2.6), middle-ear infection OR: 0.6 (0.3-1.3), pneumonia OR: 1.2 (95% CI: 0.4-3.1), throat infection OR: 1.3 (0.6-3.0); 5-17 yrs bronchitis OR: 0.6 (0.3-1.1), cold OR: 0.9 (0.5-1.6), flu OR: 1.2 (0.7-2.0), middle-ear infection OR: 0.9 (0.5-1.3), pneumonia OR: 1.2 (0.6-2.5), throat infection OR: 0.9 (0.6-1.5) | Age of house, ventilation/ purification, crowding, heating, household smoker, mold | Lower reported prevalence of bronchitis among children less than 5 years associated with residence in an older home (built before 1985) |
| **INDOOR WATER/AIR QUALITY** | | | |  |  |
| Bulkow et al., 2012 | Mold | LRTI | (UNADJUSTED) OR: 1.21 (95% CI: 0.74-1.97) | Bottle fed, medically high-risk, vomiting after feeding, woodstove, rooms with sinks in house | Hospitalizations for LRTI not associated with homes with visible mold |
| Surdu et al., 2006 | Mold | Asthma | (UNADJUSTED) OR: 0.83 (90% CI: 0.30-2.29) | See above | No relationship found between asthma and mold in homes |
| Ware et al., 2014 | Mold | Bronchitis, cold, flu, middle-ear infection, pneumonia, throat infection | (UNADJUSTED) <5 yrs bronchitis OR: 1.7 (0.6-4.3), cold OR: 2.4 (0.6-8.7), flu OR: 2.5 (1.0-6.1), middle-ear infection OR: 2.2 (1.0-5.0), pneumonia OR: 1.3 (95% CI: 0.5-3.5), throat infection OR: 1.8 (0.7-4.5); 5-17 yrs bronchitis OR: 1.6 (0.9-3.0), cold OR: 1.7 (0.9-3.3), flu OR: 2.0 (1.1-3.7), middle-ear infection OR: 1.8 (1.2-2.7), pneumonia OR: 1.6 (0.5-2.3), throat infection OR: 1.6 (1.0-2.8) | Age of house, ventilation/ purification, crowding, heating, household smoker | Non-significant elevated prevalence of reported respiratory infections associated with reported concerns about indoor mold |
| Petersen et al., 2003 | Mold | CRD | (UNADJUSTED) n=9/22 interviewees had opinions of mold as a contributing factor of CRD | Allergy, genetic/familial, inhalant abuse, nutrition practices, SE conditions | - |
| **OUTDOOR AIR QUALITY** | | | |  |  |
| Surdu et al., 2006 | Burn-barrel near home | Asthma | (UNADJUSTED) OR: 1.56 (90% CI: 0.52-4.74) | See above | Non-significant increased risk of asthma associated with outdoor air pollution (a burn-barrel within 5-minute walk from house) |
| Ware et al., 2014 | Outdoor smoke | Bronchitis, cold, flu, middle-ear infection, pneumonia, throat infection | (UNADJUSTED) <5 yrs bronchitis OR: 1.8 (0.6-4.8), cold OR: 0.9 (0.2-3.7), flu OR: 1.3 (0.5-3.6), middle-ear infection OR: 1.9 (0.7-5.4), pneumonia OR: 1.8 (95% CI 0.6-5.6), throat infection OR: 1.4 (0.5-4.4); 5-17 yrs bronchitis OR: 1.4 (0.7-2.8), cold OR: 2.0 (0.8-4.5), flu OR: 1.3 (0.7-2.4), middle-ear infection OR: 1.4 (0.7-2.9), pneumonia OR: 1.5 (0.6-3.7), throat infection OR: 1.0 (0.5-1.8) | Age of house, change ventilation/ purification, crowding, heating, household smoker, mold | Non-significant elevated prevalence of reported respiratory infections associated with reported concerns about outdoor sources of smoke |
| Petersen et al., 2003 | Steam baths/housing sand dust | CRD | (UNADJUSTED) n=22/22 interviewees had opinions of steam from outdoor baths and smoke from active/passive cigarettes and n=16/22 interviewees of dust from river sandbars, building sand pads, or roads with motorized traffic as contributing factors of CRD | See above | - |
| **FARM OPERATIONS** | |  |  |  |  |
