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Estimating Environmental Exposures to Indoor Contaminants using Residential-Dust Samples

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Estimating Environmental Exposures to Indoor Contaminants using Residential-Dust Samples

By

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ABSTRACT

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Using data from the Northern California Childhood Leukemia Study (NCCLS) and the Fresno Exposure Study this dissertation shows that concentrations of chemical contaminants in residential-dust samples can be useful surrogates for indoor chemical exposures. This dissertation focuses on dust levels of four chemicals or classes which have been associated with childhood leukemia and/or developmental effects, namely polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs), and nicotine (a surrogate for tobacco smoke). Chapter 1 assesses the state of the science of residential-dust measurements, reviews global patterns in residential-dust levels of these chemicals, identifies known determinants of these chemicals' concentrations in residential dust, and estimates relative contributions of residential dust to the overall chemical intake of these chemicals in humans. Chapter 2 describes the analytical methods developed to measure PBDEs, PCBs, and PAHs in residential-dust samples. Chapters 3-6 compare residential-dust concentrations of these chemicals measured in California homes to levels reported in other studies from around the world. Chapters 3-5 also identify questionnaire-based predictors of residential-dust concentrations of nicotine, PAHs, and PCBs (chemicals for which sufficient data were available for statistical analyses). Chapter 7 investigates the variability of residential-dust levels of these chemicals within and between California households. A major finding of this work is the demonstration that current levels of nicotine, PAHs and PCBs represent indoor contamination from the distant past (*e.g.*, over a period of years). This knowledge can be extremely useful to investigators who seek to perform retrospective assessment of exposures in studies of human health effects. The concluding Chapter 8 discusses the benefits and limitations of using residential-dust samples to estimate exposures to chemical contaminants, and presents ideas for future research in this field.

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CHAPTER 1.

ESTIMATING EXPOSURES TO INDOOR CONTAMINANTS USING RESIDENTIAL-DUST SAMPLES: A STATE-OF-THE-SCIENCE REVIEW[1]

Introduction

The principal goal of environmental epidemiology is to characterize how environmental factors affect human health. Specifically, environmental epidemiologists seek to quantify a dose-response relationship between the level of a hazardous agent in the environment and the severity of its health impact on a population. To this end, epidemiologists have generally classified potential exposures to environmental agents on the basis of self-reported information. However, self-reported exposure surrogates are generally qualitative and they may not accurately reflect true environmental exposures. When the discrepancy between estimated and true exposure levels (*i.e.*, measurement error) is substantial, the true relationship between exposure and disease will be obscured. As such, the development of quantitative and objective measures of exposure is a critical aspect of environmental epidemiology. Recently, investigators have considered estimating exposures to indoor contaminants using toxicant levels in residential-dust samples, because dust measurements are quantitative and objective. Although, in practice, few epidemiological studies (1-5) have employed estimates of exposure using dust samples, this dissertation will show that concentrations of chemical contaminants in residential dust can be useful surrogates for indoor chemical exposures

This dissertation will focus on three chemical classes which have been associated with either childhood leukemia in the Northern California Childhood Leukemia Study (NCCLS) (5, 6) or with developmental effects in other studies (7-9), namely, polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs), and polycyclic aromatic hydrocarbons (PAHs), as well as nicotine (a surrogate for cigarette smoke). All of these chemicals are ubiquitous contaminants in residential dust due to their many indoor sources. Nicotine is a specific marker of cigarette smoke; PBDEs have been used as chemical flame retardants in consumer goods (10); PCBs have been used in a host of consumer products, including fluorescent lights, televisions, and refrigerators (11); and PAHs are produced by indoor combustion sources, including cigarette smoke, wood-burning fireplaces, and gas appliances (12).

PBDE, PCB, PAH, and nicotine molecules on dust can enter the body via inhalation, via inadvertent ingestion after hand-to-mouth contact, or via direct absorption through the skin (13). For some individuals, notably children, dust likely contributes a substantial portion of the overall intake of PBDEs (13-16), PCBs (17), and PAHs (18, 19) and nicotine levels in dust offer a useful quantitative measure of cigarette smoking in the home (20).

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There have been several reviews of the use of dust as a medium for measuring chemical contamination in the home (21-24). Investigators have generally sampled residential dust by obtaining dust from subjects' household vacuum cleaners or by collecting dust from floors, carpets or other surfaces using a standardized vacuum cleaner, such as a high volume surface sampler (HVS3). Use of household vacuum cleaner bags eliminates the need for an in-home visit, which reduces study costs and minimizes the invasiveness of home sampling. In contrast, collecting dust with a standardized protocol allows investigators to know the location and time of dust collection. Some investigators have collected dust from household surfaces using a brush or broom (16, 25-29). For example, Tan *et al.* (26) collected dust from the upper surface of a fan blade to measure room-wide contamination.

Researchers have made direct comparisons between chemicals measured in dust taken from household vacuum cleaners and dust collected using a standardized protocol in the same residence (30-32). While household vacuum-cleaner dust represents contamination in several rooms over periods of months or years, interviewer-collected dust provides information about contamination that is specific to a given room at a particular time. Two studies (30, 32) found that PBDEs measured in matched samples of interviewer-collected dust and household vacuum cleaner dust were moderately correlated (r_p = 0.39-0.77 for Allen *et al*.; r_p = 0.51-0.65 for Bjorklund *et al*.) and that household vacuum dust had significantly lower concentrations of PBDEs than interviewer-collected dust. Yet, other investigators have shown that levels of PAHs and PCBs in 40 matched samples of HVS3-sampled and household vacuum cleaner dusts were correlated (r_s = 0.54-0.82) and that median concentrations from both dust collection methods were similar (31). Differences in chemical concentrations measured in dust from the two collection methods are likely to be greatest when indoor chemical sources vary from room-to-room within a residence. There is some evidence that a subject's biological levels of indoor contaminants (*i.e.*, sum of BDE 47 + 153 in breast milk) may be more closely correlated to chemical concentrations (of the sum of BDE 47 +153) measured in dust taken from their household vacuum cleaners than in dust collected from elevated surfaces in their living room (32).

Once residential dust has been collected, it is generally sieved with cut points ranging from 150 μm to 2 mm. Subsequently, the fine dust is extracted with an organic solvent; the extract is chromatographically purified; and specific analytes are detected, typically by gas chromatography-mass spectrometry (GC-MS).

This chapter will review global patterns in dust levels of PBDEs, PCBs, PAHs, and nicotine, identify known determinants of these dust levels, and estimate the relative contributions of dust contamination to human intake of these chemicals. This chapter will focus on studies that measured chemicals in residential-dust samples and omit reports of dust concentrations measured in schools, daycare centers, offices, public buildings, automobiles, etc., or in other media, such as soils or sediments.

Polybrominated diphenyl ethers in residential dust

Polybrominated diphenyl ethers (PBDEs) have been used worldwide as chemical flame retardants to treat textiles (*i.e.*, polyurethane foam in furniture) and plastics (*i.e.*, electronic housings) in consumer goods (10). Three commercial PBDE mixtures;

Penta-BDE, Octa-BDE, and Deca-BDE, have been manufactured. Each mix is comprised of several BDE congeners, but Penta-BDE is predominantly comprised of BDE-47 and BDE-99; Octa-BDE is predominantly comprised of BDE-183, BDE-196, and BDE-197; and Deca-BDE is predominantly comprised of BDE-209 (33).

The European Union banned the use of Penta-BDE and Octa-BDE in 2004 and banned the use of Deca-BDE in 2008 (34) due to concerns for public health. Similarly, PBDE producers in the U.S. phased out production and use of Penta-BDE and Octa-BDE in 2004; however, Deca-BDE is still being used in the U.S. (35). To date, there is no legislation to limit the production or use of PBDEs in Asia (36). Despite the recent regulation of PBDEs in some countries, these chemicals are likely to persist in the indoor environment due to the ubiquitous presence of PBDE-treated consumer goods which can reside in homes for decades.

Globally, PBDE consumption has varied by the quantities and mixtures of PBDEs used. Table 1 shows the regional consumption for three commercial PBDE mixtures reported in 2001 (33). In 2001, consumption of Penta-BDE, Octa-BDE, and Deca-BDE in the Americas exceeded that of Europe by 47-fold, 2-fold, and 3-fold, respectively. In comparisons between the Americas and Asia, the Americas consumed 47-fold more Penta-BDE but consumed comparable quantities of Octa-BDE and Deca-BDE. Although there is no readily available information regarding the use of PBDEs by country or state, there has likely been substantial regional variation. For example, the U.K. (37) and California (38) have stringent flammability standards that indirectly promote the use of Deca-DBE and Penta-BDE.

Global patterns in PBDE levels in residential dust

As illustrated in Table 2, levels of PBDEs measured in residential dust worldwide correspond with historical PBDE consumption. As expected, studies of dust from regions that reported use of Deca-BDE mixtures found high concentrations of BDE-209, whereas studies of dust from regions that reported use of Penta-BDE mixtures found high concentrations of BDE-47 and BDE-99.

In Figure 1, the median value of the dust concentration of BDE-99 is plotted versus that of BDE-209 for each study listed in Table 2 with at least 4 independent PBDE measurements. A global pattern of contamination emerges, as data from various regions of the world cluster together. Specifically, several studies that sampled homes in the U.S. reported median dust concentrations of at least 1 mg/g for BDE-209 and at least 0.1 mg/g for BDE-47 and BDE-99 (30, 37, 39-44). In contrast, studies conducted in continental Europe reported median dust concentrations lower than 1 mg/g for BDE-209 and lower than 0.1 mg/g for BDE-47 and BDE-99 (40, 45-55). On the other hand, the highest median concentrations of BDE-209 in dust were reported in the U.K., with estimated median values from 5 studies ranging from 2.8 to 10 mg/g (37, 40, 46, 56, 57). Levels of BDE-47 and BDE-99 in these U.K. studies were similar to those from continental Europe (*i.e.*, < 0.1 mg/g).

Although few studies of PBDE in dust have been conducted in other areas of the world, the data suggest that median PBDE dust concentrations in Australia (40, 58, 59), New Zealand (37), and Kuwait (60) are relatively low. Two studies from China (16, 29) and one from Singapore (61) reported median BDE-209 concentrations of at least 1 mg/g in dust. In contrast, studies from Japan (25, 62, 63), the Philippines (64), and

Thailand (65) reported lower levels of PBDEs. The relatively high levels of BDE-209 measured in China likely resulted from residential use of PBDE-treated products as well as environmental contamination from local electronics manufacturing facilities (16).

Three studies of PBDE dust levels from California (38, 66, 67) are not represented in Figure 1 because BDE-209 was not analyzed. These three studies have reported some of the highest median concentrations of BDE-47 (2.7, 2.7, and 3.1 mg/g, respectively) and BDE-99 (4.4, 3.8, and 5.5 mg/g, respectively) in residential dust. As noted, these BDE congeners were likely found at high levels in California due to the extensive use of Penta-BDE mixtures to treat furniture in order to comply with the state's flammability standard (68).

Several additional studies (28, 32, 69-76) are not included in Table 2 because they did not report median concentrations of individual PBDE congeners. For the most part, the findings from these studies were similar to those in Table 2, as studies from the U.S. (69, 71, 76) found relatively high concentrations of the sum of PBDEs (average of the sum of 13 PBDEs = 4,629 ng/g, median of the sum of 17 PBDEs = 11,900 ng/g, and geometric mean of the sum of 39 PBDEs = 10,050 ng/g, respectively) compared to studies from Belgium (70, 75) (median of the sum of 22 PBDEs = 125 ng/g and median of the sum of 5 PBDEs = 29 ng/g, respectively), the Czech Republic (73) (range of the sum of 16 PBDEs: 81 – 3,828 ng/g), Italy (70) (median of the sum of 22 PBDEs = 286 ng/g), Portugal (70) (median of the sum of 22 PBDEs = 91 ng/g), Romania (74) (median of the sum of 8 PBDEs = 495 ng/g), Spain (70) (median of the sum of 22 PBDEs = 98 ng/g), Sweden (32, 72) (median sum of 10 PBDEs = 510 ng/g in houses and median sum of 16 PBDEs ~ 400 ng/g in household vacuum cleaner dust), and Vietnam (28) (median of the sum of 14 PBDEs = 220 ng/g).

Importance of residential dust as a source of PBDE exposure

Several investigators observed that biological PBDE levels in various populations mirror the global patterns in PBDE dust concentrations (37, 38, 40). Indeed, it is likely that the relatively high levels of PBDEs measured in blood and breast milk from North Americans compared to Europeans are the result of higher dust concentrations of PBDEs in North American residences (77).

Researchers have also measured PBDEs in matched samples of dust and biological material (*i.e.*, serum, plasma, and breast milk) and reported positive associations between subjects' residential-dust PBDE levels and their corresponding biological levels. Such associations were observed in geographical regions with both low and high levels of PBDE in dust. In the U.S., concentrations of PBDEs in residential dust were positively correlated with matched levels of PBDEs in serum (43) and breast milk (78), as well as with various reproductive hormone levels in serum (4). Likewise, two studies from Europe (49, 79) observed significant relationships between PBDE levels in dust and plasma and one study from Sweden observed an association between PBDE levels in dust and breast milk (32).

In contrast, two studies from the U.S. (41, 69), two from Europe (51, 52), and one from Australia (59) were unable to detect positive associations between PBDEs measured in dust and matched biological samples. Two of these studies had only 10 subjects (59, 69), three did not measure (51) or could not detect (41, 52) BDE-209 (the

most abundant PBDE measured in dust in these three studies) in serum, and two observed that dust was a minor contributor to overall PBDE intake (51, 52).

The positive associations observed between PBDE levels in dust and biological samples suggest that dust is an important source of PBDE exposure worldwide. The estimated intake of PBDEs attributed to residential-dust exposure has varied widely within and between regions, but estimates from North America (13-15, 37, 39, 42, 80) and Asia (16, 61) are generally higher than estimates from Europe (37, 51-54, 74, 75, 81, 82).

Estimates of the relative contribution of dust to PBDE intake also vary somewhat across regions of the world. Two studies from Belgium (52, 75) and one from Germany (51) suggest that residential-dust ingestion was likely responsible for less than 3% of overall PBDE exposure in European adults. In contrast, two studies from Canada (14, 80) estimated that dust ingestion contributed 14 and 65% of the total PBDE intake for adults, while two U.S. studies (13, 15) estimated that dust exposure contributed 56 and 82% of adult intake (via dust ingestion and dermal contact combined), and an Asian study (16) estimated dust ingestion contributed 79% of adult intake. Based on these estimates, residential dust is expected to be the most important source of PBDE exposure for adults in geographical regions with relatively high PBDE dust levels (*e.g.*, North America and Asia). Moreover, children worldwide receive an even larger proportion of their total PBDE intake via dust ingestion compared to their adult counterparts due to hand-to-mouth behavior (14-16, 37, 39, 42, 53, 54, 61, 73, 74, 80, 81).

In summary, the available literature indicates that residential dust is an important contributor to PBDE intake in regions with heavy use of PBDEs. This suggests that levels of PBDEs in residential dust can be useful surrogates of total PBDE exposures in epidemiological studies.

Determinants of PBDE levels in residential dust

PBDEs have been incorporated into a myriad of household goods, including televisions, computers, and various other electric appliances as well as drapes, carpet, and furniture containing foam (83). PBDEs can be transferred from household items to indoor dust either as miniature fragments of foam or textiles via abrasion and weathering (84) or following vaporization of PBDEs from hot surfaces in electronics with subsequent adsorption on dust particles (85, 86).

Few studies have successfully detected significant associations between levels of PBDEs in residential dust and the number of potentially PBDE-treated items in residences. In fact, of 14 studies that inventoried the number of foam-containing pieces of furniture, the number of electronic devices, and/or the typical use of electronic devices in study residences (29, 37, 41, 49, 52, 53, 57, 59-62, 69, 78, 87), only Suzuki *et al.* (62) reported significant associations between these covariates and PBDE levels in dust. These authors reported significant correlations between total electrical appliance usage and dust concentrations of BDEs across 19 residences and 3 office buildings (62). One possible explanation for the paucity of positive associations is the wide range of bromination levels in similar consumer products (41, 63, 88). Allen *et al*. (88) used X-ray fluorescence to identify bromine-containing household goods and illustrated that by excluding furniture without bromine from counts of PBDE-treated

items, it was possible to measure a positive association between the number of electronic items and Deca-BDE congeners as well as between the number of foam-containing furniture items and Penta-BDE congeners.

Authors have examined other household characteristics (*i.e.*, residence age, type, and size; flooring, ventilation, and cleaning practices), but have identified few determinants of PBDE dust levels (30, 41, 49, 53, 58-61, 80). Stapleton *et al*. (39) found a significant negative correlation between the residence square footage and the contribution of BDE-209 to the total PBDE dust concentrations. Similarly, de Wit *et al*. (72) reported that median dust concentrations of BDE-209 were higher in apartments than in houses. In addition, Zota *et al*. (38) found that dust collected from residences in a low-income community in California had higher PBDE levels than dust collected from residences in a more affluent California community.

Polychlorinated biphenyls in residential dust

Because of their non-flammability and electrical insulation properties, polychlorinated biphenyls (PCBs) were used as coolants and lubricants in transformers, capacitors, and other electrical equipment and in a host of consumer products, including fluorescent lights, televisions, and refrigerators (11). Due to concerns for human health, PCB production and use were restricted by various international regulations beginning in the 1970s (89). Still, because of the widespread use of PCBs, their persistence in the environment, and their bioaccumulation through the food chain, these chemicals are still ubiquitous in residences around the world.

Three estimates of global PCB manufacture indicate that cumulative world-wide PCB production topped 1 million metric tons in 1980 (90) and reached somewhere between 1.3 - 1.5 million metric tons by the time PCBs were entirely phased out of production in 1993 (89, 91). Historically, the countries that have manufactured the most PCBs are the U.S., Russia, Germany, France, the U.K., and Japan, which produced 642, 174, 159, 135, 67, and 59 thousand metric tons of PCBs, respectively, by 1993 (91). Likewise, many of these nations were also major consumers of PCBs; with the U.S. consuming the largest portion (46%) of the world's PCBs, followed by Russia (8%), Germany (7%), Japan (4%), and France (4%) (92).

The worldwide restriction of PCB production was implemented at different times in various countries. In 1973, member countries of the Organization for Economic Co-operation and Development (OECD), restricted production of PCBs to certain applications (89). Japan and the U.K. banned production of PCBs in 1972 and 1978, respectively, and in 1976, the U.S. congress passed the Toxic Substances Control Act, which phased out all U.S. production of PCBs by 1979 (89). In the 1980s, limited PCB production continued in Germany and France (90); but a more stringent OECD decision in 1987 led to the cessation of all production, import, export, or sale of PCBs from these countries as well (89). Russia was the last major producer to phase-out PCB production (in 1993) (91).

Global patterns in PCB levels in residential dust

As shown in Table 3, recently reported levels of PCBs measured in residential dust from around the world correspond with reports of cumulative PCB production and consumption. Specifically, PCB concentrations measured in dust from the U.S. (3, 5,

17, 93-96); are generally higher than those measured in dust from the U.K. (17), Japan (63, 97), Singapore (26), and New Zealand (17). The relatively high levels of PCBs that were measured recently in residential dust from the U.S. reflect the high use of PCBs in the U.S. prior to 1979. In the only study of Canadian residences, dust levels of PCBs were comparable to those in the U.S. (17). While levels of Canadian PCB production were insignificant, Canada was the 6th largest PCB consumer worldwide (92). In Table 3, five additional studies were omitted (28, 66, 66, 74, 98), which measured PCBs in residential dust, but did not report individual PCB congener concentrations. Findings from these studies were qualitatively similar to those in Table 3, as the two studies from the U.S. (66, 98) found relatively high median concentrations of the sum of PCBs (sum of 65 PCBs = 710 ng/g and sum of 54 PCBs = 38.0 ng/g, respectively) compared to studies from Belgium (99) (sum of 5 PCBs = 17.2 ng/g), Romania (74) (sum of 8 PCBs = 26.5 ng/g), and Vietnam (28) (sum of 34 PCBs ~ 10 ng/g). Figure 2 summarizes the available data presented in Table 3 and shows median dust concentrations reported from each study for any of 5 major PCB congeners (PCB-105, PCB-118, PCB-138, PCB-153, or PCB-180) that were detected in at least 50% of dust samples.

Importance of residential dust as a source of PCB exposure

Dust ingestion is generally considered to be a minor source of PCB intake in adults (17, 74, 99). Roosens *et al.* (99) estimated that dust ingestion was responsible for less than 1% of overall PCB intake in Belgian adults and found no positive associations between PCB dust levels and PCB serum levels in matched samples. Dirtu and Covaci (74) estimated that dust was responsible for only 1% of total PCB intake in Romanian adults. Harrad *et al*. (17) reported low contributions from dust ingestion to overall PCB intake in adults from Canada (2.4%), New Zealand (0.6%), the U.K. (0.2%), and the U.S. (1.9%). Still, one large study (*N*=764) reported an association between matched PCB-126 concentrations measured in residential dust and serum PCB-126 levels (100).

Children are generally exposed to a relatively large proportion of their total PCB intake via dust ingestion compared to adults. Indeed, estimates of the relative contribution of dust ingestion to overall PCB intake for toddlers were 12.5, 3.6, 1.2, and 9.9% for children from Canada, New Zealand, the U.K., and the U.S., respectively (17). In the most extreme scenario, a Canadian toddler living in a home with a PCB concentration at the 95th percentile of Canadian residences could receive more than half of his or her overall PCB intake via dust ingestion (17). On the other hand, Wilson *et al*. (95) reported that inhalation and dietary ingestion were more substantial sources of PCBs for American children than dust ingestion.

In summary, the available literature indicates that residential dust is generally a minor contributor to PCB intake. Still, for some young children living in highly-contaminated homes, dust may contribute substantially to PCB intake. This suggests that levels of PCBs in residential dust could be useful surrogates of total PCB exposures in studies of childhood diseases.

Determinants of PCB levels in residential dust

Recently, investigators have reported high concentrations of PCBs in dust associated with certain construction materials, such as caulking (101) and wood floor

finish (102), as well as with a PCB-contaminated fluorescent light ballast (103) and a PCB-contaminated carpet pad (104). The prevalence of these particular PCB sources in residences is unknown; however, they are unlikely to be relevant in most homes. Ratios of indoor to outdoor PCB concentrations suggest that indoor PCB sources contribute substantially to PCB dust levels (94, 95, 98); yet, investigators have had little success identifying demographics, household characteristics, or typical household items that have an impact on PCB dust concentrations (26, 95, 98, 99).

Two studies from the U.S. have found evidence that dust from older homes or older floors is more likely to contain high levels of PCBs (3, 105). Colt *et al.* (3) reported that, in multivariable linear regression models, the age of the residence was associated with total (logged) PCB dust concentrations (sum of PCB-105, PCB-138, PCB-153, PCB-170, and PCB-180), with the highest levels found in residences built before 1960 and the lowest in residences built after 1980. Similarly, in the largest analysis of PCB determinants, Lee *et al.* (105) reported that PCB concentrations (PCB-77, PCB-81, PCB-105, PCB-114, PCB-118, PCB-123, PCB-126, PCB-156, PCB-157, PCB-167, PCB-169, and PCB-189) were significantly associated with floor age in dust from 764 Michigan residences.

Additionally, Lee *et al.* (105) identified several factors that were associated with increased concentrations of PCBs in dust, including the presence of high-pile carpet, the presence of a vegetable or flower gardens, and elevated PCB concentrations in outdoor soil. In contrast, having a dog at the residence and increased dust loading (*i.e.*, mass of dust per square meter of floor area), were associated with decreased concentrations of PCBs (105). Still, even the most comprehensive multivariable model only explained 37% of the variability of PCB concentrations in residential dust (105).

Polycyclic aromatic hydrocarbons in residential dust

Polycyclic aromatic hydrocarbons (PAHs) are molecules with two or more fused aromatic rings that are formed as products of incomplete combustion. Humans are exposed to PAHs from a variety of indoor sources including cigarette smoke, wood-burning fireplaces, gas appliances, and charred foods, as well as to outdoor sources, including vehicle exhaust (12) and treatment of pavement with coal-tar-based sealants (106). Seven PAHs that have been classified by the U.S. Environmental Protection Agency as probable carcinogens are most commonly measured in residential dust, namely, benzo(*a*)anthracene, chrysene, benzo(*b*)fluoranthene, benzo(*k*)fluoranthene, benzo(*a*)pyrene, indeno(*1,2,3-c,d*)pyrene, and dibenzo(*a,h*)anthracene (107). Table 4 shows summary statistics from studies which reported levels of these PAHs in residential dust.

Regional patterns in PAH levels in residential dust

Figure 3 shows median PAH dust concentrations reported for several studies from the U.S. (18, 93-95, 106, 108-111). As illustrated in Figure 3, there appear to be regional patterns in PAH levels across the U.S. Studies from the Northeastern U.S., specifically, from New York (93), Massachusetts (94), and Maryland (111), reported much higher PAH concentrations in residential dust, than those in the Western U.S., especially California and Arizona (93, 109). In attempting to understand these patterns, the following possible explanations are considered: (1) differential prevalence of

cigarette smoking, (2) differential use of gas/coal/wood burning heat sources, (3) differential automobile traffic densities, and (4) differential use of coal-tar to seal parking lots and roads.

The Center for Disease Control and Prevention (CDC) has estimated the prevalence of cigarette smoking in each state for the years 1998-2007 (112). In univariate regression analyses, the median dust concentrations of benzo(*a*)anthracene and benzo(*a*)pyrene reported from each study were compared to the smoking prevalence rate reported by the CDC in each state for the year 2000. As shown in a scatter plot of these data in Figure 4a, there was no evidence of correlation between the state smoking rates and the benzo(*a*)anthracene levels in dust (r_p = -0.13, P = 0.65).

Ambient temperature is one possible surrogate for the indoor use (in terms of frequency and duration) of gas/coal/wood burning heat sources. Historic average temperatures were obtained from the weather channel for January 1st in each study location (113). As shown in Figure 4b there was no apparent correlation between the mean January 1st temperatures for the study locations and the corresponding median dust concentrations of benzo(*a*)anthracene reported from each study (r_p = -0.02, P = 0.94).

Population density is a simple surrogate for automobile traffic density and likewise for PAH emissions from automobiles. Estimates of state-, county-, or metropolitan-wide population density were obtained from the U.S. Census to represent each study location (114). In Figure 4c, the plot of representative population density for each study versus the median dust concentrations of benzo(*a*)anthracene suggests a positive association (r_p = 0.27, P = 0.34). Since automobile traffic increases with population density, such an association could suggest that residential PAH levels vary geographically based, in part, on pollution from vehicular exhaust.

Although no data were publicly available regarding the regional use of coal-tar as an asphalt sealcoat in the U.S., a national survey of parking lot dust suggests that coal-tar is used less frequently west of the Rocky Mountains (115). Thus, infrequent use of coal-tar for sealing pavement in the Western U.S. could have contributed to the lower PAH concentrations reported for residential dust from California, Arizona, and Washington (93, 109) (see Figure 3).

Importance of residential dust as a source of PAH exposure

Several researchers have estimated the relative contribution of residential-dust ingestion to total PAH exposure (18, 19). Inadvertent dust ingestion contributed an estimated 42% of non-dietary PAH intake for children and 11% for adults (19). Dust is a particularly important source of exposure to the 7 PAHs classified as probable carcinogens by the EPA, with inadvertent dust/soil ingestion contributing 24% of the total intake (including diet) of these PAHs for children and 7% for adults (18).

Determinants of PAH levels in residential dust

PAH concentrations in residential dust have been reported to be higher in urban compared to rural homes (18, 22, 116), in smoking compared to nonsmoking homes (22, 116), in spring compared to summer (110), and in homes with decreased cleaning frequency (117). A recent study of dust from apartments in Texas found that residences adjacent to parking lots, which had been sealed with coal-tar containing products, had a

median total PAH (sum of 16 PAHs) dust concentration (129 μg/g) that was 25 times higher than that for residences adjacent to parking lots that had not been sealed with coal-tar containing products (5.1 μg/g) (106). One German study also observed increased PAH dust levels in homes containing parquet floor which had been installed with adhesives containing tar (118).

Nicotine in residential dust

The International Agency for Research on Cancer (IARC) concluded that active tobacco smoking causes cancer of the lung, oral cavity, pharynx, nasal cavity and paranasal sinuses, larynx, esophagus, stomach, pancreas, liver, kidney, ureter, urinary bladder, uterine cervix and bone marrow (119). Additionally, IARC asserted that involuntary smoking (exposure to secondhand smoke) also causes lung cancer (119). More recently, it has been suggested that involuntary smoking might contribute to the risk of childhood leukemia (6). Beyond active and secondhand smoking, individuals may be exposed to carcinogenic tobacco constituents which contaminate hair, clothing, furniture and dust particles (so called 'thirdhand' tobacco smoke) (120). Young children are at particular risk from exposure to thirdhand tobacco smoke due to their hand-to-mouth behavior (120).

There are over one billion tobacco smokers worldwide (119), and the prevalence of smoking varies from country to country. Generally, European nations have higher prevalence of smoking (32.0%) than the U.S. (19.8%) (112, 121). While the prevalence of tobacco smoking is generally declining in the U.S. and in Europe, smoking is becoming more common in some developing countries (119). The prevalence of smoking and trends in smoking rates vary substantially within the U.S. as well (112). In 2007, according to the Center for Disease Control, smoking prevalence was highest in Kentucky (28.3%), West Virginia (27.0%), and Oklahoma (25.8%); and lowest in Utah (11.7%), California (14.3%), and Connecticut (15.5%) (112).

Global patterns in nicotine levels in residential dust

Relatively few studies have reported levels of nicotine in residential dust (20, 120, 122-124). Nonetheless, it appears that background levels of nicotine reflect global estimates of smoking prevalence. As shown in Table 5, median nicotine concentrations in two U.S. studies of dust from non-smokers' homes were lower (120, 124) than those in two European studies (20, 123). Furthermore, the highest reported individual nicotine measurement from a non-smoker's home (125 μg/g) was reported in Denmark (20), a country with a high smoking prevalence (32.0%) (121). Likewise, the lowest reported background nicotine concentrations were from Californian residences (120) where smoking prevalence is only 14.3% (112). Interestingly, median nicotine concentrations measured in dust from smokers' homes were about 5-fold lower in the two U.S. studies (120, 124) than in the two European studies (20, 123).

Importance of residential dust as a source of exposure to tobacco constituents

Based on the 90th percentile concentrations of nicotine measured in dust from 34 homes, Hein *et al*. (20) concluded that inhalation of residential dust constitutes only a modest source of tobacco smoke constituents. The authors estimated that individuals

in smoking homes might inhale 12 ng of nicotine per hour compared to the 600-3000 ng of nicotine inhaled per hour by active smokers (20). However, Hein *et al*. did not consider that certain individuals (especially young children) are also exposed to residual tobacco smoke contamination via dust ingestion and dermal contact.

Researchers have measured matched samples of nicotine in dust and cotinine (a metabolite of nicotine) in urine and reported positive associations between subjects' environmental and biological levels of these markers of tobacco exposure (120, 122, 123). Notably, Willers *et al.* found that residential-dust concentrations of nicotine were highly correlated with urinary cotinine concentrations (r_S = 0.93, N = 13) in children exposed to cigarette smoke (123).

Determinants of nicotine levels in residential dust

Researchers have consistently reported positive relationships between subjects' self-reported smoking habits and the nicotine concentrations in their residential dust (20, 122-124). Specifically, Hein *et al*. (20) reported a positive correlation between nicotine dust concentrations in 34 homes and the mass of tobacco smoked per day by their residents (r = 0.35). Likewise, Kim *et al*. (124) found that residential-dust nicotine concentrations were positively correlated with the number of cigarettes smoked by residents in 37 homes (r_S = 0.67).

Researchers have also shown that dust nicotine concentrations can be indicative of thirdhand tobacco smoke (120, 122). Matt *et al*. (122) showed that parents who smoked cigarettes outdoors could transport nicotine (and presumably other tobacco constituents) into their homes on skin and clothing. Subsequently, the same group found that nicotine (and presumably other tobacco constituents) could persist in the dust of apartments that were formerly occupied by smokers (120). As such, both ex-situ smoking and former-smoking residents may impact nicotine concentrations in residential dust.

Aside from the smoking habits of current and former residents, one determinant of nicotine concentrations in dust may be the size of the residence. Hein *et al*. (20) reported that residence square footage was negatively associated with resdential-dust nicotine concentrations; that is, smaller residences had higher concentrations of nicotine in their dust than larger residences.

Goals of this dissertation given the state of the science of chemical measurements using residential-dust samples

Residential dust appears to be an important source of direct exposure to PBDEs and PAHs, especially for young children due to their hand-to-mouth behavior. In fact, dust exposure may be the dominant source of PBDEs (*i.e.*, >50% of total PBDE intake) for individuals from North America and Asia (13-16). Likewise, inadvertent dust ingestion could be responsible for a large proportion of overall intake of the less volatile PAHs (5-ring and 6-ring compounds), including those PAHs considered to be carcinogenic (18, 19). Although dust exposure appears to play a less important role in the intake of PCBs and tobacco smoke constituents, young children can still receive a substantial portion of their chemical intake via residential dust (17, 120). These findings support the use of residential dust as a medium to measure chemical exposures in epidemiological studies, particularly those focusing on childhood diseases.

