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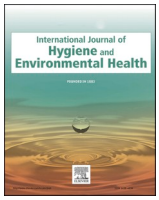

Exposure to outdoor ambient air toxics and risk of breast cancer: The multiethnic cohort

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ABSTRACT

Background: A growing literature has reported associations between traffic-related air pollution and breast cancer, however there are fewer investigations into specific ambient agents and any putative risk of breast cancer development, particularly studies occurring in populations residing in higher pollution areas such as Los Angeles.
Objectives: To estimate breast cancer risks related to ambient air toxics exposure at residential addresses.
Methods: We examined the relationships between ambient air toxics and breast cancer risk in the Multiethnic Cohort among 48,665 California female participants followed for cancer from 2003 through 2013. We obtained exposure data on chemicals acting as endocrine disruptors or mammary gland carcinogens from the National-Scale Air Toxics Assessment. Cox proportional hazards models were used to estimate breast cancer risk per one interquartile range (IQR) increase in air toxics exposure lagged by 5-years. Stratified analyses were conducted by race, ethnicity, and hormone receptor types.
Results: Among all women, increased risks of invasive breast cancer were observed with toxicants related to industries [1,1,2,2-tetrachloroethane (hazard ratio [HR] = 4.22, 95% confidence interval [95% CI] 3.18–5.60), ethylene dichloride (HR = 2.81, 95% CI 2.20–3.59), and vinyl chloride (HR = 2.27, 95% CI 1.81, 2.85); these 3 agents were correlated (r2 = 0.45–0.77)]. Agents related to gasoline production or combustion were related to increased breast cancer risk [benzene (HR = 1.32, 95% CI 1.24, 1.41), ethylbenzene (HR = 1.20, 95% CI 1.13–1.28), toluene (HR = 1.29, 95% CI 1.20–1.38), naphthalene (HR = 1.11, 95% CI 1.02–2.22), acrolein (HR = 2.26, 95% CI 1.92, 2.65)]. Higher hazard ratios were observed in African Americans and Whites compared to other racial and ethnic groups (p-heterogeneity <0.05 for traffic-related air toxics, acrolein, and vinyl acetate).
Conclusions: Our findings suggest that specific toxic air pollutants may be associated with increase breast cancer risk.

1. Introduction

Breast cancer is the most common invasive malignancy in women worldwide. In recent years an expanding literature reported associations between breast cancer and several environmental exposures, notably polycyclic aromatic hydrocarbons (PAH), dioxins, and polychlorinated biphenyls (Rodgers et al., 2018; Terry et al., 2019). The breast cancer occupational literature has been limited because studies conducted in large occupational cohorts typically have few female exposed workers, leading to low statistical power to assess female cancers. Among the few published occupational studies, findings suggest possible links between breast cancer risk and exposure to trichloroethylene, toluene and benzene while results for PAH have been mixed (Costantini et al., 2009; Glass et al., 2015; Pedersen et al., 2021a, 2021b; Peplonska et al., 2010; Petralia et al., 1998, 1999; Videnros et al., 2019). Methylene chloride and 1,1,1-trichloroethane exposures are understudied, but a Swedish

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study using a job exposure matrix found no associations for these specific solvents but reported increased breast cancer risks with more than 10 years of exposure to a group of chlorinated hydrocarbon solvents that included these chemicals (Videnros et al., 2020). As noted by the International Agency for Research on Cancer (IARC), several agents are underexplored in relation to breast cancer, including vinyl chloride and 1,3-butadiene (IARC, 2012).

Even less is known about breast cancer risk in relation to everyday life exposure to non-occupational levels of chemicals (ambient air exposures). Yet, evidence for a role of ambient traffic-related air pollution in breast cancer risk has been increasing. Studies which relied upon well-validated methods for traffic pollution exposure assessment tended to find increases in breast cancer risk, including studies utilizing land-use regression to estimate exposure to nitrogen dioxide (NO_2) or ambient fine particulate matter with diameter $\leq$2.5 μm ($PM_{2.5}$) (Cheng et al., 2020a; Crouse et al., 2010; Goldberg et al., 2017; Hystad et al., 2015; Smotherman et al., 2023) but results were not consistent (Hart et al., 2016; Reding et al., 2015).

There is some literature suggesting that residential exposure to higher ambient levels of antimony, benzene, benzidine, carbon tetrachloride, ethyl carbamate, ethylidene dichloride, arsenic, 4,4-methylene bis(2-chloroaniline), vinyl chloride, methylene chloride, biphenyl, 4-nitrophenol, cobalt, and cadmium may be related to breast cancer development (Garcia et al., 2015; Kresovich et al., 2019; Liu et al., 2015; Niehoff et al., 2019). Variation in risk by age at breast cancer diagnosis and/or estrogen receptor status was also observed. One study that found null associations for the ambient air toxics studied primarily enrolled premenopausal women, and likely had too short a follow-up period to observe associations (Hart et al., 2018). Several studies focused on White women, however residential segregation by race and ethnicity may lead to substantial variation in type and level of exposures and this may contribute to differences in findings across racial and ethnic groups (Quach et al., 2014). Here, we examine the relationships between breast cancer and ambient residential air pollution exposure to 15 human carcinogens, as identified by IARC (i.e. group 1, 2A, or 2B), mammary gland carcinogens (Rudel et al., 2007), or endocrine disruptors (The Endocrine Disruption Exchange, 2019) in a multiethnic cohort population.

2. Material and methods

The Multiethnic Cohort (MEC) is a large population-based prospective cohort and detailed study information was provided elsewhere (Cheng et al., 2020a; Kolonel et al., 2000). Briefly, the MEC study recruited participants from 1993 through 1996 among residents in Hawaii (HI) and California (CA); the current analysis focuses on California participants. Participants filled out a 26-page mailed questionnaire at baseline and were followed for a diagnosis of incident invasive breast cancer, e.g. ductal carcinoma in situ was not included. We included cases with ICD codes identified by site equal to 'C500'-'C509', excluding ICD-O-3 equal to 9050–9055, 9140, or 9590–9992. Breast cancer diagnoses were identified through linkage with the CA and HI cancer registries. The California and Hawaii Cancer Registries has been rated as Gold Certified by the North American Association of Cancer Registries, indicating >95% case ascertainment.

Risk factors and lifestyle factors including demographics, anthropometrics, smoking, medical history, family history of cancer, medication history, work history, physical activity, reproductive history, and dietary information were collected. Race and ethnicity were self-reported by participants. Residential addresses were collected (see previously published maps of residences (Cheng et al., 2020b)) and kept up-to-date by periodic mailings of newsletters, follow-up questionnaires and linkages to administrative data and registries (Cheng et al., 2020a). Addresses were routinely geocoded to latitude and longitude coordinates (Cheng et al., 2020b). Deaths were ascertained using state death certificates and the National Death Index.

For this study, eligible women included female California MEC participants who completed a baseline questionnaire, with no breast cancer diagnosis prior to cohort entry with geocoded addresses (N = 57,999). We excluded women who did not have National Air Toxics Assessment (NATA) exposure estimates during the exposure window (1998–2003) when accounting for a 5-year exposure lagging (e.g. their breast cancer diagnosis occurred too early to be included; n = 7630), women with geocoded addresses on the boundary of census tracts/out of range during their follow-up period (n = 1646), and Native Hawaiian participants (n = 58). This resulted in an analytic study population of 48,665 female participants for whom we could estimate exposures. This study population was followed from 1998 to the earliest invasive breast cancer incidence, death, or the end of study (December 31, 2013), whichever came first.