| Goldcamp et al., 2006a | Living on farm | Non-fatal injury | (UNADJUSTED) AI household youth living on farms rate of 24.0 injuries per 1,000 household youth (95% CI: ±4.4), no. of injuries 177 (95% CI: ±31), 50.9% of total injuries among racial minorities; injury rate among all racial minority youth: 12.2 (CI: ±1.7); rate ratio between injury rates for AI youth for work injuries and non-work injuries:1.3 (17.8 per 1,000 youth, 95% CI: 12.7-22.9; 13.8 per 1,000 youth, 95% CI: 11.8-15.85) | Age, farm type, race, sex, work status | AI youth living on farms had almost double the overall injury among all racial minority household youth. Work-related injury rates for AI youth living on farms were greater than non-work injuries. |
| Goldcamp et al., 2006b | Living on farm | Non-fatal injury | (UNADJUSTED) 83% of AI household youth living on farms sustained injuries on livestock farm types (rate of 27.0 injuries per 1,000 household youth), rest on crop farms (17%) (rate of 18.9 injuries per 1,000 household youth) | Age, farm type, sex, work status | More than half of all injuries to AI household youth on AI-operated farms were due to livestock operations. |
| β = beta; µg/m3 - micrograms per cubic meter of air; AI – American Indian; ALRI - acute lower respiratory illness; BTEX - benzene, toluene, ethylbenzene, o-xylene, and m,p-xylene; CI - confidence interval; CO2 – carbon dioxide; CRD – chronic respiratory disease; hMPV - human metapneumovirus; hPIV - human parainfluenza virus; IPD - invasive pneumococcal disease; LRTI - lower respiratory tract infection; OR - odds ratio; PM - particulate matter; PPM - parts per million; RH - relative humidity; RR - relative rate; RSV - respiratory syncytial virus; SE - socioeconomic; VOC – volatile organic compound. | | | | | |

Table 4. Study findings for stressors from the natural environment.

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| **Study** | **Chemical(s) of interest (media)** | **Health outcome(s)** | **Effect estimate/ measure of association/ summary measure** | **Other variables considered** | **Association(s) between chemical and health outcome(s)** |
|  |  |  |  |  |  |
| **RESIDENTIAL PROXIMITY TO POLLUTED LANDSCAPES** | | | |  |  |
| *Youth (cohort from same territory)* | | |  |  |  |
| Schell et al., 2004 | *p,p'*-DDE, HCB, mirex, PCBs, lead (blood) | Thyroid function | Sum of 8 persistent PCBs: TSH β=0.29 FT4 β=-0.30 (P≤0.05) T4 β=-0.35 T3 β=-0.08; p,p'-DDE: TSH β=0.09 FT4 β=-0.01 T4 β=-0.03 T3 β=0.07; HCB: TSH β=-0.02 FT4 β=-0.08 T4 β=-0.02 T3 β=-0.04; mirex: TSH β=-0.04 FT4 β=-0.01 T4 β=-0.09 T3 β=-0.16; lead: TSH β=0.02 FT4 β=0.03 T4 β=0.02 T3 β=0.24 | Age, lipids, other toxicants (*p,p'*-DDE, HCB, lead, mirex), sex, sum of 8 persistent PCBs as measure of PCB body burden, time of sample collection | Decreased levels of measures of thyroid function were significantly associated with increased persistent PCBs levels |
| Schell et al., 2008 | *p,p'*-DDE, HCB, PCBs, lead, mercury (blood) | Thyroid hormone levels | TSH levels: persistent 8 PCBs β=0.431 (P=0.004), *p,p'*-DDE β=-0.076 (P=0.488), HCB β=0.084 (P=0.426) lead β=-0.017 (P=0.575), mercury β=-0.026 (P=0.628); FT4 levels persistent PCBs β=-0.099 (P=0.015), p,p'-DDE β=-0.003 (P=0.926), HCB β=-0.027 (P=0.351), lead β=0.001 (P=0.885), mercury β=0.007 (P=0.617) | Age, breastfeeding, cholesterol, duration between interview and blood draw, sex, time of blood collection, triglycerides | Decreased levels of measures of thyroid function were significantly associated with increased persistent PCB levels |