Dust levels of PBDEs and PCBs appear to vary geographically based on historic patterns of production and use of these chemicals. Likewise, concentrations of PAHs in residential dust appear to vary across the U.S. due to geographic differences in traffic density and, possibly, the use of coal-tar for sealing pavement. However, aside from geographic location, researchers have had only limited success in finding determinants of chemical levels in residential dust. Even when collecting comprehensive survey information about residence characteristics, investigators have failed to identify strong predictors of chemical levels in dust (60, 80, 105).

Given the relative paucity of data regarding dust contaminants in California, one objective of this dissertation will be to use data from the NCCLS to compare dust concentrations of chemical contaminants (PBDEs, PCBs, PAHs, and nicotine) measured in California homes to levels reported in other studies from around the world. Additionally, since past investigators have failed to identify strong predictors of chemical levels in residential dust, this dissertation will employ the extensive self-reported information collected by the NCCLS to further investigate possible determinants of the concentrations of nicotine, PAHs, and PCBs in residential dust. Finally, since there is limited information regarding how concentrations of nicotine, PAHs, and PCBs vary across time and space within a residence (30, 55, 57, 111), this dissertation will characterize the variability of dust measurements within and between residences. This dissertation will conclude with a discussion of the benefits and limitations of residential-dust measurements for estimating chemical exposures, and suggestions for future research.

CHAPTER 2.

A METHOD FOR MEASURING POLYBROMINATED DIPHENYL ETHERs, POLYCHLORINATED BIPHENYLs, AND POLYCYLIC AROMATIC HYRDROCARBONs IN RESIDENTIAL-DUST SAMPLES

Introduction

As documented in Chapter 1, concentrations of chemicals in residential dust may be useful surrogates for chemical exposures in epidemiological studies. Chapter 2 describes a method developed in collaboration with investigators at the California Department of Toxic Substances Control laboratories that is being used to measure the PBDEs, PCBs, and PAHs in dust samples obtained from NCCLS households.

Methods

Northern California Childhood Leukemia Study design

The NCCLS is an ongoing case-control study conducted in the San Francisco Bay area and California Central Valley where cases aged 0-14 years are ascertained from nine pediatric clinical centers. Controls, matched to cases on date of birth, gender, race, and Hispanic ethnicity, are selected from the California birth registry (6). To date, two rounds of dust collection have been conducted to obtain information about chemical contamination in study homes. Initially, cases and controls aged 0-7 years that were living at the home they occupied at the time of diagnosis (and a similar reference date for controls) from December 1999 through November 2007 were eligible for dust collection. Among 731 subjects determined to be eligible, 629 subjects (86%) participated in this first round of dust collection from 2001-2007. Dust samples were initially collected by interviewers using the high volume surface sampler (HVS3), but in some study homes, interviewers collected the contents of household vacuum cleaners during in-home visits instead. Dust sampled during the initial collection period was analyzed for PAHs, PCBs, and nicotine at the Battelle Memorial Institute laboratories in Columbus, Ohio using methods described in Chapters 3-5. Surplus dust was stored at the Battelle lab in 2g aliquots at -20^{oc} until 2010.

In 2010, subjects participated in a second round of dust collection, where they were asked to remove the contents of their household vacuum cleaner (usually as an intact vacuum bag), place the contents in a sealable polyethylene bag, and ship the bag to a study center in Berkeley, CA in a prepaid package. To be eligible for this second round of dust collection, cases and controls needed to be living in the same home that they occupied during the first round of dust collection (and by extension, the same home they occupied at diagnosis). Thus, by design, dust collection in the NCCLS was limited to stationary residents. NCCLS interviewers attempted to contact 355 subjects that were potentially eligible for repeated dust collection, of those 270 households were confirmed to be eligible, 216 households agreed to participate in repeated dust

collection, and 204 households successfully mailed their vacuum cleaner dust to the NCCLS study center.

Figure 5 shows a schematic representation of the NCCLS dust analysis plan. For each residence, the initial dust sample (collected from 2001-2007 and subsequently archived in the Battelle Memorial Institute) was shipped to Dr. Rappaport's lab on the UC Berkeley campus in 2010. Dust samples from both collection rounds were analyzed for PBDEs, PCBs, and PAHs at the California Department of Toxic Substances Control (CA DTSC) in Berkeley, California using the method described in this chapter. Analyses in Chapter 6 are based on dust samples that were analyzed at the CA DTSC lab using the method described in this chapter. Analyses in Chapters 3-5 are based on dust samples that were analyzed at the Battelle Memorial Institute using methods described in subsequent chapters.

Written informed consent was obtained from all NCCLS children's parent or legal guardian in accordance with the Institutional Review Boards' requirements at the University of California, Berkeley and all other participating institutions.

Dust processing

Dust samples (from both collection rounds) were first sieved to remove debris larger than 150μm. For dust samples collected during 2010, household vacuum cleaner bags were cut open using pre-cleaned scissors and random portions of dust and debris were placed on a set of sieves containing from top-to-bottom: a lid, a No. 3½ sieve, a No. 100 sieve, and a collection pan (ELE International, Loveland, CO). Using a Ro-Tap test sieve shaker (W.S. Tyler, Mentor, OH) the dust was fractionated and homogenized for a period of 10 minutes. The sieve shaking was repeated with additional portions of the vacuum bag contents until 25 g of fine dust was collected. Between samples, sieves were brushed, hand-cleaned using pre-cleaned tweezers, rinsed with water, dried, and rinsed with a hexane:methylene chloride mixture (1:1). To avoid contamination, it was critical that these "dirty" processing steps took place in an isolated lab within a dedicated hood which had a separate ventilation system. Dust samples collected from 2001-2007 were sieved similarly.

Dust extraction and purification of analytes

A quantity of 0.2 g of fine dust was spiked with a mixture of isotopically labeled standards (8 PBDEs, 15 PCBs, and 1 PAH, see Table 6). The dust was placed in an 11-mL cell filled with hydromatrix (Varian, Palo Alto, CA), an inert diatomaceous earth sorbent used as a bulking agent, and extracted by accelerated solvent extraction using an ASE 200 (Dionex, Sunnyvale, CA). The extraction employed a solvent mixture of hexane:methylene chloride (95:5) with one heating and five static cycles at 100℃ and 1500 psi. Each sample extraction took 30 minutes and produced a 40 mL extract.

The extract was initially purified via silica gel chromatography. Each 100 mL chromatography column was filled sequentially with 1 cm^3 of deactivated glass wool (Alltech, Deerfield, IL), 0.25 g of deactivated sodium sulfate (EMD Chemicals, Darnstadt, Germany), 25 mL of hexane, 7.5 g of deactivated 70-230 μm mesh silica gel (Thermo Fisher Scientific, Waltham, MA), and another 0.25 g of deactivated sodium sulfate. Subsequently, excess hexane was drained to the level of the column's upper surface and the extract was poured onto the column. Target analytes were eluted using

100 mL of a hexane:methylene chloride mixture (1:1). The eluate was concentrated to 700 μL using a TurboVap evaporator (Caliper Life Sciences, Hopkinton, MA) and added to a full extraction vial using a Pasteur pipette.

The concentrated eluate was additionally purified using gel permeation chromatography (Envirogel GPC cleanup columns, Waters, Milford, MA). This additional purification step removed large molecules (*i.e*., proteins and lipids) that would otherwise interfere with chemical analysis. After this second purification, the sample was concentrated using a RapidVap/RapidTrap evaporator (Labconco, Kansas City, MO) to 250 μL. The sample was subsequently transferred to GC-MS vials using Pasteur pipettes and solvent-exchanged into 30 μL of tetradecane using a gentle stream of nitrogen. Then, the sample was spiked with a mixture of isotopically labeled recovery standards (2 PBDEs, 4 PCBs, 1 PAH, see Table 6) in 10 μL of tetradecane. For analysis of PBDEs, 4 μL of the 40 μL of concentrated sample was removed and diluted with 16 μL of tetradecane. The remaining 36 μL of the concentrated sample was split for analysis of PCBs and PAHs.

The protocol was designed for dust extraction and purification to optimize analyte recovery and to ensure quality GC-MS analysis. Table 7 shows various combinations of extraction and purification parameters that were evaluated during method development, as well as the parameters that were selected for the optimized protocol (see the bottom line of Table 7).

Chemical analysis

Twenty-two PBDE congeners were measured using isotope dilution high resolution gas chromatography-high resolution mass spectrometry (HRGC-HRMS, MAT95, Thermo Fisher Scientific, Waltham, MA) equipped with DB-5 column (15 m × 0.25-mm i.d., 0.1-μm film thickness, Agilent , Santa Clara, CA) and operated in electron impact ionization-selective ion monitoring (EI-SIM) mode. For PBDEs, pulsed splitless injection (0.5 μL) was at 30 psi and 250℃. Molecular ions were monitor ed to identify tri- to penta-BDEs, and M-2Br ions identified hexa- to deca-BDEs (see Table 6). Fifteen PCB congeners were measured using isotope dilution HRGC-HRMS equipped with RTX_Dioxin2 column (60 m × 0.25-mm i.d., 0.25-μm film thickness, Restek, Bellefonte, PA) and operated in EI-SIM mode. For PCBs, pulsed splitless injection (1 μL) was at 270℃. Molecular ions were monitored for all target P CBs (see Table 6). Twelve PAHs were measured using GC-MS (Agilent 6890/5973, Santa Clara, CA) equipped with DB-5 column (60 m × 0.25-mm i.d., 0.25-μm film thickness, Agilent , Santa Clara, CA) and operated in EI-SIM mode. For PAHs, pulsed splitless injection (2 μL) was at 275℃. Molecular ions were monitored for all target PAHs (see Table 6). Figures 6-8 show representative chromatograms obtained in the analyses of PBDEs, PCBs, and PAHs, respectively.

Quality control

Several steps were taken to ensure the quality of the results that will be generated using the newly developed method for measuring chemical contaminants in dust. First, the new method was tested for external validity. Subsequently, with each batch of 9 dust samples, a duplicate sample, a method blank, and a quality control

sample were prepared and analyzed. With a few exceptions, the method was accurate and precise. Notably, BDE-209 measurements appear to be relatively inaccurate and imprecise and method blanks were prone to contamination from BDE-209 and from volatile PAHs.

External method validation

The National Institute of Standards and Technology Standard Reference Material (NIST SRM) No. 2585 was used to test the accuracy of the method in replicate samples. NIST SRM 2585 is 10 g of residential dust that naturally contains PAHs, PCBs, and PBDEs, for which NIST has provided certified concentrations expressly for use in evaluating analytical methods. Table 8 shows the concentrations of 8 replicate NIST SRM 2585 samples that were measured using the method described above, compared to the certified NIST concentrations. For BDE-47, BDE-100, and BDE-154, each of the replicate concentrations was within 15% of the NIST certified value. For all PBDEs analyzed (except BDE-209), the average concentration from 8 replicate samples was within 30% of the certified concentration. Concentrations of BDE-209 were more variable and less accurate. PCB concentrations for 6 NIST SRM 2585 replicates were also rather variable, however, for each of the PCBs analyzed (except PCB-28) the average concentration from 6 replicate samples was within 30% of the certified concentration. For benzo(*a*)anthracene, benzo(*b*)fluoranthene, benzo(*a*)pyrene, and benzo(*g,h,i*)perylene each of the replicate concentrations was within 25% of the NIST certified value. For all PAHs analyzed [except phenanthrene, anthracene, and dibenzo(*a,h*)anthracene], the average concentration from 6 replicate samples was within 30% of the certified concentration. The measured replicate concentrations of PCB-28, phenanthrene, and anthracene were consistently lower than the certified values, possibly indicating that these more volatile contaminants were lost from the reference dust after NIST certification. Still, despite these rare inconsistencies, the method for measuring contaminants in dust generally yielded accurate results for the external quality control sample and the method was considered valid for the analysis of dust samples from study homes.

Method blanks and limits of quantitation

Samples can be contaminated in a multitude of ways, including via cross contamination between samples (*i.e.*, dirty glassware or pipettes, etc.), via ambient contamination from laboratory (*i.e*., dirty air or bench tops), or via contaminated surfaces within instruments (*i.e*., dirty syringe or injection liner, etc.). As such, it is important to monitor the extent of potential sample contamination by analyzing method blanks with each sample batch. Method blanks were treated identically to samples at each stage of the procedure (*i.e.*, extraction, clean-up, and analysis), except that extraction cells for method blanks contained only the bulking agent and corn oil (to facilitate the recovery of isotopically-labeled standards), whereas the sample extraction cells contained 0.2 g of dust and the bulking agent. To date, 13 method blanks have been analyzed along with residential-dust samples; Table 9 shows the mass of each chemical measured in each method blank. A method reporting limit (MRL) equal to 3 times the standard deviation of the method blanks was calculated for each chemical. For the 49 chemicals analyzed, PCB-114 and PCB-189 had the lowest method

reporting limits; each limit for these two PCBs was set to the limit of quantitation (LOQ = 50 pg per sample). The chemicals with the highest method reporting limits were phenanthrene and fluoranthene (MRL = 188 and 37 ng per sample, respectively). Given a typical sample mass of 0.2 g of dust, it is possible to estimate the minimum reportable concentration (MRC) for each of the analytes. Given the concentrations of PBDEs that have been recently reported in other studies from the U.S. (Table 2), most of the PBDE method reporting limits should be adequate. The method reporting limit for BDE-209 is relatively high and it may result in some data censoring (*i.e*., concentrations of BDE-209 from some homes may be below the method reporting limit). Given the concentrations of PCBs that have been recently reported from homes in California (5), it is possible that the PCB method reporting limits may result in some data censoring (*i.e*., concentrations of major PCBs from some homes will be below the method reporting limit). Given the concentrations of PAHs that have been recently reported in other studies from the U.S. (Table 4), the method reporting limits for less volatile PAHs [benzo(*a*)anthracene, chrysene,benzo(*b*)fluoranthene, benzo(*k*)fluoranthene, benzo(*a*)pyrene, indeno(*1,2,3-c,d*)pyrene, dibenzo(*a,h*)anthracene, benzo(*g,h,i*)perylene] should be adequate. However, relatively high amounts of the more volatile PAHs (phenanthrene, anthracene, fluoranthene, pyrene) have been found on the method blanks. In general, these results indicate that the method is subject to acceptable levels of contamination.

Duplicate samples

The intra-batch reproducibility of the analytical method was tested using duplicate samples. In this case, “duplicate” refers to two distinct 0.2-g sub-samples taken from a common sample of homogenized fine dust collected from a single vacuum cleaner. To date, 12 sets of duplicate samples have been analyzed along with each batch of residential-dust samples. For each chemical analyzed, Table 10 shows the relative percent difference between duplicate samples from each run. The average relative percent difference between duplicate samples ranged from 3-61% for PBDEs, from 12-40% for PCBs, and from 9-23% for PAHs. For the major PBDE congeners (*i.e.*, for BDE-47, BDE-99, BDE-100, BDE-153, BDE-154, BDE-206, and BDE-209) the average relative percent difference between duplicate samples was less than 10%. Likewise for most major PCB congeners (*i.e.*, for PCB-101, PCB-118, PCB-138, PCB-153, and PCB-180) the average relative percent difference between duplicate samples was no more than 20%. For all but one PAH [except dibenzo(*a,h*)anthracene] the relative percent difference between duplicate samples was less than 20%. These results indicate that the method has acceptable intra-batch reproducibility.

Inter-batch quality control samples

The inter-batch reproducibility of the analytical method was tested by repeatedly analyzing the same quality control dust sample alongside each batch of samples. The quality control dust was obtained from a single vacuum cleaner and a 0.2-g sub-sample of the homogenized fine quality control dust was analyzed with each set of 9 samples. Thus, the chemical concentrations measured in the inter-batch quality control samples should remain relatively constant over the course of the study. Poor inter-batch reproducibility could be indicative of instrument drift (*i.e*., the GC-MS is not providing

consistent results over time), inconsistent dust preparation, sample contamination, or improper dust storage (*i.e*., exposing the quality control sample to heat or light and thereby altering chemical concentrations).

To date, 12 inter-batch quality control samples have been analyzed along with each batch of residential-dust samples. For each chemical analyzed, Table 11 shows the coefficient of variation (CV = ratio of the standard deviation to the mean) for the 12 runs. The coefficient of variation ranged from 0.09-2.18 for PBDEs, from 0.02-0.73 for PCBs, and from 0.10-1.30 for PAHs. For most of the major BDE congeners (*i.e.*, for BDE-47, BDE-99, BDE-100, BDE-153, and BDE-154), the standard deviation from the 12 runs was less than 15% of the mean, indicating good inter-batch reproducibility. However, concentrations of BDE-209 (and its breakdown product BDE-206) were more variable in the quality control samples (CV = 0.38, 0.57, respectively). It is not clear whether the lack of reproducibility is due to analytical errors or due to the physical distribution of BDE-209 amongst dust particles. For most of the major PCB congeners (*i.e*., for PCB-101, PCB-118, PCB-138, and PCB-153), the standard deviation from the 12 runs was no more than 30% of the mean, indicating adequate inter-batch reproducibility. For most PAHs (aside from phenanthrene, anthracene, and fluoranthene), the standard deviation from the 12 runs was less than 30% of the mean. It is likely that the large variability in concentrations of phenanthrene and fluoranthene were due, at least in part, to contamination, as method blank levels of phenanthrene and fluoranthene were also highly variable from run-to-run.

Recovery of internal standards

Isotopically-labeled internal standards (9 PBDEs, 15 PCBs, and 1 PAH) were added to dust samples before chemical extraction and complimentary isotopically-labeled recovery standards (2 PBDEs, 3 PCBs, and 1 PAH) were added to dust samples immediately prior to chemical analysis. By comparing the magnitude of the signals for the internal standards with the magnitude of the signals for the recovery standards, it is possible to estimate the percent of each internal standard that was recovered for analysis. Internal standard recovery is a surrogate for sample recovery and monitoring internal standard recovery is another quality control measure. Table 12 shows the percent recovery for each internal standard for each of 12 inter-batch quality control samples. The average internal standard recovery over the course of 12 samples ranged from 55-97% for PBDEs (excluding BDE-209L), from 57-81% for PCBs, and average recovery was 69% for benzo(*a*)pyrene-L. Internal standard recovery for BDE-209L was highly variable and consistently greater than 100%. Aside from BDE-209, internal standard recovery (and by extension, sample recovery) was adequate.

Discussion

There were two goals in developing this analytical method; namely, accuracy and precision. Accuracy ensures external validity and allows for comparison to findings from other studies. Precision ensures that measured concentrations are representative of their true values and thereby prevents the misclassification of exposure. To ensure accuracy and precision, several quality control measures were employed. Firstly, the validity of the method was tested using the NIST SRM 2585 and found to be accurate. Subsequently, the accuracy of the results was confirmed by the use of method blanks

and quality control samples. Precision was evaluated using duplicate samples (intra-batch reproducibility) and quality control samples (inter-batch reproducibility). Both of these aspects of quality control provide estimates of the magnitude of error introduced by the analytical method – an important consideration when interpreting the final results of any health study based on these measurements.

Quality control assessments revealed several limitations of the analytical method. Specifically, BDE-209 measurements appear to be relatively inaccurate (based on NIST SRM 2585 testing) and imprecise (based on inter-batch quality control testing). Moreover, method blanks were prone to contamination from BDE-209. Likewise, samples were prone to contamination from volatile PAHs (phenanthrene, anthracene, fluoranthene, pyrene) and as a result, measurements of these 4 PAHs were imprecise in repeated quality control testing. It is important to consider the quality of the data when reporting results and interpreting findings.

One advantage of the method described above is its ability to analyze PBDEs, PCBs, and PAHs using a single extraction and clean-up procedure. Of course, the benefits of such an efficient protocol are savings in time and money. The disadvantage is that the method is not optimized (in terms of sample recovery) for any of three chemical classes, individually. Additionally, the method cannot be used to analyze nicotine.

CHAPTER 3.

DETERMINANTS OF NICOTINE CONCENRATIONS IN RESDENTIAL DUST[2]

Introduction

The International Agency for Research on Cancer (IARC) concluded that active tobacco smoking causes cancer of the lung, oral cavity, pharynx, nasal cavity and paranasal sinuses, larynx, esophagus, stomach, pancreas, liver, kidney, ureter, urinary bladder, uterine cervix and bone marrow (119). Additionally, IARC asserted that involuntary smoking (exposure to secondhand smoke) also causes lung cancer (119). More recently, it has been suggested that involuntary smoking might contribute to the risk of childhood leukemia (6). Beyond active and secondhand smoking, individuals may be exposed to carcinogenic tobacco constituents which contaminate hair, clothing, furniture and dust particles (so called 'thirdhand' tobacco smoke) (120). Young children are at particular risk from exposure to thirdhand tobacco smoke due to their hand-to-mouth behavior (120).

Epidemiologists generally rely on self-reported smoking histories when investigating the health effects of tobacco smoke. It is generally assumed that self-reported smoking information is reliable, and, indeed, validation studies using nicotine-specific cotinine biomarkers as "gold" standards have shown that only about 5% of professed non-smokers are actually smokers (125-127). However, deception rates as high as 25% have been observed when parents report their smoking habits in studies involving their children's health (128, 129). Thus, in studies of children's health, the use of self-reports could result in substantial misclassification of children's true exposures to cigarette smoke and introduce bias in the exposure-response relationship (130). As such, investigators from the NCCLS who are investigating the potential association between childhood leukemia and parental smoking (6), have a particular interest in developing unbiased measures of cigarette smoke exposure.

To reduce misclassification of exposure to cigarette smoke, it is beneficial to use an objective measure of exposure such as nicotine in indoor air (131), cotinine in urine (132), or nicotine in hair (133). Alternatively, researchers have suggested using nicotine levels in residential dust as surrogates for in-home exposures to cigarette smoke (20, 122-124). Indeed, previous research has shown that nicotine concentrations in residential dust are highly correlated with children's levels of urinary cotinine (r_S = 0.93, N = 13) in smoking households (123). However, previous investigations of nicotine levels in residential dust involved small numbers of households (N = 72, 49, 23, and 37 respectively) and were unable to thoroughly examine the determinants of nicotine concentrations in residential dust (20, 122-124).

[2] A similar version of this manuscript has been published: Whitehead T, Metayer C, Ward MH, Nishioka MG, Gunier R, Colt JS, Reynolds P, Selvin S, Buffler P, Rappaport SM (2009). Is House-Dust Nicotine a Good Surrogate for Household Smoking? *American Journal of Epidemiology*. 169(9):1113-23. Oxford University Press.

Chapter 3 reports results from 469 households for which nicotine was measured in residential dust and where extensive questionnaire data, including smoking habits, were also obtained from residents. This chapter also compares levels of nicotine in residential dust to self-reported smoking at various times before and during the child's life, and identifies determinants of levels of nicotine in residential dust. Although this information is directly relevant to researchers considering the effect of parental smoking on childhood leukemia risk, it should also be pertinent for any epidemiologic study that seeks to quantify exposure to cigarette smoke.

Methods

Study population

From 2001-2007, dust samples were collected from 629 households participating in the NCCLS (see Chapter 2 for NCCLS details), nicotine was analyzed in dust samples from 469 residences.

Residential-dust collection

Residential-dust samples were collected using a high-volume surface sampler (HVS3) or household vacuum cleaners, as previously described (31); data from both methods were used in the statistical analyses of this chapter. Briefly, for HVS3 samples, parents were asked to identify the room (other than the kitchen or the child's bedroom) in which the child spent the most time while awake. For most subjects, this was the living room or family room. The interviewer marked an area (~2 m^2) with tape and vacuumed the surface in 8-cm strips, making four passes back and forth on each strip, until 10 mL of dust had been collected. In HVS3-sampled homes, the area of the carpet sampled was a variable that could be included in statistical analyses. The HVS3 sampling train was cleaned with isopropyl alcohol and dried between uses at each home. Although HVS3-sampled dust was collected initially, household vacuum-cleaner dust was substituted starting in 2006.

Nicotine analysis

For nicotine analyses, each 0.5-g portion of fine (<150μm) dust was spiked with 250 ng of d_4-nicotine, extracted by ultra-sonication in methylene chloride, concentrated, and analyzed using a GC-MS in the multiple ion detection mode. The GC analysis employed a DB-1701 column (30 m, 0.25-mm id, 0.15-μm film), that was programmed from 130 to 220℃ at 2℃/min, and then from 220 to 280℃ at 10℃/min. Dibromobiphenyl was used as an internal standard; a 9-point calibration curve (range: 2-750 ng/mL) and a zero-level standard were analyzed with each sample set [12 field samples, a duplicate, a duplicate spike (250 ng), and a solvent method blank]. To correct for variable nicotine recovery on a sample-by-sample basis, d_4-nicotine was used as a surrogate recovery standard (SRS). Recoveries of nicotine and d_4-nicotine in spiked samples were 57 ± 45% and 59 ± 45%, respectively. The median relative percent difference for duplicates was 17% after SRS correction.

Self-reported smoking

Parents, primarily the mother (97%), responded to two sets of questionnaires, each with inquiries about smoking habits, as outlined in Figure 9. The initial interview ascertained the smoking status of the mother, father, and others in the household at several time points of interest. Additionally, the first interview asked the respondent for the number of cigarettes smoked per day for some but not all of the time periods. A subsequent interview at the time of dust collection ascertained the total number of cigarettes smoked per day inside the residence during the previous month. This additional question dealt specifically with smoking inside the home and was, therefore, expected to correspond to the concurrent residential-dust nicotine measurements. However, responses from the first interview were also considered as potential determinants of the concentrations of nicotine in residential dust, because nicotine is known to persist indoors (134) where it is protected from degradation by moisture, sunlight, and microbial action.

Statistical analysis

Because the distribution of nicotine in residential dust was highly skewed, the nonparametric Kruskal-Wallis one-way analysis of variance (KW ANOVA) was used to compare the distribution of nicotine in residential dust between various groups throughout the analysis. The data had an approximate log-normal distribution, so the natural log of the concentration was used in all analyses involving the continuous variable. Residential-dust nicotine measurements below the limit of detection, *i.e.*, 20 ng/g, (N = 53, 11% of residences) were assigned a value of one-half the limit of detection. Pairwise correlation coefficients between the natural log-transformed residential-dust nicotine concentrations and self-reported cigarette consumption (as well as other variables of interest) were estimated. Although Pearson correlation coefficients are reported, results were similar when using Spearman rank coefficients.

Seven groups of variables were considered for inclusion in the residential-dust nicotine regression models: self-reported smoking, parental demographics, residence characteristics, child-specific variables, sampling conditions, time effects, and ethnicity (see Table 13 for full list of variables considered). Groups of highly correlated variables were analyzed by principal components analysis to produce simpler, but meaningful, summary measures of the variables within these groups for inclusion in the final residential-dust nicotine regression models (135). The remaining groups of candidate variables were modeled individually using backwards elimination ($P < 0.10$) to identify other variables used in the final models. In addition to main effects, significant interactions ($P < 0.10$) between self-reported smoking variables and parental demographic variables and between self-reported smoking variables and case-control status were included.

Using the variables identified in group screening, two subsequent regression analyses were performed with case and control households combined. The first analysis used all possible households regardless of the sampling method (both HVS3 and vacuum cleaner dust samples were used). The second analysis used only HVS3-sampled households; this analysis included size of sampling area, a variable that was only relevant in homes where HVS3 sampling was done.

Results

Nicotine in residential dust

The analysis included 233 cases and 236 controls with residential-dust nicotine measurements. Nicotine was detected in 89% (416 of 469) of the residences. The nicotine concentrations ranged from not detected (less than 20 ng/g) to a maximum of 35,000 ng/g, with a median value of 265 ng/g and an interquartile range between 96 and 612 ng/g. Table 14 shows the prevalence of smoking during various time periods, the median concentration of nicotine in residential dust for smokers and non-smokers in each category, and the *P*-value from the Kruskal-Wallis one-way ANOVA comparing the distributions of concentrations of nicotine from residences with smokers versus those residences without smokers. Significant differences in concentrations of nicotine in residential dust were observed for all self-reported smoking categories.

Univariate analysis

Pearson correlation coefficients for covariates of interest (those that were continuous and significantly correlated with the log-transformed residential-dust nicotine concentrations) are shown in Table 15. The group of smoking variables was highly correlated as was the group of parental demographic variables, whereas the two groups of variables were negatively correlated with each other. Other variables correlated with residential-dust nicotine were age of residence, breastfeeding duration, size of sampling area (HVS3 dust samples only), and vacuum use frequency.

Principal components analysis

Tables 16 and 17 show the results of the principal components analysis for the two groups of highly correlated variables, *i.e.*, self-reported smoking and parental demographics. Three meaningful factors were chosen to represent the 15 self-reported smoking variables and 2 factors were chosen to represent the 5 parental demographic variables. A variable was said to load on a given component if the factor loading was 0.40 or greater (135). Using this criterion, 12 variables describing parental smoking were found to load on the first smoking component, which was subsequently labeled the parental smoking component. Similarly, the 4 father's smoking variables loaded on the second smoking component (father smoking component) and 3 variables, describing other household smoking, loaded on the third component (other household smoking component). Combined, the smoking-related principal components accounted for 65% of the total variance of all smoking variables. The demographic variable group, shown in Table 17 was described by a parental socioeconomic status (SES) component, which was loaded by parental education and income, and a parental age component, which was loaded by the mother's age and father's age. Combined, the summary demographic principal components accounted for 80% of the total variance explained by all demographic variables.

Multivariable regression models

For the model with all homes (Table 18), 13 variables were identified based on *a priori* screening of groups of variables for significant associations with logged residential-dust nicotine concentrations. The variables are ordered in Table 18 by their

significance in the final model. Two significant interactions between the parental SES component and the father smoking component and between the parental age component and father smoking component were included. After adjustment for the model degrees of freedom, the overall model fit was $R^2_{adj} = 0.31$. Table 19 shows predicted concentration of nicotine in residential dust for various combinations of smoking scenarios and parental demographics based on the model with all homes.

Restricting the analysis to only HVS3-sampled homes (and including the variable size of sampling area), yielded a model with similar regression coefficients and *P*-values (Table 18, HVS3 Homes). The variable size of sampling area was significant in the model with only HVS3-sampled homes.

Discussion

Several determinants of concentrations of nicotine in residential dust were identified (Table 18). Notably, two principal components summarizing self-reported smoking variables (parental and father smoking components) were highly significant predictors of residential-dust nicotine in the final models ($P < 0.0001$). These principal components represented self-reported smoking for time periods of months and years before dust collection. Based on the regression model results, nicotine concentrations in residential dust seem to reflect cumulative smoking habits of residents over periods of up to several years rather than simply the current smoking pattern in the home.

To verify the hypothesis that levels of nicotine in residential-dust samples reflect past smoking habits, it was useful to examine NCCLS households that reported changes in their smoking status between the initial interview and dust collection. Of the households that reported no smoking in the month before dust collection, 90 households (21%) had previously reported some smoking at the initial interview. Nicotine concentrations in residential-dust samples from these 90 households did, indeed, remain elevated (median 681 ng/g vs. 201 ng/g for consistently smoke-free homes, KW ANOVA $P < 0.0001$). This finding suggests that nicotine (and other harmful tobacco smoke constituents) may contaminant homes long after cigarette smoking has ceased, a phenomenon referred to as “thirdhand smoke”. In fact, investigators have reported that children living in apartments that were formerly occupied by smokers had elevated levels of residential-dust nicotine and urinary cotinine (120).

Additionally, of the NCCLS households that reported some smoking at the time of dust collection, 5 (24%) reported no smoking at the initial interview. These 5 households had lower concentration of nicotine in residential dust than households that consistently reported smoking (median 314 ng/g vs. 1,730 ng/g, KW ANOVA $P = 0.22$). Both of these findings support the conjecture that current concentrations of nicotine in residential dust may be particularly good measures of cumulative household smoking habits. Furthermore, these findings suggests that, in studies that aim to estimate prenatal or postnatal cigarette smoking exposures retrospectively, concentration of nicotine in residential dust could be a more useful surrogate than short-term exposure markers such as concentrations of nicotine in air or of cotinine in urine.

After considering self-reported smoking, the age of the residence was a significant predictor of concentrations of nicotine in residential dust. Since concentrations of nicotine in residential dust increase with the age of the residence,

nicotine evidently accumulates in household carpets. Thus, nicotine concentrations in residential dust likely reflect cumulative smoking habits in a household.

Two measures of parental demographics, namely, the parental SES component and the parental age component, remained significant predictors of the concentrations of nicotine in residential dust, after accounting for self-reported smoking. Table 19 illustrates that, in general, after adjusting for self-reported smoking, concentrations of nicotine in residential dust decreased with increasing parental SES and age.

Interestingly, when considering the 211 households that reported no smoking at any time, the households with below median income had significantly higher concentration of nicotine in their residential dust than the households with above median income (median 279 vs. 113 ng/g, KW ANOVA $P < 0.0001$). Thus, even when no smoking was reported, low-income households had elevated concentrations of nicotine in their residential dust compared to high-income households. There are several possible explanations for the discrepancy in levels of nicotine in residential dust from self-reported non-smoking households: (a) low-SES residences may be physically different from high-SES residences, due to unmeasured differences in ventilation, carpet types, light, moisture or microbial action; (b) low-SES parents may be more likely to be exposed to passive cigarette smoke, and may convey nicotine into their homes on their skin or clothing; (c) low-SES households may be more likely to have residual nicotine in residential dust from previous residents; (d) low-SES households may use more smokeless tobacco products or; (e) low-SES households may have underreported their smoking habits. If differential self-reporting by SES or age is present, then an objective measure of exposure to household smoking, such as concentrations of nicotine in residential dust, would be advantageous.

