Original Contribution

Coarse Particles and Respiratory Emergency Department Visits in California

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Although respiratory disease has been strongly connected to fine particulate air pollution (particulate matter <2.5 μm in diameter (PM$_{2.5}$)), evidence has been mixed regarding the effects of coarse particles (particulate matter from 2.5 to 10 μm in diameter), possibly because of the greater spatial heterogeneity of coarse particles. In this study, we evaluated the relationship between coarse particles and respiratory emergency department visits, including common subdiagnoses, from 2005 to 2008 in 35 California counties. A time-stratified case-crossover design was used to help control for time-invariant confounders and seasonal influences, and the study population was limited to those residing within 20 km of pollution monitors to mitigate the influence of spatial heterogeneity. Significant associations between respiratory emergency department visits and coarse particle levels were observed. Asthma visits showed associations (for 2-day lag, excess risk per 10 μg/m$^3$ = 3.3%, 95% confidence interval: 2.0, 4.6) that were robust to adjustment by other common air pollutants (particles <2.5 μm in diameter, ozone, nitrogen dioxide, carbon monoxide, and sulfur dioxide). Pneumonia and acute respiratory infection visits were not associated, although some suggestion of a relationship with chronic obstructive pulmonary disease visits was present. Our results indicate that coarse particle exposure may trigger asthma exacerbations requiring emergency care, and reducing exposures among asthmatic persons may provide benefits.

air pollution; asthma; case-crossover; emergency medical services; hospitalization; particulate matter; respiratory tract diseases

Abbreviations: COPD, chronic obstructive pulmonary disease; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; PM$_{2.5}$ and PM$_{10}$, particulate matter <2.5 and <10 μm in diameter, respectively.
visits, we examined the relationship between coarse particles and respiratory emergency department visits. Emergency visits were of particular interest because they have been rarely studied in relation to coarse particles, especially in the United States (5, 13, 15, 16), and they encompass a broader scope of impact than more grave outcomes such as mortality. They are also plentiful, providing sufficient cases to confine our study population to those living near coarse particle monitors, as determined by residential zip code. This degree of required proximity, often used in long-term or birth outcome studies of air pollution (22–25) but not often applied in acute studies because of difficulties in securing individual-level location data, should reduce the exposure misclassification by examining only those for whom our monitor measurements are most relevant. California also has extensive monitoring of other common air pollutants, providing an opportunity to account for them when assessing the independent effects of coarse particles. Our study leverages these available resources with the aim of providing a clearer look at the relationship between coarse particles and respiratory health.

MATERIALS AND METHODS

Health outcome data

Emergency department visit data from 2005 through 2008 were compiled from 2 databases maintained by the California Office of Statewide Health Planning and Development, one containing outpatient emergency department visits and the other containing inpatient admissions to licensed California hospitals. Our final data set included both outpatient visits and inpatient visits specifically originating in the emergency department.

We utilized information on the patient’s date of visit, principal International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), diagnosis, and zip code of residence. For this analysis, we focused on respiratory visits (ICD-9-CM codes 460–519), specifically noting visits for asthma (ICD-9-CM code 493), COPD excluding asthma (ICD-9-CM codes 490–492 and 494–496), pneumonia (ICD-9-CM codes 480–486), and acute respiratory infections (ICD-9-CM codes 460–466). In addition, we extracted information on each patient’s age, sex, race/ethnicity, and expected method of payment.

Air pollution, weather, and neighborhood data

Data on particulate matter <10 μm in diameter (PM_{10}) and PM_{2.5} were provided by the California Air Resources Board (26). Coarse particle levels were calculated by subtracting PM_{2.5} readings from collocated PM_{10} readings taken on the same day. These data were recorded every 3 or 6 days. For 9 counties, daily PM_{2.5} measures were also available. Daily measures of ozone (O_3), nitrogen dioxide (NO_2), carbon monoxide (CO), and sulfur dioxide (SO_2) were also extracted from the California Air Resources Board database to evaluate them as possible confounders. Daily values for gaseous pollutants were reported as maximum 1-hour concentrations, and particulate measures were provided as 24-hour averages.

Hourly temperature and humidity data were compiled from 3 public databases provided by the National Climatic Data Center, the US Environmental Protection Agency, and the California Irrigation Management and Information System (27–29). Hourly apparent temperature was calculated from the temperature and relative humidity by using methods previously reported (30) and then averaged for each day to create daily measures. Data from the 2000 US Census provided the proportion of residents in urban areas for each zip code tabulation area, which is a census-defined aggregation of census blocks approximating postal zip code boundaries.