| Schell et al., 2009 | *p,p'*-DDE, HCB, PCB groups by chlorination and structure (blood) | Thyroid function | TPOAb levels among those who were breastfed: *p,p'*-DDE β=0.34 (P=0.05); HCB β=0.05 (P=0.76); mirex β=0.09 (P=0.56) | Age, BMI, breastfeeding, diet, education, height, material well-being, sex, tobacco/alcohol use, weight | Increased TPOAb levels associated with significantly higher levels of all PCB groupings (except non-persistent PCBs) and levels of *p,p'*-DDE |
| Newman et al., 2006 | PCBs (sum of 16 PCB congeners detected in 50% or more of samples) (blood) | Cognitive function | (ADJUSTED) Relationships between summary PCB levels (ΣPCB50%) and cognitive outcome measures with P-values <0.05: long term memory tests - Delayed Recall Index β = -3.563, Long Term Retrieval β = -6.894; and Comprehension-Knowledge β = -4.590 | Mother (e.g., cognition, smoking); adolescent (e.g., breastfeeding, other toxicants (*p,p'*-DDE, HCB, lead, mercury, mirex)) | Decreased test scores for long-term memory and comprehension-knowledge associated with increased concentrations of PCBs |
| Newman et al., 2009 | PCBs (specific congeners grouped by structure: dioxin-like or non-dioxin-like and by persistence: high or low) (blood) | Cognitive function | (ADJUSTED) Relationships with P-values <0.05: Σdioxin-like PCBs50%: Ravens (measure of intellectual ability and reasoning skills) β=-0.16 r2=18%, Delayed Recall β=-0.16 r2=13%, Long Term Retrieval β=-0.16 r2=11%; Σnon-dioxin-like PCBs50%: Ravens β=-0.08 r2=17%, Delayed Recall β=-0.21 r2=13%, Long Term Retrieval β=-0.25 r2=11%; Σpersistent PCBs50%: Delayed Recall β=-0.22 r2=13%, Long Term Retrieval β=-0.20 r2=12%, Auditory Processing β=-0.23 r2=12%; Σlow-persistent PCBs50%: Delayed Recall β=-0.16 r2=13%, Long Term Retrieval β=-0.22 r2=12% | Age, BMI, breastfeeding, cholesterol/ triglyceride level, other toxicants (HCB, *p,p'*-DDE, mirex, blood lead, mercury), maternal BMI/ cognitive scores, smoking during pregnancy, SE status, sex | Decreased test scores for long-term memory (Delayed Recall and Long Term Retrieval) associated with increased concentrations of PCB groupings by persistence and dioxin-like/non-dioxin-like congeners |
| Newman et al., 2014 | PCBs (sum of persistent congeners that may have been active throughout participants' lives or prenatally, found in at least 50% of participants) (blood) | ADHD | (ADJUSTED) Only association with P-value <0.05 between summary measure of persistent PCBs and ADHD score (Impulsive-hyperactive Conners parent T-scores) β=-3.84 | Age, BMI, lipids, maternal factors (BMI, breastfeeding duration, cognitive ability, pregnancy, SE status, smoking during pregnancy), other toxicants (*p,p'*-DDE, lead, HCB, mercury), tobacco/ alcohol use | No evidence of adverse effects of persistent PCB levels on ADHD-like behavior |
| Denham et al., 2005 | *p,p'*-DDE, HCB, mirex, PCBs, lead, mercury | Timing of menarche | Pre- or post-menarcheal status (binary logistic regression) mean-centered levels: *p,p'*-DDE (ppb) β=-0.37 (P=0.66), group of estrogenic PCBs (ppb) β=2.13 (P=0.04), HCB (ppb) β=0.12 (P=0.93), lead (µg/dL) β=-1.29 (P=0.01), mercury (µg/dL) β=0.16 (P=0.78) | Age, BMI, SE status | Lower probability of reaching menarche significantly associated with higher lead levels and earlier age at menarche with higher PCB levels |