Three other variables were significant predictors of nicotine concentrations in residential dust after adjusting for self-reported smoking and parental demographics, residence is apartment, residence is townhouse, and size of sampling area. Since apartments and townhouses generally have less square footage than single family homes, the positive regression coefficient for the variables residence is apartment and residence is townhouse are consistent with the observation of Hein *et al.* (20) who found that residential-dust nicotine concentrations increased with decreasing square footage of the residence. The negative regression coefficient for the variable size of sampling area in the final model with HVS3-sampled homes indicates that, as the size of carpet sampled increased, the concentration of nicotine measured in residential dust decreased. This relationship could be a limitation of the HVS3 sampling method and it suggests that this variable should be measured and adjusted for in models of residential-dust nicotine concentrations using HVS3 sampling. Still, including size of sampling area in the regression model had little effect on the other parameters.

Given that the ultimate purpose of the NCCLS is to compare leukemia cases and controls, the effect of case-control status on measured nicotine concentration was examined. Interestingly, case-control status was not a significant predictor of nicotine concentrations and there was no indication that case parents were reporting their smoking differently than controls (data not shown). This finding suggests that there was little differential misclassification of exposures in case and control households in the previous analysis of self-reported cigarette smoking in the NCCLS population (6).

The concentrations of nicotine measured in dust from smoking and non-smoking NCCLS residences (Table 14) were lower than those previously reported (Table 5). Specifically, the median concentrations of nicotine for self-reported non-smoking NCCLS homes (as reported for the month before dust collection) was 0.3 μg/g, substantially lower than median levels reported for non-smoking homes in previous studies (ranged from 2.9-20 μg/g). As discussed in Chapter 1, lower levels of background nicotine contamination might be explained by the low prevalence of smoking in California. Alternatively, these differences may partly reflect differences in analytical methodology. Despite the lower levels of nicotine measured in the NCCLS, the nicotine concentrations in residential-dust samples were correlated with concurrently self-reported household cigarette consumption (r_P = 0.29, in log scale).

Although concentrations of nicotine in residential dust are specific indicators of cigarette smoke contamination, the use of dust to assess children's exposure to secondhand cigarette smoke has limitations. First, it must be assumed that children are in the home when smoking occurs. This is a reasonable expectation given the young age of the children in the NCCLS (median 3.6 years at reference date). Secondly, it must be assumed that nicotine in residential dust originated from cigarettes smoked in the home. However, a previous study found that nicotine levels in residential dust were elevated in homes where parents reported only smoking outdoors compared to homes where parents reported no smoking (122). Thus, parents that are exposed to cigarette smoke (either active or passive) may convey nicotine into carpets, via their skin, clothing, or shoes without exposing their children to secondhand cigarette smoke. The risks of exposing children to residual tobacco smoke contamination (in the absence of active smoking or secondhand smoke exposure) are not well understood. Future studies should consider using a long-term biomarker of exposure to cigarette smoke, such as hair nicotine, to investigate the relationship between concentrations of nicotine in residential dust and the corresponding biological dose of nicotine in children.

Since parents may have tracked nicotine into their homes after smoking outside, the results of the residential-dust nicotine models may have been somewhat obscured. Specifically, the variable describing household cigarette consumption during the month before dust collection was specific to in-home smoking and it was a relatively weak predictor of nicotine concentrations in dust. In contrast, the highly significant parental and father smoking components were based on general smoking habits (reported for smoking inside and outside of the home, collectively). It is possible that the variable describing household cigarette consumption during the month before dust collection was a relatively weak predictor of nicotine levels, because outdoor smoking was excluded.

In summary, results reported in this chapter confirmed previous findings that concentrations of nicotine in residential dust were significantly associated with self-reported household smoking. Chapter 3 also presents evidence that residual smoke contamination (*i.e.*, thirdhand smoke), could persist in homes long after cigarette smoking ceased. Finally, these results suggest that concentrations of nicotine in residential dust can be used as long-term surrogates for exposures to cigarette smoke in the home.

CHAPTER 4.

DETERMINANTS OF POLYCYCLIC AROMATIC HYDROCARBON CONCENRATIONS IN RESDENTIAL DUST[3]

Introduction

Polycyclic aromatic hydrocarbons (PAHs) are formed as products of incomplete combustion and there are a variety of indoor PAH sources including cigarette smoke, wood-burning fireplaces, gas appliances, and charred foods, as well as outdoor sources, including vehicle exhaust (12) and coal-tar-based pavement sealants (106). Occupational exposures to PAHs have been associated with increased risks of lung, skin, and bladder cancers (136). Likewise, increased levels of PAH-DNA adducts have been associated with lung cancer (137) in the general population. Moreover, in-utero PAH exposures, as measured by maternal personal air monitoring during pregnancy, have been associated with IQ deficits (8), cognitive developmental delays (7), decreased gestational size (138), and respiratory effects (139, 140).

Surrogates of PAH exposure have been measured in several environmental and biological media, including air (141-143), residential dust (18, 19, 22, 94, 95, 110, 117, 144-146), urine (147-149), and blood (150, 151). Because chemicals can accumulate in carpets (23), concentrations of PAH in residential dust may be long-term predictors of indoor PAH exposures. Moreover, because inadvertent dust ingestion could be responsible for as much as 42% of non-dietary PAH exposure in young children (19), levels of PAHs in residential dust may be particularly relevant to the uptake of PAHs in children.

Although measurements of chemicals in residential dust are specific measures of indoor exposures, such data have rarely been collected in epidemiologic investigations. Rather, epidemiologists have classified potential exposures to chemicals based on self-reported information and/or ambient levels of chemicals measured at outdoor monitoring sites. Since self-reports and estimated outdoor air levels may not be good surrogates for indoor exposures, it is important to know the extent to which these indirect measures predict residential levels of environmental agents. Chapter 4 evaluates the predictive value of self-reported and geographic data in estimating measured levels of 9 PAHs in residential-dust samples.

[3] A similar version of this manuscript has been published: Whitehead T, Metayer C, Gunier RB, Ward MH, Nishioka MG, Buffler P, Rappaport SM (2011). Determinants of polycyclic aromatic hydrocarbon levels in house dust. *Journal of Exposure Science and Environmental Epidemiology*. 21(2):123-32. doi:10.1038/jes.2009.68.
Available at: http://www.nature.com/jes/journal/v21/n2/full/jes200968a.html

Methods

Study population

From 2001-2007, dust samples were collected from 629 households participating in the NCCLS (see Chapter 2 for NCCLS details), PAHs were analyzed in dust samples from 583 residences.

Residential-dust collection

Residential-dust samples were collected using a high-volume surface sampler (HVS3) or household vacuum cleaners, as previously described (see Chapter 3 for details); data from both methods were used in the statistical analyses of this chapter.

PAH analysis

The 9 PAHs analyzed were benzo(*a*)anthracene, chrysene, benzo(*a*)pyrene, benzo(*b*)fluoranthene, benzo(*k*)fluoranthene, indeno(1,2,3-*c,d*)pyrene, dibenzo(*a,h*)anthracene, coronene, and dibenzo(*a,e*)pyrene. For the PAH analyses, 0.5-g portions of fine (<150μm) dust were spiked with 250 ng of each of two surrogate recovery standards $^{13}C_6$-benzo(*k*)fluoranthene and $^{13}C_6$-dibenzo(*a,e*)pyrene. Dust samples were then extracted by ultra-sonication in 1:1 hexane:acetone, solvent exchanged into hexane, purified via solid phase extraction (using sequential elution of hexane, 15% diethyl ether in hexane, and methylene chloride on 1 g silica cartridges), concentrated to 1 mL, spiked with the internal standard d_{12}-benzo(*e*)pyrene, and analyzed using GC-MS in the multiple ion detection mode. The GC separation employed an RTx-5 MS column (30 m, 0.25-mm i.d., 0.25-μm film) that was programmed from 130 to 220 ℃ at 2 ℃/min, and then from 220 to 300 ℃ at 10 ℃/min. A 9-point calibration curve (range 2-750 ng/mL) and a zero-level standard were analyzed with each sample set [12 field samples, a duplicate, a duplicate spike (250 ng), and a solvent method blank]. The internal standard method of quantification was used, with linear least squares determination of the calibration curve. To correct for variable PAH recovery on a sample-by-sample basis, $^{13}C_6$-benzo(*k*)fluoranthene and $^{13}C_6$-dibenzo(*a,e*)pyrene were used as surrogate recovery standards. The average recoveries for the two surrogate recovery standards in the dust samples were 83±23% and 99±78% for $^{13}C_6$-benzo(*k*)fluoranthene (*N* = 583) and $^{13}C_6$-dibenzo(*a,e*)pyrene (*N* = 579), respectively. The average relative difference between analytes in duplicate samples was 27%.

Self-reported exposure surrogates

Parents participated in an in-home interview designed to ascertain information pertinent to childhood leukemia. A subset of questions that may be related to possible sources of indoor PAHs, including household heating appliances, household cooking practices, household cigarette smoking, and presence of an attached garage were selected for the analysis. Furthermore, effects of household characteristics (*i.e.*, residence age and type), sampling conditions (*i.e*., season, vacuuming frequency, sampling method, and sampling area), parental demographics (*i.e.*, parental age, education, income, and ethnicity), and child-specific variables (*i.e*., child's case–control

status, sex, and age) on PAH concentrations in residential dust were also considered (see Table 20 for full list of variables considered). .

GIS-derived exposure surrogates

A global-positioning-system device was used to determine the latitude and longitude coordinates for each residence. Subsequently, three surrogates for outdoor PAH concentrations: traffic density, modeled predictions of outdoor PAH concentrations, and urban or rural location were considered. Traffic density was estimated as described previously (152). Briefly, a 500-m radius was drawn around each residence and traffic density was defined as the sum of the annual average daily traffic count from 2000, multiplied by the length of the road for all roads within the buffer, divided by the buffer's area (153). The estimates of outdoor PAH concentrations were taken from the EPA's 2002 National-Scale Air Toxics Assessment (154). The outdoor PAH concentrations were estimated at a census-tract resolution using an air dispersion model and National Emissions Inventory data, which includes major stationary sources (*i.e.*, power plants), area sources (*i.e.*, commercial and residential emissions), and mobile sources (*i.e.*, automobiles and trucks). The estimated outdoor PAH concentration represented 7 of the 9 individual PAHs measured in the residential dust. Since both outdoor PAH estimates and traffic density were approximately log-normally distributed, their logged values were used for statistical analyses. The urban indicator variable was coded as either 1, for residences in census blocks classified as "urban" (population density of at least 1000 people per square mile); or 0, for those classified as "rural" or "other" by the 2000 U.S. Census (155).

Statistical analysis

As previously described (see Chapter 3), principal components analysis was used to summarize 15 highly correlated household cigarette smoking variables with 3 meaningful principal components (*i.e.*, parental, father-only, and other household smoking components). Likewise, five highly correlated parental demographic variables were summarized with two principal components (*i.e.*, parental age and socioeconomic status). Residence age, a categorical variable, was treated as a continuous variable by subtracting the mid-point year from the construction date range reported from the median year of dust collection (*i.e.*, if respondent reported a residence constructed between 1950-1959, residence age = 2004 -1955 = 49 years or 4.9 decades).

Pairwise correlation coefficients between the natural log-transformed residential-dust PAH concentrations and covariates of interest were estimated. Although Pearson correlation coefficients (of logged PAH levels) are reported, results were similar when using Spearman rank coefficients.

Multiple imputation of missing data

A multiple-imputation procedure was used to borrow information from available measurements to impute values for missing data. In simulation studies, multiple imputation has been shown to produce unbiased effect estimates and appropriate confidence intervals (156-158). The data had three types of missing data: missing residential-dust PAH values, residential-dust PAH values below the limit of detection, and missing covariate data. Overall, 70 (1.3% of N = 5247) residential-dust PAH

measurements were missing for 56 subjects. These PAH measurements were missing as a result of interference from co-eluting compounds during GC-MS analysis, which made detection of some individual PAHs impossible. In addition, there were 63 (1.2% of N = 5247) residential-dust PAH measurements below the limit of detection in 44 participant households. Finally, 246 (42%) of the subjects had at least one missing covariate, because respondents were either unable or unwilling to complete all of the survey questions (*i.e.*, respondent answered "don't know").

Because the 9 individual PAHs were correlated in the data, the multiple imputation strategy was particularly useful. Specifically, using Proc MI (SAS v.9.1, Cary, NC) the joint multivariate normal distribution for the 9 correlated PAHs was estimated. Then, for each missing value, a probability distribution was created conditional upon the values for the non-missing PAHs (generally the 8 other PAHs). Next, five possible imputations for the missing value were randomly drawn from the conditional probability distribution bounded so that each of the randomly drawn values was greater than the limit of detection. The random sampling addressed uncertainty due to missing values and resulted in more valid statistical inferences than single imputation. Additionally, the relative magnitude of missing PAH estimates reflected the profile of the corresponding non-missing PAHs for the same subjects.

A similar procedure was used to estimate five possible values for each PAH measurement below the limit of detection and each missing covariate of interest. Covariate imputation was based on the distribution of non-missing covariates only. Again, logical bounds were set on the randomly selected values so that the estimates were reasonable (*i.e.*, gas heating must be assigned as 0 or 1 and all estimates for measurements below the limit of detection must be less than the detection limit). Ultimately, five complete data sets were created with five imputed values for each of the three types of missing data. Regression analyses were performed separately on each data set (as described below) and the results were combined to produce inferential results.

Model selection

The goal of the regression analysis was to build a model that would be useful in predicting concentrations of PAH in residential dust given the questionnaire- and GIS-based variables. As such, the deletion-substitution-addition (DSA) algorithm, a tool for model selection written in R (159-161), was used to choose an optimal model from the list of candidate variables. All households and all imputed values (average of five imputations) were included in the DSA procedure. For each model considered, the DSA algorithm performed a 10-fold cross validation procedure with 10 repeated rounds. Each round of cross-validation involved randomly partitioning the data into 10 complementary subsets, fitting a regression model based on 9/10 of the data, and validating the model by comparing predicted and measured values in the remaining data (the validation set). This process was repeated 10 times each round so that each partition was used as the validation set once. Finally, to reduce variability, 10 rounds of cross-validation were performed using different partitions, and the regression coefficients were averaged over the rounds. The 'best' model was the one that minimized the mean error between the predicted and observed values in 100 validation sets. The parameters in this 'best' model should be the most useful in predicting residential dust PAH concentrations in

other households from the NCCLS population. The search for the 'best' model began with the intercept-only model and proceeded iteratively by comparing the best model at each step with: 1) a deletion step which removed a term from the model, 2) a substitution step which replaced one term with another, and 3) an addition step which added a term to the model. Initially, the DSA algorithm was restricted so that it produced a model with only linear effects and no interaction terms. However, after narrowing the model selection to the most informative variables, the DSA procedure was repeated and 2nd order non-linear terms and two-way interactions that improved the model fit were added.

Regression analysis

Because the PAH data had approximate log-normal distributions, the natural log of the total residential-dust PAH concentration was used for all analyses. After selecting the optimal model using the DSA algorithm, three regression analyses were performed with case and control households combined. The primary analysis used data from all possible households regardless of the sampling method (both HVS3 and vacuum cleaner dust samples) or missing data (both observed and imputed values). The second analysis used only HVS3-sampled households and utilized imputed data; this analysis included the size of sampling area variable. The third analysis included households with both HVS3 and vacuum cleaner dust, but excluded subjects with any missing data. The first two regressions analyzed the five imputed data sets separately and combined the results to infer appropriate confidence intervals (SAS v.9.1, PROC MI Analyze). For the third analysis standard least-squares linear regression (SAS v.9.1, PROC Reg) was used.

Results

PAHs in residential dust

Statistical analyses in this chapter included 277 cases and 306 controls with PAH residential-dust measurements. As shown in Table 21, individual PAH detection rates ranged from 94-100% and individual PAH concentrations ranged from below detection (limit of 2 or 4 ng/g) to a maximum of 2,450 ng/g. The sum of the 9 residential-dust PAH concentrations (hereafter referred to as total PAH concentration in residential dust) for the 583 residences ranged from 54-11,170 ng/g, with a median value of 479 ng/g. Table 22 shows the Pearson correlation coefficients between individual log-transformed residential-dust PAH concentrations. In general, levels of the 9 PAHs were moderately to highly correlated.

Table 23 shows the Pearson correlation coefficients between total log-transformed residential-dust PAH concentrations and covariates of interest for the multiple imputation analysis (N = 583 x 5 data sets) and for the participants with complete covariate and PAH data. In general, the correlation coefficients were similar regardless of how missing data were treated. In the bivariate analysis, residence age, traffic density, and outdoor PAH concentrations were the covariates most strongly correlated with total PAH concentrations in residential dust. Table 23 also shows the number of subjects with missing values for the variables of interest. Table 24 shows the sum of the 9 PAH concentrations by covariates of interest.

Multivariable regression models

Based on the DSA algorithm that used all homes and included imputed values, six main effects were selected for the optimal model of logged total PAH concentrations in residential dust and subsequently two non-linear terms were added. Table 25 shows the parameter estimates and 95% confidence intervals for the optimal logged residential-dust PAH concentration model given the uncertainty introduced by the multiple imputation analysis (Table 25, Model 1). Restricting the analysis to only HVS3-sampled homes (and including the variable size of sampling area), yielded a model with similar parameter estimates, but with slightly larger confidence intervals (Table 25, Model 2). The variable size of sampling area was marginally significant in the model with only HVS3-sampled homes. Similarly, restricting the analysis to only subjects with complete data yielded a model with parameter estimates similar to those in Model 1, but with slightly larger confidence intervals (Table 25, Model 3).

The overall fit of Model 1 was $R^2 = 0.15$. During cross validation of Model 1, the average difference between the predicted total PAH concentration in residential dust and the measured total PAH concentration in residential dust was 0.67 (in log scale). For comparison, the average difference between any measured total PAH concentration in residential dust and the average total PAH concentration in residential dust was 0.72. Figure 10 compares the measured and predicted total PAH concentrations in residential dust (in log scale). Table 26 shows predicted total PAH concentrations in residential dust for various combinations of the six variables using parameter estimates from Model 1. Table 26, demonstrates the added effect of each term in the model on total residential-dust PAH concentration. For example, while holding all other variables constant, the added effect of indoor gas heating increased the predicted total PAH concentration in residential dust from 510 to 600 ng/g.

Discussion

Two suspected sources of indoor PAHs, *i.e.*, indoor gas heating and estimated outdoor PAH levels, were significant predictors of total residential-dust PAH concentrations in the models. Interestingly, the age of the residence had the most significant effect on total residential-dust PAH concentrations, with older residences having higher PAH concentrations. The age of residence had a similar effect in the previous analysis of nicotine concentrations in residential dust (see Chapter 3). Previous researchers have shown that only about 5% of the total dust loading present in a 10 year-old carpet is available as surface dust, whereas the larger portion resides deep within the carpet and is not removed by typical cleaning (162, 163). Taken together, these findings suggest that environmental contaminants can accumulate in household carpets over years or decades (23).

The child's age at enrollment was also a significant predictor of PAH concentrations in residential dust. Older children appeared to have higher concentrations of PAHs in their residential dust. In bivariate analyses, a child's age at enrollment was positively correlated with the amount of time his or her family had lived in the current residence ($r_p = 0.61$) and with the age of the carpet sampled ($r_p = 0.13$). While duration at residence and carpet age were not significant predictors of PAH levels, child's age may be a more reliably reported surrogate for the age of the dust

collected. If so, the positive regression coefficient for the child's age variable is further evidence that PAHs accumulate in residential dust over time.

Residence in an apartment/condominium, duplex/townhouse, or mobile home compared to a single family home, was also a significant predictor of the PAH concentrations in residential dust, with higher concentrations seen for multiple family dwellings. In Model 1, if the residence was not a single family home, the predicted total PAH concentration increased (Table 26). Because apartments, mobile homes, and townhouses are typically smaller than single family homes, this result is consistent with a previous finding that concentrations of environmental contaminants in residential dust increased with decreasing square footage of the residence (20). Presumably, given a constant number of PAH sources (*i.e.*, heaters, stoves, smokers); a smaller residence would have a greater PAH concentration.

The mother's ethnicity was also a significant predictor of PAH concentrations in residential dust. Hispanic mothers appeared to have lower PAH concentrations in their residential dust than non-Hispanic mothers. Notably, Hispanic mothers were also more likely to report that their carpets were vacuumed more than once a week (76% v. 36% for Hispanic v. non-Hispanic) and were less likely to live in an urban census tract (66% v. 78% for Hispanic v. non-Hispanic). Although these other factors were not selected as variables in the optimal residential-dust PAH model, in bivariate analyses, vacuum frequency was negatively correlated with PAH concentrations and urban location was positively correlated with PAH concentrations.

While the DSA algorithm identified several significant determinants of total PAH concentrations in residential dust, even the optimal model only explained a small portion of the total variability of the data (R^2=0.15). Moreover, during cross validation, the optimal model was only marginally better at predicting PAH concentrations in residential dust than the intercept model (average residuals of 0.67 and 0.72, respectively). Ultimately, it seems that even the most relevant self-reported and GIS-based data provided only limited information about residential PAH levels; this underscores the importance of making environmental or biological measurements.

As discussed, dust samples were collected using both the HVS3 and household vacuum cleaners. Restricting the regression analysis to only those homes with dust collected by the HVS3 did little to change the estimates of the parameters used in Model 1 (Table 25). This reinforces previous findings from the NCCLS (31) and suggests that collecting residential dust from household vacuum cleaners is a useful alternative to the more expensive and labor-intensive HVS3 sampling method.

An implicit assumption of the multiple imputation procedure is that the distribution of the missing data depends only on the observed data. This assumption is plausible given the large size and correlation of the set of predictors used for imputation (164). Moreover, restricting the regression to participants with complete data had little impact on the estimates of the parameters used in Model 1 (Table 25). Indeed, whereas the parameter estimates were similar, the standard errors and confidence intervals were smaller for Model 1 than for Model 3. Thus, it appears that the multiple imputation of missing data was useful. The one variable that was substantially different in Model 3 was the variable identifying the residence as an apartment. However, because this variable had only one missing observation, the discrepancy probably points to data censoring in Model 3 rather than to failure of the imputation process.

The PAH concentrations measured in residential dust in this chapter were generally lower than those previously reported (see Table 4) for residences in Durham, NC (95, 144, 145), in the Rio Grande Valley, TX (110), in Cape Cod, MA (94), in Long Island, NY (146), and in Ottawa, Canada (117). However, a recent study of dust from residences in Kuwait (19) found PAH concentrations similar to those reported in this chapter. The wide range of reported residential-dust PAH concentrations probably reflects true geographical variability. Specifically, one possible explanation for the relatively low levels of PAH in California homes is the infrequent use of coal-tar for sealing pavement in the Western U.S. (discussed in Chapter 1).

Interestingly, several factors that have been related to residential-dust PAH levels in previous studies; *i.e.*, smoking (22), vacuum use frequency (117), season (110), and urban location (18), were not important determinants in this analysis. However, some variables that were omitted from the optimal model (Model 1), were correlated with residential-dust PAH concentrations in bivariate analyses. Specifically, the variables urban location (r_p = 0.11), traffic density (r_p = 0.21), and vacuum use frequency (r_p = -0.07) were correlated with PAH levels. Moreover, PAH levels were higher in residences where some household smoking was reported compared to residences with no household smoking ($P_{t\text{-}test}$ = 0.18). Still, these variables were not important predictors of PAH concentrations when more informative variables were included in the model (*i.e*., mother's ethnicity and outdoor PAH estimate). Conversely, variables describing cooking habits, fireplace use, and season did not appear to be correlated with residential-dust PAH concentrations in bivariate or multivariable regression analyses (data not shown). Unfortunately, the variables describing cooking habits were crude (*i.e*., number of meat servings per week) and no information was available for most of the NCCLS population (N = 129). Notably, the case-control status was not an important determinant of PAH concentrations when more informative variables were included in the model. The potential importance of reporting bias in the optimal model can be discounted, because case and control parents would not be expected to differentially report the important predictor variables, namely, address, child's age, and residence construction date.

These analyses of total PAH concentrations assume that the 9 PAHs would have similar characteristics. To examine differences across PAHs, the variable set selected for the total PAH model was used to create a model for each individual PAH. The regression coefficients for each of the 9 individual PAH models were fairly consistent, with each individual regression coefficient falling within the 99% confidence interval of the regression coefficient from the total PAH model (data not shown). The consistency of the regression results across individual PAH models and the correlation between individual PAHs, suggests that the 9 PAHs measured have similar determinants.

In summary, these analyses identified several determinants of PAH concentrations in residential dust and confirmed that gas heating and elevated outdoor PAH concentrations were significant predictors of indoor PAH levels. Moreover, the regression results suggest that PAHs measured in residential dust could be used as long-term surrogates for residential exposures to PAHs. Nonetheless, despite the large number of dust measurements and the extensive questionnaire- and GIS-based data developed by the NCCLS, the optimal model was only able to explain a small portion of

the overall variability in PAH levels in residential dust (R^2 = 0.15). Hence, it is important to directly measure PAH levels in epidemiologic studies.

CHAPTER 5.

DETERMINANTS OF POLYCHLORINATED BIPHENYL CONCENRATIONS IN RESDENTIAL DUST[4]

Introduction

Residential dust can act as a reservoir for indoor chemical contamination (162, 163) and persistent organic chemicals like PCBs accumulate in carpets (3, 105). As such, PCB concentrations measured in residential dust may be long-term predictors of indoor PCB exposures. Moreover, because inadvertent dust ingestion could be responsible for a substantial portion of total PCB exposure in some young children (17), levels of PCBs in residential dust may be particularly relevant to the uptake of PCBs in children (see Chapter 1).

The health impact of PCB exposure has not been fully characterized. Recently, investigators have reported that ambient exposure to PCBs (as measured by PCB serum concentrations) was associated with an increased risk of type-2 diabetes (165). PCBs (measured in dust and blood) have also been associated with the risk of non-Hodgkin's lymphoma (3, 166). Similarly, investigators from the NCCLS noted that elevated levels of PCBs in residential dust were associated with the development of childhood leukemia (5).

Because timely collection of biological and environmental samples is particularly challenging in case-control studies, interview-based exposure assessment is commonly employed. Investigators have shown that certain demographic and lifestyle factors, including country of origin, sex, parity, body mass index, age, breastfeeding, and educational level, can influence biological levels of persistent chemicals (167). However, less is known about the relationship between self-reports and levels of PCBs in residential dust (see Chapter 1). Notably, one previous study identified floor age as an important predictor of PCB concentrations in residential dust (105). Chapter 5 assesses the predictive value of self-reported data in estimating measured levels of 6 PCBs in residential dust from 583 households in California, and discusses the implications for using questionnaires to classify PCB exposures in epidemiological studies more generally.

Methods

Study population

From 2001-2007, dust samples were collected from 629 households participating in the NCCLS (see Chapter 2 for NCCLS details), PCBs were analyzed in dust samples from 583 residences.

[4] A similar version of this manuscript will be submitted for publication. Whitehead TP, Metayer C, Ward MH, Colt JS, Nishioka MG, Buffler P, Rappaport SM (to be submitted). Determinants of Polychlorinated Biphenyls in Residential Dust.

Residential-dust collection

Residential-dust samples were collected using a high-volume surface sampler (HVS3) or household vacuum cleaners, as previously described (see Chapter 3 for details); data from both methods were used in analyses for this chapter.

PCB analysis

Six PCB congeners (PCB-105, PCB-118, PCB-138, PCB-153, PCB-170, and PCB-180) were analyzed using gas chromatography-mass spectrometry (GC-MS). For the PCB analyses, 0.5-g portions of fine (<150μm) dust were spiked with 250 ng of carbon-labeled surrogate recovery standards. Dust samples were then extracted by ultra-sonication in 1:1 hexane:acetone, solvent exchanged into hexane, purified via solid phase extraction (using sequential elution of hexane, 15% diethyl ether in hexane, and methylene chloride on 1 g silica cartridges), concentrated to 1 mL, spiked with the internal standard p,p = -dibromophenyl, and analyzed using GC-MS in the multiple ion detection mode. The GC separation employed an RTx-5 MS column (30 m, 0.25-mm i.d., 0.25-μm film) that was programmed from 130 to 220 ℃ at 2 ℃/min, and then from 220 to 300 ℃ at 10 ℃/min. A 9-point calibration cu rve (range 2-750 ng/mL) and a zero-level standard were analyzed with each sample set [12 field samples, a duplicate, a duplicate spike (250 ng), and a solvent method blank]. The internal standard method of quantification was used, with linear least squares determination of the calibration curve.

Self-reported exposure surrogates

Parents, primarily the biological mother (97%), participated in in-home interviews designed to ascertain information pertinent to childhood leukemia. Specific questions thought to provide information about possible sources of indoor PCBs, including contamination from construction materials associated with recent remodeling (*i.e.*, painting, re-flooring, or roofing), and track-in contamination from parents occupationally-exposed to PCBs (*i.e.*, construction workers, electricians) were evaluated. Furthermore, the effects of household characteristics [*i.e.*, residence age (constructed before or after 1980) and residence type], sampling conditions [*i.e*., season, vacuuming frequency, sampling method (HVS3 or household vacuum cleaner), and sampling area], parental demographics (*i.e.*, parental age, education, income, and ethnicity), and child-specific variables (*i.e*., child's case–control status, sex, and age) on PCB concentrations in residential dust were also considered (see Table 27 for complete list of candidate variables). Some parents were unable or unwilling to complete certain aspects of the questionnaires (*e.g.*, 70 respondents did not know their residence's construction date); as a result, statistical analyses used a limited subset of households that had complete questionnaire information available.

Statistical analysis

Depending upon the particular PCB congener, between 45 and 91% of PCB measurements were below analytical limits of detection (Table 28). Since such high proportions of the dust samples had non-detectable levels of PCBs, multivariable logistic regression models were used to predict the probability that a particular PCB congener would be detected based upon the self-reported explanatory variables. The

deletion–substitution–addition (DSA) algorithm, a cross-validation tool for model selection written in R (159-161), was used to choose optimal models from the list of candidate variables (as described in Chapter 4). Briefly, the DSA algorithm partitioned the data into 10 complementary subsets, fit a candidate logistic regression model based on 9/10 of the data, and validated that model by comparing predicted and measured values in the remaining 1/10 of the data (the validation set). After iteratively evaluating combinations of different variables, the optimal model was the one that minimized the mean squared error between the predictions (probabilities that the PCB concentration in dust from a given residence was above the limit of detection) and the observations in 100 validation sets. The DSA algorithm was restricted so that it identified main effects and 2^{nd} order interaction terms that predicted the detectable presence of PCBs. This process was repeated 6 times so that each PCB congener had an optimal logistic model. Finally, for all observations above detection limits, multivariable linear regression were used to evaluate whether the variables that were selected by the DSA algorithm (to predict PCB detection) were also associated with PCB concentrations in residential dust. Since the PCB congeners had approximate log-normal distributions, the natural log of the PCB concentrations were used for linear regression.

Results

Individual PCB congeners ranged from below the detection limit (1 or 2 ng/g) to a maximum of 273 ng/g (Table 28). The DSA algorithm identified few predictors of the detectable presence of PCBs (Table 29). For PCB-105, the intercept-only model performed better in cross validation than any alternative models containing predictor variables. Likewise, the optimal models for PCB-118, PCB-138, PCB-153, and PCB-180 each contained only one interaction term; and the optimal models for PCB-170 contained only two variables. In Table 29, regression coefficients for non-significant main effects are shown along with the corresponding interaction terms selected by the DSA algorithm. Residence age and parental age were common predictors of the presence of the PCB congeners in 5 of 6 final models (PCB-118, PCB-138, PCB-153, PCB-170, PCB-180). The 6 logistic models explained between 8 and 22% of the variance in PCB detection. The 6 linear models explained between 1 and 10% of the variance in logged PCB concentrations.

Residences that were built before 1980 were more likely to have detectable levels of PCBs than those constructed in 1980 or thereafter (Table 30). In older residences, households with older mothers (at least 31 years-old at the time of their child's birth) were more likely to have detectable levels of PCBs than those with younger mothers. Indeed, for each PCB congener, detection frequency followed a consistent pattern, *i.e.*, the percentage of households with detectable levels of PCB in older homes with older mothers > in older homes with younger mothers > in newer homes.

Likewise, residences that were built before 1980 had higher median PCB concentrations than more recently constructed homes (Table 31). Furthermore, in older residences, households with older mothers had higher median PCB concentrations than those with younger mothers. Indeed, for 5 of 6 PCB congeners, concentrations followed a consistent pattern, *i.e.*, PCB dust concentrations in older homes with older mothers > in older homes with younger mothers > in newer homes.

Discussion

The age of the residence was the strongest predictor of the detectable presence of PCB in residential dust. For example, PCB-153 was detected in 74% of residences built before 1980, but it was only detected in 32% of more recently constructed homes (Table 30). Since U.S. production of PCBs was banned in 1979 (89), homes built before 1980 were expected to have more PCB contamination than those constructed more recently.

Parental age was also useful in predicting the detectable presence of PCB in residential dust from older homes. For example, PCB-118 was detected in 55% of older homes occupied by older mothers, but it was only detected in 36% of older homes occupied by younger mothers (Table 30). Perhaps this observation is attributable to older parents owning older items that contain PCBs. Alternatively, this observation could be explained by the fact that older parents tended to have older carpets.

As shown in Table 3, the PCB concentrations measured in the NCCLS residential-dust samples were generally lower than those previously reported for residences in the U.S. (17, 93, 95). However, one recent study reported similarly low median PCB concentrations in dust collected from residences in Michigan (96).