2.1. Exposure assessment

The National Air Toxics Assessment (NATA) is an ongoing review of air toxics published by the United States Environmental Protection Agency (U.S. EPA, 2018). Approximately every 3 years, EPA compiles a national emissions inventory of air toxics sources, then models ambient concentration estimates using the Assessment System for Population Exposure Nationwide (ASPEN) model. The ASPEN Model combines estimates of toxic pollutant emissions with National Weather service data to estimate air toxic concentrations. They also estimate human exposures with the Hazardous Air Pollutant Exposure Model (HAPEM), using estimated ambient concentrations (i.e., ASPEN model results) as input to the model. HAPEM models make use of census data, human activity patterns, ambient air quality levels, climate data and indoor/outdoor concentrations to generate an expected inhalation exposure concentration for humans. We utilized the HAPEM data for exposure assessment because it was available during the years of interest in this analysis.

Because of the expected latency period of breast cancer, we began by focusing on exposures modelled at the earliest time period that NATA estimates were available. EPA does not recommend combining NATA results across years because the modeling methods used to estimate exposures have been modified over the years. However, NATA 1999 and 2002 data were compatible in the models they used for exposure assessment (HAPEM5), thus we relied solely on these two models for exposure assessment in this study. Geocoded addresses for 1998–2000 and 2001–2003 were linked to the 1999 and 2002 NATA models according to 2000 census tracts, respectively, as has been done elsewhere (Symanski et al., 2016).

The 2002 NATA model provides estimates for 181 agents, from which we selected for inclusion in analyses agents identified as endocrine disruptors (The Endocrine Disruption Exchange, 2019), mammary gland carcinogens in animal bioassays (Rudel et al., 2007), or suspected or established carcinogens in humans (World Health Organization, 2019). We excluded air toxics with zero-values in >80% of the study period (e.g. no related pollution sources within 50 km and/or background levels equal to zero) and/or when estimates needed to be imputed for >35% of subjects, leaving 57 chemicals. We then examined the distributions of the 57 chemicals in the Los Angeles (LA) air basin, and found that most (N = 41) were not widely used in LA or did not have meaningful exposure contrasts during the study period (as assessed by review of maps and emissions data) and were therefore excluded.

2.2. Statistical analysis

Air toxics that arise from the same sources can be highly correlated. We used Pearson correlations to describe the correlations among chemicals. Pollutants were grouped as traffic-related toxics (correlations $r > 0.70$) and industry-related toxics. For all reported chemicals, we also generated maps showing their geographic distribution in the greater LA area, using NATA 2002 exposure concentration data (Fig. 1). We tested for linearity and removed one pollutant, xylenes, that did not exhibit

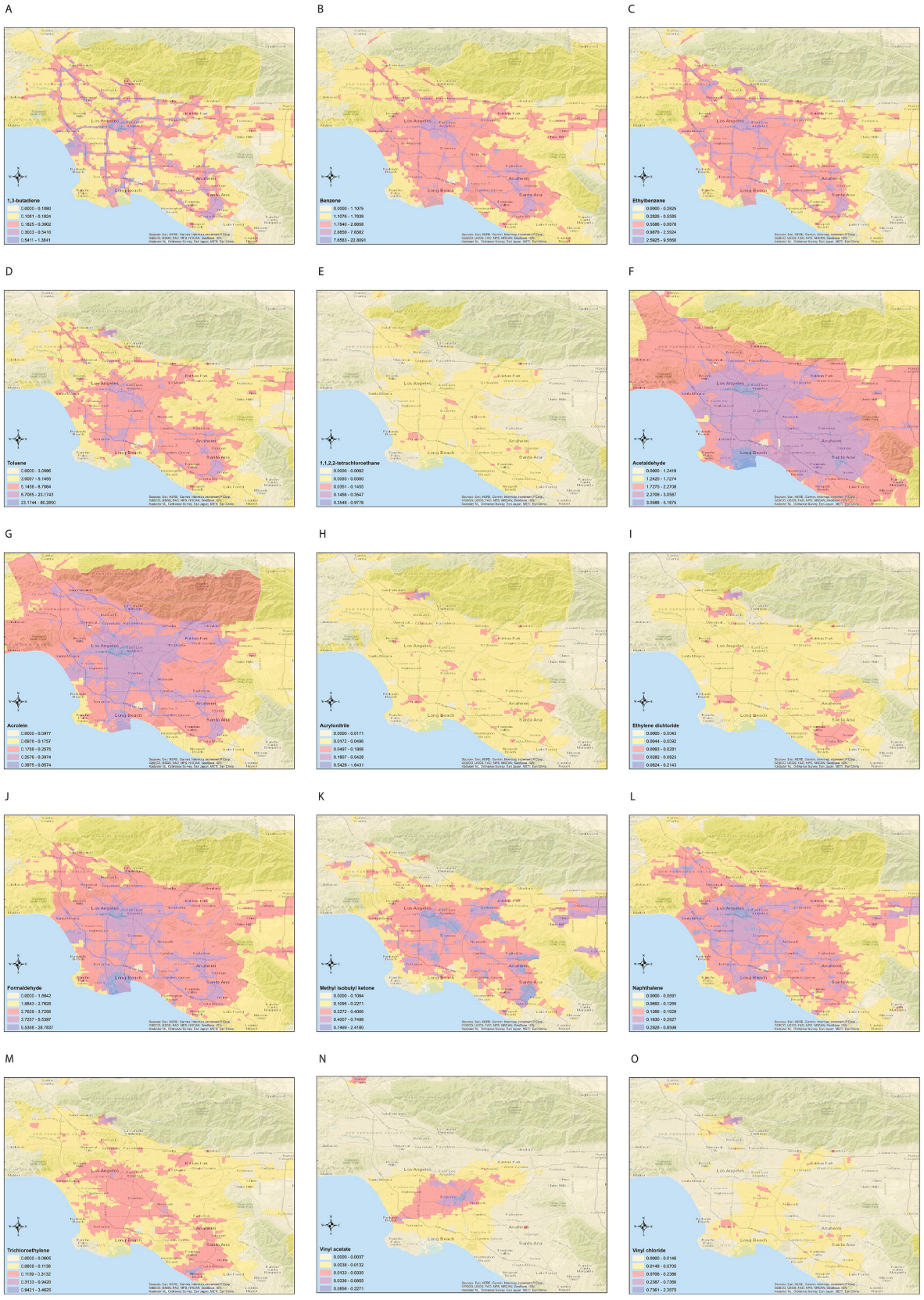

Fig. 1. Exposure concentration of chemicals reported, the greater Los Angeles area, NATA 2002; (A) 1,3-butadiene, (B) Benzene, (C) Ethylbenzene, (D) Toluene, (E) 1,1,2,2-tetrachloroethane, (F) Acetaldehyde, (G) Acrolein, (H) Acrylonitrile, (I) Ethylene dichloride, (J) Formaldehyde, (K) Methyl isobutyl ketone, (L) Naphthalene, (M) Trichloroethylene, (N) Vinyl acetate, (O) Vinyl chloride.

linearity. After these exclusions, the following 15 chemicals that are prevalent in the LA air basin remained for analyses: 1,1,2,2-tetrachloroethane, ethylene dichloride, 1,3-butadiene, benzene, ethylbenzene, formaldehyde, toluene, acrylonitrile, acetaldehyde, acrolein, methyl isobutyl ketone, naphthalene, trichloroethylene, vinyl acetate, vinyl chloride. EPA provides a confidence rating for each chemical which we have included in Supplemental Table 1.