| Ernst et al., 1986 | Fluoride from aluminum smelter (urine) | Lung function | Only significant association of lung function with exposure: among boys, lung function CV/VC% high exposure adjusted mean 8.25 (SEE=1.02) low exposure mean=5.36 (SEE=1.07) P-value for differences=0.05; only significant association of lung function with urinary fluoride: among boys, CV/VC% slope 4.78 (P=0.02); among girls, CV/VC% 4.40 (P=0.01) | Age, height, smoking, time since last cold, weight | Increased closing volume (may be indicative of small airway abnormalities) significantly associated with living near smelter 60% of lifetime among boys and increasing levels of urinary fluoride |
| Gallo et al., 2011 | *p,p'*-DDE, HCB, PCBs (blood) | - | Geometric mean concentrations breastfed/non-breastfed: total PCBs 0.87/0.78 (P=0.04); Σ14 PCB50% 0.47/0.40 (P=0.02); Σ9 persistent PCBs 0.35/0.29 (P<0.01)); Σ5 non-persistent PCBs 0.10/0.11 (P=0.41); *p,p'*-DDE 0.33/0.32 (P=0.69); HCB 0.03/0.03 (P=0.27) | Age, BMI, breastfeeding, diet, education, medications, recreational/traditional activities, SE status, sex, tobacco/ alchohol use | - |
| Schell et al., 2003 | *p,p'*-DDE, HCB, mirex, PCBs, lead, mercury (blood) | - | Breastfed/non-breastfed ratios of geometric mean concentrations: total PCBs 1.13=1.74/1.53 (P≤0.001); ΣPCB50% (congeners with ≥50% detection rate) 1.28=0.76/0.59 (P≤0.001); ΣPCB75% 1.32=0.60/0.45 (PP≤0.001); Σpersistent PCBs 1.39=0.46/0.33 (P≤0.001); *p,p*'-DDE 1.45=0.45/0.31 (P≤0.001); HCB 1.07=0.04/0.03; mirex 1.26~0.02/0.02 (P=0.059); lead 1.03=0.72/0.70 (P=0.869); mercury 0.96~0.09/0.09 (P=0.639) | - | - |
| *Youth (other AI cohort)* | |  |  |  |  |
| Malcoe et al., 2002 | Lead from former uranium mining region (blood concentrations and residential environmental levels in dust, paint, soil, water) | - | Median blood lead levels (mg/kg) for American Indian (5.0) and White (5.0) children (P=0.48); median mean soil levels (mg/kg) for American Indians (103) and Whites (148) (P=0.03) mean soil correlation 0.32 (P<0.001) front yard soil 0.32 (P<0.001) back yard soil 0.27 (P<0.001) mean sill dust 0.19 (P=0.005) mean floor dust 0.34 (P<0.001) child's bedroom floor dust 0.24 (P<0.001) exterior paint index 0.12 (P=0.080) interior paint index 0.13 (P=0.051) water -0.01 (P=0.92); associations with P-values <0.05 mean soil lead β=0.74 (P=0.002) mean floor dust lead loading β=0.45 (P=0.02) | Caregiver education, child's hygiene, mouthing, poverty | - |
| *Mothers/infants (cohort from same territory)* | | | | | |
| Fitzgerald et al., 1998 | PCBs (total PCBs - summed each of 68 PCB-containing zones or peaks) (breast milk) | - | (ADJUSTED) Geometric mean breast milk total PCB concentration (ppm, fat basis) AI and control (rural White) mothers who gave birth 1986-1989: 0.602 vs. 0.375 (P<0.01); 1990: 0.352 vs. 0.404; 1991-1992 0.254 vs. 0.318. Geometric mean breast milk concentrations (ppb, fat basis) for greatest concentrations of specific PCB congeners 1986-1989 AI vs. control mothers, all pairwise comparisons had P-values less than 0.05: #138 53.5 vs. 29.9; #153 49.8 vs. 32.8; #99 32.9 vs. 14.8. | Alcohol consumption/ antibiotic use before pregnancy, maternal age, previous breastfeeding | - |
| Fitzgerald et al., 2004 | PCBs (air, blood, local fruit and vegetable, local meat, soil, wild duck concentrations among pregnant women) | - | (UNADJUSTED) Geometric mean (median) of total PCBs (summed congener concentrations of 68 PCB containing zones or peaks) concentrations in serum of pregnant women: 1.2 ppb (maximum: 7.8); geometric means of 3 leading serum congener-specific PCB concentrations (ppb) IUPAC Nos.: #153 0.092; #138 0.0345; #180 0.0142; surface soil total PCB average (range) concentration (ppb): 62.02 (<0.2-886); local meat: 20.10 (<0.2-69.1); wild duck: 481.54 (<0.2-5970); local fruits and vegetables: 5.33 (<0.2-149.5); average total PCB in air in winter: ≤1 ng/m3 and maximum averages in spring/summer: 9.2-10.8 | - | - |