Previous investigators have observed that PCB concentrations were elevated in dust from older residences (3) and in dust from older floor surfaces (105). It was noted earlier that concentrations of PAHs (Chapter 4) and nicotine (Chapter 3) measured in dust from NCCLS households were also positively associated with residence age. Taken together, these findings suggest that chemical contaminants may persist in household carpets for decades, and that residential dust represents an excellent resource for investigations of long-term chemical exposures in the home.

Previous investigators have also reported that some construction materials, such as wood-floor finishes (102) and caulk (101) can contain high concentrations of PCBs. However, in these analyses, recent construction activities, including re-flooring, were not predictive of PCB detection.

In summary, the DSA algorithm identified few determinants of PCB levels in a large sample of residential dust (N = 583). In fact, the age of the residence and the age of its occupants were the only determinants of the detectable presence and concentrations of PCBs in residential dust. The lack of other questionnaire-based determinants of PCB contamination underscores the importance of directly measuring PCB levels in epidemiological studies. The results from this chapter suggest that PCBs measured in dust could be used as indicators of long-term residential PCB contamination.

CHAPTER 6.

POLYBROMINATED DIPHENYL ETHER CONCENRATIONS IN RESDENTIAL DUST

Introduction

Because residential dust can act as a reservoir for chemical contamination (162, 163), chemicals with indoor sources, such as PBDEs, can accumulate in carpets. Since inadvertent dust ingestion is the dominant source of PBDE exposure for Americans (13, 15) (see Chapter 1); PBDE concentrations measured in residential dust may be particularly effective long-term predictors of PBDE exposures.

The health impact of PBDE exposure has not been fully characterized. Investigators have shown that exposure to PBDEs is associated with altered hormone levels in men (4), reduced fecundability in women (168), and neurodevelopmental effects in young children (9). Moreover, since PBDEs are structurally similar to other halogenated molecules (*i.e.*, PCBs and Dioxin) that cause cancer, there is some concern about the potential carcinogenicity of PBDEs as well. As such, the NCCLS is investigating whether exposure to PBDE-contaminated residential dust could contribute to childhood leukemia risk.

Chapter 6 reports preliminary results for concentrations of 22 PBDEs measured in residential dust from 81 households in California and compares the levels measured in the NCCLS to other recent studies from California and around the world.

Methods

Study population

From 2001-2007, dust samples were collected from 629 households participating in the NCCLS (see Chapter 2 for NCCLS details), PBDEs were analyzed in dust samples from 81 residences.

Residential-dust collection

Residential-dust samples were collected using household vacuum cleaners from 2001-2007 and stored at -20^{oc} at Battelle Memorial Institute until their shipment to Dr. Rappaport's UC Berkeley laboratory in 2010. PBDE chemical analyses were performed during 2010 at the CA DTSC.

PBDE analysis

Twenty-two PBDE congeners (*i.e.*, BDE-28, BDE-32, BDE-47, BDE-66, BDE-71, BDE-99, BDE-100, BDE-153, BDE-154, BDE-155, BDE-179, BDE-183, BDE-190, BDE-196, BDE-197, BDE-201, BDE-202, BDE-203, BDE-206, BDE-207, BDE-208, BDE-209) were measured using isotope dilution high resolution gas chromatography-high resolution mass spectrometry (HRGC-HRMS), as described in Chapter 2.

Statistical analysis

All values below the limit of detection were assigned a concentration equal to the limit of detection divided by the square root of 2 (169). Spearman correlation coefficients between concentrations of PBDE congeners are reported. Highly correlated concentrations of the 22 PBDE congeners were analyzed by principal components analysis to produce simpler, but meaningful, summary measures of PBDE contamination (135).

Results

As shown in Table 32, detection rates for PBDE congeners ranged from 26-100% and concentrations of PBDE congeners ranged from below the limits of detection (LODs from 0.3 - 400 ng/g) to a maximum of 109,409 ng/g (for BDE-209). Mean and median concentrations of BDE-47, BDE-99, and BDE-209 were higher than other congeners (each greater than 1,000 ng/g). Figure 11 shows median concentrations of BDE-47, BDE-99, and BDE-100 measured in the NCCLS dust samples compared to recently reported values from 3 other studies in California (38, 66, 67).

Figure 12 shows the relative contribution of the 22 PBDE congeners to total PBDE dust concentrations (*i.e.*, sum of all congeners measured) in the 81 dust samples. BDE-209 was the predominant congener in 42 dust samples and BDE-99 was the predominant congener in the remaining 39 samples. The median ratio of total nona-BDE dust concentrations (*i.e*., sum of BDE-206 + BDE-207 + BDE-208) to BDE-209 dust concentrations for 81 residences was 7% and the maximum ratio was 14%.

Table 33 shows the Spearman correlation coefficients between concentrations of 22 PBDE congeners. In general, the correlations between PBDE congeners in Table 33 reflected the congener patterns in the three commercially available PBDE mixtures. Specifically, concentrations of each of the PBDE congeners found in the Penta-BDE commercial mix (*i.e.*, BDE-28, BDE-47, BDE-66, BDE-99, BDE-100, BDE-153, BDE-154, BDE-155) were highly correlated ($r_S \geq 0.80$) in the 81 dust samples. Likewise, concentrations of each of the PBDE congeners found in the Deca-BDE commercial mix (*i.e.*, BDE-206, BDE-207, BDE-208, BDE-209) were highly correlated ($r_S \geq 0.84$) as were several of the major PBDE congeners found in the Octa-BDE commercial mix (*i.e.*, BDE-183, BDE-196, BDE-197) ($r_S \geq 0.70$).

Table 34 shows the results of the principal components analysis for the concentrations of 22 PBDE congeners. Three meaningful factors were chosen to represent the 22 PBDE congeners. A congener was said to load on a given component if the factor loading was 0.50 or greater. Using this criterion, 9 PBDE congeners (BDE-28, BDE-32, BDE-47, BDE-66, BDE-99, BDE-100, BDE-153, BDE-154, BDE-155) were found to load on the first component, which was subsequently labeled the Penta-BDE component. Similarly, 6 PBDE congeners (BDE-183, BDE-190, BDE-196, BDE-197, BDE-202, BDE-203) were found to load on the second component, which was subsequently labeled the Octa-BDE component. Finally, 5 PBDE congeners (BDE-201, BDE-206, BDE-207, BDE-208, BDE-209) were found to load on the third component, which was subsequently labeled the Deca-BDE component. Combined, three principal components accounted for 82% of the total variance in concentrations of the 22 PBDE congeners.

Discussion

Concentrations of PBDEs in 81 dust samples from NCCLS homes were relatively high compared to levels measured around the world (see Table 2). However, as shown in Figure 11, in comparison to homes from other studies in California (38, 66, 67), the NCCLS homes had relatively modest median concentrations of BDE-47, BDE-99, and BDE-100. In roughly half of the residential-dust samples from the NCCLS, BDE-209 was the predominant BDE congener, suggesting extensive historical use of the commercial Deca-BDE mix in California. The NCCLS is the first study from California to report concentrations of BDE-209 in residential dust.

Results from Spearman correlations (Table 33) and principal component analysis (Table 34) revealed clear patterns in PBDE contamination. Specifically, 22 PBDE congeners were resolved into three principal components that reflected distinct sources of PBDEs; *i.e.*, the Penta-BDE, Octa-BDE, and Deca-BDE commercial mixtures. These findings suggest that relatively few indicator PBDE congeners (*i.e.*, BDE-99, BDE-183, BDE-209) could be used to describe PBDE contamination in homes.

Although BDE-202 has not been reported at detectable levels in any PBDE commercial mixtures, the median concentration of BDE-202 from 81 NCCLS dust samples was 3 ng/g and concentrations were as high as 77 ng/g. The presence of BDE-202 in the NCCLS dust samples points to degradation of BDE-209 molecules (loss of 2 bromine atoms) in the environment. Likewise, the ratios of total nona-BDE to BDE-209 in the 81 dust samples from NCCLS residences (median = 7%, maximum = 14%) were much greater than the ratio typically found in the commercial Deca-BDE mix (<3%) (33). Additionally, Table 33 shows that concentrations of each nona-brominated diphenyl ether (*i.e.*, BDE-206, BDE-207, BDE-208) were highly correlated with concentrations of BDE-209. Taken together, these findings suggest that BDE-209 can break down into nona-brominated and octa-brominated diphenyl ethers in the environment. Since lower-brominated congeners are thought to be more toxic than BDE-209 (33), debromination of BDE-209 could lead to more harmful indoor contamination.

In summary, NCCLS residences had some of the highest median concentrations of BDE-47, BDE-99, and BDE-209 reported in North America (see Tables 2 and 32). Two PBDE congeners, BDE-99 and BDE-209, were found to predominate in dust samples from 81 Californian homes. Additionally, there was suggestive evidence of BDE-209 debromination in the indoor environment.

CHAPTER 7.

MEASURING EXPOSURES TO CHEMICALS USING RESIDENTIAL-DUST SAMPLES: IMPLICATIONS OF VARIABILITY[5]

Introduction

Although many researchers have measured chemicals in residential dust (see Chapter 1), most studies have been limited to the collection of only one dust sample from each home. Indeed, few researchers have sampled dust repeatedly in the same residences (30, 102, 170, 171) or characterized the variability of dust measurements within and between residences (111, 172). In two studies that reported variance components of dust levels (of pesticides, lead, and phenanthrene), large variance ratios (*i.e.*, ratio of within-residence variance component to between-residence variance component, designated here as λ) were observed (111, 172). Since, the degree of exposure measurement error increases directly with λ, large values of this ratio indicate imprecise exposure classification. In an epidemiological study, exposure measurement error will result in risk estimates that are smaller than the true risks, a phenomenon referred to as attenuation bias. To employ residential-dust concentrations as surrogates for chemical exposure with confidence, investigators need to know how variable these measurements are within a given residence, that is, they need some measure of their reliability.

Chapter 7 quantifies the reliability of residential-dust chemical concentrations as exposure measures for future studies of human health. Nine PAHs, six PCBs, and nicotine were analyzed in repeated samples of residential dust. Using random-effects models of repeated measurements from residential dust, variance ratios for each of these chemicals were estimated. Subsequently, these variance ratios were used to estimate the amount of attenuation bias that would be expected in independent case-control studies that used these residential-dust chemicals as exposure measures.

Methods

Study population

Dust samples were obtained from 21 residences in Fresno County, CA, from 2003-2005, as part of the Fresno Exposure Study, an investigation to estimate chemical exposures in residences located in agricultural communities. The study protocols were approved by the Institutional Review Boards at Colorado State University and the National Cancer Institute, and written informed consent was obtained from all participating subjects.

[5] A similar version of this manuscript has been submitted for publication: Whitehead TP, Nuckols JR, Ward MH, Rappaport SM (submitted). House-dust Chemicals as Measures of Exposure: Implications of Variability. *Emerging Themes in Epidemiology*.

Residential-dust collection

Residential-dust samples were collected using a high-volume surface sampler (HVS3) as previously described (31). Briefly, the interviewer selected a room on the side of the residence that faced agricultural crops, marked an approximately 2 m^2 area of a carpet or rug with tape, and vacuumed the surface until a specified amount of fine dust had been collected. All repeated dust samples for a given subject were collected from the same residence (*i.e.*, all subjects were residentially stationary) and, with few exceptions, all repeated samples from a given residence were collected from the same room. The median number of measurements per residence was n = 3 (range of n: 1 – 7) and the median duration between repeated visits was 5 months (range of 3-15 months).

Chemical analyses

Nine PAHs [benzo(*a*)anthracene, chrysene, benzo(*a*)pyrene, benzo(*b*)fluoranthene, benzo(*k*)fluoranthene, indeno(1,2,3-*c,d*)pyrene, dibenzo(*a,h*)anthracene, coronene, and dibenzo(*a,e*)pyrene], six PCBs (PCB-105, PCB-118, PCB-138, PCB-153, PCB-170, and PCB-180), and nicotine were analyzed in 68 dust samples as previously described (see Chapters 3-5). Briefly, 0.5 g of fine dust (<150 μm) was extracted with either a 1:1 hexane:acetone mixture (PAHs, PCBs) or methylene chloride (nicotine). Then the extract was cleaned using solid phase extraction (for PAHs and PCBs), and the concentrated eluate was analyzed with GC-MS using isotopically labeled internal standards for quantitation.

Statistical analyses

Since the chemical concentrations were approximately log-normally distributed, the natural log-transformed values were used for all statistical analyses. All values below the limit of detection were assigned a concentration equal to the limit of detection divided by the square root of 2 (169). Chemicals that were detected in less than 75% of the dust samples were excluded from the random-effects modeling (*i.e.,* PCB-105, PCB-118, and PCB-170).

Random-effects models

To estimate variance components, the one-way random-effects model was used:

$$Y_{ij} = \ln\left(X_{ij}\right) = \mu_Y + b_i + e_{ij}, \quad (1)$$

for i = 1,2,…, k residences and j = 1,2,…, n repeated measurements, where
X_{ij} = the residential-dust chemical concentration for the i^{th} residence on the j^{th} repeated measurement;
Y_{ij} = the natural log-transform of X_{ij};
μ_Y = the true (logged) mean residential-dust chemical concentration for the population;
b_i = μ_{Yi} - μ_Y, and represents the random deviation of the i^{th} residence's true mean (logged) residential-dust chemical concentration, μ_{Yi}, from μ_Y;
e_{ij} = Y_{ij} - μ_{Yi}, and represents the random deviation of the observed (logged) residential-dust chemical concentration, Y_{ij}, from μ_{Yi} for the i^{th} residence on the j^{th} repeated measurement.

It is assumed b_i and e_{ij} are mutually independent and normally distributed random variables, with means of zero and variances σ^2_{bY} and σ^2_{wY}, representing the between-residence and within-residence variances, respectively. These assumptions have been validated using repeated measurements of occupational chemical exposures (173-175).

Using Proc Mixed (SAS v.9.1, Cary, NC), Equation 1 was fit to the data and the variance components ($\hat{\sigma}^2_{bY}$, $\hat{\sigma}^2_{wY}$, and $\hat{\sigma}^2_Y = \hat{\sigma}^2_{wY} + \hat{\sigma}^2_{bY}$) and variance ratios, $\hat{\lambda} = \frac{\hat{\sigma}^2_{wY}}{\hat{\sigma}^2_{bY}}$ were estimated. Subsequently, the expected fold ranges for 95% of measurements (*i.e.*, the expected ratio of the 97.5th percentile concentration to the 2.5th percentile concentration) within residences $\left[{}_w\hat{R}_{0.95} = \exp\left(3.92 \times \hat{\sigma}_{wY}\right)\right]$ and across residences $\left[{}_b\hat{R}_{0.95} = \exp\left(3.92 \times \hat{\sigma}_{bY}\right)\right]$ were estimated (175).

Estimating attenuation bias

In the context of a case-control study, the following logistic model could be used to assess the risk of disease associated with concentrations a particular chemical in residential dust:

$$\text{Logit}\left(Z_i\right) = \ln\left(\frac{Z_i}{Z_i - 1}\right) = \beta_0 + \beta_1 \overline{Y_i}\ , \qquad (2)$$

where
Z_i = the disease status (1 or 0) of an individual in the ith residence and
$\overline{Y_i}$ = the (logged) mean residential-dust chemical concentration for the ith residence.

In this case, the expected value of the estimated logistic regression coefficient, E[$\hat{\beta}_1$], is related to the true logistic regression coefficient, β_1, by the variance ratio, λ, as follows (176):

$$\text{E}\left[\hat{\beta}_1\right] = \frac{\beta_1}{1 + \frac{\lambda}{n}}. \qquad (3)$$

Here, attenuation bias is defined as the normalized difference between the expected value of the estimated logistic regression coefficient and the true logistic regression coefficient:

$$B = \frac{\text{E}\left[\hat{\beta}_1\right] - \beta_1}{\beta_1}. \qquad (4)$$

Equations 3 and 4 were used to estimate the attenuation bias that would be expected in case-control studies using residential-dust chemicals as independent variables in logistic regression analyses. Using estimates of the variance ratio, $\hat{\lambda}$, and an assumed true odds ratio of 1.5, the expected value for $\hat{\beta}_1$, the expected odds ratio, $\text{E}\left[\widehat{OR}\right]$, and the expected attenuation bias were each estimated. In these calculations,

measurement error is assumed to be non-differential (*i.e.*, the variance ratios for the case and control populations are assumed to be equal).

Investigators can improve the precision of exposure estimates and, thereby, limit attenuation bias by making repeated exposure measurements and finding an average exposure level for each study subject over time. Combining Equations 3 and 4, it is possible to calculate the number of repeated measurements per residence, *n*, that would be necessary to limit attenuation bias to a certain level as follows:

$$n = \frac{\hat{\lambda}}{\frac{1}{1+B} - 1}. \qquad (5)$$

The number of repeated measurements that would be necessary to limit the magnitude of attenuation bias to 20% in a case-control study using these residential-dust chemicals as measures of exposure was calculated based on the variance ratio estimates from the random-effects models.

Results

Chemical concentrations in residential dust

Analyses included 68 residential-dust measurements from 21 residences in the Fresno Exposure Study. As shown in Table 35, individual chemical detection rates ranged from 38 to 100% and, as shown in Table 36, individual chemical concentrations ranged from below the limits of detection (LODs from 1 - 20 ng/g) to a maximum of 7,776 ng/g (for nicotine). The 9 PAHs were detected in a higher percentage of samples, and at higher median concentrations, than the 6 PCBs. The range in concentrations of nicotine was larger than those of either PAHs or PCBs.

Estimated variance components

Table 37 shows the results of the analysis using random-effects models for the 13 chemicals with at least a 75% detection rate. For all models, the between-residence variance component was greater than the within-residence variance component (*i.e.*, $\hat{\lambda} < 1$). The median within-residence variance component estimate for PAHs was $\hat{\sigma}^2_{wY}$ = 0.38 (Interquartile range, IQR: 0.21 – 0.42), for PCBs it was $\hat{\sigma}^2_{wY}$ = 0.41 (IQR: 0.36 – 0.51), and for nicotine it was $\hat{\sigma}^2_{wY}$ = 1.33. For each of the 13 individual chemicals, the within-residence variance component ranged from $\hat{\sigma}^2_{wY}$ = 0.16 (coronene) to $\hat{\sigma}^2_{wY}$ = 1.33 (nicotine). Correspondingly, 95% of repeated coronene measurements from a residence in the Fresno Exposure Study would be expected to lie within a 5-fold range versus a 92-fold range for repeated nicotine measurements. The median between-residence variance component estimate for PAHs was $\hat{\sigma}^2_{bY}$ = 1.20 (IQR: 1.00 – 1.27), for PCBs it was $\hat{\sigma}^2_{bY}$ = 1.29 (IQR: 1.24 – 1.46), and for nicotine it was $\hat{\sigma}^2_{bY}$ = 1.85. For each of the 13 individual chemicals, the between-residence variance component ranged from $\hat{\sigma}^2_{bY}$ = 0.77 [benzo(*k*)fluoranthene] to $\hat{\sigma}^2_{bY}$ = 1.85 (nicotine). Correspondingly, 95% of the mean benzo(*k*)fluoranthene concentrations from different residences in the Fresno

Exposure Study would be expected to lie within a 31-fold range versus a 207-fold range for mean nicotine levels.

Expected attenuation bias

Table 38 shows the amount of attenuation that would be expected in odds ratios if case-control studies were to use each of the residential-dust chemicals as independent variables in logistic regression analyses. For each of the 13 chemicals with at least a 75% detection rate, the expected bias was calculated using Equations 3 and 4 along with estimates of the variance ratio from Table 37. By definition, the expected bias increased with the size of the estimated variance ratio. For example, for benzo(*b*)flouranthene, the chemical with the smallest variance ratio ($\hat{\lambda}$ = 0.13), the expected odds ratio would be 1.43 assuming only one measurement from each residence (*i.e.*, *n* = 1), indicating a -12% bias (true odds ratio = 1.5). However, for nicotine, the chemical with the highest variance ratio ($\hat{\lambda}$ = 0.72), the expected odds ratio under the same conditions is 1.27, a -42% bias.

Figure 12 shows the relationship between the expected odds ratio and the number of repeated measurements per residence, using the estimated variance ratios from Table 37 and assuming a true odds ratio of 1.5 for PCB-153, benzo(*a*)pyrene, and nicotine. For each of the chemicals measured in residential dust, Table 38 indicates that the number of repeated measurements necessary to limit attenuation bias to -20% ranged from 1 to 3 per residence.

Discussion

Results from these analyses can guide epidemiologists in developing sampling strategies for residential dust as a medium for estimating exposures to PAHs, PCBs, or nicotine in their studies. Generally, investigators can improve the precision of their exposure estimates and limit attenuation bias by making repeated exposure measurements in each residence. However, the analytical advantages of a repeated sampling design must be balanced with the practical concerns of a study's schedule and budget. As shown in Table 39, calculations that employed estimated variance ratios from the Fresno Exposure Study suggest that three repeated dust measurements per residence would be sufficient to reduce the magnitude of attenuation bias to less than 20% for each chemical measured in the current study. Moreover, if repeated measurements would not be feasible, Table 38 indicates that for 10 of the 13 chemicals analyzed, the expected magnitude of attenuation bias would still be less than 30%.

Because the results shown in this chapter are based on a limited sample size (68 dust measurements from 21 residences), the variance ratio estimates are somewhat imprecise (see Table 37). However, these findings should be externally valid and useful for other investigators measuring these same chemicals in residential dust. Notably, the concentrations of chemicals measured in dust from the Fresno Exposure Study residences (Table 36) were generally similar to the concentrations reported for the NCCLS homes with respect to both the medians and the ranges of concentrations (Chapters 3-5). Unfortunately, it is difficult to compare the results from this chapter to those from two other studies that repeatedly sampled dust from the same residences over time and reported corresponding variance components (111, 172), because these studies published estimates for different chemicals in dust (*i.e.*, pesticides, lead, and

phenanthrene). However, estimated variance ratios for the Fresno Exposure Study residences (Table 37) were quite similar to those estimated using unpublished data from Egeghy *et al.* for several PAHs that were measured in residential dust from both studies (Table 39). The similarity of variance ratios from two independent populations lends credibility to the findings reported in Chapter 7 and suggests that the levels of variability observed in concentrations of chemicals measured in dust from the Fresno Exposure Study residences may be generalized to other populations.

In using the random-effects model to estimate variance components, it is implicitly assumed that each residence has a true underlying dust concentration for each chemical that remains constant over the course of the study [*i.e.*, $\exp(\mu_Y + b_i)$, equivalent to the geometric mean concentration in the i^{th} household]. As such, any deviation from a residence's true level is interpreted as measurement error or random within-residence variability. It is possible that some of the "random" variability that was observed is due to changes in the sources of chemical contamination in homes during the course of the study. Indeed, since the Fresno Exposure Study dust samples were collected over the period of 3 years, it is possible that true concentrations of chemicals in household dust changed systematically over time. Consequently, the long-term timing of the dust sampling could have artificially inflated the within-household variance component, resulting in an overestimate of the variance ratios and the associated attenuation bias. Nevertheless, the random-effects model should provide a conservative estimate of the reliability of chemicals in residential dust as measures of exposure. Indeed, the results from Chapter 7 indicate that residential dust would be a valuable tool for retrospective exposure assessment given the modest within-residence variability observed for dust measurements collected several months apart.

A limitation of the method used for predicting attenuation bias is the implicit assumption that measurement error is non-differential (*i.e.*, the variance ratios from the case and control populations are assumed to be equal). In the more complex situation where case and control populations have different variance ratios, Equation 3 would be only approximate.

In summary, estimates of variance ratios for concentrations of PAHs ($0.13 \leq \hat{\lambda} \leq 0.64$), PCBs ($0.25 \leq \hat{\lambda} \leq 0.37$), and nicotine ($\hat{\lambda} = 0.72$) measured in residential dust were modest for the 21 homes in the Fresno Exposure Study. Though based on a limited number of measurements ($N = 68$), these findings suggest that the use of residential-dust measurements as markers of exposure to these 13 chemicals will result in relatively small levels of attenuation bias due to exposure measurement error. Likewise, these results indicate that residential dust would be a valuable tool for retrospective exposure assessment.

CHAPTER 8.

ESTIMATING EXPOSURES TO INDOOR CONTAMINANTS USING RESIDENTIAL-DUST SAMPLES: BENEFITS, LIMITATIONS, AND FUTURE DIRECTIONS

The previous chapters indicate that residential dust offers a convenient matrix for estimating levels of chemical exposure in the home. In this chapter, both the strengths and weaknesses of residential dust measurements will be discussed and opportunities for future work will be suggested.

Benefits of using residential-dust levels as measures of chemical exposure

In multivariable regression analyses, it was observed that the age of the residence was a consistent determinant of the concentrations of nicotine (Chapter 3), PAHs (Chapter 4), and PCBs (Chapter 5) in residential dust. This finding suggests that these chemicals accumulate in carpets over years or decades. This conclusion was supported by evidence that dust from homes of former smokers had higher nicotine concentrations than dust from homes of nonsmokers (Chapter 3), indicating that residual nicotine contamination could persist in dust for years after smoking cessation. Likewise dust levels of PCBs were higher in homes constructed before 1980 than in newer homes (Chapter 5), demonstrating that these chemicals remained inside homes more than three decades after PCBs were banned in the U.S. The persistence of chemicals in residential dust offers an advantage for the estimation of long-term chemical exposures compared to air or biological measurements, which generally provide only a "snapshot" of current chemical exposures (177). As such, chemicals measured in residential dust may be useful measures of cumulative exposure in epidemiologic studies, especially for diseases with long latency periods.

Another advantage of using residential-dust levels as measures of chemical exposure is the fact that dust levels provide information that questionnaires cannot. Whereas dust measurements are specific and quantitative indicators of chemical contamination in the home, questionnaires generally offer only qualitative measures of chemical exposure. Indeed, even the extensive survey information developed by the NCCLS offered only weak predictions of residential-dust levels of PAHs (R^2 = 0.15, Chapter 4) or PCBs (R^2 = 0.02 - 0.12, Chapter 5) and modest predictions of dust levels of nicotine (R^2_{adj} = 0.31, Chapter 3). Since questionnaire-based exposure surrogates appear to be poor predictors of indoor levels of chemical contamination, they are also likely to be poor predictors of chemical exposure. Thus, it is recommended that residential dust measurements be used instead of, or in addition to, questionnaires when evaluating exposures to chemicals.

Another benefit of using residential dust for exposure assessment is the simple, inexpensive, and non-invasive nature of sample collection. By using dust from household vacuum cleaners and collecting samples via the mail, it is possible to obtain dust samples without ever visiting subjects' homes (Chapter 6). In the NCCLS, analyses of chemical levels in dust obtained from household vacuum cleaners were

indistinguishable from those obtained with the more rigorous and expensive high-volume surface (HVS3) sampler (Chapters 3 and 4).

Finally, residential dust can be an important source of chemical exposures. For example, dust ingestion may be the dominant route of exposure to PBDEs for individuals from North America and Asia (13-16), and investigators have observed strong correlations between levels of PBDEs in matched samples of dust and biological specimens have been observed (4, 32, 43, 49, 78, 79). Although dust exposure appears to play a more minor role in the intake of other chemicals, investigators have still observed correlations between dust concentrations and biomarkers of PCBs (100) and nicotine (120, 122, 123). Thus, there is evidence that dust measurements can be useful not only as markers of residential chemical contamination, but as surrogates of chemical uptake and dose. Moreover, since dust is a particularly important source of chemical exposure for young children, dust measurements could be especially useful in studies of childhood diseases.

Limitations of using residential-dust levels as measures of chemical exposure

It is important to keep in mind that residential dust provides only one piece of the complete 'puzzle' of chemical exposure. For example, a dust measurement would not necessarily provide information about a subject's potential chemical exposures via the inhalation of contaminated air, particularly for volatile substances, or the ingestion of contaminated food. Thus, measuring the concentration of chemicals in residential dust allows an investigator to estimate directly only one route of exposure (*i.e.*, ingestion of/dermal contact with dust). In some populations and for some chemicals, contaminated dust may not be a relevant source of chemical exposure, and in these scenarios, dust may not be the ideal medium for assessing exposures.

In some cases, it is appropriate to use chemicals measured in dust as surrogates for total chemical intake, even if dust ingestion is only a minor source of exposure. For example, in Chapter 3 it was shown that residential-dust nicotine measurements could be used as surrogates for secondhand smoke exposures. However, nicotine can be conveyed into the home not only by residential smoking, but also via the skin, clothing, or shoes of smokers (122). Moreover, nicotine concentrations can remain elevated in dust collected from non-smoking families living in apartments formerly occupied by smokers (120). As such, dust contamination is not necessarily indicative of exposures received via inhalation or other routes.

Residential dust contamination will be an ineffective measure of chemical exposures for some individuals. For example, concentrations of chemicals measured in residential dust from a subject's current home may not be representative of chemical concentrations in dust from their previous home. As such, it may be difficult to use residential-dust samples to estimate past exposures in residentially mobile study populations. Likewise, residential dust does not provide information about potential chemical exposures that may occur outside of the home, such as exposures received at work, while commuting, or in public spaces. Of course, dust could potentially be collected from these other microenvironments to provide more complete information about chemical exposures, but that would be difficult in most cases. Alternatively,

investigators could use residential dust to assess exposures in less mobile subjects (*i.e.*, very young children), who are mostly exposed to chemicals in their own homes.

Some diseases are the result of a chemical exposure during a specific time window of development (*e.g.*, during pregnancy). However, since residential dust measurements are long-term measures of exposure, it can be difficult to use dust to estimate exposures at a specific time of interest.

Investigators that plan to use dust measurements to estimate exposures need to consider the complexity of the analytical method. As described in Chapter 2, the dust measurement protocol requires several preparatory steps (*i.e.*, fractionation, extraction, and clean-up) prior to GC-MS analysis. In all, the current method requires extensive time, expertise, and instrumentation. Other researchers have used simpler methods for dust analyses, but the method described in Chapter 2 was optimized to minimize GC-MS interferences and maximize analyte sensitivity.

Future directions

Since there is limited information regarding how concentrations of chemicals in dust vary across time and space within a residence, it would be useful to use a larger dataset to verify the findings from Chapter 7. Specifically, investigators should determine whether a single dust measurement can effectively represent indoor contamination from the distant past (*e.g.*, over a period of years), as would be necessary when performing retrospective exposure assessment. Investigators should also use data from repeated measurements collected from case-control study populations to investigate differences in measurement errors between case and control populations.

Since investigators have struggled to find determinants of PBDEs, future researchers should identify factors that impact PBDE levels in residential dust. Specifically, researchers should investigate the hypothesis that differences in PBDE contamination across California may be a function of inter-community income disparities. It would also be worthwhile to evaluate whether PBDE levels and congener patterns have changed significantly over time as a result of recent restrictions of the commercial Penta-BDE and Octa-BDE mixtures. Finally, future work should assess the degradation of BDE-209 in the environment, as this phenomenon may increase the prevalence of more harmful lower-brominated BDE molecules in dust.

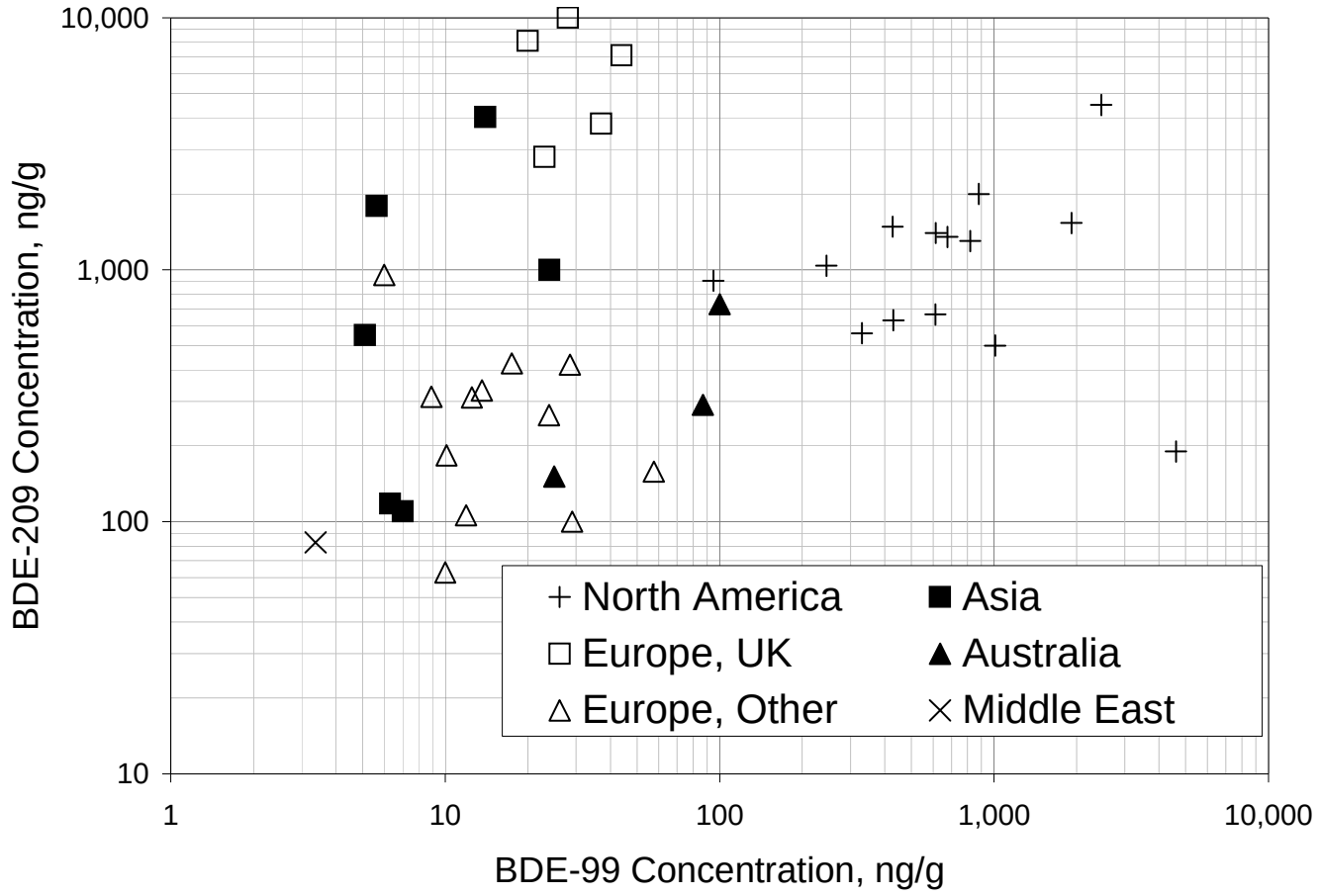
Researchers should also follow-up on the findings of Matt *et al.* (120), who reported that residual nicotine contamination could persist in apartments of former smokers. Specifically, investigators should use longitudinal data to evaluate changes in nicotine dust levels over time for households with changing smoking habits. For example, it would be useful to assess the impact of smoking cessation on dust nicotine levels.