We computed monthly estimates by dividing annual estimates into 12 months; this allowed us to assign values based on the month and year at each residential address. The remaining chemicals had very few zero values (<1%). Time-dependent monthly average exposures were computed as a weighted mean of monthly exposure estimates for addresses in each participant's residential history during the study duration until the event (breast cancer, censor, death, or end of study, whichever came first).

We employed Cox proportional hazard models to assess time-dependent air toxics exposure and evaluated its effects on breast cancer risk per interquartile range (IQR) increase. We tested the proportional hazards assumption by plotting the residuals against time for all covariates and found no violation of the assumption. Crude and adjusted hazard ratios were calculated using age as the time scale and age group at entry (5-year interval) as a stratum variable. Using the Cox model we generated risk-set based estimates through a counting process.

We also accounted for clustering of subjects due to the assignment of exposure based on census tract by adding an ID statement with COVS (AGGREGATE) option in models. Potential confounding variables were chosen *a priori* based on our prior experience with MEC and air pollution research. A complete case analysis was conducted. All models were adjusted for race and ethnicity and additionally for body mass index ((BMI) under <18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), obese (≥30 kg/m^2)), family history of breast cancer (first degree relatives only; yes/no), age at first live birth (nulliparous, <20, 21–30, >30 years), age at menarche (≤12, 13–14, >14 years), number of children (0, 1, 2–3, 4+), menopausal status (self-reported at baseline; pre-menopause, natural menopause, oophorectomy, hysterectomy), hormone replacement therapy (self-report; no estrogen use, past estrogen use, current estrogen use only, current estrogen use with past or current progesterone use), physical activity (none and quartiles of physical activity levels), energy intake (kilocalories per day; quintiles), alcohol use (non-drinker and drinker (>0 g/day)), smoking (never, former, and current), educational attainment (≤ high school graduate, some college, college graduate, graduate and professional school), and neighborhood socioeconomic status (at baseline and end of follow-up). A neighborhood socioeconomic status (nSES) composite measure was assigned based on census block group and categorized into quintiles based on the nSES distribution of Los Angeles County block groups (Cheng et al., 2020b).

In order to compare to previous studies that employed the EPA ASPEN model, we generated results using that model. Findings were similar to the HAPEM5 model, thus we report the HAPEM5 results in main tables and also report estimated long-term mean inhalation exposure using ASPEN (Supplemental Table 2).

Exposure lagging was conducted by 5, 10 and 15 years but we only present 5-year lagged results due to sparse data when employing 10 and 15-year lags. We conducted stratified analyses comparing associations by hormone receptor-positive (HR+) breast cancers [positive for estrogen receptors or progesterone receptors (ER + or PR+)] vs. hormone receptor-negative (HR-) breast cancers [negative for estrogen and progesterone receptors (ER- and PR-)]. We conducted stratified analyses by race and ethnicity and tested for heterogeneity in effects by racial and ethnic groups using a global simultaneous test based on the Wald test.

In sensitivity analyses, we conducted stratified analyses by moving status (movers vs. non-movers during the follow-up period). Non-movers had one residential address across the study period, while movers had more than one address. We additionally examined results in non-smokers. We did an additional sensitivity analysis to adjust for traffic-related air pollution. Finally, because main results were done with a complete case analyses, we also conducted multiple imputation, conditional on age and ethnicity, to estimate covariates that were missing, and we reran analyses to determine if results changed.

Spatial joining and mapping were done in ArcGIS 10.8 and data management and statistical analyses were done using SAS 9.4.

3. Results

Among the 48,665 female California MEC participants in our study, 40.4% described themselves as Hispanic or Latino (hereafter, Latino), 33.5% African Americans, 14.9% Whites, and 11.2% Japanese Americans (Table 1). Fifty-three percent of the women had an education level of high school or lower. Only 10% of the sample was premenopausal at baseline. African American and Latino women were more likely to live in the lowest two quintiles of SES neighborhoods at baseline (66.2% and 58.8% respectively) than White and Japanese American women (23.5% and 17.0%, respectively).

Mean values of each agent are shown in Table 2 and Pearson correlation coefficients between reported chemicals are shown in Supplemental Table 3. Maps indicated that industry-related toxics, while dispersed widely across the LA Basin, had higher modelled exposure concentrations in census tracts located in Torrance, Anaheim and Santa Ana while traffic-related air toxics were modelled as being higher close to freeways (Fig. 1).

The results for breast cancer risk in all women combined and modelled air toxics exposure with 5-year exposure lagging are shown in Table 3. An increased risk of breast cancer was observed with increased exposure to most air toxics, with largest hazard ratios (HR > 2.0) for acrolein, 1,1,2,2-tetrachloroethane, ethylene dichloride, vinyl acetate, and vinyl chloride. All traffic-related pollutants also consistently exhibited positive associations with HRs ranging from 1.20 to 2.04.

In analyses stratified by hormone receptor status (Table 4), point estimates were similar across hormone receptor status, with overlapping confidence intervals.

Mean exposure values by racial and ethnic group are shown in Supplemental Table 4, and stratified results by racial and ethnic group are shown in Supplemental Table 5. For African American women, we could not model breast cancer risks with some of the industrial-related air toxics due to very homogenous exposure levels in areas where these women resided. Hazard ratios were similar across racial and ethnic groups with overlapping confidence intervals. We detected statistical evidence of heterogeneity in effects by race and ethnicity for pollutants including some traffic-related air toxics, 1,1,2,2-tetrachloroethane, ethylene dichloride, and vinyl acetate (all with P heterogeneity <0.01).

The associations for air toxics with breast cancer risk were similar in movers and non-movers (Supplemental Table 6). In analyses in non-smokers, the sample size decreased by half (N = 688 breast cancer cases) yet most results did not change substantially (Supplemental Table 7). Among non-smokers, there were increases in the risk estimate for acrolein [hazard ratio (HR) = 2.08; 95% confidence interval (CI) 1.69, 2.55), vinyl chloride (HR = 3.04, 95% CI 2.42, 3.81), and trichloroethylene (HR = 1.25, 95% CI 1.18, 1.32).

The sensitivity analysis with adjustment for traffic pollution yielded results that were similar or slightly higher than main results (Supplemental Table 8). When we utilized multiple imputation for missing information in covariates, results were nearly identical to main findings (Supplemental Table 9).

4. Discussion

In this population-based cohort from the California MEC, we observed some notable increases in breast cancer risk with exposure to air toxics according to the NATA (HAPEM5 and ASPEN) models. Our findings of associations between traffic-related toxics and breast cancer are in line with most other studies on breast carcinogenicity of traffic

Table 1
Characteristics of study population at baseline.