Methods

Using the population-weighted centroid of each patient’s reported residential zip code as his/her presumed location, we assigned exposure from the closest pollution monitor with available data for that day. To increase the validity of our pollution exposure metrics, we assigned exposures only to zip codes and, consequently, cases within 20 km of a reporting monitor. The proximity requirement for temperature monitors was 25 km. Geographical assignment was performed by using ArcGIS 9.2 (31) with the Hawth’s Tools extension (32).

We selected a case-crossover design time stratified by month to study acute effects of coarse particle exposure on respiratory emergency department visits and our chosen subdiagnoses. This method helps to control for time-invariant confounders and seasonal trends by design. For each case, referent periods were chosen in 3- or 6-day increments from the case day within that month, depending on the availability of particulate matter monitoring. For our exposure metric, we chose to separately examine coarse particle levels on the same day as the cases and controls (lag 0), 1 day prior (lag 1), and 2 days prior (lag 2). Our analysis consisted of 2 steps. First, county-level conditional logistic regressions were performed by using SAS, version 9.2, software (33). The baseline model included a linear term for a coarse particle lag; linear and squared terms for lag 0 apparent temperature, which better accounted for a nonlinear temperature–emergency department visit relationship; and dummy variables for day of week, to control for weekday patterns in emergency department visits. To provide an overall estimate, we combined the county-level estimates using a random-effects meta-analysis using R, version 12.2.2 (34). We report them as percent excess risk (defined as (odds ratio − 1) × 100) per 10 μg/m³ of coarse particles. Only counties with at least 50 cases were included in overall estimates. For context, we also report results of parallel analyses of PM_{2.5} and PM_{10} from the same monitors.

We conducted a number of sensitivity analyses. To test whether the exposures we assigned by monitor became less relevant among cases living greater distances from the monitor, we compared pooled estimates for those within 10 km of a monitor with those between 10 and 20 km away. We also examined nonlinearity of effects by introducing a squared term for coarse particles in the model and comparing model goodness-of-fit using the Akaike Information Criterion. To determine whether extreme values influenced our
findings, we ran analyses excluding the highest and lowest 5% of calculated coarse particle levels for each model. To assess possible confounding by other air pollutants, we introduced each pollutant separately into the base model. For the gases, we averaged pollution levels of the same day and the 2 days prior. For PM$_{2.5}$, our primary method of adjustment used single-day readings matching the lag of coarse particles. However, we also performed analyses with the 3-day average of PM$_{2.5}$ using the few counties where daily readings were available. We compared estimates from these models with those from the baseline model to assess the extent of confounding.

Finally, for outcomes found to be significantly associated with coarse particles, we conducted stratified analyses to assess possible effect modification. These included stratifications by sex, age, and race/ethnicity. To examine interaction by socioeconomic status, we compared cases expected to pay with the help of Medi-Cal, California’s Medicaid program, or other programs that aid lower income individuals with those not expected to use such programs. This comparison was limited to individuals under 65 years of age because of the widespread availability of government-provided Medicare beginning at that age. We also examined external factors including warmer (November–April) season of visit and percentage of urban residents in a participant’s zip code tabulation area. To make more direct comparisons, we limited tests between strata to counties with a minimum of 50 cases in each stratum.

RESULTS

Thirty-five of California’s 58 counties had the minimum 50 cases necessary in each outcome subgroup of interest to be included in the analysis (Figure 1). Eligible respiratory emergency department cases with same-day coarse particle data totaled 487,068, including 224,893 acute respiratory infection cases, 74,978 asthma cases, 70,967 pneumonia cases, and 57,903 COPD cases. Cases by county ranged from 632 (San Benito) to 135,133 (Los Angeles). Totals were similar for 1- or 2-day lags. Children 0–18 years of age were well represented, numbering 45% of total cases. Hispanics and non-Hispanic whites comprised 38% and 36% of cases, respectively, although race/ethnicity was quite variable by county: Hispanic cases comprised anywhere from 4% to 82% of county-level visits, and non-Hispanic blacks ranged from 0% to 27%. Thirty-eight percent of cases under 65 years of age involved payment through low-income assistance, although this also varied widely by county (range, 24%–63%). More than 80% were outpatient visits, and 62% of the visits took place during the cooler months of November through April; 57% lived in entirely urban zip code tabulation areas, and approximately 63% lived within 10 km of a monitor. A fair degree of coarse particle variation was observed in our study area, with county means ranging from 5.6 to 34.4 μg/m$^3$ (Table 1). Coarse particles showed low to moderate within-county correlations with temperature and other air pollutants. Coarse particles were typically most correlated with apparent temperature and ozone (median county-level Spearman correlations = 0.40 and 0.38, respectively). Other median pollutant correlations with coarse particles ranged from 0.14 (carbon monoxide) to 0.31 (PM$_{2.5}$).