There have been few studies that reported levels of PBDEs, PCBs, PAHs, or nicotine in residential dust from geographic regions outside of North America or Western Europe. Reports of residential-dust levels from the developing world are particularly sparse. The ease with which residential-dust samples can be obtained (*e.g.*, by collecting vacuum cleaner bags or brushing surfaces) creates an opportunity to use dust as a medium for measuring indoor chemical contamination in the developing world.

Another possibility for future research could be to identify techniques for the remediation of chemical contamination. For example, PBDE-contaminated e-waste from the U.S. is frequently exported to recycling centers in developing countries, a practice that is neither equitable nor sustainable. Measurement of PBDEs in dust samples before and after remediation would be useful in gauging the impact of these efforts on reducing contaminant levels. Likewise, investigators could use nicotine levels in residential dust to determine the effectiveness of various methods for removing residual tobacco smoke from residences formerly occupied by smokers.

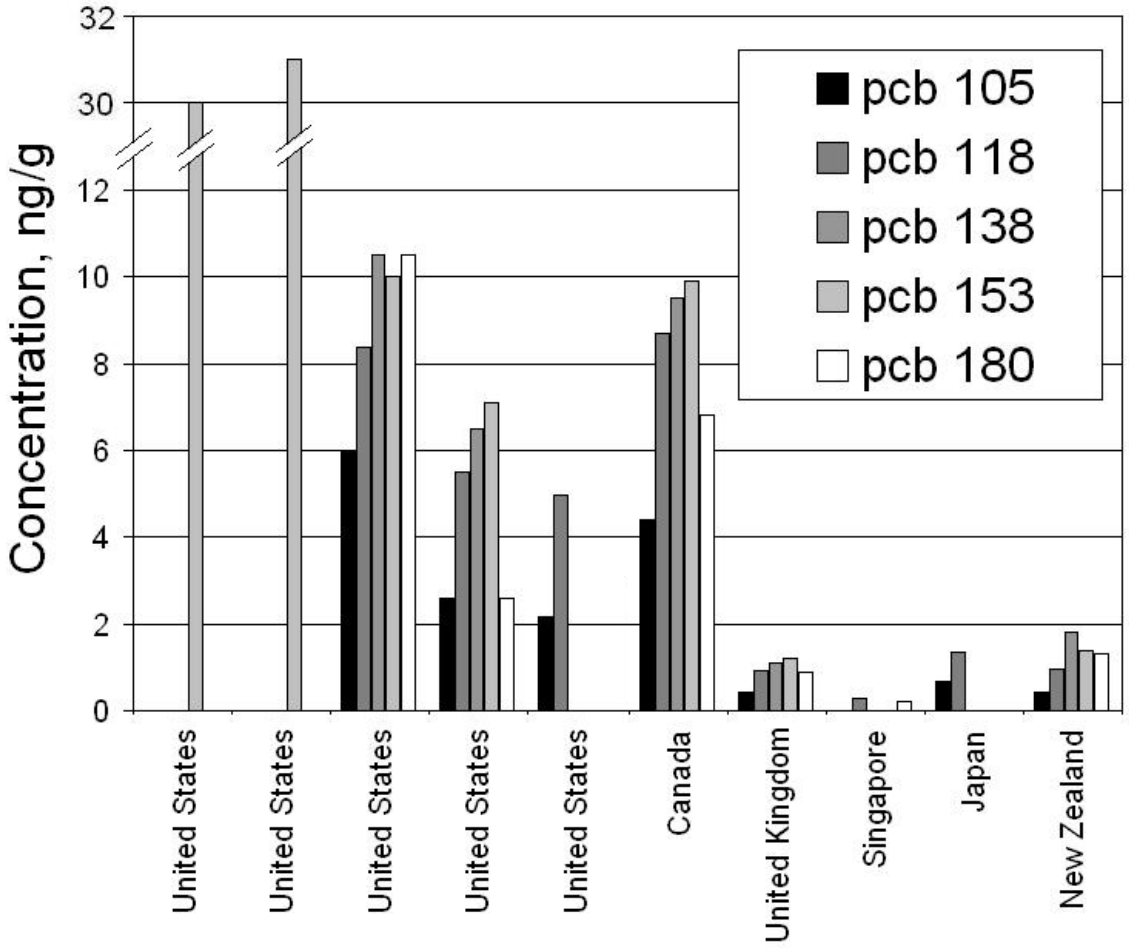
FIGURES

Figure 1. Global patterns in median concentrations of major polybrominated diphenyl ether congeners measured in residential-dust samples from selected studies.



Note: Median BDE-209 values shown for Wu *et al.*, 2007 and Al Bitar *et al.* 2004 are set at the limit of detection, actual median BDE-209 values were below the limit of detection; median BDE-99 values for Roosens *et al*., 2009; Wang *et al*., 2010; and Webster *et al*., 2010; were not reported, maximum median values were inferred from reported group medians (*i.e.*, the median for BDE-47 must be less than the reported median for all tetra-BDEs).

Figure 2. Median concentrations of major polychlorinated biphenyl congeners measured in residential-dust samples from selected studies.



Note: Camann *et al.* (93) median PCB-105 values were below method detection limits; all other missing data in Figure 2 indicate PCBs that were not analyzed. References shown in Figure 2 (from left to right) are Camann *et al.*, 2000 (NY); Camann *et al.*, 2000 (MI); Wilson *et al*., 2003; Harrad *et al.*, 2009 (U.S.); Hedgeman *et al*., 2009; Harrad *et al*., 2009 (Canada); Harrad *et al.*, 2009 (U.K.); Tan *et al*., 2007a; Saito *et al*., 2003; and Harrad *et al*., 2009 (New Zealand).

Figure 3. Regional patterns in median concentrations of benzo(*a*)anthracene and benzo(*a*)pyrene measured in residential-dust samples from selected studies.

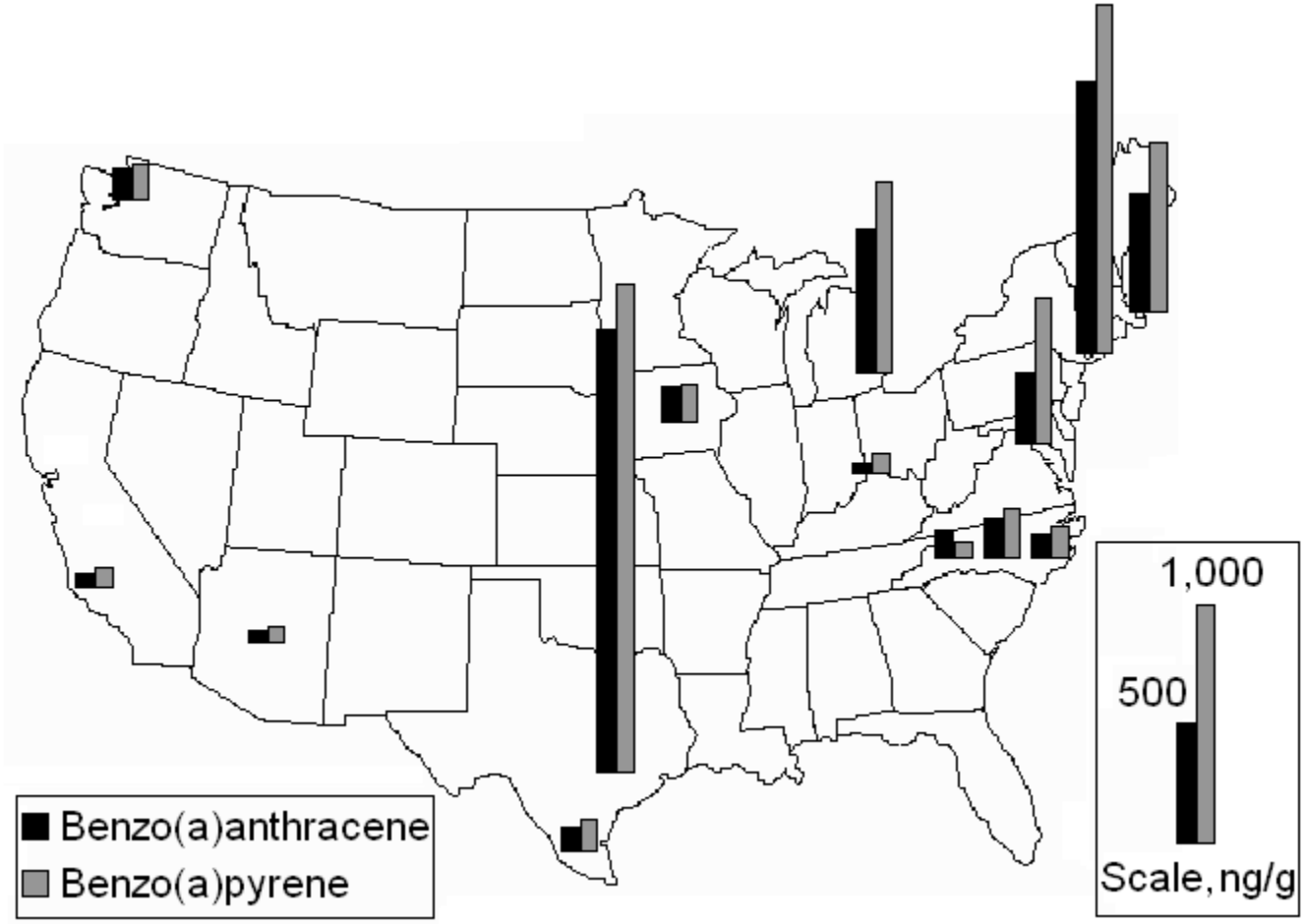


Figure 4. Univariate regression analyses of median benzo(*a*)anthracene residential-dust concentrations regressed on (a) state-wide smoking rates, (b) typical winter day temperatures, and (c) population densities for the study locations.

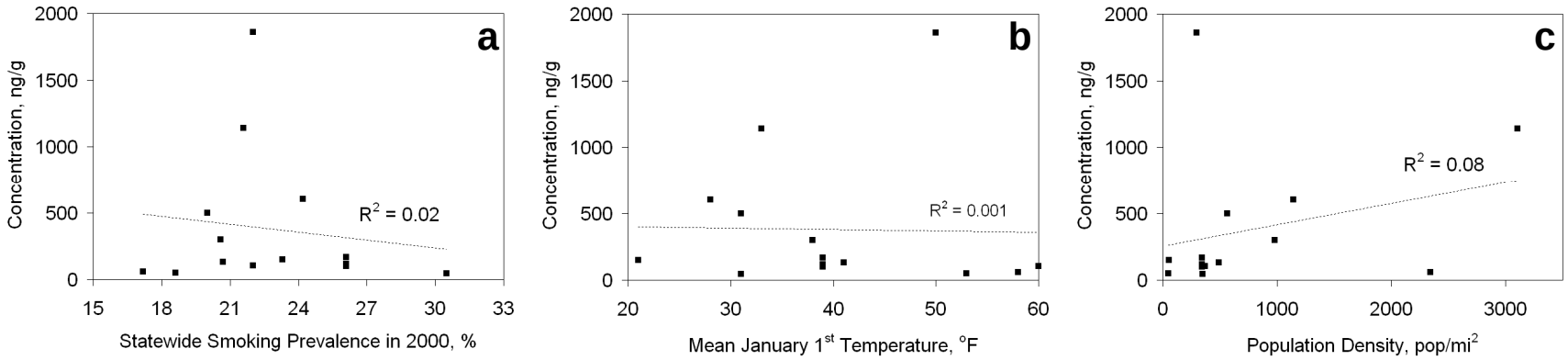


Figure 5. Schematic representation of the Northern California Childhood Leukemia Study residential-dust sample analysis plan.

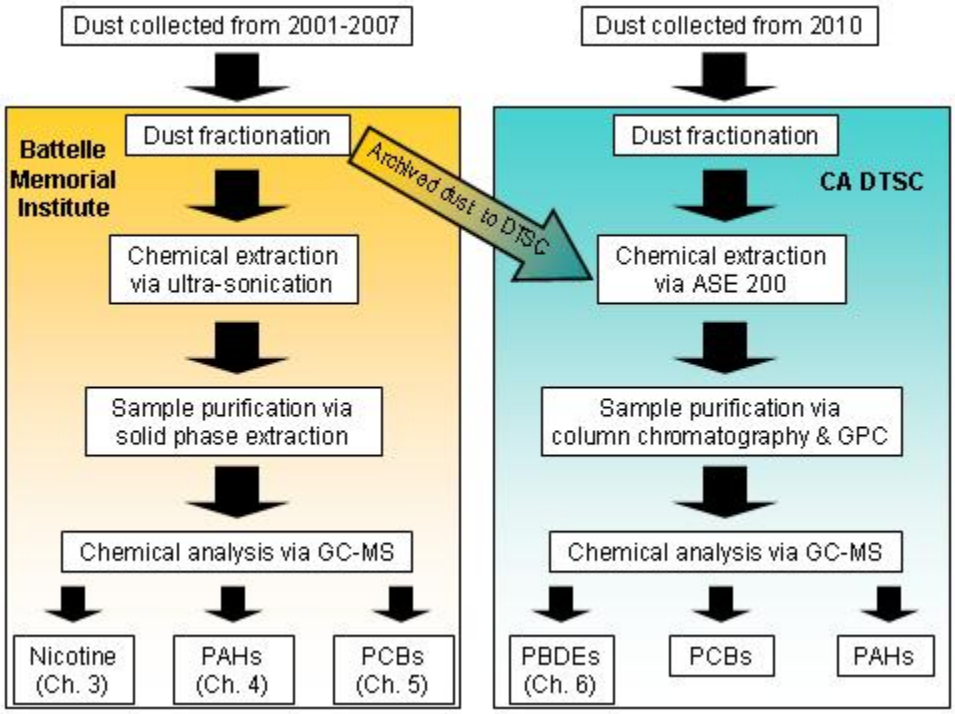


Figure 6. Representative GC-MS chromatogram for PBDE analytical standard.

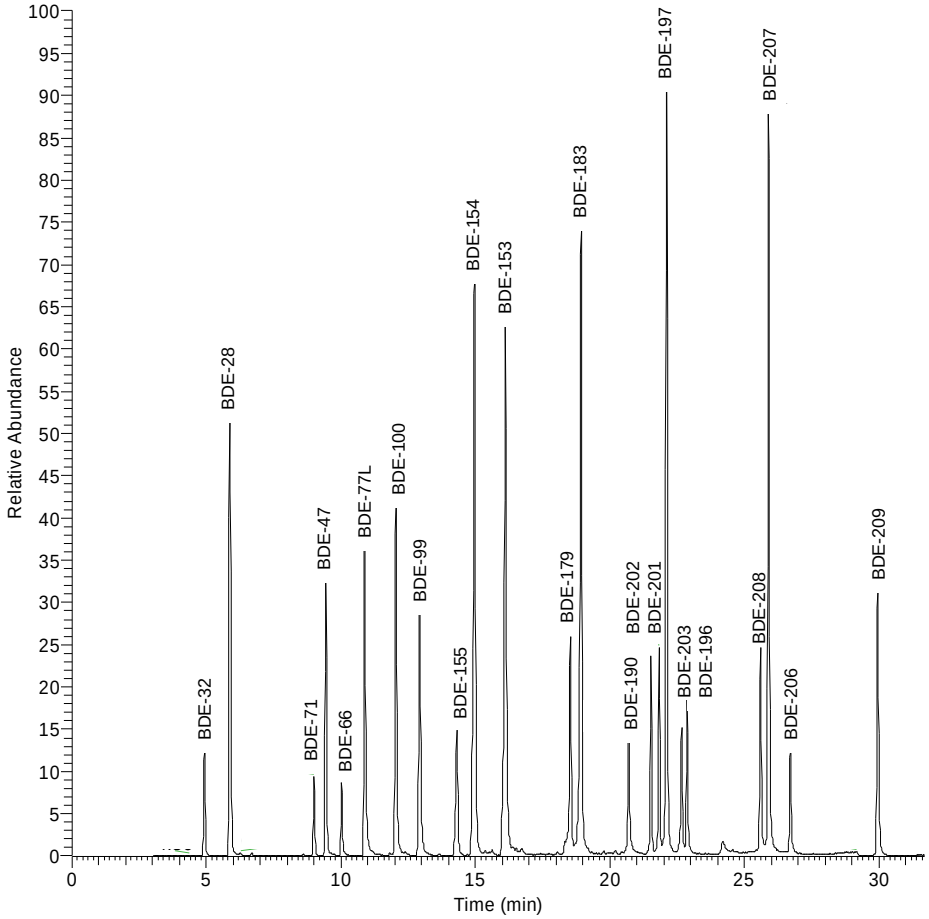


Figure 7. Representative GC-MS chromatogram for PCB analytical standard.

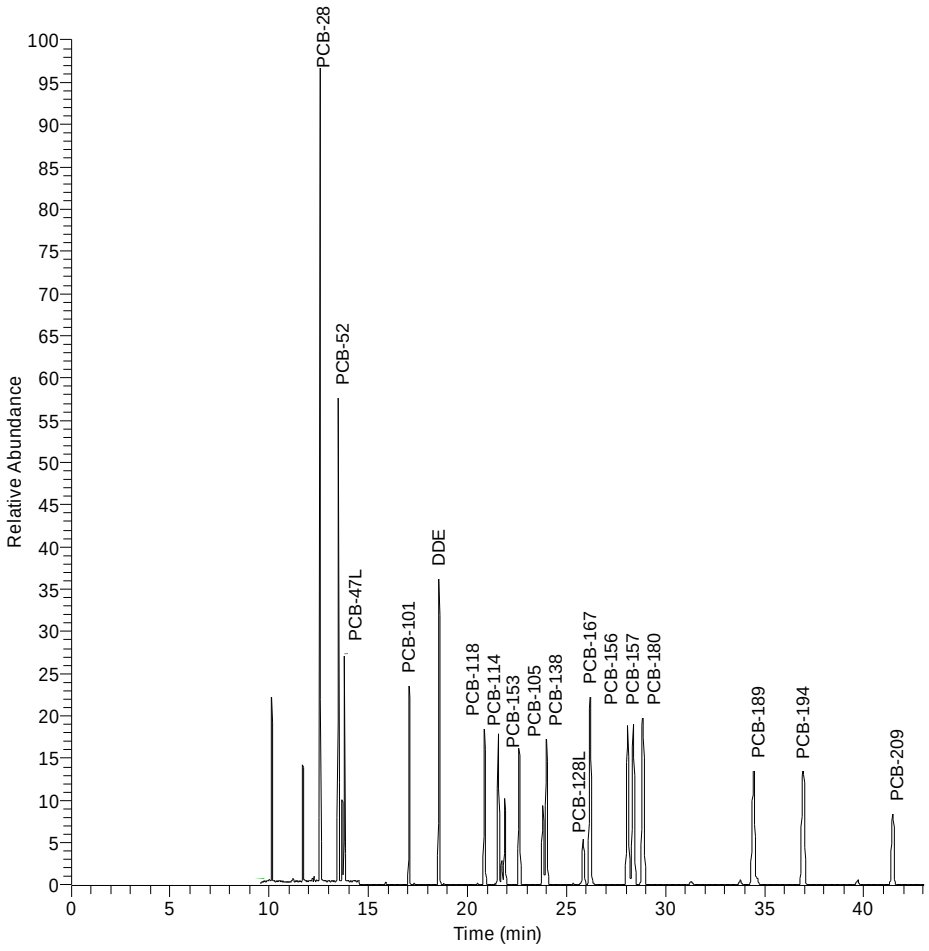


Figure 8. Representative GC-MS chromatogram for PAH analytical standard.

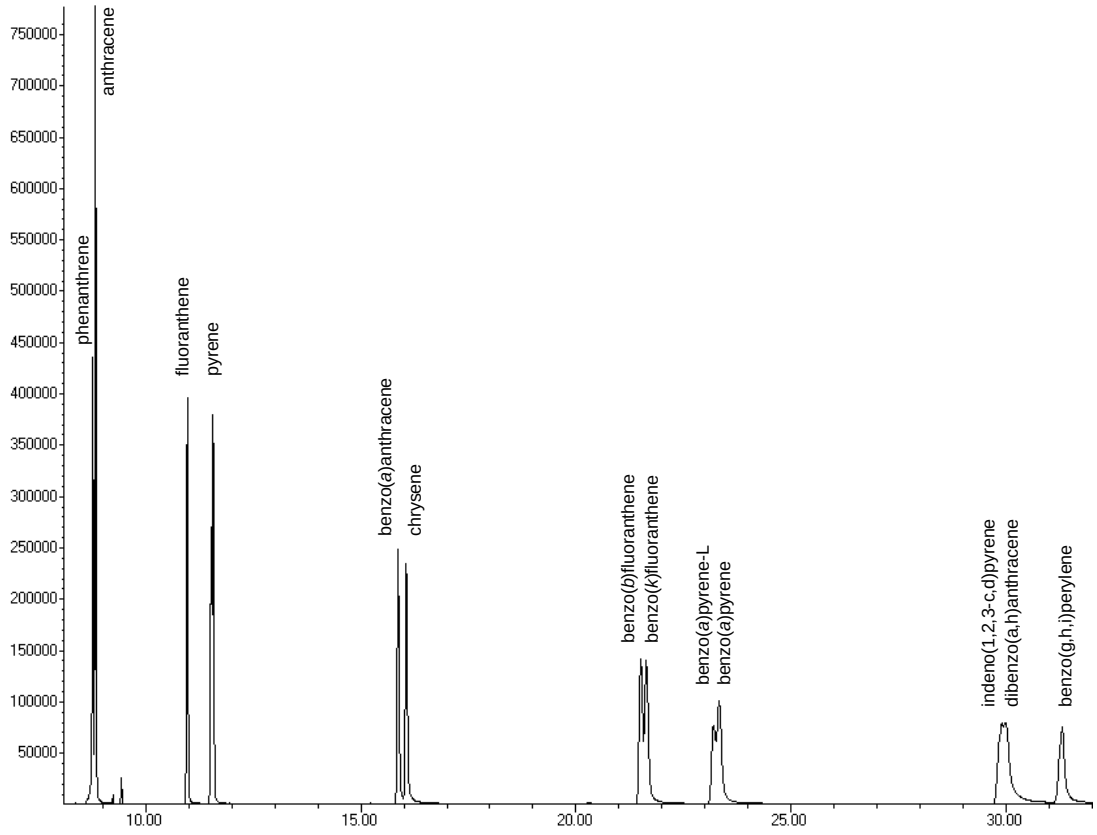
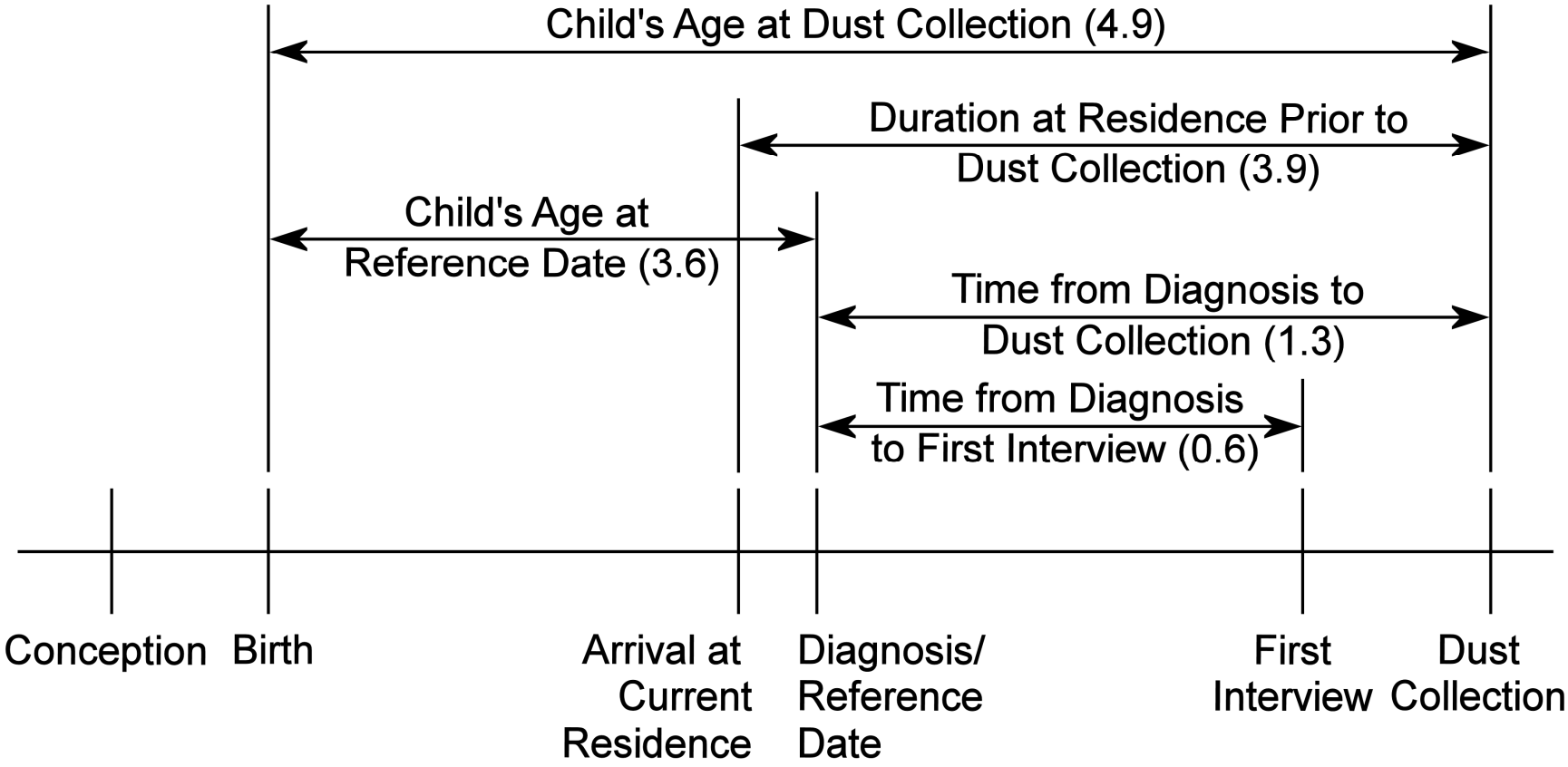


Figure 9. Conceptual timeline of Northern California Childhood Leukemia Study, 1999-2007.



Note: The timeline displays time variables that were included in the statistical analysis of Chapter 3 as potential modifiers of nicotine concentrations in residential-dust samples. For each variable, the median value for the study population (measured in years) is shown in parenthesis.

Figure 10. Total PAH concentrations measured in residential-dust samples collected from 81 households participating in the Northern California Childhood Leukemia study from 2001-2007 compared to PAH concentrations predicted using Model 1.

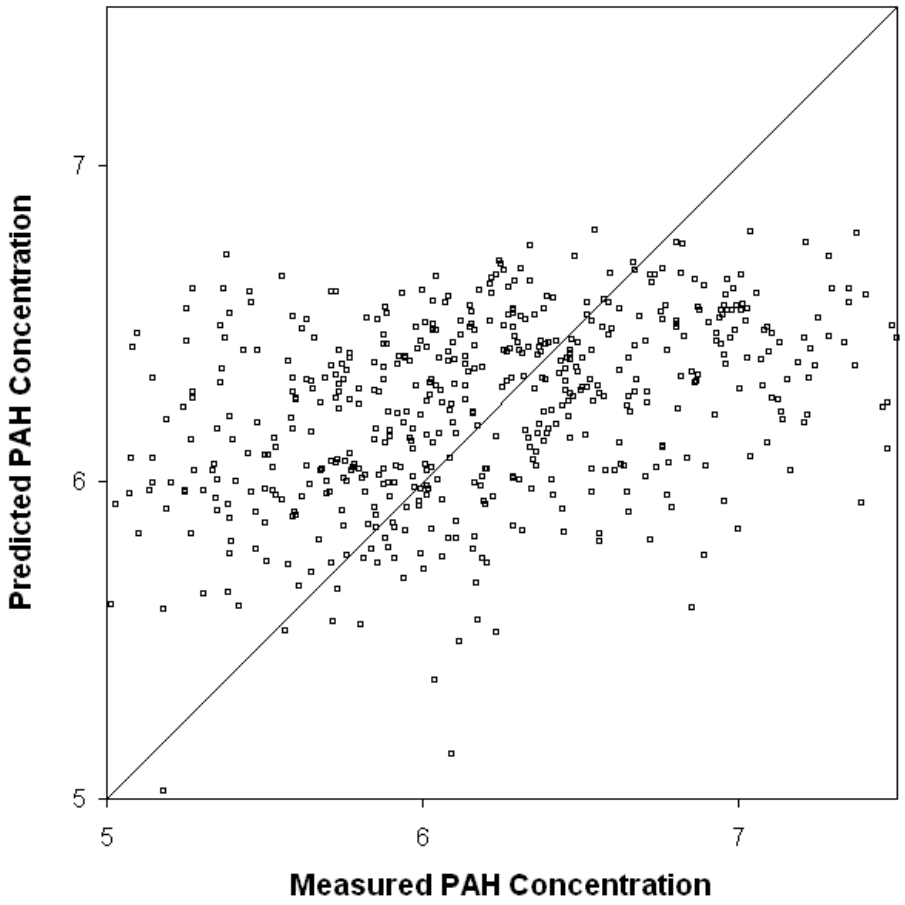


Figure 11. Median concentrations of BDE-47, BDE-99, and BDE-100 (ng/g) measured in residential-dust samples collected from 81 households participating in the Northern California Childhood Leukemia study from 2001-2007 compared to recently reported values from 3 other studies in California.