Characteristics	All Women (N = 48,665)	African Americans (N = 16,296)	Japanese Americans (N = 5446)	Latinos (N = 19,669)	Whites (7,254)
	n (%)	n (%)	n (%)	n (%)	n (%)
Age at cohort entry					
45-49	6977 (14.3)	2741 (16.8)	718 (13.2)	2605 (13.2)	913 (12.6)
50-54	7284 (15.0)	2596 (15.9)	686 (12.6)	3050 (15.5)	952 (13.1)
55-59	9553 (19.6)	2486 (15.3)	847 (15.6)	4753 (24.2)	1467 (20.2)
60-64	9164 (18.8)	2206 (13.5)	976 (17.9)	4516 (23.0)	1466 (20.2)
65-69	8097 (16.6)	3094 (19.0)	979 (18.0)	2765 (14.1)	1259 (17.4)
70+	7590 (15.6)	3173 (19.5)	1240 (22.8)	1980 (10.1)	1197 (16.5)
Family history of breast cancer in mother or sisters					
Yes	4754 (10.6)	1703 (11.3)	525 (10.1)	1612 (9.1)	914 (13.3)
No	40109 (89.4)	13329 (88.7)	4654 (89.9)	16181 (90.9)	5945 (86.7)
Missing	3802	1264	267	1876	395
Menopausal status					
Pre-Menopause	5390 (11.2)	1935 (12.0)	716 (13.2)	2023 (10.5)	716 (9.9)
Natural Menopause	23563 (49.1)	6380 (39.6)	3087 (57.0)	10339 (53.6)	3757 (52.2)
Surgical Menopause (oophorectomy with or without hysterectomy)	7085 (14.8)	2856 (17.7)	687 (12.7)	2344 (12.2)	1198 (16.6)
Other Surgery that causes periods to stop (hysterectomy, endometrial ablation)	9533 (19.9)	4073 (25.3)	589 (10.9)	3589 (18.6)	1282 (17.8)
Period stopped but reason unknown (including women with aged 65+ at baseline)	2436 (5.1)	860 (5.3)	333 (6.2)	995 (5.2)	248 (3.4)
Missing	658	192	34	379	53
Age at menarche					
<12	22968 (48.1)	7886 (49.5)	2464 (45.9)	9027 (46.8)	3591 (50.1)
13-14	18461 (38.7)	5974 (37.5)	2165 (40.4)	7495 (38.9)	2827 (39.4)
>14	6320 (13.2)	2068 (13.0)	736 (13.7)	2761 (14.3)	755 (10.5)
Missing	916	368	81	386	81
Hormone replacement therapy use					
Never estrogen use, with or without past or current progesterone use	26027 (57.0)	9278 (60.5)	2951 (55.9)	10644 (59.0)	3154 (45.0)
Past estrogen use, with or without past progesterone use	8359 (18.3)	3116 (20.3)	680 (12.9)	3295 (18.3)	1268 (18.1)
Current estrogen use alone	5741 (12.6)	1835 (12.0)	708 (13.4)	2048 (11.4)	1150 (16.4)
Current estrogen use with progesterone - past or current	5543 (12.1)	1104 (7.2)	941 (17.8)	2060 (11.4)	1438 (20.5)
Missing	2995	963	166	1622	244
Age at first live birth					
No children	5544 (11.8)	2019 (12.9)	922 (17.3)	1555 (8.2)	1048 (14.7)
15-20	17515 (37.1)	7315 (46.7)	386 (7.2)	7765 (40.7)	2049 (28.8)
21-30	21332 (45.2)	5649 (36.0)	3452 (64.8)	8728 (45.8)	3503 (49.2)
>30	2784 (5.9)	691 (4.4)	569 (10.7)	1010 (5.3)	514 (7.2)
Missing	1490	622	117	611	140
Parity					
0 children (nulliparous)	5418 (11.3)	1987 (12.4)	913 (16.9)	1484 (7.7)	1034 (14.4)
1 child	5421 (11.3)	2536 (15.8)	642 (11.9)	1355 (7.0)	888 (12.4)
2–3 children	18676 (39.0)	5883 (36.7)	3005 (55.6)	6315 (32.8)	3473 (48.4)
4 or more children	18329 (38.3)	5612 (35.0)	845 (15.6)	10090 (52.4)	1782 (24.8)
Missing	821	278	41	425	77
Body mass index					
Underweight	711 (1.5)	130 (0.8)	321 (5.9)	132 (0.7)	128 (1.8)
Normal	16565 (34.6)	3681 (23.3)	3756 (69.1)	5871 (30.2)	3257 (45.0)
Overweight	17176 (35.9)	5938 (37.7)	1108 (20.4)	7858 (40.4)	2272 (31.4)
Obese	13436 (28.1)	6024 (38.2)	250 (4.6)	5583 (28.7)	1579 (21.8)
Missing	777	523	11	225	18
Alcohol use					
Yes	17777 (38.2)	5896 (37.9)	1453 (27.8)	6703 (35.6)	3725 (54.1)
No	28764 (61.8)	9670 (62.1)	3783 (72.3)	12149 (64.4)	3162 (45.9)
Missing	2124	730	210	817	367
Smoker					
Current smoker	6486 (13.7)	3036 (18.9)	478 (8.9)	1829 (9.8)	1143 (16.0)
Former smoker	13669 (28.9)	5362 (33.4)	1252 (23.2)	4512 (24.1)	2543 (35.6)
Never smoker	27151 (57.4)	7646 (47.7)	3663 (67.9)	12379 (66.1)	3463 (48.4)
Missing	1359	252	53	949	105
Physical activity, hours/day					
0	3718 (7.9)	799 (5.1)	120 (2.2)	2558 (13.7)	241 (3.4)
Quartile 1, <0.4	8143 (17.4)	2830 (18.1)	775 (14.4)	3740 (20.0)	798 (11.2)
Quartile 2, 0.4-<0.7	11707 (25.0)	4647 (29.7)	1410 (26.2)	4115 (22.0)	1535 (21.5)
Quartile 3, 0.7-<1.2	10860 (23.2)	3784 (24.2)	1366 (25.4)	3888 (20.8)	1822 (25.5)
Quartile 4, 1.2-<13.3	12423 (26.5)	3578 (22.9)	1704 (31.7)	4404 (23.5)	2737 (38.4)
Missing	1814	658	71	964	121
Energy intake, kcal/day					
Quintile 1, 417.4-<1158.5	9114 (19.6)	3797 (24.4)	977 (18.7)	3023 (16.0)	1317 (19.1)
Quintile 2, 1158.5-<1539.8	9296 (20.0)	3146 (20.2)	1337 (25.5)	3159 (16.8)	1654 (24.0)
Quintile 3, 1539.8-<1961.1	9334 (20.1)	2956 (19.0)	1325 (25.3)	3477 (18.4)	1576 (22.9)
Quintile 4, 1961.1-<2633.8	9385 (20.2)	2885 (18.5)	1070 (20.4)	3964 (21.0)	1466 (21.3)

(*continued on next page*)

Table 1 (*continued*)

Characteristics	All Women (N = 48,665)	African Americans (N = 16,296)	Japanese Americans (N = 5446)	Latinos (N = 19,669)	Whites (7,254)
	n (%)	n (%)	n (%)	n (%)	n (%)
Quintile 5, 2633.8-<7211.3	9412 (20.2)	2782 (17.9)	527 (10.1)	5229 (27.7)	874 (12.7)
Missing	2124	730	210	817	367
Education					
<High school	25474 (53.2)	6450 (40.2)	1919 (35.6)	14284 (74.2)	2821 (39.3)
High school graduate	13836 (28.9)	6002 (37.4)	1959 (36.3)	3495 (18.2)	2380 (33.2)
College	4478 (9.4)	1873 (11.7)	943 (17.5)	709 (3.7)	953 (13.3)
Graduate school	4091 (8.5)	1727 (10.8)	572 (10.6)	771 (4.0)	1021 (14.2)
Missing	786	244	53	410	79
Baseline neighborhood SES					
Quintile 1 - Low	12157 (25.0)	5990 (36.8)	259 (4.8)	5384 (27.4)	524 (7.2)
Quintile 2	12804 (26.3)	4790 (29.4)	661 (12.2)	6173 (31.4)	1180 (16.3)
Quintile 3	9669 (19.9)	2567 (15.8)	1323 (24.3)	4191 (21.3)	1588 (21.9)
Quintile 4	8471 (17.4)	2279 (14.0)	1679 (30.9)	2561 (13.0)	1952 (26.9)
Quintile 5 - High	5553 (11.4)	668 (4.1)	1520 (27.9)	1357 (6.9)	2008 (27.7)
Missing	11	2	4	3	2

