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Using Syndromic Surveillance to Evaluate the Respiratory Effects of Fine Particulate Matter

To the Editor:

Particulate air pollution is a prevalent exposure in urban areas and has been linked to mortality and adverse respiratory conditions, including asthma, chronic obstructive pulmonary disease, lower respiratory infection, and lung cancer (1–3). Studies of daily changes in fine particulate matter (aerodynamic diameter < 2.5 μm [$PM_{2.5}$]) and acute respiratory effects often use data from the healthcare system, typically acute care events, such as emergency department visits, hospital admissions, and to a lesser extent provider visits (4–6). However, this approach may overlook some events, because patients presenting with subacute complaints may not initially seek care in these ways due to access (e.g., travel time), insurance coverage (e.g., copayments), or other factors such as presence of comorbidities (e.g., ability to travel). In addition, some subacute symptoms may not warrant emergency care but instead can be addressed through a primary care physician visit or contact with a nurse via phone or email.

We adopted a syndromic surveillance framework to examine the relationship between ambient $PM_{2.5}$ concentrations and respiratory symptoms in a large health maintenance organization–based healthcare system in the Mid-Atlantic region of the United States. Syndromic surveillance identifies changes in disease activity using either clinical features detected before diagnosis is confirmed or activities prompted by the onset of symptoms (7). We hypothesized that calls and e-mails related to respiratory symptoms would represent an association with $PM_{2.5}$ similar to the associations observed with emergency department and urgent care visits.

Methods

We constructed an innovative database of information collected during routine provision of medical care by Kaiser Permanente Mid-Atlantic States (KPMAS), which serves approximately 700,000 residents of the northern Virginia, District of Columbia, Maryland, and Baltimore areas. This study was approved by institutional review boards at KPMAS and Georgia State University.

Healthcare utilization data were collected from the comprehensive electronic health databases of KPMAS. We identified four types of utilization events for 2013 and 2014: *1*) any phone contact or e-mail message (member or provider initiated); *2*)

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any outpatient provider face-to-face visit (nurse or physician) that was not an urgent care visit; *3*) emergency department and urgent care visits; and *4*) hospital admissions. Only utilization events likely related to respiratory issues were counted, such as *International Classification of Diseases, Ninth Revision*, Clinical Modification codes for 466.0 (acute bronchitis), 493.22 (chronic obstructive asthma with exacerbation), and 518.81 (acute respiratory failure).

KPMAS members and utilization events were aggregated by census block of residence and date of utilization. Utilization event rates were defined for each day as the number of persons with any of the four types of utilization events divided by the number of members as of December 31, 2013 (the middle of the study period). Utilization event rates were expressed as a value per 100,000 KPMAS members per day.

Data on ambient concentrations of $PM_{2.5}$ were obtained from 63 air monitoring stations. Monitoring stations were owned and operated by state environmental agencies with data housed within the Air Quality System of the U.S. Environmental Protection Agency, which we accessed via the AirData website (8). Data were obtained from each monitor as well as latitude and longitude to assign daily average $PM_{2.5}$ concentrations to each census block. We evaluated the potential for delayed effects of ambient $PM_{2.5}$ concentrations by considering daily averages from the current day, 1-day lag, 3-day distributed lag, and a 3-day moving average. The association of $PM_{2.5}$ concentration and utilization events related to respiratory issues was estimated using linear regression. Models included significant predictors of the outcome and potential confounders, including day of week, month, and year; temperature and temperature squared; and census tract-level socioeconomic variables (median household income and percent of adults with high school education or less).

Results

The mean level of $PM_{2.5}$ across all census block groups for 2013 to 2014 was 9.15 $\mu g/m^3$ (standard deviation, 0.78 $\mu g/m^3$), comparable to previously reported concentrations (9, 10) (Table 1). There was variation throughout the year, although the highest concentrations occurred during cooler compared with warmer weather. Table 2 displays associations between ambient $PM_{2.5}$ concentrations and utilization events for each of the four model specifications. The effects of ambient $PM_{2.5}$ are remarkably

Table 1. Distribution of utilization events for respiratory symptoms in the Kaiser Permanente Mid-Atlantic States, 2013 to 2014

Event Type	Calls/ E-mails	Provider Visits	ED/UC Visits	Hospital Admissions
Total No. of events	70,324	221,686	62,639	11,740
No. of events/d	96.3	303.7	85.8	16.1
Events per 100,000 member-days, mean (SD)	29.9 (24.6)	94.4 (55.0)	26.7 (22.7)	5.0 (12.9)

Definition of abbreviations: ED/UC = emergency department and urgent care; SD = standard deviation.