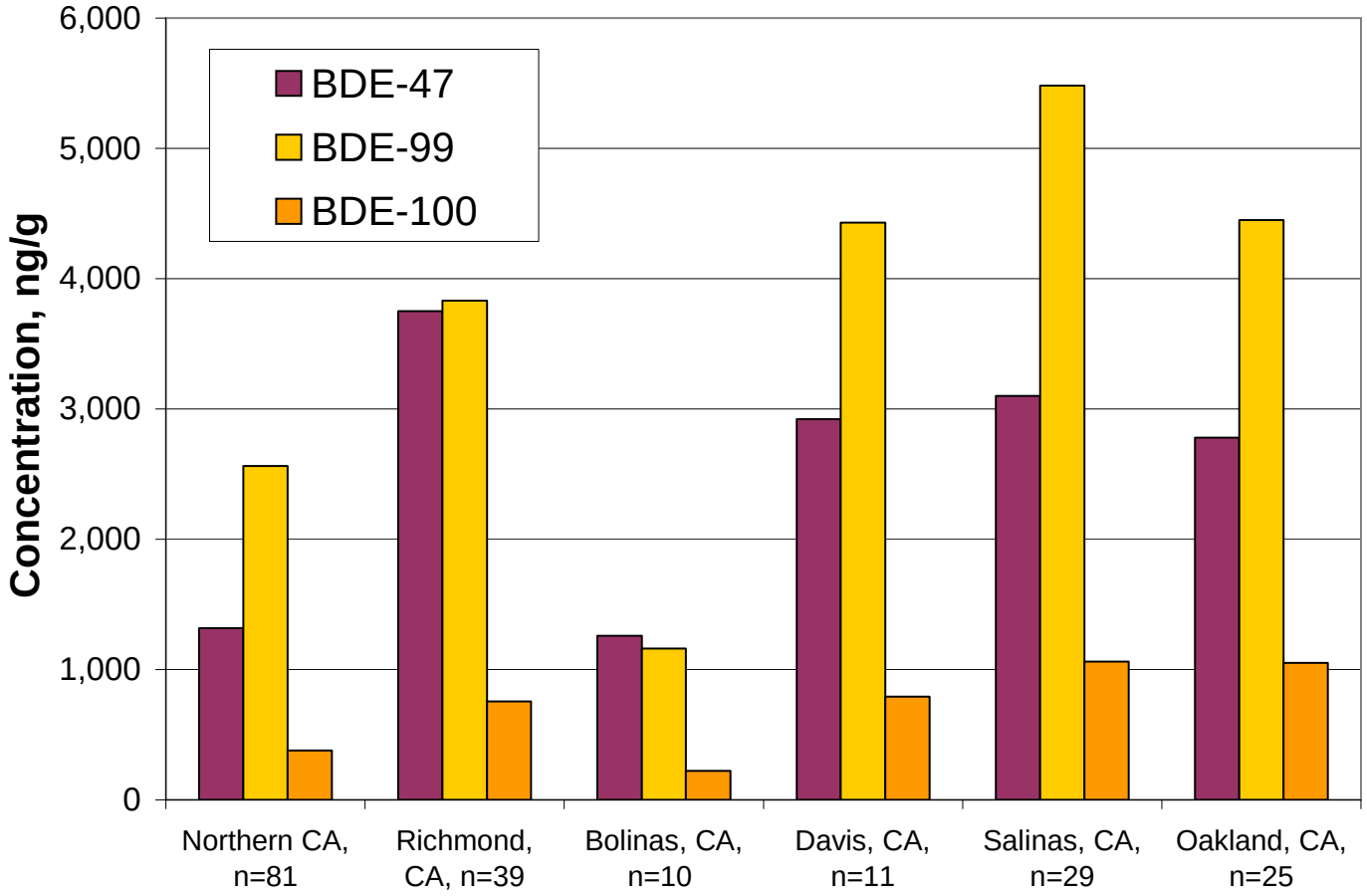
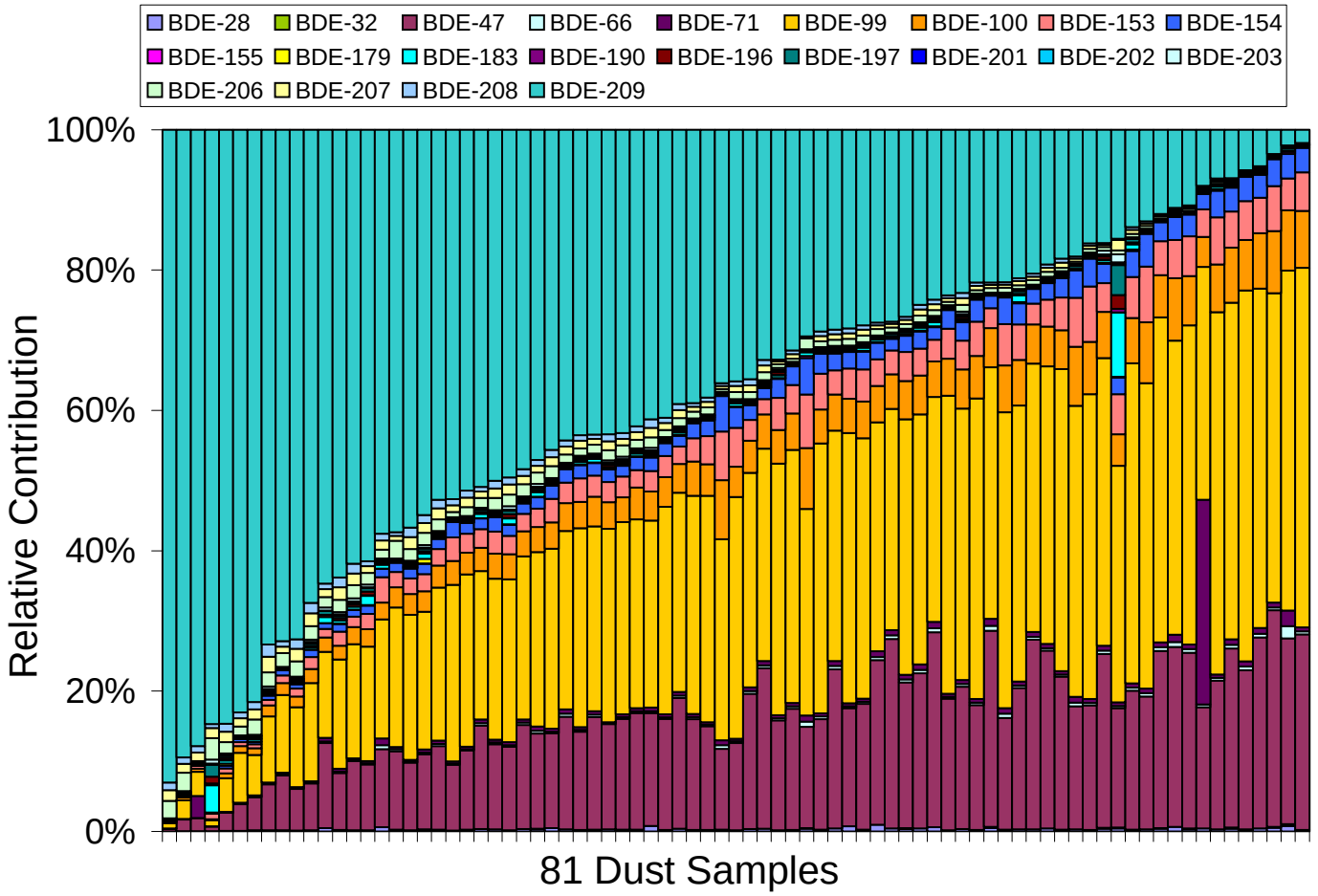
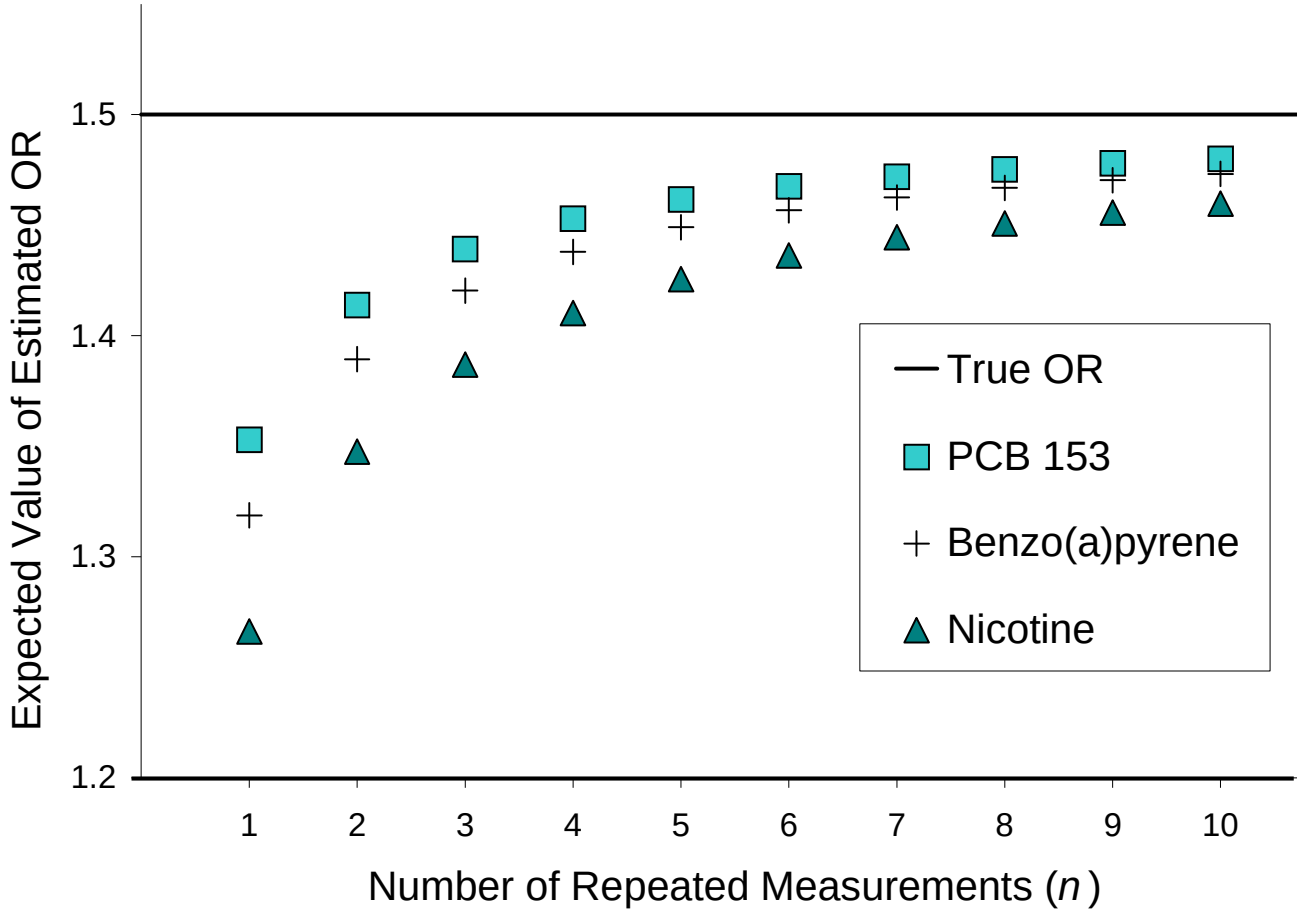


Figure 12. Relative contribution of 22 PBDE congeners to total PBDE dust concentrations in residential-dust samples collected from 81 households participating in the Northern California Childhood Leukemia Study from 2001-2007.



Note: Dust samples are ordered on the horizontal axis by the relative contribution of BDE-209, from most to least.

Figure 13. Expected odds ratio attenuation in case-control studies that use (logged) residential-dust chemical concentrations as measures of exposure, given various sampling strategies.



TABLES

Table 1. Global consumption (metric tons) of three commercial mixtures of polybrominated diphenyl ethers (PBDEs) in 2001.

Region	Penta-BDE	Octa-BDE	Deca-BDE	Total PBDE
Americas	7100	1500	24500	33100
Europe	150	610	7600	8360
Asia	150	1500	23000	24650
Other	100	180	1050	1330

Source: Birnbaum *et al*. (33)

Table 2. Median and maximum concentrations (ng/g) of major polybrominated diphenyl ether congeners in residential-dust samples, 2003-2010.

					BDE-47		BDE-99		BDE-100		BDE-153		BDE-183		BDE-209	
Region	Country	Year	Ref	N	Median	Max	Median	Max	Median	Max	Median	Max	Median	Max	Median	Max
North America	Canada	2005	(80)	68	300	33000	430	60000	73	21000	49	25000	19	650	630	10000
North America	Canada	2008	(37)	10[d]	140	720	330	1800	65	420	43	260	9	30	560	1100
North America	United States	2003	(94)	120	<400	9860	304	22500	<300	3400	-	-	-	-	-	-
North America	United States	2005	(178)[a]	9	364	10538	612	13841	103	2605	61	1097	19	44	665	65777
North America	United States	2005	(39)	17	644	7610	676	13800	119	2090	64	1510	18	168	1350	8750
North America	United States	2007	(78)	11	670	14610	1010	14800	170	2780	110	560	-	-	<500	9600
North America	United States	2008	(30)[b,c]	20	1865	16840	2460	24510	436	4274	234	2377	28	230	4502	184600
North America	United States	2008	(37)	20[d]	410	3300	820	6000	160	840	110	1800	16	170	1300	3300
North America	United States	2008	(66)[a]	11	2920	8830	4430	11700	793	2000	-	-	-	-	-	-
North America	United States	2008	(40)	10	430	3000	880	3700	150	660	140	650	70	4000	2000	21000
North America	United States	2008	(179)	1	1042	1042	747	747	111	111	42	42	5	5	40	40
North America	United States	2008	(38)	49	2700	107000	3800	170000	684	30900	-	-	-	-	-	-
North America	United States	2009	(87)	20	2000	46000	4600	79000	1200	78000	110	790	220	7600	190	66000
North America	United States	2009	(41)[b]	38	520	-	614	-	120	-	73	-	-	-	1398	-
North America	United States	2009	(15)	12	40	354	95	664	16	122	26	82	<21	64	903	9210
North America	United States	2009	(4)	24	500	7620	838	9220	180	2830	-	-	-	-	-	-
North America	United States	2009	(42)[a,c]	4	205	617	245	1278	44	199	20	141	7	28	1038	4156
North America	United States	2010	(43)[c]	50	390	8627	427	12967	100	2164	56	1352	17	688	1482	32366
North America	United States	2010	(44)[b]	30	<1918[f]	-	<1918[f]	-	<1918[f]	-	<1918[f]	-	<78	-	1534	-
North America	United States	2011	(67)[c]	29	3100	29200	5480	43200	1060	7490	-	-	-	-	-	-
Europe	Belgium	2004	(48)	23[e]	<20	751	29	944	<20	207	<20	86	<20	75	<100	303677
Europe	Belgium	2008	(180)[a]	8	-	-	-	-	-	-	-	-	-	-	144	292
Europe	Belgium	2009	(52)	19	<12[f]	-	<12[f]	-	<12[f]	-	<12[f]	-	<12[f]	-	106	588
Europe	Belgium	2010	(54)	43	8	>62[g]	9	>110[g]	1	>12[g]	2	>44[g]	1	>10[g]	313	>1513
Europe	Denmark	2003	(46)	1	66	66	<0.1	<0.1	11	11	23	23	11	11	260	260
Europe	Denmark	2010	(55)	42	17	962	14	1764	2	292	2	182	4	47	332	58064
Europe	Finland	2003	(46)	1	10	10	9	9	4	4	4	4	<0.1	<0.1	100	100

Table 2. continued

					BDE-47		BDE-99		BDE-100		BDE-153		BDE-183		BDE-209	
Region	Country	Year	Ref	N	Median	Max	Median	Max	Median	Max	Median	Max	Median	Max	Median	Max
Europe	Germany	2003	(49)	40	17	1910	24	2850	4	314	6	420	6	464	265	19100
Europe	Germany	2003	(51)	1[e]	31	31	37	37	8	8	-	-	2	2	2800	2800
Europe	Germany	2008	(45)	10	<14	22	10	28	<6	7	<6	22	<6	120	63	410
Europe	Germany	2009	(54)	34	9	255	13	390	2	81	3	41	4	60	312	1460
Europe	Italy	2003	(51)	1[e]	23	23	36	36	7	7	-	-	62	62	1600	1600
Europe	Portugal	2010	(55)[a]	9	19	52	6	32	2	7	3	8	4	21	953	1832
Europe	Romania	2008	(188)	1	-	-	-	-	-	-	-	-	-	-	27	27
Europe	Spain	2003	(51)	4[e]	13	16	18	21	4	4	-	-	4	39	425	1700
Europe	Spain	2006	(189)	4	22	59	26	64	5	20	3	3	-	-	-	-
Europe	Spain	2007	(53)	6	12	70	10	60	2	18	3	9	22	142	184	1615
Europe	Spain	2008	(188)	1	-	-	-	-	-	-	-	-	-	-	138	138
Europe	Sweden	2007	(52)[a]	5	26	160	58	194	9	92	5	7	2	17	158	1560
Europe	United Kingdom	2003	(50)	10[e]	25	1980	44	2100	9	230	23	170	10	87	7100	19900
Europe	United Kingdom	2006	(58)	9	16	62	37	85	6	16	7	10	9	20	3796	54795
Europe	United Kingdom	2008	(59)	30	10	58	20	180	3	17	5	110	4	550	8100	2200000
Europe	United Kingdom	2008	(42)	28[d]	13	160	23	320	4	50	5	110	13	550	2800	520000
Europe	United Kingdom	2008	(45)	10	22	180	28	300	4	52	5	53	5	18	10000	54000
Asia	China	2010	(34)	76	8	237	6	304	1	61	4	118	6	47	1792	9602
Asia	China	2010	(4)	27	<10[f]	-	<14[f]	-	<14[f]	-	<5[f]	-	<8[f]	-	4039	40500
Asia	Japan	2006	(64)	19	5	22	5	39	1	6	3	11	8	50	550	2600
Asia	Japan	2007	(30)[a]	13	7	2800	7	1700	1	260	2	150	3	16	110	3200
Asia	Japan	2009	(65)[a]	2	2	3	3	3	1	1	2	4	-	-	390	620
Asia	Philippines	2010	(66)	25	4	91	6	411	1	32	2	41	2	10	118	524
Asia	Singapore	2007	(63)	31	20	1500	24	6300	4	1200	7	1400	9	180	1000	13000
Asia	Thailand	2008	(67)	53	2	59	3	138	1	21	1	17	-	-	-	-
Other	Australia	2008	(45)	10	60	1400	100	3400	18	550	13	410	14	99	730	13000
Other	Australia	2009	(61)	10	56	-	87	-	18	-	7	-	3	-	291	-
Other	Australia	2009	(60)[a]	5	18	54	25	82	5	17	7	14	10	28	151	587
Other	Kuwait	2006	(62)	17	3	65	3	36	1	9	1	4	1	25	83	338
Other	New Zealand	2008	(42)	20[d]	24	150	51	380	9	70	5	35	-	-	-	-

Table 2. continued

[a] Median values were not reported; medians were calculated from reported raw data for use in this table
[b] Median values were not reported; reported geometric means were used in place of medians in this table
[c] Additional data from this reference are available; for Allen *et al.* (30) data for dust collected by high-volume surface sampler in the living room is presented, for Johnson *et al.* (43) data from the first round of dust sampling (for which more BDE congeners were analyzed) is presented, for Wei *et al.* (42) data from the first round of dust sampling is presented, for Quiros-Alcala *et al*. (67) data for dust collected in Salinas, CA is presented
[d] The number of dust samples analyzed varied by BDE congener
[e] The number of dust samples analyzed includes "pooled" samples that were amalgamations of dust from several residences
f Median values for individual congeners were not reported; maximum median values from reported group medians were inferred (*i.e.*, the median for BDE-47 must be less than the reported median for all tetra-BDEs)
[g] Maximum values were not reported; minimum maximum values were inferred from reported 95th percentiles

Table 3. Median and maximum concentrations (ng/g) of major polychlorinated biphenyl congeners in residential-dust samples, 2000-2009.

					PCB-105		PCB-118		PCB-138		PCB-153		PCB-180	
Region	Country	Year	Reference	*N*	Median	Maximum	Median	Maximum	Median	Maximum	Median	Maximum	Median	Maximum
North America	United States	2000	(93) (NY)	661	<30[c]	>140[d]	-	-	-	-	31	>340[e]	-	-
North America	United States	2000	(93) (MI)	38	<50[c]	>150[d]	-	-	-	-	32	>600[e]	-	-
North America	United States	2000	(93) (IA)	60	<20[c]	>50[d]	-	-	-	-	<20	>70[e]	-	-
North America	United States	2000	(93) (WA)	57	<30[c]	>80[d]	-	-	-	-	<20	>300[e]	-	-
North America	United States	2000	(93) (CA)	42	<30[c]	>40[d]	-	-	-	-	<20	>40[e]	-	-
North America	United States	2003	(94)	120	<200	16500	-	-	-	-	<200	35300	-	-
North America	United States	2003	(95)[a]	9	6	18	8	35	10	22	10	25	10	22
North America	United States	2005	(3)	1046	<20.8	3860	-	-	<20.8	10200	<20.8	6460	<20.8	2870
North America	United States	2009	(17)	20	3	20	6	44	7	31	7	22	3	20
North America	United States	2009	(96)	764	2	984	5	1760	-	-	-	-	-	-
North America	United States	2009	(5)	396	<1	49	<1	95	<1	145	<1	176	<2	108
North America	Canada	2009	(17)	10	4	23	9	55	10	49	10	36	7	24
Euroe	United Kingdom	2009	(17)	20	0.4	24	1	56	1	50	1	32	1	8
Asia	Singapore	2007	(26)	31	-	-	0.3	8	-	-	-	-	0.2	2
Asia	Japan	2003	(97)[a]	10	1	3	1	5	-	-	-	-	-	-
Asia	Japan	2009	(63)[b]	2	<5	<7	<5	<7	<1	<2	<1	<2	<0.5	<0.6
Other	New Zealand	2009	(17)	20	0.4	53	1	14	2	11	1	12	1	10

[a] Median values were not reported, a lognormal distribution was assumed and median values were estimated using the reported minimum and maximum values, *i.e.*, estimated median = exp ([ln(min) + ln(max)] / 2)
[b] Median values for individual congeners were not reported; maximum values for medians and maximums were inferred from reported group data (*i.e.*, the median for PCB-105 must be less than the reported median for all penta-chlorinated biphenyls)
[c] Maximum PCB-105 median values inferred from reported 75th percentiles of PCB-105
[d] Minimum PCB-105 maximum values inferred from reported 90th percentiles of PCB-105
[e] Minimum PCB-153 maximum values inferred from reported 90th percentiles of PCB-153

Table 4. Median and maximum concentrations (ng/g) of 7 polycyclic aromatic hydrocarbons (classified by the US EPA as probably carcinogenic to humans) in residential-dust samples, 1997-2010.

				B(*a*)a		Chr		B(*b*)f		B(*k*)f		B(*a*)p		I(*c,d*)p		D(*a,h*)a	
Location	Year	Ref.	*N*	Med	Max	Med	Max	Med	Max	Med	Max	Med	Max	Med	Max	Med	Max
Arizona	1997	(109)[a]	22	49	468	101	685	-[f]	-[f]	-[f]	-[f]	63	68	101	727	25	158
California	2000	(93)	42	60	>120[e]	-	-	-	-	-	-	80	>180[g]	-	-	-	-
Iowa	2000	(93)	60	150	>700[e]	-	-	-	-	-	-	160	>900[g]	-	-	-	-
Kentucky	1996	(108)[b]	4	44	220	124	360	-[f]	-[f]	-[f]	-[f]	82	190	82	210	22	98
Maryland	2005	(111)[a]	126	298	300000	585	343000	879	265000	466	275000	611	338000	244	273000	79	64000
Massachusetts	2003	(94)	120	499	10000	-	-	-	-	-	-	712	18100	-	-	-	-
Michigan	2000	(93)	38	600	>2200[e]	-	-	-	-	-	-	800	>3300[g]	-	-	-	-
New York	2000	(93)	661	1,140	>8700[e]	-	-	-	-	-	-	1,460	>10900[g]	-	-	-	-
North Carolina	1997	(109)[a]	13	117	1465	162	1052	-[f]	-[f]	-[f]	-[f]	63	931	88	879	19	240
North Carolina	1999	(18)[b]	24	166	690	347	2410	-[f]	-[f]	-[f]	-[f]	210	630	187	700	91	410
North Carolina	1999	(145)	1[d]	230	230	410	410	550	550	300	300	280	280	340	340	80	80
North Carolina	2003	(95)[b]	9	99	519	176	838	276	1440	97	496	136	768	184	963	69	294
Texas	1997	(110)[c]	9	103	-	193	-	162	-	108	-	128	-	140	-	32	-
Texas	2010	(106)[a]	23	1860	20800	5020	38300	4000	38400	1380	15200	2050	24200	2050	18700	570	5270
Washington	2000	(93)	57	130	>700[e]	-	-	-	-	-	-	150	>900[g]	-	-	-	-
Brisbane, Australia	2005	(182)	12	<10	80	40	240	170	300	-	-	80	170	40	90	-	-
Ottawa, Canada	2008	(117)	51	696	32100	1190	35100	1660	54000	532	19000	803	38800	911	33500	185	6270
Berlin, Germany	2004	(183)	61	290	1410	550	2000	540	1900	370	1910	270	1390	330	1170	50	290
Palermo, Italy	2008	(116)[a]	28	33	712	147	1413	73	1051	41	662	46	608	56	363	63	451
Kuwait	2007	(19)	24	-	203	-	501	-	289	-	341	-	398	-	88	-	23

Legend: B(*a*)a=benzo(*a*)anthracene, Chr=chrysene, B(*b*)f=benzo(*b*)fluoranthene, B(*k*)f=benzo(*k*)fluoranthene, B(*a*)p=benzo(*a*)pyrene, I(*c,d*)p=indeno(*1,2,3-c,d*)pyrene, D(*a,h*)a=dibenzo(*a,h*)anthracene

[a]Median values were not reported; medians were calculated from reported raw data for use in this table

[b]Median values were not reported, a lognormal distribution was assumed and median values were estimated using the reported minimum and maximum values, *i.e.*, estimated median = exp ([ln(min) + ln(max)] / 2)

[c]Additional data from Murkerjee *et al.* (110) is available; data for dust collected in the spring is presented

[d]Dust sample analyzed was a "pooled" sample that was an amalgamation of dust from several residences

[e]Minimum benzo(*a*)anthracene maximum values inferred from reported 90th percentiles of benzo(*a*)anthracene

[f]benzofluoranthenes not resolved

[g]Minimum benzo(*a*)pyrene maximum values inferred from reported 90th percentiles of benzo(*a*)pyrene

Table 5. Median and maximum concentrations (ng/g) of nicotine in residential-dust samples, by residents' smoking status, 1991-2011.

			Smoking Homes			Non-smoking Homes		
Year	Reference	Location	*N*	Median	Maximum	*N*	Median	Maximum
1991	(20)	Denmark	38	242	1592	34	18	125
2004	(123)[a]	Sweden	15	212	393	8	20	78
2008	(124)	Maryland	30	43	300	7	12	27
2011	(120)[b]	California	93	40	52	50	2.9	4.0

[a]Additional data from Willers *et al.* is available; data for dust collected using the modified vacuum cleaner is presented
[b]Median values were not reported, geometric means are presented

Table 6. Details of residential dust chemical analyses, Northern California Childhood Leukemia Study, 2010.

Chemical	Structural Description	Internal Standard[a]	Recovery Standard[b]	Molecular Weight	Quantification Ion	Retention Time, Min.
BDEs						
BDE-32	2,4',6-Tribrominated diphenyl ether	BDE-28L	BDE-77L	406.90	405.8021	4.51
BDE-28	2,4,4'-Tribrominated diphenyl ether	BDE-28L	BDE-77L	406.90	405.8021	5.80
BDE-71	2,3',4',6-Tetrabrominated diphenyl ether	BDE-47L	BDE-77L	485.80	485.7106	8.98
BDE-47	2,2',4,4'-Tetrabrominated diphenyl ether	BDE-47L	BDE-77L	485.80	485.7106	9.50
BDE-66	2,3',4,4'-Tetrabrominated diphenyl ether	BDE-47L	BDE-77L	485.80	485.7106	10.10
BDE-100	2,2',4,4',6-Pentabrominated diphenyl ether	BDE-100L	BDE-77L	564.69	563.6211	12.13
BDE-99	2,2',4,4',5-Pentabrominated diphenyl ether	BDE-99L	BDE-77L	564.69	563.6211	13.00
BDE-155	2,2',4,4',6,6'-Hexabrominated diphenyl ether	BDE153L	BDE-154L	643.59	483.6950	14.40
BDE-154	2,2',4,4',5,6'-Hexabrominated diphenyl ether	BDE153L	BDE-154L	643.59	483.6950	14.93
BDE-153	2,2',4,4',5,5'-Hexabrominated diphenyl ether	BDE153L	BDE-154L	643.59	483.6950	16.19
BDE-179	2,2,3,3',5,6,6'-Heptabrominated diphenyl ether	BDE-183L	BDE-154L	722.48	561.6055	18.62
BDE-183	2,2',3,4,4',5',6-Heptabrominated diphenyl ether	BDE-183L	BDE-154L	722.48	561.6055	19.01
BDE-190	2,3,3',4,4',5,6-Heptabrominated diphenyl ether	BDE-183L	BDE-154L	722.48	561.6055	20.76
BDE-202	2,2',3,3',5,5',6,6'-Octabrominated diphenyl ether	BDE-197L	BDE-154L	801.38	641.5140	21.62
BDE-201	2,2',3,3',4,5',6,6'-Octabrominated diphenyl ether	BDE-197L	BDE-154L	801.38	641.5140	21.92
BDE-197	2,2',3,3',4,4',6,6'-Octabrominated diphenyl ether	BDE-197L	BDE-154L	801.38	641.5140	22.20
BDE-203	2,2',3,4,4',5,5',6-Octabrominated diphenyl ether	BDE-197L	BDE-154L	801.38	641.5140	22.79
BDE-196	2,2',3,3',4,4',5,6'-Octabrominated diphenyl ether	BDE-197L	BDE-154L	801.38	641.5140	22.98
BDE-208	2,2',3,3',4,5,5',6,6'-Nonabrominated diphenyl ether	BDE-207L	BDE-154L	880.28	719.4245	25.70
BDE-207	2,3',3,3',4,4',5,6,6'-Nonabrominated diphenyl ether	BDE-207L	BDE-154L	880.28	719.4245	26.00
BDE-206	2,2',3,3',4,4',5,5',6-Nonabrominated diphenyl ether	BDE-207L	BDE-154L	880.28	719.4245	26.81
BDE-209	Decabrominated diphenyl ether	BDE-209L	BDE-154L	959.17	799.3329	30.08
PCBs						
PCB-28	2,4,4'-Trichlorinated biphenyl	PCB-28L	PCB-47L	257.55	255.9608	12.68
PCB-52	2,2',5,5'-Tetrachlorinated biphenyl	PCB-52L	PCB-47L	291.99	291.9189	13.59
PCB-101	2,2',4,5,5'-Pentachlorinated biphenyl	PCB-101L	PCB-128L	326.44	325.8799	17.16
PCB-118	2,3',4,4',5-Pentachlorinated biphenyl	PCB-118L	PCB-128L	326.44	325.8799	20.95
PCB-114	2,3,4,4',5-Pentachlorinated biphenyl	PCB-114L	PCB-128L	326.44	325.8799	21.66
PCB-153	2,2',4,4',5,5'-Hexachlorinated biphenyl	PCB-153L	PCB-178L	360.88	359.8409	22.04
PCB-105	2,3,3',4,4'-Pentachlorinated biphenyl	PCB-105L	PCB-128L	326.44	325.8799	22.72
PCB-138	2,2',3,4,4',5-Hexachlorinated biphenyl	PCB-138L	PCB-178L	360.88	359.8409	23.94
PCB-167	2,3',4,4',5,5'-Hexachlorinated biphenyl	PCB-167L	PCB-178L	360.88	359.8409	26.36
PCB-156	2,3,3',4,4',5-Hexachlorinated biphenyl	PCB-156L	PCB-178L	360.88	359.8409	28.27
PCB-157	2,3,3',4,4',5'-Hexachlorinated biphenyl	PCB-157L	PCB-178L	360.88	359.8409	28.59
PCB-180	2,2',3,4,4',5,5'-Heptachlorinated biphenyl	PCB-180L	PCB-178L	395.33	393.8019	29.08
PCB-189	2,3,3',4,4',5,5'-Heptachlorinated biphenyl	PCB-189L	PCB-178L	395.33	393.8019	34.69
PCB-194	2,2',3,3',4,4',5,5'-Octachlorinated biphenyl	PCB-194L	PCB-178L	429.77	429.7600	37.24
PCB-209	Decachlorinated biphenyl	PCB-209L	PCB-178L	498.66	497.6821	41.80

Table 6. continued

Chemical	Structural Description	Internal Standard[a]	Recovery Standard[b]	Molecular Weight	Quantification Ion	Retention Time, Min.
PAHs						
phenanthrene	Tricyclic aromatic hydrocarbon	benzo(*a*)pyrene-L	pyrene-L	178.2	178.2	8.75
anthracene	Tricyclic aromatic hydrocarbon	benzo(*a*)pyrene-L	pyrene-L	178.2	178.2	8.80
fluoranthene	Tetracyclic aromatic hyrdrocarbon	benzo(*a*)pyrene-L	pyrene-L	202.3	202.3	10.95
pyrene	Tetracyclic aromatic hyrdrocarbon	benzo(*a*)pyrene-L	pyrene-L	202.3	202.3	11.60
benzo(*a*)anthracene	Tetracyclic aromatic hyrdrocarbon	benzo(*a*)pyrene-L	pyrene-L	228.3	228.3	15.90
chrysene	Tetracyclic aromatic hyrdrocarbon	benzo(*a*)pyrene-L	pyrene-L	228.3	228.3	16.10
benzo(*b*)fluoranthene	Pentacyclic aromatic hydrocarbon	benzo(*a*)pyrene-L	pyrene-L	252.3	252.3	21.50
benzo(*k*)fluoranthene	Pentacyclic aromatic hydrocarbon	benzo(*a*)pyrene-L	pyrene-L	252.3	252.3	21.60
benzo(*a*)pyrene	Pentacyclic aromatic hydrocarbon	benzo(*a*)pyrene-L	pyrene-L	252.3	252.3	23.50
indeno(*1,2,3-c,d*)pyrene	Hexacyclic aromatic hydrocarbon	benzo(*a*)pyrene-L	pyrene-L	276.3	276.3	29.90
dibenzo(*a,h*)anthracene	Pentacyclic aromatic hydrocarbon	benzo(*a*)pyrene-L	pyrene-L	278.3	278.3	30.05
benzo(*g,h,i*)perylene	Hexacyclic aromatic hydrocarbon	benzo(*a*)pyrene-L	pyrene-L	276.3	276.3	31.30

[a] Here, “internal standard” refers to an isotopically labeled standard that is spiked into dust before extraction
[b] Here, “recovery standard” refers to an isotopically labeled standard that is spiked into the concentrated extract before chemical analysis

Table 7. Parameter optimization for dust extraction and purification protocol, Northern California Childhood Leukemia Study, 2010.