*Native Hawaiians (N = 58) not shown in Table 1 due to small sample size.

pollution, for which point estimates ranged from 1.1 to 1.9; hence, our results are comparable with the literature (Cheng et al., 2020a; Crouse et al., 2010; Goldberg et al., 2017; Hystad et al., 2015). There is a more limited literature on these agents in the occupational literature representing studies primarily on benzene, with effect estimates ranging from 30 to 90% breast cancer increases with occupational benzene exposure (Costantini et al., 2009; Petralia et al., 1998). Results are also in line with animal bioassays examining exposure due to inhalation or ingestion of traffic-related agents that reported associations with mammary tumors (Huff et al., 1989; Maltoni et al., 1985, 1997). In our study acrolein was moderately to strongly correlated with traffic pollutants, reflecting its use as an additive in gasoline ($r^2 = 0.71–0.89$). Hence, the associations we observed may be due to its correlations with traffic-related agents in our study. At present there is a limited literature on the carcinogenicity of acrolein (IARC, 2021).

Previous studies on ambient air toxics and breast cancer have included a variety of different agents, plausibly due to the types of industries that are located in different geographic regions. Hence, we were unable to examine certain agents of interest which were noted elsewhere. The California Teachers' Study (CTS), which also used NATA models (ASPEN) to estimate breast cancer risk, differed from our study both racially and geographically, as it included largely White women (89%) recruited across California with oversampling in rural areas; thus, agents they could study only partially overlap with our study. Yet, both California studies found increases in breast cancer risk with vinyl chloride. The CTS only examined one traffic-related pollutant, benzene; somewhat comparable to our findings, the CTS reported increases in risk with traffic-related pollutants but only for ER-/PR-tumors (benzene HR = 1.45; (Garcia et al., 2015).

Our results support those from a nationwide US study, the Sister Study, which reported increases in breast cancer risk with ethylene dichloride (HR = 1.13) and toluene (HR = 1.13), although only in subgroups of women with high BMI and low physical activity. Overall the Sister study reported more null associations compared to our study, including for vinyl chloride (Niehoff et al., 2019). As we showed, differences between the ASPEN and HAPEM5 models were small, thus the use of different models does not explain the differences in study findings. A possible reason for the discrepant findings across studies is the size of census tracts, which have a far larger geographic size in rural areas, up to 7992 square miles in rural California in comparison to Los Angeles County, where the census tracts were as small as 0.042 square miles in a 2017 analysis (median census tract size in Los Angeles County = 0.459 square miles) (McMillen and Powers, 2017). This would suggest studies with more rural participants are potentially subject to greater misclassification of exposure. Further, the urban setting of our study with high traffic and industrial pollutant levels (vs. the Sister Study's nationwide recruitment) as well as a higher pollution burden in neighborhoods with a high concentration of historically marginalized racial and ethnic groups— as reported elsewhere (Pastor et al., 2004)— would suggest that chemical exposure levels varied between our and the two previously published studies. In addition, the Sister Study included only women whose sisters had been diagnosed with breast cancer, suggesting different genetic risk in the populations.

There was some heterogeneity of results by race and ethnicity, although confidence intervals often overlapped across groups. It is likely that differences observed by race and ethnicity reflect the varying pollution levels across neighborhoods of residence and not inherent differences by race and ethnicity in susceptibility to these air toxics. During the study period, African American participants lived primarily within the area bordered by the 10, 405, 105, and 110 freeways (Inglewood) with high levels of traffic related and specific agents compared to White participants (Cheng et al., 2020a; Cushing et al., 2015; National Center for Biotechnology Information, 2021). Japanese American participants lived across Los Angeles but with larger numbers in northeast LA (Monterey Park) and in certain west side neighborhoods (Torrance and South Bay). Both White and Latino MEC participants resided across the LA basin, but Whites were slightly more likely to live west and Latinos east of downtown Los Angeles. The variation in effect estimates may at least partially reflect varying concentrations of exposures in these distinct neighborhoods of residence.

In California, the primary sources of 1,1,1,2-tetrachloroethane emissions are aircraft and aircraft parts manufacturing (CARB, 1997). A study in experimental animals reported increases in mammary gland fibroadenoma with 1,1,1,2-tetrachloroethane exposure. In humans, 1,1,1,2-tetrachloroethane accumulates in fat tissue; it appears to be genotoxic, but studies are limited. This toxicant is an understudied exposure: a 2014 IARC review was not able to identify any carcinogenicity studies in humans (IARC, 2014).

Vinyl chloride is primarily used in the manufacturing of polyvinyl chloride plastic and vinyl products. It is a colorless gas found near landfills, sewage treatment plants, and hazardous waste sites in California. Knowledge of the human carcinogenicity of vinyl chloride stems largely from several large occupational cohort studies of polyvinyl chloride manufacturing workers, but these studies included few women. Hence, knowledge about a putative effect on breast cancer is lacking. Multiple animal studies have observed that inhalation of vinyl chloride increases the incidence of mammary tumors in mice, rats, and hamsters (IARC, 2012). Vinyl chloride is genotoxic, inducing unscheduled DNA synthesis, increasing the frequency of sister chromatid exchange in rat and human cells, and increasing the frequency of chromosomal aberrations and micronucleus formation.

Human studies of the carcinogenicity of ethylene dichloride,

Table 2
Mean concentration of the individual air toxics (ug/m3), NATA 2002, by race and ethnicity.