We observed statistically significant associations between coarse particles and respiratory emergency department visits (per 10 μg/m$^3$ coarse particles, excess risk for 1-day lag = 0.7%, 95% confidence interval: 0.3, 1.1) using single-pollutant models (Figure 2). Analyses of specific respiratory diagnoses indicated that asthma visits were a strong contributor to the overall association (excess risk for 2-day lag = 3.3%, 95% confidence interval: 2.0, 4.6). Effect estimates were also elevated for COPD visits when coarse particle levels 2 days prior were considered. There was notable between-county heterogeneity; lag 1 for all respiratory visits and lag 2 for asthma had $I^2$ statistics of 33% and 52%, respectively. For COPD, it was lower, at 2%. Acute respiratory infections or pneumonia was not associated with coarse particles, but all outcomes were associated with PM$_{2.5}$. PM$_{10}$ effect estimates typically fell between coarse particles and PM$_{2.5}$ estimates.

The coarse particle associations with respiratory and asthma persisted after extreme values were excluded from the analysis. Adding a squared term for coarse particles to address possible nonlinearity did not improve the model’s goodness of fit.

When stratifying by distance to the monitor (within 10 km vs. 10–20 km), we found that both groups maintained significant associations with asthma visits (Figure 3). Among those residing closer, we did observe stronger associations for asthma; the lag 1 estimate was nearly twice as high for that group. However, differences between the distance groups were not statistically significant. No consistent pattern was observed for overall respiratory visits. The COPD relationship at lag 2 remained elevated for those living closer to the monitor, but it was not present among those farther away. Exposure misclassification due to distance did not appear to obscure relationships with other respiratory outcomes, because no new associations were present in the 0–10 km analyses.

Associations observed for asthma were robust to the addition of other pollutants in the model, with our significant findings persisting in all 2-pollutant models (Figure 4). Overall respiratory disease associations were more sensitive to the addition of nitrogen dioxide and carbon monoxide; lag 1 associations remained elevated but were no longer statistically significant. Addition of collocated simultaneous PM$_{2.5}$ also attenuated the coarse particle effect, although it remained statistically significant. The 3-day average PM$_{2.5}$ metric was not a strong confounder.

Few consistent differences were observed when comparing effect estimates for asthma among subgroups (Figure 5). Associations were significantly weaker for adults over 65 years and children under 5 at lags 1 and 2, respectively. However, other lags for those groups remained significant. Lag 2 effects among Hispanics and blacks were greater than those of whites, and effects were stronger in the warm season, but none of those differences was statistically significant. Restricting cases to outpatient emergency room visits resulted in only minimally higher effect estimates. Differences observed for sex or method of payment did not approach statistical significance and lacked consistency over the 2 lags. Limiting analyses to counties with both completely urban and...
more rural zip codes revealed no compelling evidence that zip code urbanicity impacted the magnitude of effect; significant effects were seen in both populations. This was also true when all counties were considered (not shown).

**DISCUSSION**

In our study of respiratory emergency department visits in California, we observed strong associations between coarse particle exposures and emergency department visits for asthma that remained even after accounting for other common air pollutants. Two Canadian studies found similarly robust effects on asthma hospitalizations (4, 35), although other asthma emergency studies saw previously significant associations attenuated after such adjustment (9, 15). The latter studies were limited to a smaller range of exposures measured from 1 monitor, which may have reduced their ability to detect such an association. Single-pollutant studies of coarse particles in Atlanta, Georgia; Seattle, Washington; and Zonguldak, Turkey reported associations with outpatient or inpatient visits for asthma, although the outpatient findings in Atlanta were not present for a later time period (10, 11, 36, 37). Smaller-scale, longitudinal studies of asthmatic cohorts in California and Maryland also noted exacerbations with outdoor or indoor coarse particle exposure, respectively, even after adjustment for demographic and in-home factors (38, 39). Findings for indoor coarse particles in the 2011 study reported by McCormack et al. (39) were also robust to adjustment for indoor PM$_{2.5}$ and outdoor PM$_{2.5}$. Nitrogen dioxide adjustment in the 2010 study by Mann et al. (38) reduced the coarse particle effect by only 10%, but it was no longer statistically significant.