	Column chromatography			
ASE Extraction solvent(s)	Column contents	Elution solvent(s)	GPC	Result
Hexane				Poor PCB/BDE recovery
Hexane:methylene chloride (95:5)				Acceptable PCB/BDE recovery; delayed retention times
Hexane:methylene chloride (80:20)				Some particulate in extract
Hexane:methylene chloride (50:50)				Heavy particulate in extract
Methylene chloride				Heavy particulate in extract
Hexane:methylene chloride (95:5)	2g silica gel	20 mL hexane		Poor BDE recovery; delayed retention times
Hexane:methylene chloride (95:5)	1g acid silica, 1g silica	20 mL hexane		Poor BDE recovery; delayed retention times
Hexane:methylene chloride (95:5)	2g fluorosil, 2g silica	50 mL hexane		Poor PCB/BDE recovery; delayed retention times
Hexane:methylene chloride (95:5)	2g silica, 2g acid silica, 2g alumina	75 mL hexane	Yes	Acceptable PCB/PBDE recovery and chromatography; poor PAH recovery
	3g silica, 3g acid silica, 3g silica	100 mL hexane	Yes	Poor PAH recovery
	3g silica, 3g acid silica, 3g silica	100 mL hexane:methylene chloride (1:1)	Yes	Poor PAH recovery
	3g silica, 3g acid silica, 3g silica	100 mL hexane:acetone (1:1)	Yes	Poor PAH recovery
	3g silica, 3g acid silica, 3g silica	100 mL methylene chloride	Yes	Poor PAH recovery
	7.5g silica	100 mL hexane	Yes	Poor PAH recovery
	7.5g silica	100 mL cyclohexane	Yes	Poor PAH recovery
	7.5g silica	100 mL hexane:methylene chloride (1:1)	Yes	Acceptable PAH recovery
Hexane:methylene chloride (95:5)	7.5g silica	100 mL hexane:methylene chloride (1:1)	Yes	Acceptable recovery for all analytes

Table 8. Concentrations (ng/g) of 8 replicate samples of National Institute of Standards and Technology (NIST) Standard Reference Material 2585 compared to certified values, Northern California Childhood Leukemia Study, 2010.

Chemical	Certified NIST	Replicate Average	Average RPD	1	2	3	4	5	6	7	8
BDE-28	47	46	-3%	52	47	45	45	43	48	42	41
BDE-47	497	497	0%	547	509	508	505	454	541	469	440
BDE-66	30	30	1%	36	30	31	31	24	33	27	27
BDE-100	145	147	2%	164	149	145	146	135	160	142	137
BDE-99	892	1135	27%	1323	931	1186	1214	1070	1285	1058	1015
BDE-154	84	84	1%	96	84	86	82	79	89	79	79
BDE-153	119	147	23%	172	141	136	138	141	159	149	137
BDE-183	43	50	16%	57	44	48	50	48	58	46	48
BDE-190	5	4	-18%	4	5	4	4	4	4	4	4
BDE-203	37	42	13%	43	42	38	41	36	54	38	41
BDE-206	271	211	-22%	199	257	199	203	187	245	199	195
BDE-209	2510	4160	66%	4621	3919	2795	2824	5166	4144	4964	4843
PCB-28	13.4	9	-36%	9	-	10	10	-	8	7	8
PCB-52	21.8	17	-23%	20	-	18	19	-	15	14	15
PCB-101	29.8	30	0%	36	-	31	38	-	27	23	23
PCB-118	26.3	22	-15%	27	-	25	25	-	21	19	18
PCB-105	13.2	11	-19%	12	-	12	12	-	10	9	9
PCB-153	40.2	30	-25%	32	-	36	39	-	28	21	24
PCB-138	27.6	30	9%	34	-	33	37	-	27	26	24
PCB-180	18.4	18	-5%	13	-	24	24	-	13	17	14
phenanthrene	1920	1037	-46%	1382	758	938	1028	1110	1005	-	-
anthracene	96	46	-52%	75	19	42	44	48	46	-	-
fluoranthene	4380	3104	-29%	4014	2612	2522	3468	3130	2880	-	-
pyrene	3290	2443	-26%	3129	2043	2026	2687	2484	2287	-	-
benzo(*a*)anthracene	1160	1000	-14%	1197	920	931	1005	951	996	-	-
chrysene	2260	2451	8%	3002	2259	2242	2500	2275	2427	-	-
benzo(*b*)fluoranthene	2700	2994	11%	3199	3101	2850	2999	2778	3040	-	-
benzo(*k*)fluoranthene	1330	1616	22%	2125	1413	1594	1518	1382	1664	-	-
benzo(*a*)pyrene	1140	949	-17%	1087	953	893	942	883	938	-	-
indeno(*1,2,3-c,d*)pyrene	2080	1751	-16%	1903	1761	1824	1642	1467	1906	-	-
dibenzo(*a,h*)anthracene	301	500	66%	448	424	565	499	471	593	-	-
benzo(*g,h,i*)perylene	2280	2155	-5%	2314	2162	2257	2048	1817	2333	-	-

Legend: RPD = relative percent difference between certified NIST SRM 2585 values and replicate average

Table 9. Mass of chemicals (pg) measured in 13 method blanks, Northern California Childhood Leukemia Study, 2010.

Chemical	1	2	3	4	5	6	7	8	9	10	11	12	13	MRL, pg	LOQ, pg	MRC, ng/g
Major BDEs																
BDE-47	-	1124	2868	332	361	1082	1474	1555	2151	459	-	-	908	2447	12	12
BDE-100	-	291	451	73	72	153	313	182	549	93	-	-	118	500	12	3
BDE-99	-	2057	2880	544	562	880	2002	1542	3577	434	-	-	673	3283	12	16
BDE-154	-	143	152	37	33	54	167	ND	238	41	-	-	55	223	24	1
BDE-153	-	237	274	108	58	104	312	123	487	72	-	-	98	413	24	2
BDE-206	-	3177	98	ND	24	ND	170	ND	296	296	-	-	34	3446	24	17
BDE-209	-	81454	3440	ND	ND	2007	4351	2144	7467	5147	-	-	1134	82725	480	414
Other BDEs																
BDE-32	-	ND	ND	ND	ND	ND	ND	38	13	ND	-	-	ND	53	12	0.3
BDE-28	-	48	139	ND	11	55	67	ND	48	20	-	-	35	118	12	0.6
BDE-71	-	ND	119	ND	16	44	80	34	64	22	-	-	ND	109	12	0.5
BDE-66	-	37	64	539	600	18	41	31	36	12	-	-	ND	711	12	4
BDE-155	-	ND	ND	ND	ND	7	18	ND	20	ND	-	-	18	17	24	0.1
BDE-179	-	ND	ND	ND	ND	22	13	ND	ND	29	-	-	18	20	24	0.1
BDE-183	-	93	192	90	ND	120	150	ND	103	130	-	-	60	122	24	0.6
BDE-190	-	ND	17	ND	ND	ND	ND	ND	ND	124	-	-	ND	227	24	1
BDE-201	-	350	79	118	10	46	26	ND	ND	145	-	-	ND	348	24	2
BDE-202	-	ND	9	ND	ND	21	55	ND	50	194	-	-	ND	223	24	1
BDE-197	-	316	83	120	11	60	118	ND	55	217	-	-	43	290	24	1
BDE-203	-	521	64	ND	ND	43	168	ND	ND	342	-	-	ND	606	24	3
BDE-196	-	469	82	ND	ND	55	92	ND	56	265	-	-	ND	499	24	2
BDE-208	-	2582	101	ND	31	85	248	72	170	510	-	-	37	2467	24	12
BDE-207	-	3185	145	ND	42	107	316	109	242	518	-	-	71	3025	24	15
Major PCBs																
PCB-52	-	67	360	6	20	95	110	292	106	77	101	176	-	326	50	2
PCB-101	-	115	635	13	30	183	112	103	150	49	25	55	-	525	50	3
PCB-118	-	40	254	14	23	90	61	47	140	26	6	56	-	217	50	1
PCB-153	-	54	670	53	60	196	123	63	317	79	19	96	-	570	50	3
PCB-138	-	330	658	254	355	428	466	404	607	352	288	378	-	376	50	2
PCB-180	-	81	730	89	105	284	204	90	321	21	33	100	-	614	50	3
Other PCBs																
PCB-28	-	18	213	8	13	84	56	109	31	17	17	23	-	186	50	0.9
PCB-114	-	ND	ND	ND	ND	ND	ND	ND	ND	ND	2	ND	-	-	50	0.3
PCB-105	-	26	72	ND	14	36	14	21	40	10	4	14	-	60	50	0.3
PCB-167	-	6	38	5	ND	13	8	19	12	ND	ND	10	-	32	50	0.2
PCB-156	-	9	48	7	9	13	12	22	25	ND	ND	16	-	38	50	0.2
PCB-157	-	ND	ND	ND	ND	ND	1	15	4	ND	ND	4	-	18	50	0.1
PCB-189	-	ND	ND	ND	ND	ND	ND	12	ND	ND	ND	ND	-	-	50	0.3
PCB-194	-	35	146	ND	28	74	54	39	68	2	5	29	-	126	50	0.6
PCB-209	-	5	ND	ND	2	ND	ND	9	8	ND	ND	ND	-	10	50	0.1

Table 9. continued

Chemical	1	2	3	4	5	6	7	8	9	10	11	12	13	MRL, pg	LOQ, pg	MRC, ng/g
PAHs																
Phenanthrene	3666	4005	219307	1510	12726	109014	70790	27210	34628	6628	6526	14206	3195	188042	800	940
Anthracene	47	365	2130	30	234	1218	927	326	417	193	197	306	129	1789	800	9
Fluoranthene	1516	3036	45600	485	2501	19437	9228	4984	5618	1626	1750	3212	2211	37246	800	186
Pyrene	875	2877	16011	522	1193	6193	3000	2085	2875	1403	904	1416	2193	12366	800	62
benzo(*a*)anthracene	219	1567	85	39	133	159	67	65	220	76	48	53	180	1226	800	6
Chrysene	1703	2240	718	157	315	1082	368	367	1326	323	214	238	663	1964	800	10
benzo(*b*)fluoranthene	1237	592	197	63	139	478	176	136	909	146	90	148	323	1078	800	5
benzo(*k*)fluoranthene	1205	475	80	26	99	381	86	206	436	143	153	108	424	945	800	5
benzo(*a*)pyrene	14	119	318	128	97	350	132	131	497	209	221	194	245	380	800	2
indeno(*1,2,3-c,d*)pyrene	827	196	53	38	83	281	63	63	511	10	53	54	84	715	800	4
dibenzo(*a,h*)anthracene	139	70	1	5	3	66	3	18	117	6	21	29	42	137	800	0.7
benzo(*g,h,i*)perylene	846	292	379	80	119	549	195	115	1275	76	87	107	488	1086	800	5

Legend: MRL = method reporting limit; LOQ = limit of quantitation; MRC = minimum reportable concentration

Table 10. Relative percent difference between 12 sets of duplicate residential-dust samples, Northern California Childhood Leukemia Study, 2010.

Chemical	1	2	3	4	5	6	7	8	9	10	11	12	Average
Major BDEs													
BDE-47	5	1	1	2	7	0.01	5	3	0.1	6	-	-	3
BDE-100	11	1	6	0	2	2	4	3	0.2	8	-	-	4
BDE-99	3	0.1	8	5	8	4	7	7	3	2	-	-	5
BDE-154	8	1	8	3	1	1	0.4	0.3	1	3	-	-	3
BDE-153	11	0.5	4	2	1	0.1	4	4	1	2	-	-	3
BDE-206	-	-	13	3	10	6	22	6	2	9	-	-	9
BDE-209	11	22	4	6	-	2	3	10	1	16	-	-	8
Other BDEs													
BDE-32	-	-	-	-	-	42	-	7	9	-	-	-	19
BDE-28	4	4	1	5	1	0.04	7	1	5	4	-	-	3
BDE-71	193	4	0.04	6	2	1	1	4	4	1	-	-	21
BDE-66	7	4	3	16	17	5	16	20	18	0.1	-	-	11
BDE-155	1	7	12	8	0.1	0.1	4	5	6	5	-	-	5
BDE-179	-	-	-	-	-	19	-	74	-	77	-	-	57
BDE-183	17	8	120	4	3	0.2	7	2	14	12	-	-	19
BDE-190	24	127	123	4	1	46	-	13	38	32	-	-	45
BDE-201	58	143	2	6	33	13	58	29	34	23	-	-	40
BDE-202	57	11	9	5	25	4	31	41	35	11	-	-	23
BDE-197	45	11	100	9	5	4	15	31	53	11	-	-	28
BDE-203	34	30	33	10	7	14	40	40	43	9	-	-	26
BDE-196	27	33	55	10	11	10	30	26	35	14	-	-	25
BDE-208	-	-	12	4	22	2	50	17	18	20	-	-	18
BDE-207	-	-	10	6	16	1	46	20	16	16	-	-	17
Major PCBs													
PCB-52	14	50	24	11	7	4	18	4	58	-	-	-	21
PCB-101	1	75	34	5	8	8	9	1	5	-	-	-	16
PCB-118	21	79	51	1	0	2	19	5	2	-	-	-	20
PCB-153	5	25	65	7	6	13	10	18	17	-	-	-	19
PCB-138	13	29	-	-	1	5	12	24	7	-	-	-	13
PCB-180	0	47	46	20	7	2	45	7	8	-	-	-	20
Other PCBs													
PCB-28	17	17	12	1	3	19	17	8	-	-	-	-	12
PCB-114	-	73	-	-	-	-	-	-	8	-	-	-	40
PCB-105	22	87	36	1	2	2	12	8	2	-	-	-	19
PCB-167	16	31	47	-	2	2	14	15	9	-	-	-	17
PCB-156	5	54	52	2	15	3	15	7	1	-	-	-	17
PCB-157	32	69	55	-	28	-	1	72	2	-	-	-	37
PCB-189	-	22	-	-	-	-	91	-	6	-	-	-	40
PCB-194	7	57	39	-	5	5	42	12	9	-	-	-	22
PCB-209	7	15	33	38	16	4	11	21	6	-	-	-	17

Table 10. continued

Chemical	1	2	3	4	5	6	7	8	9	10	11	12	Average
PAHs													
Phenanthrene	9	2	7	2	1	31	20	12	11	3	2	9	9
Anthracene	15	25	4	3	15	15	36	12	5	18	7	36	16
Fluoranthene	46	17	8	7	5	10	24	16	5	6	7	6	13
Pyrene	46	13	1	8	4	2	21	2	2	2	5	8	10
benzo(*a*)anthracene	45	23	11	3	11	1	31	19	2	7	7	33	16
Chrysene	33	17	7	6	7	10	14	10	3	4	9	13	11
benzo(*b*)fluoranthene	42	20	7	5	10	11	2	5	11	9	3	8	11
benzo(*k*)fluoranthene	44	12	11	20	25	14	42	11	0.2	3	24	14	18
benzo(*a*)pyrene	46	16	28	13	7	7	26	13	4	8	2	17	16
indeno(*1,2,3-c,d*)pyrene	37	15	4	3	0.3	9	15	10	8	4	2	5	9
dibenzo(*a,h*)anthracene	52	16	3	47	18	24	58	11	27	7	3	17	23
benzo(*g,h,i*)perylene	35	14	9	4	9	5	17	6	8	2	4	1	9

Table 11. Concentrations (ng/g) of 12 inter-batch quality control residential-dust samples, Northern California Childhood Leukemia Study, 2010.

Chemical	1	2	3	4	5	6	7	8	9	10	11	12	CV
Major BDEs													
BDE-47	303	302	289	271	265	266	344	344	310	381	-	-	0.13
BDE-100	70	72	70	60	60	59	75	73	71	79	-	-	0.10
BDE-99	424	420	398	347	343	343	400	418	388	438	-	-	0.09
BDE-154	24	21	23	20	19	21	23	24	22	26	-	-	0.09
BDE-153	34	32	34	27	26	30	32	37	31	36	-	-	0.11
BDE-206	68	47	23	27	42	53	40	25	22	38	-	-	0.38
BDE-209	3265	1792	806	955	ND	1536	1660	791	750	1071	-	-	0.57
Other BDEs													
BDE-32	ND	ND	ND	ND	ND	ND	ND	3	2	3	-	-	0.10
BDE-28	6	6	6	5	5	5	8	7	7	8	-	-	0.15
BDE-71	9	8	9	8	8	ND	10	9	10	13	-	-	0.16
BDE-66	5	5	5	4	5	4	7	6	5	7	-	-	0.19
BDE-155	2	1	2	1	1	2	2	2	2	ND	-	-	0.11
BDE-179	ND	ND	ND	ND	ND	0	0	31	0	0	-	-	2.18
BDE-183	5	5	15	4	5	5	6	40	6	6	-	-	1.14
BDE-190	1	1	1	0	1	ND	ND	2	1	ND	-	-	0.81
BDE-201	5	3	2	3	4	5	1	0	0	1	-	-	0.76
BDE-202	2	1	1	1	1	2	2	2	1	2	-	-	0.27
BDE-197	6	4	7	4	5	5	4	17	3	4	-	-	0.69
BDE-203	9	6	6	6	6	8	6	9	4	7	-	-	0.24
BDE-196	8	6	7	6	6	7	4	11	3	5	-	-	0.36
BDE-208	50	26	18	22	32	39	20	15	13	19	-	-	0.47
BDE-207	65	35	24	27	39	48	28	23	17	24	-	-	0.44
Major PCBs													
PCB-52	3	3	5	3	3	3	4	7	2	4	5	5	0.33
PCB-101	6	7	9	6	6	8	9	11	9	10	9	9	0.20
PCB-118	3	3	4	3	3	4	4	5	4	4	4	4	0.18
PCB-153	2	6	4	2	3	4	4	5	4	3	3	5	0.30
PCB-138	3	7	7	3	4	6	6	7	5	5	5	7	0.27
PCB-180	1	5	4	1	1	4	3	2	1	1	1	7	0.73
Other PCBs													
PCB-28	1	1	2	1	1	2	1	2	0.4	1	1	1	0.57
PCB-114	ND	ND	ND	ND	ND	ND	0.1	ND	ND	ND	0.1	ND	0.02
PCB-105	1	1	2	1	1	1	2	2	1	2	2	2	0.21
PCB-167	0.1	0.2	0.2	0.1	0.1	0.1	0.2	0.3	0.1	0.2	0.1	0.2	0.37
PCB-156	0.2	0.5	0.4	0.2	0.2	0.4	0.4	0.5	0.3	0.3	0.2	1	0.35
PCB-157	0.1	0.1	0.1	0.05	0.04	0.03	0.1	0.2	0.1	0.1	0.0	0.02	0.58
PCB-189	0.02	0.1	ND	ND	ND	ND	0.0	ND	ND	ND	0.0	ND	0.70
PCB-194	1	2	1	0.5	1	1	1	1	1	0.4	1	2	0.51
PCB-209	0.1	0.1	0.1	0.2	0.1	0.1	0.1	0.2	0.1	0.2	0.1	0.2	0.26

Table 11. continued

Chemical	1	2	3	4	5	6	7	8	9	10	11	12	CV
PAHs													
phenanthrene	82	114	1331	124	173	1341	275	179	211	157	116	144	1.30
anthracene	4	7	16	9	8	19	7	6	7	10	7	7	0.49
fluoranthene	184	237	457	214	290	437	316	196	234	379	291	224	0.32
pyrene	240	309	338	280	340	336	314	239	252	393	327	255	0.16
benzo(*a*)anthracene	75	120	85	88	109	72	127	70	74	131	99	78	0.24
chrysene	365	420	356	364	396	363	404	344	344	472	430	364	0.10
benzo(*b*)fluoranthene	210	222	224	196	302	206	282	209	210	286	278	182	0.18
benzo(*k*)fluoranthene	108	132	113	90	97	96	148	96	99	165	167	107	0.23
benzo(*a*)pyrene	97	132	105	89	111	98	151	93	107	163	172	67	0.28
indeno(*1,2,3-c,d*)pyrene	118	141	138	96	117	116	171	120	118	166	194	109	0.22
dibenzo(*a,h*)anthracene	31	38	36	26	32	22	45	22	24	32	34	21	0.25
benzo(*g,h,i*)perylene	213	231	232	176	186	200	273	206	199	257	284	189	0.16

Legend: CV = coefficient of variation (average/standard deviation)

Table 12. Percent recovery of internal standards in 12 internal quality control residential-dust samples, Northern California Childhood Leukemia Study, 2010.

Chemical	1	2	3	4	5	6	7	8	9	10	11	12	Avg	Min	Max
BDE-28L	68	62	90	85	66	56	75	52	68	43	-	-	67	43	90
BDE-47L	66	64	82	79	72	51	74	57	71	38	-	-	65	38	82
BDE-100L	61	64	79	73	75	51	77	58	71	42	-	-	65	42	79
BDE-99L	49	54	64	61	62	44	71	50	63	36	-	-	55	36	71
BDE153L	76	79	86	80	80	56	84	66	83	48	-	-	74	48	86
BDE-183L	59	61	70	58	67	45	71	51	66	41	-	-	59	41	71
BDE-197L	83	78	95	66	82	56	87	62	78	45	-	-	73	45	95
BDE-207L	134	136	135	87	103	79	97	68	84	51	-	-	97	51	136
BDE-209L	467	641	317	176	303	155	190	102	122	106	-	-	258	102	641
PCB-28L	57	67	78	71	78	45	71	261	6	46	67	68	76	6	261
PCB-52L	58	66	78	75	71	44	72	50	73	43	63	65	63	43	78
PCB-101L	63	67	77	79	72	50	79	58	77	46	72	75	68	46	79
PCB-118L	73	68	82	84	78	52	80	58	74	49	71	79	71	49	84
PCB-114L	78	70	87	80	76	56	80	65	75	47	71	85	73	47	87
PCB-105L	79	68	82	80	79	56	78	59	75	43	78	76	71	43	82
PCB-153L	82	83	93	97	86	61	84	62	67	45	80	69	76	45	97
PCB-138L	80	80	90	91	89	67	91	56	71	50	77	82	77	50	91
PCB-167L	77	85	98	93	93	69	86	61	74	49	76	78	78	49	98
PCB-156L	79	85	99	95	92	63	83	62	74	48	79	77	78	48	99
PCB-157L	79	84	96	92	95	68	86	62	77	46	78	77	78	46	96
PCB-180L	75	80	98	90	92	65	85	61	71	49	81	76	77	49	98
PCB-189L	81	87	99	90	98	62	88	62	70	48	72	80	78	48	99
PCB-194L	52	53	64	61	62	40	74	48	57	40	62	68	57	40	74
PCB-209L	78	83	94	82	121	69	95	57	80	49	85	83	81	49	121
Benzo(a)pyrene-L	67	65	80	71	76	52	93	63	76	45	70	70	69	45	93

Legend: avg = average, min = minimum, max = maximum

Table 13. Variables used in statistical analyses of nicotine concentrations measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007.

Variable group	Variable	Units
Self-reported smoking	Lifetime smoking status of mother	Dichotomous
	Smoking status of mother three months before conception	Dichotomous
	Smoking status of mother while pregnant	Dichotomous
	Smoking status of mother after birth	Dichotomous
	Smoking status of mother at initial interview	Dichotomous
	Cigarette consumption of mother three months before conception	Continuous (cig/d)
	Cigarette consumption of mother while pregnant	Continuous (cig/d)
	Cigarette consumption of mother after birth	Continuous (cig/d)
	Lifetime smoking status of father	Dichotomous
	Smoking status of father three months before conception	Dichotomous
	Smoking status of father at initial interview	Dichotomous
	Cigarette consumption of father three months before conception	Continuous (cig/d)
	Smoking status of others in residence before birth	Dichotomous
	Smoking status of others in residence after birth	Dichotomous
	Household cigarette consumption during month before dust collection	Continuous (cig/d)
Parental Demographics	Mother's age	Continuous (y)
	Father's age	Continuous (y)
	Mother's education	Categorical
	Father's education	Categorical
	Household annual income	Categorical
Residence characteristics	Residence is apartment	Dichotomous
	Residence is townhouse	Dichotomous
	Residence is mobile home	Dichotomous
	Age of residence	Categorical
Child-specific variables	Case-control status	Dichotomous
	Sex	Dichotomous
	Age at reference date	Continuous (y)
	Down syndrome status	Dichotomous
	Birth weight	Continuous (g)
	Breastfeeding duration	Continuous (months)

Table 13. continued

Variable group	Variable	Units
Sampling conditions	Sampling method	Dichotomous
	Sampling temperature	Continuous (oF)
	Sampling humidity	Continuous (% R.H.)
	Size of sampling area	Continuous (sq. m)
	Age of carpet sampled	Continuous (y)
	Room throughway distinction	Dichotomous
	Vacuum use frequency	Categorical
	Interview respondent	Dichotomous
Time effects	Time from diagnosis to initial interview	Continuous (d)
	Time from diagnosis to dust collection	Continuous (d)
	Year of dust collection	Continuous
	Season is spring	Dichotomous
	Season is summer	Dichotomous
	Season is fall	Dichotomous
	Residence stability	Continuous (y)
Ethnicity	Child is white	Dichotomous
	Child is neither Hispanic nor white	Dichotomous
	Mother is white	Dichotomous
	Mother is neither Hispanic nor white	Dichotomous
	Father is white	Dichotomous
	Father is neither Hispanic nor white	Dichotomous

Table 14. Prevalence of smoking at various time periods indicated by variables derived from interviews of Northern California Childhood Leukemia Study subjects conducted from 1999–2007.

Self-Reported Cigarette Smoking Variable	Response			Median Nicotine Concentration (ng/g)		
	Yes	No	% Yes	Yes	No	P[b]
Mother ever smoked	137	326	30	465	203	<0.0001
Mother smoked at first interview	41	422	9	1256	240	<0.0001
Mother smoked during 3 months before conception[a]	53	410	11	1071	237	<0.0001
Mother smoked during pregnancy[a]	29	434	6	1634	245	<0.0001
Mother smoked after birth[a]	53	409	11	847	235	<0.0001
Father ever smoked	182	277	40	415	184	<0.0001
Father smoked at first interview	76	380	17	774	214	<0.0001
Father smoked during 3 months before conception[a]	95	363	21	613	215	<0.0001
Anyone else smoked during one year before birth	25	438	5	1109	252	<0.0001
Anyone else smoked during one year after birth	17	443	4	1109	255	<0.0001
Anyone smoked in residence during month before dust collection[a]	21	446	4	1256	256	<0.0001

[a] Indicates cigarettes consumption (cig. per day) was obtained for this category
[b] Kruskal-Wallis one-way ANOVA

Table 15. Pearson correlation coefficient matrix of continuous variables significantly correlated ($P < 0.05$) with (logged) concentrations of nicotine measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007.

	ln(HDN)	Father's cig. conc.	Mother's cig. conc.	Mother's cig. preg.	Mother's cig. after	House cig.	Mother's age	Father's age	Mother's ed.	Father's ed.	Income	Res. Age	Breast-feeding	Size of samp. area	Vacuum
	469	454	463	462	462	467	463	459	469	458	469	413	462	385	457
ln (residential-dust nicotine concentration)	1	0.37**	0.24**	0.17*	0.31**	0.29**	-0.26**	-0.16*	-0.27**	-0.28**	-0.24**	0.13*	-0.18**	-0.16*	0.15*
Cig. consumption[a] of father 3 months before conception		1	0.41**	0.20**	0.46**	0.29**	-0.14*	-0.05	-0.18*	-0.21**	-0.16*	0.00	-0.08	-0.05	0.12*
Cig. consumption of mother 3 months before conception			1	0.75**	0.87**	0.30**	-0.13*	-0.04	-0.11*	-0.09*	-0.01	-0.04	-0.07	-0.02	0.04
Cig. consumption of mother while pregnant				1	0.63**	0.26**	-0.09*	-0.08	-0.06	-0.03	0.00	-0.01	-0.06	0.03	-0.01
Cig. consumption of mother after birth					1	0.38**	-0.15*	-0.07	-0.14*	-0.12*	-0.04	-0.04	-0.10*	-0.08	0.08
Household cig. consumption at dust collection						1	-0.12*	-0.03	-0.16*	-0.15*	-0.14*	0.04	-0.07	-0.03	0.09
Mother's age							1	0.75**	0.42**	0.39**	0.37**	0.11*	0.24**	0.11*	-0.26**
Father's age								1	0.36**	0.34**	0.32**	0.09	0.20**	0.05	-0.23**
Mother's education									1	0.69**	0.60**	0.06	0.17*	0.06	-0.35**
Father's education										1	0.59**	0.03	0.23**	0.09	-0.37**
Household annual income											1	-0.05	0.11*	0.13	-0.33**
Age of residence												1	0.10*	-0.14*	-0.04
Breastfeeding duration													1	0.00	-0.21**
Size of sampling area														1	0.09
Vacuum use frequency															1

** $P < 0.0001$, * $P < 0.05$

Legend: ln(HDN) = ln(residential-dust nicotine concentration); Father's cig. conc. = cigarette consumption of father 3 months before conception; Mother's cig. conc. = cigarette consumption of mother 3 months before conception; Mother's cig. preg. = cigarette consumption of mother while pregnant; Mother's cig. after = cigarette consumption of mother after birth; House cig. = household cigarette consumption at dust collection; Mother's ed. = mother's education; Father's ed. = father's education; Income = household annual income; Res. Age = age of residence; Breast-feeding = breastfeeding duration; Size of samp. area = size of sampling area; Vacuum = vacuum use frequency

[a] Cigarettes smoked per day

Table 16. Principal components analysis factor loadings for self-reported smoking variables derived from interviews of Northern California Childhood Leukemia Study subjects conducted from 1999–2007.

Variable	Component Loadings 1	2	3
Lifetime smoking status of mother	0.59[a]	-0.13	-0.22
Smoking status of mother at initial interview	0.74[a]	-0.23	-0.18
Smoking status of mother three months before conception[b]	0.83[a]	-0.29	-0.11
Smoking status of mother while pregnant	0.74[a]	-0.35	0.07
Smoking status of mother after birth	0.80[a]	-0.19	-0.19
Cigarette consumption of mother three months before conception	0.85[a]	-0.28	0.09
Cigarette consumption of mother while pregnant	0.65[a]	-0.39	0.04
Cigarette consumption of mother after birth	0.84[a]	-0.19	0.09
Lifetime smoking status of father	0.43[a]	0.60[a]	-0.25
Smoking status of father at initial interview	0.49[a]	0.71[a]	-0.14
Smoking status of father three months before conception	0.60[a]	0.67[a]	-0.16
Cigarette consumption of father three months before conception	0.65[a]	0.56[a]	0.02
Smoking status of others in residence before birth	0.39	0.18	0.65[a]
Smoking status of others in residence after birth	0.20	0.14	0.58[a]
Household cigarette consumption during month before dust collection	0.34	0.19	0.50[a]
Proportion of group variance explained	41%	15%	8%
Label	**Parental Smoking**	**Father Smoking**	**Other Household Smoking**

[a] A variable was said to load on a given component if the factor loading was ≥ 0.40
[b] Cigarettes smoked per day

Table 17. Principal components analysis factor loadings for parental demographic variables derived from interviews of Northern California Childhood Leukemia Study subjects conducted from 1999–2007.

Variable	Component Loadings 1	2
Father's education	0.86	0.19
Mother's education	0.85	0.23
Household annual income	0.81	0.20
Father's age	0.27	0.89
Mother's age	0.18	0.92
Proportion of group variance explained	59%	21%
Label	**Parental SES**	**Parental Age**

[a] A variable was said to load on a given component if the factor loading was ≥ 0.40

Table 18. Multivariable regression analyses for concentrations of nicotine measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007.

Variable	All Homes (*N*=381)			HVS3 Homes (*N*=312)		
	β	*t*	*P*	β	*t*	*P*
Intercept	5.09			5.51		
Parental smoking component[a]	0.55	7.5	<0.0001	0.50	6.3	<0.0001
Father smoking component[a]	0.34	4.5	<0.0001	0.32	4.0	<0.0001
Age of residence[b]	0.11	3.8	0.0002	0.09	2.7	0.008
Parental socioeconomic status component[a]	-0.26	-3.0	0.003	-0.26	-2.7	0.007
Parental age component[a]	-0.20	-2.6	0.011	-0.18	-2.1	0.035
Residence is apartment[c]	0.84	2.3	0.022	0.93	2.4	0.015
Residence is townhouse[c]	0.61	1.9	0.056	0.56	1.5	0.13
Season is fall[c]	-0.25	-1.5	0.13	-0.33	-1.6	0.11
Breastfeeding duration[d]	-0.02	-1.5	0.13	-0.01	-1.2	0.24
Residence is mobile home[c]	0.65	1.2	0.23	0.58	1.1	0.28
Other household smoking component[a]	0.09	1.1	0.26	0.06	0.7	0.47
Child is neither Hispanic nor white[c]	-0.10	-0.6	0.56	-0.13	-0.7	0.51
Vacuum use frequency[e]	0.02	0.3	0.80	0.05	0.5	0.59
Father smoking*parental SES	0.34	3.8	0.0002	0.30	3.1	0.002
Father smoking*parental age	0.18	2.4	0.019	0.17	2.0	0.042
Size of sampling area				-0.16	-2.4	0.018

[a]Each principal component is a unitless variable with mean 0 and standard deviation of 1; values calculated based on component loadings shown in Tables 16 and 17
[b]Categorical variable (age in 5-year increments)
[c]Dichotomous variable
[d]Continuous variable (duration in months)
[e]Categorical variable (vacuum frequency less than once a month, 1-3 times a month, once a week, or more than once a week)
[f]Continuous variable (area in m^2)

Table 19. Predicted concentrations of nicotine (ng/g) in residential-dust samples for various combinations of self-reported smoking and parental demographics, Northern California Childhood Leukemia Study.