	All women			African Americans			Japanese Americans			Latinos			Whites		
	Mean	Min.	Max.	Mean	Min.	Max.	Mean	Min.	Max.	Mean	Min.	Max.	Mean	Min.	Max.
Traffic-related toxics															
1,3-butadiene	0.0508	0.0006	0.3738	0.0468	0.0091	0.2796	0.0522	0.0089	0.3362	0.0547	0.0054	0.3738	0.0475	0.0006	0.3622
Acetaldehyde	0.4931	0.0616	0.9676	0.5074	0.1024	0.8646	0.4910	0.1232	0.9676	0.4963	0.1004	0.9676	0.4544	0.0616	0.9192
Acrolein	0.0689	0.0008	0.3063	0.0735	0.0010	0.2091	0.0686	0.0054	0.2091	0.0680	0.0009	0.3063	0.0612	0.0008	0.3063
Benzene	0.4812	0.0383	2.1288	0.4703	0.0751	1.6260	0.4867	0.0947	2.0116	0.5023	0.0756	2.1288	0.4404	0.0383	2.0555
Ethylbenzene	0.1788	0.0025	2.4961	0.1738	0.0026	0.7188	0.1836	0.0159	0.8875	0.1875	0.0025	2.4961	0.1611	0.0026	0.9219
Formaldehyde	0.6899	0.0584	2.0508	0.6995	0.1525	1.5836	0.6887	0.1595	1.9761	0.7026	0.1177	2.0508	0.6332	0.0584	2.0508
Naphthalene	0.0342	0.0006	0.1089	0.0370	0.0007	0.1089	0.0333	0.0040	0.0861	0.0341	0.0006	0.1089	0.0292	0.0007	0.1040
Toluene	1.3033	0.0343	5.5380	1.2732	0.0889	4.3817	1.2991	0.1702	5.4237	1.3665	0.1109	5.5380	1.1913	0.0343	5.2909
Industry-related toxics															
1,1,2,2-tetrachloroethane	0.0116	0.0004	0.0615	0.0111	0.0007	0.0230	0.0117	0.0008	0.0592	0.0119	0.0007	0.0615	0.0117	0.0004	0.0592
Acrylonitrile	4.18E-03	1.79E-04	9.32E-02	3.65E-03	3.22E-04	2.40E-02	4.21E-03	4.87E-04	3.29E-02	4.49E-03	1.79E-04	9.32E-02	4.41E-03	2.06E-04	6.87E-02
Ethylene dichloride	0.0067	0.0003	0.0553	0.0065	0.0004	0.0180	0.0068	0.0004	0.0553	0.0068	0.0004	0.0553	0.0067	0.0003	0.0553
Methyl isobutyl ketone	3.48E-02	3.64E-05	2.83E-01	3.53E-02	2.06E-04	2.46E-01	3.42E-02	2.17E-03	2.01E-01	3.62E-02	3.64E-05	2.83E-01	3.00E-02	1.19E-04	2.83E-01
Trichloroethylene	0.0205	0.0012	0.1890	0.0205	0.0039	0.1890	0.0202	0.0052	0.0743	0.0208	0.0039	0.1221	0.0199	0.0012	0.1074
Vinyl acetate	8.14E-03	7.93E-07	4.87E-02	8.68E-03	1.68E-05	3.22E-02	8.08E-03	1.02E-04	3.59E-02	8.14E-03	3.93E-06	3.68E-02	6.98E-03	7.93E-07	4.87E-02
Vinyl chloride	1.42E-02	1.89E-05	1.36E-01	1.33E-02	5.47E-05	4.01E-02	1.42E-02	4.41E-04	4.32E-02	1.47E-02	7.50E-05	1.36E-01	1.45E-02	1.89E-05	1.03E-01

Table 3
Hazard ratios and 95% confidence intervals for the association between one interquartile range (IQR) increase in air toxic exposure and breast cancer risk, with 5-year exposure lagging, accounting for cluster effects (N = 48,665).

Air Toxic	Crude Hazard Ratio [a,b]	Adjusted Hazard Ratio [a,c]
	N cases: 1520	N cases: 1261
Traffic-related toxics		
1,3-butadiene [d,e,f]	1.13 (1.08, 1.18)	1.18 (1.13, 1.23)
Acetaldehyde [d,e]	1.58 (1.38, 1.81)	1.95 (1.63, 2.33)
Acrolein [d]	1.84 (1.60, 2.12)	2.26 (1.92, 2.65)
Benzene [d,e,f]	1.23 (1.15, 1.30)	1.32 (1.24, 1.41)
Ethylbenzene [d,e]	1.14 (1.08, 1.21)	1.20 (1.13, 1.28)
Formaldehyde [d,e]	1.17 (1.09, 1.26)	1.28 (1.18, 1.39)
Naphthalene [e]	1.02 (0.95, 1.09)	1.11 (1.02, 1.22)
Toluene [e]	1.19 (1.12, 1.27)	1.29 (1.20, 1.38)
Industry-related toxics		
1,1,2,2-tetrachloroethane [d]	3.78 (2.81, 5.07)	4.22 (3.18, 5.60)
Acrylonitrile [e,f]	1.01 (0.99, 1.04)	1.02 (0.99, 1.05)
Ethylene dichloride [d,f]	2.47 (1.92, 3.17)	2.81 (2.20, 3.59)
Methyl isobutyl ketone [d]	0.73 (0.67, 0.80)	0.74 (0.66, 0.82)
Trichloroethylene [e]	1.06 (1.04, 1.09)	1.07 (1.04, 1.11)
Vinyl acetate [d,e]	3.59 (2.87, 4.50)	5.27 (4.14, 6.73)
Vinyl chloride [d,f]	2.13 (1.68, 2.70)	2.27 (1.81, 2.85)

[a] Excluded air toxics with imputed estimates >35% or with zero-values >80%.
[b] Covariates adjusted in the crude model: age at entry (as a strata variable, 5-year categories), race and ethnicity.
[c] Covariates adjusted in the adjusted model: age at entry (as a strata variable, 5-year categories), race and ethnicity, BMI, family history of breast cancer, age at first live birth, age at menarche, number of children, menopausal status, hormone replacement therapy, physical activity, energy intake, alcohol use, smoking, education and neighborhood SES (baseline and current).
[d] Group 1, 2A, or 2B carcinogen.
[e] Endocrine disruptor.
[f] Mammary glad carcinogen in animal bioassays.

naphthalene, and vinyl acetate are lacking. The US EPA classifies ethylene dichloride as a probable human carcinogen, and naphthalene as a possible carcinogen; vinyl acetate has not been classified (U.S. EPA, 2016a, b, c). Ethylene dichloride is used in production of vinyl chloride, as solvents in organic synthesis, and as an additive lead scavenger in leaded gasoline. Naphthalene is used in the production of phthalic anhydride and is in carbamate insecticides, surface active agents and resins, as a dye intermediate, as a synthetic tanning agent, as a moth repellent, and in other chemicals. Vinyl acetate is used in the production of polyvinyl acetate and polyvinyl alcohol, among other uses.

Limitations of our study include that NATA models only provide air pollution estimates at the census tract level, limiting precision. It should be noted that the available chemicals are not exhaustive and its possible that the examined agents are correlated with other unmeasured chemical exposures. A further limitation is that we were only able estimate exposures during the study period and therefore we may be missing important earlier life exposures. Further, we were not able to adjust for noise pollution. Our results may vary from similar studies due to the analytic strategy and the population studied. Although many of the studied agents were not strongly correlated, future analyses may consider the role of mixtures in disease risk. Strengths of this study include the prospective analysis, detailed questionnaire information allowing us to adjust for multiple covariates while maintaining statistical power, and the detailed residential histories available for residents who lived in California during the study period. By utilizing an ongoing prospective multiethnic cohort with large sample size, we had the ability to stratify and compare results across racial and ethnic groups.

5. Conclusions

In summary, our findings show the importance of local industry related and traffic sources of air toxics in neighborhoods for breast

Table 4
Hazard ratios and 95% confidence intervals for the association between one interquartile range (IQR) increase in air toxic exposure and breast cancer risk stratified by breast cancer subtypes, with 5-year lagging and accounting for cluster effects (N = 48,559).