Our study also noted associations for overall respiratory visits, although they were attenuated when either nitrogen dioxide or carbon monoxide was jointly considered with coarse particles. An extensive multisite study of older adults in the...
United States found that coarse particle associations with total respiratory hospitalizations were not significant, even prior to adjustment for other pollutants (3). Our detection of an effect could be attributable to our decision to study only cases living near monitors or to population differences in disease severity and demographics; the vast majority of our cases were outpatient, and 83% were not old enough for Medicare. While confounding due to PM2.5 was weak at best in our study, it was found to be an important confounder in other studies of pneumonia hospitalizations, COPD hospitalizations, combined COPD–asthma hospitalizations, and respiratory mortality (8, 40–42). However, a Hong Kong
study of emergency respiratory admissions and studies of respiratory mortality in the United States and the Canary Islands found PM$_{2.5}$-independent coarse particle effects (9, 43, 44). Studies in Vancouver, Canada, found associations for respiratory hospitalizations in very young children and older adults to be robust to adjustment for gaseous pollutants, and studies in Rome, Italy, and Mexico City, Mexico, found coarse particles to be associated with mortality from respiratory diseases, even after adjustment for ozone (45–48). However, significant associations observed for respiratory

Figure 2. Effect estimates for different particulate matter sizes on emergency department visits in 35 California counties, 2005–2008, using A) single particulate and B) 2 particulate pollutant models, by outcome. Bars, 95% confidence interval. COPD, chronic obstructive pulmonary disease; CP, coarse particles; PM$_{2.5}$ and PM$_{10}$, particulate matter <2.5 and <10 μm in diameter, respectively; Resp, respiratory.
admissions, COPD, and respiratory infections in Toronto, Canada, were not present in gas-adjusted models (4). Nitrogen dioxide and carbon monoxide, strong markers for traffic pollution, appeared to confound the coarse particle–respiratory emergency department visit relationship in our analysis. Ultimately, because of their own relationships with respiratory health, PM$_{2.5}$ and gaseous air pollutants should be considered when one is trying to identify the independent effects of coarse particles.

There was some concern about assignment of coarse particle exposures based on central site monitors given the degree of spatial heterogeneity coarse particles typically exhibit. Monitoring studies deploying multiple monitors in Los Angeles, Philadelphia, St. Louis, and Rochester observed notable variability in coarse particle readings at nearby sites, sometimes even at distances as close as 2 km (20, 21, 49, 50). Proximity of monitors to local coarse particle sources, such as reentrained dust from heavy vehicular traffic or agricultural fields, exerted a sizeable influence on the discordance of readings with nearby monitors (20, 21). Indeed, traffic and agriculture are strongly present in many of the areas we studied. We addressed this problem by limiting our study to those living within 20 km of monitors, but we also compared the effects for those living within 10 km of a monitor with those 10–20 km away. We observed greater magnitudes for asthma and COPD associations among those living closer, suggesting that exposure misclassification by distance does have some influence, even within our defined radius. But asthma associations were still significant for the group living farther, implying that a typical individual’s movement beyond his/her residence may be expansive enough to make exposures measured at that distance relevant for an epidemiologic context. Statistical examinations of the influence of coarse particle exposure error in the Medicare data set also found that it did not materially affect the findings observed (3, 51). Ultimately, exposure models able to account for specific sources, or personal monitoring, would help to refine estimates of coarse particle health effects. Absent those, researchers using central monitoring should evaluate their population’s distance from the monitor and weigh the tradeoffs between sample size and exposure misclassification when designing coarse particle studies.

The strong associations with asthma observed here seem to agree with experimentally derived research on coarse particles. Particles of this size can reach and deposit in the tracheobronchial airways most involved in asthmatic disease (1). In vitro and in vivo studies of animals have observed evidence that coarse particles may incite allergic or inflammatory airway responses (19, 52–56). Controlled exposure to concentrated ambient coarse particles can also produce increases in neutrophils in healthy humans (17, 18). Such inflammatory responses are a major component of asthmatic disease and may incite or exacerbate other respiratory conditions (57, 58).