Description of Self-Reported Smoking	Parental Demographics		
	Younger & Lower SES[b]	Median Age & Median SES[c]	Older & Higher SES[d]
No smoking by anyone, at any time	210	130	90
Only mother smoked – stopped at least 3 months before conception[e]	230	130	90
Only father smoked – stopped at least 3 months before conception[e]	210	160	130
Both mother and father smoked – stopped at least 3 months before conception[e]	230	170	130
No parental smoking at any time, only others smoked in home before and after birth[e]	400	330	280
Only mother smoked – at all time periods[f]	1000	230	70
Only father smoked – at all time periods[f]	230	370	530
Both mother and father smoked – at all time periods[f]	1100	650	420
Both mother and father smoked at all time periods[f] & in-home smoking reported at dust collection[f]	1300	800	540
Both mother and father smoked at all time periods[f] & others smoked before and after birth[e]	2200	1700	1300
Both mother and father smoked at all time periods[f] & others smoked before and after birth[e] & in-home smoking reported at dust collection[f]	2500	2000	1700

[a] Predicted values based on the "All Homes" model, assuming 10-year old single family house, measurement season is not fall, no breastfeeding, child is white or Hispanic, and usual vacuum frequency of less than once a month
[b] 25th percentile values: mother's age (yrs) = 26, father's age = 28, household annual income = $30-44,000, parents have high school degrees
[c] Median values: mother's age (yrs) = 30, father's age = 33, household annual income = $60-74,000, parents have some post-high school education
[d] 75th percentile values: mother's age (yrs) = 34, father's age = 37, household annual income = $75,000+, parents have bachelor's degrees
[e] Dichotomous (yes/no) smoking variable
[f] Continuous smoking variable, showing model predictions for cigarette consumption of 5 cigarettes per day

Table 20. Variables used in statistical analyses of PAH concentrations measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007.

Variable	Type
Spatial characteristics	
Urban location	Dichotomous
Traffic density	Continuous
Modeled predictions of outdoor PAH concentrations	Continuous
Residential characteristics	
Residence construction date	Continuous
Residence is townhouse or apartment or mobile home	Dichotomous
Heating source was gas	Dichotomous
Heating source was fireplace	Dichotomous
Heating source was electric	Dichotomous
Residence has attached garage	Dichotomous
Sampling Conditions	
Dust collection was performed with HVS3 sampler	Dichotomous
Dust collection was performed with household vacuum cleaner	Dichotomous
Dust collection season was winter	Dichotomous
Dust collection season was spring	Dichotomous
Dust collection season was fall	Dichotomous
Parental demographics	
Mother's age	Continuous
Father's age	Continuous
Annual household income (<$15k, $15-30k, $30-45k, $45-60k, $60-75k, >$75k)	Categorical
Mother's education (no high school degree, high school degree, some college, college degree)	Categorical
Father's education (no high school degree, high school degree, some college, college degree)	Categorical
Mother is non-Hispanic white	Dichotomous
Mother is non-Hispanic non-white	Dichotomous
Child's characteristics	
Case-control status	Dichotomous
Child's sex	Dichotomous
Child's age at diagnosis (or reference date)	Continuous
Other variables	
Principal component describing household smoking[a]	Continuous
Time at residence before diagnosis (or reference date)	Continuous
Time at residence before dust collection	Continuous
Household vacuum cleaner frequency (<1/month, 1-3 times a month, 1/week, >1/ week)	Categorical

[a] See Chapter 3 for details on principal component analysis of smoking variables (“other household smoking”)

Table 21. Table 21. Summary of PAH measurements in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007.

Individual PAH	Molecular Weight	Missing	Below Detection	Percent Detected	Non-missing & Above Detection	Concentration (ng PAH/g dust)		
						Min.	Median	Max.
Benzo(*a*)anthracene[a,c,d]	228	1	5	99.1%	577	<2	25	834
Chrysene[a,c,d]	228	1	0	100.0%	582	7	73	1547
Benzo(*a*)pyrene[a,c,d]	252	16	9	98.4%	558	<2	40	1948
Benzo(*b*)fluoranthene[a,c,d]	252	5	1	99.8%	577	<2	59	2450
Benzo(*k*)fluoranthene[a,c,d]	252	11	0	100.0%	572	3	40	814
Indeno(123-*c*,*d*)pyrene[a,c,d]	276	0	1	99.8%	582	<2	53	2371
Dibenzo(*a,h*)anthracene[a,c,d]	278	6	35	93.9%	542	<2	14	393
Coronene[b]	300	25	8	98.6%	550	<4	94	636
Dibenzo(*a,e*)pyrene[b]	302	5	4	99.3%	574	<4	27	713

Legend: min = minimum, max = maximum
[a] Detection limit 2 ng/g dust.
[b] Detection limit 4 ng/g dust.
[c] Classified as probable human carcinogen by U.S. Environmental Protection Agency.
[d] Used in EPA's 2002 National-Scale Air Toxics Assessment outdoor PAH model

Table 22. Pearson correlation coefficients between logged concentrations of PAHs measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007.

	ln[B(*a*)A]	ln[Chry]	ln[B(*a*)P]	ln[B(*k*)F]	ln[B(*b*)F]	ln[I(*c,d*)P]	ln[D(*a,h*)A]	ln[Cor]	ln[D(*a,e*)P]
N, non-missing & above detection	577	582	558	572	577	582	542	554	570
ln[Benzo(*a*)anthracene]	1	0.91	0.70	0.65	0.81	0.82	0.60	0.46	0.49
ln[Chrysene]		1	0.61	0.64	0.82	0.76	0.57	0.46	0.39
ln[Benzo(*a*)pyrene]			1	0.57	0.61	0.70	0.63	0.37	0.51
ln[Benzo(*k*)fluoranthene]				1	0.55	0.57	0.48	0.36	0.27
ln[Benzo(*b*)fluoranthene]					1	0.79	0.58	0.46	0.42
ln[Indeno(1,2,3-*c,d*)pyrene]						1	0.66	0.58	0.69
ln[Dibenzo(*a,h*)anthracene]							1	0.35	0.41
ln[Coronene]								1	0.58
ln[Dibenzo(*a,e*)pyrene]									1

Legend: ln[B(*a*)A]=ln[Benzo(*a*)anthracene]; ln[Chry]=ln[Chrysene]; ln[B(*a*)P]= ln[Benzo(*a*)pyrene]; ln[B(*k*)F]=ln[Benzo(*k*)fluoranthene]; ln[B(*b*)F]=ln[Benzo(*b*)fluoranthene]; ln[I(*c,d*)P]= ln[Indeno(1,2,3-*c,d*)pyrene); ln[D(*a,h*)A]= ln[Dibenzo(*a,h*)anthracene]; ln[Cor]= ln[Coronene]; ln[D(*a,e*)P]= ln[Dibenzo(*a,e*)pyrene]

Table 23. Pearson correlation coefficients between study covariates and the total logged concentrations of PAH measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007.

Variable	r_p, After Multiple Imputation	Number Imputed	r_p, Complete Data	*N* with Complete Data
Residence age, years	0.26	70	0.28	431
ln(Traffic density, veh-mi/mi^2/d)	0.21	156	0.23	352
ln(Outdoor PAH estimate, ng/m^3)	0.20	82	0.20	411
Duration at residence prior to enrollment, years	0.11	55	0.12	437
Size of sampling area, m^2	0.09	0	0.09	334
Mother's education[a]	0.08	0	0.09	489
Vacuum frequency[a]	-0.07	13	-0.06	480
Child's age at enrollment, years	0.07	0	0.09	489
Household annual income[a]	0.04	19	-0.04	489
Mother's age, years	0.02	0	-0.04	489
Household cigarette consumption, cig/d	-0.02	1	0.03	488

[a] Categorical variable

Table 24. Total PAH concentrations measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007, by study covariates.

				Concentration (ng PAH/g dust)		
Variable	Category	*N*	%	Median	25th Percentile	75th Percentile
Residence age	1990-present	162	28	362	254	510
	1985-1989	38	7	383	284	537
	1980-1984	29	5	469	350	622
	1970-1979	76	13	592	390	972
	1960-1969	60	10	566	371	935
	1950-1959	69	12	601	417	963
	1940-1949	45	8	620	395	900
	1939-earlier	34	6	570	439	924
	Unknown	70	12	522	347	944
Gas heating	Present	407	70	521	339	839
	Absent	171	29	402	286	639
	Unknown or Missing	5	1	374	347	479
Residence type	Single family home	488	84	472	308	753
	Duplex or townhouse	36	6	584	386	1049
	Apartment or condo	47	8	538	371	903
	Mobile home	11	2	419	320	1126
	Unknown	1	0	374	374	374
Mother's ethnicity	Hispanic	172	30	430	305	686
	Not Hispanic	411	70	501	331	793
Household smoking	None	553	95	475	318	770
	>= 1 cigarette/day	29	5	586	412	839
	Unknown	1	0	304	304	304

Table 25. Multivariable regression analyses for concentrations of total PAH measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007, using the optimal variable set selected with deletion-substitution-addition algorithm.

	Model 1; All Homes, Imputed Values (*N* = 583)				Model 2; HVS3-Sampled Homes, Imputed Values (*N* = 417)				Model 3; All homes, No Imputed Values (*N* = 307)			
Parameter	Estimate	SE	95% CI	Partial R^2	Estimate	SE	95% CI	Partial R^2	Estimate	SE	95% CI	Partial R^2
Intercept	5.43	0.11	(5.22, 5.64)	-	5.16	0.16	(4.85, 5.47)	-	5.51	0.14	(5.24, 5.78)	-
Residence age	0.21	0.05	(0.11, 0.30)	0.07	0.26	0.06	(0.14, 0.38)	0.07	0.24	0.06	(0.13, 0.35)	0.09
ln(EPA estimate of outdoor PAH)	0.22	0.07	(0.08, 0.36)	0.02	0.28	0.07	(0.14, 0.41)	0.02	0.16	0.07	(0.02, 0.30)	0.01
Gas heating	0.16	0.06	(0.04, 0.29)	0.02	0.18	0.07	(0.04, 0.33)	0.02	0.20	0.08	(0.04, 0.36)	0.04
Residence is apartment/townhouse	0.18	0.08	(0.02, 0.33)	0.01	0.12	0.09	(-0.07, 0.30)	0.01	-0.13	0.11	(-0.35, 0.08)	0.002
Child's age at diagnosis	0.04	0.02	(0.01, 0.07)	0.01	0.04	0.02	(0.00, 0.08)	0.01	0.03	0.02	(-0.01, 0.07)	0.01
Mother's ethnicity is Hispanic	-0.12	0.06	(-0.24, 0.01)	0.002	-0.10	0.08	(-0.24, 0.05)	0.001	-0.09	0.08	(-0.25, 0.07)	0.003
$(\text{Residence age})^2$	-0.02	0.01	(-0.03,-0.01)	0.02	-0.02	0.01	(-0.04,-0.01)	0.03	-0.02	0.01	(-0.04,-0.01)	0.03
$[\ln(\text{EPA estimate of outdoor PAH})]^2$	-0.05	0.02	(-0.09,-0.01)	0.01	0.06	0.03	(0.00, 0.12)	0.02	-0.03	0.02	(-0.07, 0.01)	0.005
Size of sampling area	-	-	-	-	-0.06	0.02	(-0.10,-0.02)	0.01	-	-	-	-

Table 26. Predicted total PAH concentrations in residential-dust samples, using parameter estimates from Model 1, Northern California Childhood Leukemia Study.

	Median values	New house	Old house	Young child	Old child	No gas heating	Low ambient PAH	High ambient PAH	Hispanic mother	Res. is apt.	Worst case scenario	Best case scenario
Residence age, years	30[a]	**10[b]**	**50[c]**	30[a]	30[a]	30[a]	30[a]	30[a]	30[a]	30[a]	56	0
Child's age at enrollment, years	3.5[a]	3.5[a]	3.5[a]	**2.3[b]**	**5.0[c]**	3.5[a]	3.5[a]	3.5[a]	3.5[a]	3.5[a]	8.0	0
Gas heating	Yes	Yes	Yes	Yes	Yes	**No**	Yes	Yes	Yes	Yes	Yes	No
Outdoor PAH estimate, ng/m^3	3.0[a]	3.0[a]	3.0[a]	3.0[a]	3.0[a]	3.0[a]	**1.6[b]**	**5.4[c]**	3.0[a]	3.0[a]	10.8	0.2
Mother's ethnicity is Hispanic	No	No	No	No	No	No	No	No	**Yes**	No	No	Yes
Residence is apartment/townhouse	No	No	No	No	No	No	No	No	No	**Yes**	Yes	No
Predicted total PAH concentrations in residential dust, ng/g	600	460	670	560	640	510	540	630	530	710	1060	120

Legend: Res. is apt. = residence is apartment

[a] Median value

[b] 25th percentile value

[c] 75th percentile value

Table 27. Variables used in statistical analyses of PCB concentrations measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007.

Variable	Type
Recent remodeling	
Residents recently performed any remodeling	Dichotomous
Residents recently painted	Dichotomous
Residents recently replaced carpet	Dichotomous
Residents recently replaced flooring	Dichotomous
Residents recently weatherproofed their home	Dichotomous
Residents recently performed construction on their home	Dichotomous
Residents recently replaced roof	Dichotomous
Residents recently performed other remodeling	Dichotomous
Parental occupations	
Resident is electrician, lineman, or cable puller	Dichotomous
Resident is worker in manufacturing, assembly, or industrial operations	Dichotomous
Resident is cleaner or janitor	Dichotomous
Resident is construction worker	Dichotomous
Resident is lab worker	Dichotomous
Residence characteristics	
Residence built before 1980	Dichotomous
Residence is townhouse	Dichotomous
Residence is apartment	Dichotomous
Residence is mobile home	Dichotomous
Heating source was gas	Dichotomous
Heating source was fireplace	Dichotomous
Heating source was electric	Dichotomous
Residence has attached garage	Dichotomous
Sampling Conditions	
Dust collection was performed with HVS3 sampler	Dichotomous
Dust collection was performed with household vacuum cleaner	Dichotomous
Dust collection season was winter	Dichotomous
Dust collection season was spring	Dichotomous
Dust collection season was fall	Dichotomous

Table 27. continued

Variable	Type
Parental demographics	
Mother's age	Continuous
Father's age	Continuous
Annual household income (<$15k, $15-30k, $30-45k, $45-60k, $60-75k, >$75k)	Categorical
Mother's education (no high school degree, high school degree, some college, college degree)	Categorical
Father's education (no high school degree, high school degree, some college, college degree)	Categorical
Mother is non-Hispanic white	Dichotomous
Mother is non-Hispanic non-white	Dichotomous
Child's characteristics	
Case-control status	Dichotomous
Child's sex	Dichotomous
Child's age at diagnosis (or reference date)	Continuous
Other variables	
Residents smoked cigarettes in the home during the month before dust collection	Dichotomous
Principal component describing parental smoking before, during, and after pregnancy[a]	Continuous
Time at residence before diagnosis (or reference date)	Continuous
Time at residence before dust collection	Continuous
Residents remove shoes when entering home	Dichotomous

Table 28. Summary statistics for 6 PCBs measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007.

Congener	Percent Detected, %	*N*, Below Detection	Concentration, ng/g				
			Detection Limit	Median	75th Percentile	95th Percentile	Maximum
PCB-105	12	512	1	<1	<1	10	68
PCB-118	32	395	1	<1	4.1	18	102
PCB-138	55	261	1	2.3	6.5	29	201
PCB-153	55	265	1	1.7	5.3	21	273
PCB-170	8.9	531	2	<2	<2	8.2	93
PCB-180	42	340	2	<2	3.7	13	223

Table 29. Optimal logistic regression models for 6 PCBs measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007.

Congener	Variable	Logistic regression models			Linear regression models		
		N[a]	Coefficient	Max-rescaled R^2 [b]	N[c]	Coefficient	R^2
PCB-105	Intercept	421	-1.94		53	2.31	
PCB-118	Intercept	421	-2.54	0.15	145	2.43	0.02
	Residence built before 1980		0.08			-0.39	
	Mother's age		0.03			-0.02	
	Residence built before 1980 * Mother's age		0.04			0.02	
PCB-138	Intercept	421	0.37	0.15	235	1.76	0.03
	Residence built before 1980		-0.91			-0.22	
	Mother's age		-0.03			-0.0001	
	Residence built before 1980 * Mother's age		0.07 *			0.02	
PCB-153	Intercept	421	-2.09	0.23	233	1.47	0.04
	Residence built before 1980		1.11			-0.23	
	Mother's age		0.04			0.001	
	Residence built before 1980 * Mother's age		0.02			0.02	
PCB-170	Intercept	421	-3.61	0.08	40	-0.76	0.12
	Residence built before 1980		1.10 *			0.29	
	Father's age		-0.03			0.13	
	Father's age^2		0.001			-0.001	
PCB-180	Intercept	421	-2.46		179	1.50	
	Residence built before 1980		1.03	0.22		-0.61	0.03
	Father's age		0.03			0.001	
	Residence built before 1980 * Father's age		0.02			0.02	

Note: Each PCB congener has one logistic regression model for PCB detection and one linear regression model for (logged) PCB concentrations.

* $P < 0.05$

[a] All households with complete case data (*i.e.*, data available for all candidate variables in Table 27)

[b] Max-rescaled R^2 is a generalized coefficient of determination, see Nagelkerke (193) for details

[c] All households with complete case data and detectable concentrations of PCB

Table 30. Percentage of residences[a] in the Northern California Childhood Leukemia Study with detectable concentrations of PCB measured in residential-dust samples collected from 2001-2007, stratified by residence construction date and mother's age.

Congener	Residence built before 1980			Residence built in 1980 or thereafter
	All mothers (*N* = 284)	Older mothers[b] (*N* = 151)	Younger mothers (*N* = 133)	All mothers (*N* = 229)
PCB-105	13	13	13	10
PCB-118	46	55	36	18
PCB-138	70	75	64	38
PCB-153	74	83	64	32
PCB-170	12	14	11	5
PCB-180	60	66	53	21

[a] *N* = 151 + 133 + 229 = 513 residences with PCB measurements and data available for residence age

[b] Older mothers were at least 31 years old at the time of their child's birth, the median age for mothers in the study population. Younger mothers were less than 31 years old.

Table 31. Concentrations of PCB (ng/g) measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007, stratified by residence construction date and mother's age.

Congener	Residence built before 1980			Residence built in 1980 or thereafter
	All Mothers	Older Mothers	Younger Mothers	All Mothers
PCB-105	9.3	9.6	7.7	7.2
PCB-118	6.5	6.5	6.4	5.6
PCB-138	6.3	7.1	5.9	4.6
PCB-153	4.9	5.3	4.5	4.2
PCB-170	10.6	10.6	13.9	6.1
PCB-180	5.0	5.0	4.9	3.8

[a] *N* = 151 + 133 + 229 = 513 residences with PCB measurements and data available for residence age; to find the number of residences in each cell, multiply *N* from column headers in Table 30 by detection frequencies in Table 30, *i.e.*, PCB-105 was detected in 13% of 284 residences built before 1980, so *N* = 0.13 X 284 = 37 residences for the upper left-hand corner cell

Table 32. Summary statistics for 22 PBDE congeners measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007.

		Dust Concentration, ng/g			
Congeners	Detection Rate, %	Minimum	Median	Mean	Maximum
Major BDEs					
BDE-47	100%	86	1,228	1,886	7,443
BDE-100	100%	25	304	604	4,675
BDE-99	100%	162	2,176	3,579	15,876
BDE-154	100%	13	146	294	2,790
BDE-153	100%	23	263	487	3,841
BDE-206	94%	<17	66	177	2,920
BDE-209	96%	<400	2,872	7,330	109,409
Other BDEs					
BDE-32	26%	<0.3	0.2	3	44
BDE-28	100%	2	20	34	164
BDE-71	98%	<1	35	184	7,036
BDE-66	99%	<4	24	44	323
BDE-155	100%	1	9	17	132
BDE-179	30%	<0.1	0.1	2	45
BDE-183	100%	5	21	87	2,531
BDE-190	72%	<1	2	6	156
BDE-201	73%	<2	4	8	53
BDE-202	86%	<1	3	5	77
BDE-197	99%	<1	12	41	1,115
BDE-203	98%	<3	12	29	401
BDE-196	98%	<2	12	33	620
BDE-208	93%	<12	42	95	1,249
BDE-207	95%	<15	58	136	1,823

Table 33. Spearman correlation coefficients between concentrations of 22 PBDEs measured in residential-dust samples collected from Northern California Childhood Leukemia Study households from 2001-2007.

Congener	28	32	47	66	71	99	100	153	154	155	179	183	190	196	197	201	202	203	206	207	208	209
N	81	81	81	81	81	81	81	81	81	81	81	81	81	81	81	81	81	81	81	81	81	81
BDE-28	1	0.24	0.91	0.90	0.92	0.84	0.85	0.80	0.81	0.83	0.09	0.57	0.48	0.28	0.31	0.17	0.23	0.23	0.15	0.20	0.12	0.16
BDE-32		1	0.24	0.29	0.26	0.20	0.21	0.20	0.19	0.20	0.28	0.15	0.17	-0.14	-0.08	-0.45	0.09	-0.11	-0.08	-0.23	-0.32	-0.14
BDE-47			1	0.97	0.96	0.97	0.98	0.90	0.94	0.96	0.13	0.59	0.43	0.24	0.28	0.15	0.16	0.18	0.09	0.14	0.06	0.12
BDE-66				1	0.98	0.95	0.95	0.90	0.92	0.94	0.10	0.61	0.47	0.25	0.30	0.13	0.19	0.19	0.10	0.15	0.07	0.14
BDE-71					1	0.92	0.93	0.87	0.90	0.92	0.12	0.61	0.48	0.27	0.32	0.15	0.20	0.21	0.08	0.17	0.09	0.16
BDE-99						1	0.99	0.94	0.98	0.99	0.12	0.57	0.40	0.23	0.26	0.20	0.13	0.16	0.07	0.13	0.06	0.10
BDE-100							1	0.94	0.98	0.99	0.11	0.57	0.41	0.23	0.27	0.18	0.13	0.16	0.07	0.12	0.05	0.10
BDE-153								1	0.98	0.95	0.13	0.67	0.51	0.33	0.37	0.25	0.21	0.26	0.16	0.22	0.14	0.20
BDE-154									1	0.99	0.11	0.60	0.43	0.26	0.30	0.22	0.15	0.19	0.09	0.15	0.08	0.13
BDE-155										1	0.09	0.57	0.40	0.23	0.26	0.19	0.12	0.16	0.07	0.12	0.05	0.10
BDE-179											1	0.16	0.20	0.04	0.08	-0.21	0.13	0.05	0.01	0.00	0.03	0.06
BDE-183												1	0.83	0.70	0.82	0.30	0.53	0.62	0.46	0.49	0.37	0.48
BDE-190													1	0.75	0.80	0.36	0.69	0.72	0.57	0.62	0.52	0.60
BDE-196														1	0.94	0.71	0.81	0.97	0.77	0.87	0.78	0.81
BDE-197															1	0.59	0.74	0.88	0.68	0.79	0.69	0.74
BDE-201																1	0.48	0.69	0.49	0.71	0.71	0.55
BDE-202																	1	0.89	0.83	0.87	0.81	0.84
BDE-203																		1	0.83	0.90	0.83	0.85
BDE-206																			1	0.88	0.84	0.91
BDE-207																				1	0.96	0.94
BDE-208																					1	0.90
BDE-209																						1

Table 34. Principal components analysis factor loadings for PBDE concentrations measured in residential-dust samples from Northern California Childhood Leukemia Study households from 2001-2007.

	Component Loadings		
	1	2	3
BDE-28	0.89[a]	0.05	-0.02
BDE-32	0.52[a]	0.25	-0.18
BDE-47	0.93[a]	0.00	-0.05
BDE-66	0.94[a]	-0.01	-0.03
BDE-71	0.22	-0.07	0.17
BDE-99	0.96[a]	-0.01	-0.02
BDE-100	0.98[a]	-0.03	0.01
BDE-153	0.95[a]	0.07	0.03
BDE-154	0.95[a]	-0.01	0.04
BDE-155	0.97[a]	-0.03	0.02
BDE-179	0.19	0.01	-0.14
BDE-183	0.05	0.99[a]	0.04
BDE-190	0.04	0.99[a]	0.05
BDE-196	0.01	0.95[a]	0.31
BDE-197	0.01	0.99[a]	0.10
BDE-201	0.03	0.15	0.85[a]
BDE-202	0.01	0.91[a]	0.38
BDE-203	-0.01	0.87[a]	0.47
BDE-206	-0.05	0.37	0.80[a]
BDE-207	-0.05	0.30	0.94[a]
BDE-208	-0.06	0.09	0.98[a]
BDE-209	-0.03	0.22	0.95[a]
Variance explained	34%	34%	13%
Label	Penta-BDE	Octa-BDE	Deca-BDE

[a] A variable was said to load on a given component if the factor loading was ≥ 0.50

Table 35. Limits of detection and frequency of detection for chemicals measured in 68 residential-dust samples collected from 21 homes in Fresno County, CA from 2003-2005.

Chemical	LOD, ng/g	Detected	% Detected
Nicotine[a]	20	44	77
Benzo(*a*)anthracene[b]	2	67	100
Chrysene	2	68	100
Benzo(*b*)fluoranthene	2	68	100
Benzo(*k*)fluoranthene	2	68	100
Benzo(*a*)pyrene	2	66	100
Indeno(*1,2,3-c,d*)pyrene	2	68	100
Dibenzo(*a,h*)anthracene	2	66	97
Coronene	4	68	100
Dibenzo(*a,e*)pyrene	4	68	100
PCB-105	1	26	38
PCB-118	1	45	66
PCB-138	1	52	76
PCB-153	1	59	87
PCB-170	2	28	41
PCB-180	2	51	75

Legend: LOD = limit of detection
[a] *N* = 57 for nicotine due to chemical interference during GC-MS analysis
[b] *N* = 67 for benzo(*a*)anthracene due to chemical interference during GC-MS analysis

Table 36. Summary statistics for chemicals measured in 68 residential-dust samples collected from 21 homes in Fresno County, CA from 2003-2005 compared to results from the Northern California Childhood Leukemia Study.

	Concentration in Residential Dust (ng/g)					
	Fresno Exposure Study, 2003-2005			NCCLS, 2001-2007[a]		
Chemical	Minimum	Median	Maximum	Minimum	Median	Maximum
Nicotine	<20	250	7776	<20	265	35000
Benzo(*a*)anthracene	5	27	1272	<2	25	834
Chrysene	18	69	2867	7	73	1547
Benzo(*b*)fluoranthene	18	55	2660	<2	59	2450
Benzo(*k*)fluoranthene	13	66	2413	3	40	814
Benzo(*a*)pyrene	4	33	2127	<2	40	1948
Indeno(*1,2,3-c,d*)pyrene	3	48	3609	<2	53	2371
Dibenzo(*a,h*)anthracene	<2	10	570	<2	14	393
Coronene	9	55	802	<4	94	636
Dibenzo(*a,e*)pyrene	6	21	1551	<4	27	713
PCB-105	<1	<1	54	<1	<1	68
PCB-118	<1	3	150	<1	<1	102
PCB-138	<1	5	118	<1	2.3	201
PCB-153	<1	4	100	<1	1.7	273
PCB-170	<2	<2	45	<2	<2	93
PCB-180	<2	3	114	<2	<2	223

[a] Summary statistics for Northern California Childhood Leukemia Study taken from Chapter 3 (nicotine); Chapter 4 (PAHs); and Chapter 5 (PCBs)

Table 37. Variance parameter estimates from random-effects model regression analyses of repeated measurements of 68 residential-dust samples collected from 21 homes in Fresno County, CA from 2003-2005.

Chemical	Logged Study Mean $\left(\hat{\mu}_Y\right)$	Total Variance $\left(\hat{\sigma}_Y^2\right)$	Between-residence variance $\left(\hat{\sigma}_{bY}^2\right)$	95% Confidence Interval	Within-residence variance $\left(\hat{\sigma}_{wY}^2\right)$	95% Confidence Interval	Between-residence fold range $\left({}_b\hat{R}_{0.95}\right)$	Within-residence fold range $\left({}_w\hat{R}_{0.95}\right)$	Variance Ratio $\left(\hat{\lambda}\right)$
Nicotine	5.5	3.18	1.85	(0.33, 3.37)	1.33	(0.75, 1.91)	207	92	0.72
Benzo(*a*)anthracene	3.5	1.55	1.24	(0.36, 2.11)	0.32	(0.19, 0.45)	78	9	0.26
Chrysene	4.5	1.28	1.07	(0.34, 1.80)	0.21	(0.12, 0.29)	58	6	0.19
Benzo(*b*)fluoranthene	4.4	1.36	1.20	(0.40, 1.99)	0.16	(0.10, 0.23)	73	5	0.13
Benzo(*k*)fluoranthene	4.3	1.27	0.77	(0.13, 1.41)	0.49	(0.29, 0.70)	31	16	0.64
Benzo(*a*)pyrene	3.8	2.07	1.41	(0.28, 2.55)	0.66	(0.38, 0.94)	106	24	0.47
Indeno(*1,2,3-c,d*)pyrene	4.2	1.69	1.27	(0.35, 2.20)	0.42	(0.25, 0.59)	83	13	0.33
Dibenzo(*a,h*)anthracene	2.6	1.70	1.30	(0.33, 2.27)	0.40	(0.23, 0.56)	88	12	0.31
Coronene	4.1	1.10	0.94	(0.30, 1.58)	0.16	(0.10, 0.23)	45	5	0.17
Dibenzo(*a,e*)pyrene	3.4	1.37	1.00	(0.25, 1.74)	0.38	(0.22, 0.53)	50	11	0.38
PCB-138	1.5	2.25	1.64	(0.38, 2.91)	0.60	(0.35, 0.85)	152	21	0.37
PCB-153	1.6	1.61	1.20	(0.31, 2.08)	0.41	(0.24, 0.58)	73	12	0.34
PCB-180	1.5	1.60	1.29	(0.39, 2.18)	0.32	(0.19, 0.44)	85	9	0.25

Table 38. Expected attenuation bias due to errors in repeated measurements of 68 residential-dust samples collected from 21 homes in Fresno County, CA from 2003-2005.

Chemical	True Odds Ratio (OR)	True Logistic Regression Coefficient (β_1)	Estimated Variance Ratio $\left(\hat{\lambda}\right)$	Expected Logistic Regression Coefficient $\left(\mathrm{E}\left[\hat{\beta}_1\right]\right)$	Expected Odds Ratio $\left(\mathrm{E}\left[\widehat{OR}\right]\right)$	Expected Attenuation Bias (B)	No. of Repeats to Limit Bias to 20% (n)
Nicotine	1.50	0.41	0.72	0.24	1.27	-0.42	3
Benzo(*a*)anthracene	1.50	0.41	0.26	0.32	1.38	-0.21	2
Chrysene	1.50	0.41	0.19	0.34	1.40	-0.16	1
Benzo(*b*)fluoranthene	1.50	0.41	0.13	0.36	1.43	-0.12	1
Benzo(*k*)fluoranthene	1.50	0.41	0.64	0.25	1.28	-0.39	3
Benzo(*a*)pyrene	1.50	0.41	0.47	0.28	1.32	-0.32	2
Indeno(*1,2,3-c,d*)pyrene	1.50	0.41	0.33	0.30	1.36	-0.25	2
Dibenzo(*a,h*)anthracene	1.50	0.41	0.31	0.31	1.36	-0.23	2
Coronene	1.50	0.41	0.17	0.35	1.41	-0.15	1
Dibenzo(*a,e*)pyrene	1.50	0.41	0.38	0.29	1.34	-0.27	2
PCB-138	1.50	0.41	0.37	0.30	1.35	-0.27	2
PCB-153	1.50	0.41	0.34	0.30	1.35	-0.25	2
PCB-180	1.50	0.41	0.25	0.33	1.38	-0.20	1

Note: Expected logistic regression coefficients were calculated using Equation 3 assuming a true odds ratio of 1.5, a case-control study without repeated measurements, and the variance ratios for chemicals measured in residential-dust samples from 21 households of Fresno County, California from 2003-2005. Estimates of *B* and *n* were calculated using Equations 4 and 5, respectively.

Table 39. External comparison of variance parameter estimates from random-effects model regression analyses using data from Egeghy *et al.*

	Fresno County, CA, 2003-2005			Baltimore, MD[a], 1995-1996		
Chemical	$\hat{\sigma}^2_{bY}$	$\hat{\sigma}^2_{wY}$	$\hat{\lambda}$	$\hat{\sigma}^2_{bY}$	$\hat{\sigma}^2_{wY}$	$\hat{\lambda}$
Benzo(*a*)anthracene	1.24	0.32	0.26	1.54	0.48	0.31
Chrysene	1.07	0.21	0.19	1.51	0.43	0.29
Benzo(*b*)fluoranthene	1.20	0.16	0.13	1.46	0.59	0.40
Benzo(*k*)fluoranthene	0.77	0.49	0.64	1.86	0.55	0.29
Benzo(*a*)pyrene	1.41	0.66	0.47	1.92	0.57	0.30
Indeno(*1,2,3-c,d*)pyrene	1.27	0.42	0.33	1.96	0.74	0.38
Dibenzo(*a,h*)anthracene	1.30	0.40	0.31	1.18	0.54	0.45

[a] Based on unpublished data accompanying Egeghy *et al.*

Note: The model in Equation 1 was used to estimate variance ratios for unpublished data from Egeghy *et al*. (105), an independent study that repeatedly sampled dust from residences over time. Egeghy *et al*. collected 126 residential-dust samples from 50 households in Baltimore, MD from 1995-1996 using an HVS3 sampler. The authors reported variance components for only three chemicals in dust (chlorpyrifos, lead, and phenathrene), but made additional results available to the public (online at www.epa.gov/heds). Variance ratios were calculated for 7 PAHs that were analyzed in dust from both the Egeghy *et al*. study and in the Fresno Exposure Study. The median estimated variance ratio from the data of Egeghy *et al*. was $\lambda = 0.31$ (interquartile range: 0.30 - 0.39) compared to Fresno Exposure Study median of $\lambda = 0.31$ (interquartile range: 0.23 - 0.40) for concentrations of the 7 PAHs.

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