Air Toxic	HR- (ER- AND PR-)		HR+ (ER + OR PR+)	
	Crude Hazard Ratio [a,b]	Adjusted Hazard Ratio [a,c]	Crude Hazard Ratio [a,b]	Adjusted Hazard Ratio [a,c]
	N cases: 272	N cases: 226	N cases: 1142	N cases: 952
Traffic-related toxics				
1,3-butadiene	1.18 (1.09, 1.27)	1.24 (1.14, 1.35)	1.12 (1.07, 1.17)	1.17 (1.11, 1.23)
Acetaldehyde	1.62 (1.20, 2.20)	2.31 (1.58, 3.37)	1.54 (1.33, 1.78)	1.83 (1.50, 2.22)
Acrolein	1.85 (1.39, 2.47)	2.54 (1.85, 3.47)	1.80 (1.55, 2.10)	2.15 (1.80, 2.57)
Benzene	1.29 (1.15, 1.44)	1.42 (1.26, 1.61)	1.21 (1.14, 1.29)	1.30 (1.21, 1.39)
Ethylbenzene	1.17 (1.09, 1.26)	1.23 (1.14, 1.33)	1.14 (1.08, 1.20)	1.20 (1.13, 1.27)
Formaldehyde	1.19 (1.02, 1.39)	1.37 (1.16, 1.62)	1.17 (1.09, 1.27)	1.26 (1.15, 1.39)
Naphthalene	1.00 (0.84, 1.18)	1.19 (0.98, 1.45)	1.03 (0.95, 1.12)	1.11 (1.00, 1.24)
Toluene	1.28 (1.14, 1.44)	1.41 (1.24, 1.61)	1.17 (1.10, 1.25)	1.26 (1.16, 1.36)
Industry-related toxics				
1,1,2,2-tetrachloroethane	4.35 (3.26, 5.81)	4.74 (3.57, 6.30)	3.66 (2.73, 4.90)	4.14 (3.12, 5.50)
Acrylonitrile	1.02 (0.98, 1.07)	1.02 (0.97, 1.07)	1.01 (0.99, 1.04)	1.02 (0.99, 1.05)
Ethylene dichloride	2.51 (2.01, 3.13)	3.28 (2.54, 4.24)	2.56 (1.94, 3.36)	3.35 (2.38, 4.71)
Methyl isobutyl ketone	0.69 (0.56, 0.85)	0.75 (0.59, 0.96)	0.75 (0.68, 0.82)	0.74 (0.66, 0.83)
Trichloroethylene	1.08 (1.04, 1.11)	1.08 (1.04, 1.12)	1.06 (1.03, 1.09)	1.07 (1.04, 1.10)
Vinyl acetate	4.03 (3.10, 5.23)	7.09 (5.18, 9.70)	3.36 (2.69, 4.19)	4.77 (3.70, 6.15)
Vinyl chloride	2.22 (1.73, 2.85)	2.41 (1.87, 3.10)	2.10 (1.66, 2.65)	2.24 (1.79, 2.81)

[a] Excluded air toxics with imputed estimates >35% or with zero-values >80%.
[b] Covariates adjusted in the crude model: age at entry (as a strata variable, 5-year categories), race and ethnicity.
[c] Covariates adjusted in model: age at entry (as a strata variable, 5-year categories), race and ethnicity, BMI, family history of breast cancer, age at first live birth, age at menarche, number of children, menopausal status, hormone replacement therapy, physical activity, energy intake, alcohol use, smoking, education and neighborhood SES (baseline and current).

cancer risk. Individuals who have experienced historical environmental injustices due to the location of polluting sources appear to be at elevated risk of breast cancer.

CRediT authorship contribution statement

Julia E. Heck: Conceptualization, Funding acquisition, Investigation, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Di He:** Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Sam E. Wing:** Formal analysis, Writing – review & editing. **Beate Ritz:** Methodology, Supervision, Writing – review & editing. **Chandra D. Carey:** Writing – review & editing. **Juan Yang:** Formal analysis, Writing – review & editing. **Daniel O. Stram:** Data curation, Writing – review & editing. **Loïc Le Marchand:** Data curation, Writing – review & editing. **Sungshim Lani Park:** Data curation, Writing – review & editing. **Iona Cheng:** Data curation, Resources, Writing – review & editing. **Anna H. Wu:** Data curation, Resources, Writing – review & editing.

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Appendix A. Supplementary data

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References

CARB, 1997. Toxic air contaminent identified list summaries. In: California Air Resources Board (CARB).
Cheng, I., Tseng, C., Wu, J., Yang, J., Conroy, S.M., Shariff-Marco, S., Li, L., Hertz, A., Gomez, S.L., Le Marchand, L., Whittemore, A.S., Stram, D.O., Ritz, B., Wu, A.H., 2020a. Association between ambient air pollution and breast cancer risk: the multiethnic cohort study. Int. J. Cancer 146, 699–711.
Cheng, I., Tseng, C., Wu, J., Yang, J., Conroy, S.M., Shariff-Marco, S., Li, L., Hertz, A., Gomez, S.L., Le Marchand, L., Whittemore, A.S., Stram, D.O., Ritz, B., Wu, A.H., 2020b. Association between ambient air pollution and breast cancer risk: the multiethnic cohort study. Int. J. Cancer 146, 699–711.
Costantini, A.S., Gorini, G., Consonni, D., Miligi, L., Giovannetti, L., Quinn, M., 2009. Exposure to benzene and risk of breast cancer among shoe factory workers in Italy. Tumori 95, 8–12.
Crouse, D.L., Goldberg, M.S., Ross, N.A., Chen, H., Labreche, F., 2010. Postmenopausal breast cancer is associated with exposure to traffic-related air pollution in Montreal, Canada: a case-control study. Environ. Health Perspect. 118, 1578–1583.
Cushing, L., Faust, J., August, L.M., Cendak, R., Wieland, W., Alexeeff, G., 2015. Racial/ethnic disparities in cumulative environmental health impacts in California: evidence from a statewide environmental justice screening tool (CalEnviroScreen 1.1). Am. J. Publ. Health 105, 2341–2348.
Garcia, E., Hurley, S., Nelson, D.O., Hertz, A., Reynolds, P., 2015. Hazardous air pollutants and breast cancer risk in California teachers. Environ. Health 14, 14.
Glass, D.C., Heyworth, J., Thomson, A.K., Peters, S., Saunders, C., Fritschi, L., 2015. Occupational exposure to solvents and risk of breast cancer. Am. J. Ind. Med. 58, 915–922.
Goldberg, M.S., Labreche, F., Weichenthal, S., Lavigne, E., Valois, M.F., Hatzopoulou, M., Van Ryswyk, K., Shekarrizfard, M., Villeneuve, P.J., Crouse, D., Parent, M.E., 2017. The association between the incidence of postmenopausal breast cancer and concentrations at street-level of nitrogen dioxide and ultrafine particles. Environ. Res. 158, 7–15.
Hart, J.E., Bertrand, K.A., DuPre, N., James, P., Vieira, V.M., Tamimi, R.M., Laden, F., 2016. Long-term particulate matter exposures during adulthood and risk of breast cancer incidence in the nurses' health study II prospective cohort. Cancer Epidemiol. Biomarkers Prev. 25, 1274–1276.
Hart, J.E., Bertrand, K.A., DuPre, N., James, P., Vieira, V.M., VoPham, T., Mittleman, M. R., Tamimi, R.M., Laden, F., 2018. Exposure to hazardous air pollutants and risk of incident breast cancer in the nurses' health study II. Environ. Health 17, 28.
Huff, J.E., Haseman, J.K., DeMarini, D.M., Eustis, S., Maronpot, R.R., Peters, A.C., Persing, R.L., Chrisp, C.E., Jacobs, A.C., 1989. Multiple-site carcinogenicity of benzene in Fischer 344 rats and B6C3F1 mice. Environ. Health Perspect. 82, 125–163.
Hystad, P., Villeneuve, P.J., Goldberg, M.S., Crouse, D.L., Johnson, K., Canadian Cancer Registries Epidemiology Research, G., 2015. Exposure to traffic-related air pollution and the risk of developing breast cancer among women in eight Canadian provinces: a case-control study. Environ. Int. 74, 240–248.
IARC, 2012. A Review of Human Carcinogens: Chemical Agents and Related Occupations. IARC Monographs on the Identification of Carcinogenic Risks to Humans. 100F. WHO Press, Lyon, France.
IARC, 2014. Trichloroethylene, Tetrachloroethylene, and Some Other Chlorinated Agents. IARC Monographs on the Identification of Carcinogenic Risks to Humans. 106. WHO. Press, Lyon.
IARC, 2021. Acrolein, crotonaldehyde, and arecoline. IARC Monographs on the Identification of Carcinogenic Risks to Humans 128. WHO Press, Lyon.
Kolonel, L.N., Henderson, B.E., Hankin, J.H., Nomura, A.M., Wilkens, L.R., Pike, M.C., Stram, D.O., Monroe, K.R., Earle, M.E., Nagamine, F.S., 2000. A multiethnic cohort in Hawaii and Los Angeles: baseline characteristics. Am. J. Epidemiol. 151, 346–357.
Kresovich, J.K., Erdal, S., Chen, H.Y., Gann, P.H., Argos, M., Rauscher, G.H., 2019. Metallic air pollutants and breast cancer heterogeneity. Environ. Res. 177, 108639.
Liu, R., Nelson, D.O., Hurley, S., Hertz, A., Reynolds, P., 2015. Residential exposure to estrogen disrupting hazardous air pollutants and breast cancer risk. Epidemiology 26, 365–373.
Maltoni, C., Ciliberti, A., Pinto, C., Soffritti, M., Belpoggi, F., Menarini, L., 1997. Results of long-term experimental carcinogenicity studies of the effects of gasoline, correlated fuels, and major gasoline aromatics on rats. Ann. N. Y. Acad. Sci. 837, 15–52.
Maltoni, C., Conti, B., Cotti, G., Belpoggi, F., 1985. Experimental studies on benzene carcinogenicity at the Bologna Institute of Oncology: current results and ongoing research. Am. J. Ind. Med. 7, 415–446.