There are a number of weaknesses present in this analysis. First, because coarse particle measures were only available every 3 or every 6 days, data for cases were not simultaneously present for multiple lag days. Thus, analyses examining lag 0 looked only at the set of cases occurring on monitored days, lag 1 at the set occurring 1 day following monitored days, and so on. Any between-lag comparisons by the reader should note that these analyses tested mutually

Figure 3. Effect estimates for coarse particles on emergency department visits in California, 2005–2008, by outcome and distance. Bars, 95% confidence interval. COPD, chronic obstructive pulmonary disease; RI, respiratory infection(s).
Figure 4. Effect estimates for coarse particles in California, 2005–2008, adjusted for air pollutants, on A) respiratory and B) asthma emergency department visits. Bars, 95% confidence interval. Adj, adjusted; CO, carbon monoxide; NO₂, nitrogen dioxide; O₃, ozone; PM₂·₅, particulate matter <2·5 μm in diameter; SO₂, sulfur dioxide; Unadj, unadjusted.

exclusive case populations, so the differences observed could also be influenced by random population differences. Hopefully, increased daily monitoring will permit the use of distributed lag models to better assess independent impacts of lags and the possibility that cumulative lags are stronger predictors. Another issue is that our referent periods include days fairly close to the case period. This makes examination of longer lags problematic because lagged referent periods can overlap with case-proximate periods and compromise the ability to detect differences between them. Future studies using other setups should examine longer lags, as some studies have observed associations with extended lags (11).

Second, the reported visit day may be less accurate for hospitalized cases. Our hospitalization database reports the date of admission for inpatient care; the patient may have arrived at the emergency department the day prior, leading to some exposure misclassification among the hospitalized. We observe marginally higher estimates in emergency room–only analyses (not shown), suggesting the presence of this misclassification, but other differences between inpatient and outpatient cases may also influence these estimates. Some misclassification of exposure may have been introduced by our measure of coarse particles, which is indirectly calculated by using PM$_{10}$ and PM$_{2.5}$ measurements and subject to errors in either reading. Our calculations produced some negative values for coarse particles; a sensitivity analysis using a data set trimmed of extremes showed that removing these values did not impact our findings. Increased direct measurement of coarse particles in the future would address this problem.

Coarse particles are heterogeneous in composition, and this study does not specifically address whether specific components bear greater responsibility. Toxicological studies indicate that coarse particles from different areas can have different inflammatory effects (59–61), likely owing to different sources and constituents. Coarse particles are most often linked with soil or crustal materials because of the presence of elements like silicon and calcium, but they may also contain elements from non–combustion traffic sources, such as road, brake, or tire wear (62). Transition metals present in these sources may have proinflammatory effects in pulmonary tissue (63). Endotoxin and other biological components are present in the coarse fraction, and they may also incite inflammatory responses (64). However, some evidence suggests that inflammatory potential of coarse particles exists independently of endotoxin (17). Biomass burning may also generate particularly toxic coarse particles (65). We compared the effects in urban versus more rural areas as a rough proxy for comparing the effects of more traffic-sourced coarse

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**Figure 5.** Effect estimates for coarse particles on asthma emergency department visits in California, 2005–2008, by lag and possible effect modifiers. Bars, 95% confidence interval. Apr, April; B, black; F, females; H, Hispanic; Low Inc. Prog., payment assistance programs for low income patients; M, males; Nov, November; Oct, October; W, white.
particles versus agriculture and crustal-sourced particles and observed little difference in potency. Controlling for traffic pollutants, such as nitrogen dioxide and carbon monoxide, as we did when assessing confounding, may actually compromise the ability to detect traffic-derived coarse particle effects, because they share a common source, leading to an underestimation of coarse particle impact. Monitoring of coarse particle species is quite rare but would be valuable in identifying whether specific sources or compounds may be especially harmful.

In this multicounty study of coarse particles and emergency room visits for respiratory disease, we observed evidence that coarse particle levels impact respiratory morbidity, specifically asthma and COPD-related morbidity, independently of the effects of PM$_{2.5}$, which was associated with all the outcomes studied, and other common air pollutants. Although PM$_{2.5}$ is often the focus of researchers and regulatory agencies, this study contributes evidence that reductions in coarse particles may also improve public health, particularly for asthmatic persons.

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