| Hong et al., 1994 | PCBs (breast milk) | - | (UNADJUSTED) Mean (range) total coplanar PCB (sum of 12 non-ortho- and mono-ortho-substituted PCBs) concentrations in milk fat: 49 ng/g (3.4-178) for AI mothers vs. 55 ng/g (8.4-179) for control mothers (P=0.47). Main contributions of individual non-ortho- and mono-ortho-substituted PCB congeners to total calculated toxic equivalent values were PCB congeners #118 (25.8 pg/g lipid); #126  (25 pg/g lipid); #105 (10.8 pg/g lipid); and 156 (7.4 pg/g lipid). | - | - |
| Fitzgerald et al., 2001 | *p,p'*-DDE, HCB, mirex (breast milk) | - | (ADJUSTED) Geometric mean breast milk concentrations (ppb, fat basis) of AI vs. control (rural White) mothers: 1986-1989: *p,p'*-DDE: 420 vs. 198 (P<0.05), HCB: 1.8 vs. 1.7, mirex: 2.6 vs. 1.2 (P<0.10); 1990: *p,p'*-DDE: 198 vs. 113 (P<0.05), HCB: 8.7 vs. 11.0, mirex: 2.3 vs. 1.0 (P<0.10); 1991-1992: *p,p'*-DDE: 183 vs. 190, HCB: 12.5 vs. 14.4, mirex: 3.0 vs. 1.4 (P<0.05) | Antibiotic use before pregnancy, BMI, breastfeeding, education, maternal age/height, occupation, parity, tobacco/ alcohol use | - |
| *Mothers/infants (other AI/AN cohorts)* | | | |  |  |
| Gilbreath et al., 2006a | Potential exposure to hazardous waste and waste disposal methods from maternal residence in village with open dumpsite(s) at time of birth | Fetal/neonatal deaths, congenital anomalies | (ADJUSTED) All deaths: high hazard dumpsite contents rate ratio: 2.04 (95% CI:0.48-8.57) vs. moderate hazard dumpsite contents; other congenital anomalies: high hazard dumpsite contents rate ratio: 4.27 (1.76-10.36) compared to moderate hazard dumpsite contents | Gender, healthcare options, interpregnancy interval, maternal age/education, missing values, piped water, prenatal care, race, tobacco/alcohol use | Infants from mothers who lived in villages containing open dumpsites with high hazard dumpsite contents were more likely to have other congenital defects |
| Gilbreath et al., 2006b | Potential exposure to hazardous waste and waste disposal methods from maternal residence in village with open dumpsite(s) at time of birth | Adverse birth outcomes | (ADJUSTED) Low birthweight: high hazard dumpsite ranking OR 2.06 (95% CI: 1.28-3.32), intermediate dumpsite hazard OR 1.73 (1.06-2.84) compared to infants from mothers in villages with low hazard dumpsite rankings; IGR: high hazard dumpsite OR 3.98 (1.93-8.21), intermediate hazard dumpsite OR 4.38 (2.20-8.77); preterm birth: high hazard OR 1.24 (0.89-1.74), intermediate hazard OR 0.77 (0.52-1.12) | Gender, health care options, interpregnancy interval, maternal age/education, missing values, parity, piped water, prenatal care, race, tobacco/alcohol use | Higher proportion of infants from mothers in villages with high or intermediate hazard ranked open dumpsites had low birth weight or intrauterine growth retardation compared to infants from mothers in villages containing low ranked dumpsites |