McMillen, D.P., Powers, E.T., 2017. The eldercare landscape: evidence from California. Health Econ. 26 (Suppl. 2), 139–157.
National Center for Biotechnology Information, 2021. PubChem Compound Summary for CID 7839, 1,2-Dibromoethane. National Center for Biotechnology Information. Retrieved December 17, 2021 from. https://pubchem.ncbi.nlm.nih.gov/compound/1_2-Dibromoethane.
Niehoff, N.M., Gammon, M.D., Keil, A.P., Nichols, H.B., Engel, L.S., Sandler, D.P., White, A.J., 2019. Airborne mammary carcinogens and breast cancer risk in the Sister Study. Environ. Int. 130, 104897.
Pastor, M., Sadd, J.L., Morello-Frosch, R., 2004. Waiting to inhale: the demographics of toxic air release facilities in 21st-century California. Soc. Sci. Q. 85, 420–440.
Pedersen, J.E., Strandberg-Larsen, K., Andersson, M., Hansen, J., 2021a. Breast cancer among Danish women occupationally exposed to diesel exhaust and polycyclic aromatic hydrocarbons, 1964–2016. Scand. J. Work. Environ. Health 47, 154.
Pedersen, J.E., Strandberg-Larsen, K., Andersson, M., Hansen, J., 2021b. Occupational exposure to specific organic solvents and risk of subtypes of breast cancer in a large population of Danish women, 1964–2016. Occup. Environ. Med. 78, 192–198.
Peplonska, B., Stewart, P., Szeszenia-Dabrowska, N., Lissowska, J., Brinton, L.A., Gromiec, J.P., Brzeznicki, S., Yang, X.R., Sherman, M., Garcia-Closas, M., Blair, A., 2010. Occupational exposure to organic solvents and breast cancer in women. Occup. Environ. Med. 67, 722–729.
Petralia, S.A., Chow, W.H., McLaughlin, J., Jin, F., Gao, Y.T., Dosemeci, M., 1998. Occupational risk factors for breast cancer among women in Shanghai. Am. J. Ind. Med. 34, 477–483.
Petralia, S.A., Vena, J.E., Freudenheim, J.L., Dosemeci, M., Michalek, A., Goldberg, M.S., Brasure, J., Graham, S., 1999. Risk of premenopausal breast cancer in association with occupational exposure to polycyclic aromatic hydrocarbons and benzene. Scand. J. Work. Environ. Health 25, 215–221.
Quach, T., Liu, R., Nelson, D.O., Hurley, S., Von Behren, J., Hertz, A., Reynolds, P., 2014. Disaggregating data on Asian American and Pacific Islander women to provide new insights on potential exposures to hazardous air pollutants in California. Cancer Epidemiol. Biomarkers Prev. 23, 2218–2228.
Reding, K.W., Young, M.T., Szpiro, A.A., Han, C.J., DeRoo, L.A., Weinberg, C., Kaufman, J.D., Sandler, D.P., 2015. Breast cancer risk in relation to ambient air pollution exposure at residences in the sister study cohort. Cancer Epidemiol. Biomarkers Prev. 24, 1907–1909.
Rodgers, K.M., Udesky, J.O., Rudel, R.A., Brody, J.G., 2018. Environmental chemicals and breast cancer: an updated review of epidemiological literature informed by biological mechanisms. Environ. Res. 160, 152–182.
Rudel, R.A., Attfield, K.R., Schifano, J.N., Brody, J.G., 2007. Chemicals causing mammary gland tumors in animals signal new directions for epidemiology, chemicals testing, and risk assessment for breast cancer prevention. Cancer 109, 2635–2666.
Smotherman, C., Sprague, B., Datta, S., Braithwaite, D., Qin, H., Yaghjyan, L., 2023. Association of air pollution with postmenopausal breast cancer risk in UK Biobank. Breast Cancer Res. 25, 83.
Symanski, E., Tee Lewis, P.G., Chen, T.Y., Chan, W., Lai, D., Ma, X., 2016. Air toxics and early childhood acute lymphocytic leukemia in Texas, a population based case control study. Environ. Health 15, 70.
Terry, M.B., Michels, K.B., Brody, J.G., Byrne, C., Chen, S., Jerry, D.J., Malecki, K.M.C., Martin, M.B., Miller, R.L., Neuhausen, S.L., Silk, K., Trentham-Dietz, A., Breast, C., the Environment Research, P., 2019. Environmental exposures during windows of susceptibility for breast cancer: a framework for prevention research. Breast Cancer Res. 21, 96.
The Endocrine Disruption Exchange, I., 2019. TEDX List of Potential Endocrine Disruptors Paonia. CO.
U.S. EPA, 2016a. Ethylene Dichloride (1,2-Dichloroethane). U.S. EPA.
U.S. EPA, 2016b. Naphthalene.
U.S. EPA, 2016c. Vinyl Acetate. U.S. EPA.
U.S. EPA, 2018. National Air Toxics Assessment.
Videnros, C., Selander, J., Wiebert, P., Albin, M., Plato, N., Borgquist, S., Manjer, J., Gustavsson, P., 2019. Postmenopausal breast cancer and occupational exposure to chemicals. Scand. J. Work. Environ. Health 642–650.
Videnros, C., Selander, J., Wiebert, P., Albin, M., Plato, N., Borgquist, S., Manjer, J., Gustavsson, P., 2020. Investigating the risk of breast cancer among women exposed to chemicals: a nested case-control study using improved exposure estimates. Int. Arch. Occup. Environ. Health 93, 261–269.
World Health Organization, 2019. Agents Classified by the IARC Monographs, Volumes 1-124 World Health Organization.