| Orr et al., 2002 | COIs, inorganic compounds, nitrates/nitrites, pesticides, VOCs from mother's residence at time of delivery in same census tract as hazardous waste sites | Birth defect | (ADJUSTED) Greatest OR among AI/Alaska Natives for spina bifada (OR: 7.35, 95% CI: 1.01-53.44), NTDs (OR: 5.51, 0.74-40.87), oral clefts (OR: 2.45, 0.70-8.56); greatest OR among Hispanic/Latinos for anencephaly 1.70 (95% CI: 0.69-4.18); greatest OR among Black/African Americans for integument 1.19 (95% CI: 0.77-1.83); greatest OR among Asian/Pacific Islanders for anencephaly 4.30 (95% CI: 1.42-13.03); greatest ORs between potential exposure and any birth defect for all groups for COIs (OR: 1.30, 1.02-1.67), nitrates/nitrites (OR: 1.27, 0.68-2.36), pesticides (OR: 1.18, 0.97-1.43) | Maternal age, prenatal care | Greatest increased risk of adverse birth outcomes among AI/Alaska Natives from potential exposure to contaminants vs. controls (same counties, no birth defect) |
| Shields et al., 1992 | Radiation from former uranium mining region | Adverse birth outcomes | Only statistical significant association when mother lived near tailings/mine dump and adverse birth outcome (group of outcomes included hip dysplasias and dislocations OR 2.71, 95% CI: 1.09-7.64). Significant associations found when mother (OR=2.05, 1.16-3.76) or father (OR=2.56, 1.14-6.28) worked at electronics plant (worker exposures included variety of chemicals/solvents) and all adverse birth outcomes and for group of outcomes as above when mother worked at plant (OR=2.71, 1.09-7.64). | Mother's co-morbidities (e.g., tobacco/alcohol use), period of birth by 6-yr intervals | Increased risk of adverse birth outcomes significantly associated with mother living near uranium mine tailings/dumps; also independently associated when either parent worked at electronics plant |
| **DIETARY CONSUMPTION** | |  |  |  |  |
| Monheit et al., 2008 | Herbicide (fluridone concentrations in aquatic vegetation, sediment, water) | - | (UNADJUSTED) Maximum fluridone concentration in vegetation: 3.4 ppb; sediment: 65 ppb; water: 0.3 ppb; hazard quotient (compared ADD with non-carcinogenic reference dose) for child "worse-case" scenario for vegetation: sub-chronic (1 yr): 4.0E-05, chronic (6 yrs): 2.5E-04; sediment sub-chronic: 1.1E-06, chronic: 6.8E-06; water sub-chronic: 2.5E-07, chronic: 1.5E-06. Found little to no hazard of adverse effects from consuming vegetation. | Tule vegetation harvesting | - |
| Xue et al., 2014 | PCBs (blood) | - | (ADJUSTED) Among younger age group (12-≤30 years), A/P/N/M had highest total PCB concentrations (0.6 ng/g) compared to other racial/ethnic groups. Among younger age group, highest daily average fish consumption for A/P/N/M = 0.3 g/kg. Pearson correlation coefficient=0.07 (P<0.01) between fish consumption and total blood PCB concentrations | Age, gender, region, other racial/ethnic groups, survey periods | - |
| β = beta; *p,p'*-DDE - *p,p'*- dichlorophenyldichloroethylene; r2- coefficient of determination; ADD - average daily dose; ADHD - attention deficit hyperactivity disorder; AI/AN – American Indian/Alaska Native; A/P/N/M - Asian/Pacific/Native American/Other Multiracial; BMI - body mass index; CI - confidence interval; COI - cytochrome oxidase inhibitor; CV/VC% = closing volume as percent of vital capacity; FT4 - free thyroxine; HCB - hexachlorobenzene; IGR – intrauterine growth retardation; MUS - musculoskeletal; NTD - neural tube defect; OR - odds ratio; PCB - polychlorinated biphenyl; PPM - parts per million; PPB - parts per billion; SE - socioeconomic; SEE - standard error of estimate; T3 - triidothyronine; T4 - total thyroxine; TPOAb - anti-thyroid peroxidase; TSH - thyroid stimulating hormone; VOC - volatile organic compound. | | | | | |