Table 2. Association between ambient particulate matter with an aerodynamic diameter <2.5 μm and utilization events for respiratory symptoms within the Kaiser Permanente Mid-Atlantic States, 2013 to 2014

$PM_{2.5}$	Calls/E-mails				Provider Visits				ED/UC Visits				Hospital Admissions			
	Model 1	Model 2	Model 3	Model 4	Model 1	Model 2	Model 3	Model 4	Model 1	Model 2	Model 3	Model 4	Model 1	Model 2	Model 3	Model 4
Current day	**0.08**	—	0.07	—	**0.25**	—	**0.24**	—	**0.16**	—	**0.19**	—	0.02	—	0.03	—
95% CI	**0.02 to 0.14**		0.00 to 0.14		**0.14 to 0.35**		**0.12 to 0.36**		**0.10 to 0.22**		**0.12 to 0.26**		0.00 to 0.05		0.00 to 0.06	
1-d lag	—	0.05	0.02	—	—	−0.08	−0.10	—	—	0.04	−0.05	—	—	0.01	−0.03	—
95% CI		−0.01 to 0.10	−0.06 to 0.10			−0.03 to 0.19	−0.25 to 0.04			−0.02 to 0.09	−0.12 to 0.03			−0.02 to 0.03	−0.06 to 0.01	
2-d lag	—	—	0.00	—	—	—	0.08	—	—	—	−0.01	—	—	—	0.03	—
95% CI			−0.07 to 0.07				−0.05 to 0.21				−0.08 to 0.06				0.00 to 0.06	
3-d MA	—	—	—	**0.10**	—	—	—	**0.20**	—	—	—	**0.12**	—	—	—	0.03
95% CI				**0.02 to 0.18**				**0.05 to 0.35**				**0.04 to 0.20**				0.00 to 0.06

Definition of abbreviations: CI = confidence interval; ED/UC = emergency department and urgent care; MA = moving average; PM2.5 = particulate matter with an aerodynamic diameter <2.5 μm.
Bold typeface represents statistically significant effect estimates. Model 1 is current-day exposure; Model 2 is 1-day lag, Model 3 is a distributed lag model of current day, 1-day, and 2-day; Model 4 is a 3-day moving average of the past 3 days.

Table 3. Difference in daily event rates for respiratory symptoms per 100,000 members associated with selected particulate matter with an aerodynamic diameter <2.5 μm metrics

Current Day $PM_{2.5}$	Calls/E-mails	Provider Visits	ED/UC Visits	Hospital Admissions
Absolute change in daily event rates per 100,000 members				
1.25 ug/m^3 (IQR)	**0.10**	**0.31**	**0.20**	0.03
95% CI	**(0.03 to 0.17)**	**(0.18 to 0.44)**	**(0.12 to 0.27)**	(0.00 to 0.06)
10.0 μg/m^3 increase	**0.78**	**2.48**	**1.59**	0.21
95% CI	**(0.21 to 1.35)**	**(1.44 to 3.51)**	**(1.00 to 2.18)**	(−0.03 to 0.46)
Percent change in daily event rates per 100,000 members				
1.25 ug/m^3 (IQR)	**0.33**	**0.33**	**0.74**	0.53
95% CI	**(0.09 to 0.57)**	**(0.19 to 0.46)**	**(0.47 to 1.02)**	(−0.07 to 1.14)
10.0 μg/m^3 increase	**2.61**	**2.63**	**5.96**	4.20
95% CI	**(0.71 to 4.53)**	**(1.53 to 3.72)**	**(3.73 to 8.15)**	(−0.57 to 9.13)

Definition of abbreviations: CI = confidence interval; ED/UC = emergency department and urgent care; IQR = interquartile range; $PM_{2.5}$ = particulate matter with an aerodynamic diameter <2.5 μm.
Bold typeface represents statistically significant effect estimates.

consistent across event types. Higher current-day exposure is associated with statistically significant ($P < 0.05$) higher calls/e-mails, provider visits, and emergency department/urgent care visits for respiratory reasons per 100,000 members per day.

Table 3 shows a 1.25 μg/m^3 and 10.0 μg/m^3 change in current-day $PM_{2.5}$ concentration and the associated prevalence of utilization events for respiratory symptoms as absolute and percentage values. The numerator for computing percent increases in utilization events is obtained from Table 2, and the denominator is the average event rate for an event type and exposure type displayed in Table 1. An elevation in utilization events by type is meaningful, because the denominators for different event types vary substantially in magnitude. Thus, a small absolute effect may be a large relative effect if the average event rate is low, and vice versa. For example, a 10.0 μg/m^3 change in $PM_{2.5}$ is associated with a 0.78 (95% confidence interval [CI], 0.21–1.35) higher absolute prevalence in calls/e-mails per 100,000 members, which corresponds to 2.61% (95% CI, 0.71–4.53%). The highest effect is seen in emergency department/urgent care visits, where a 10.0 μg/m^3 change in $PM_{2.5}$ is associated with higher prevalence of 1.59 (95% CI, 1.00–2.18) events per 100,000 members, which is equivalent to 5.96% (95% CI, 3.73–8.15%).

Conclusions

Consistent with several prior studies, we found associations between higher ambient $PM_{2.5}$ concentrations and higher urgent care/emergency department visits (4, 9, 11–13). As hypothesized, we also found higher utilization event rates in nonurgent, nonemergent services—calls or e-mails between patients and providers as well as face-to-face provider visits. Each of these types of services requires time and resources and adds to the overall costs and complexity of healthcare delivery—in a manner that is more subtle and less dramatic than urgent or emergent care but nevertheless burdensome. Because all healthcare utilization incurs costs to healthcare systems and patients, society stands to benefit from public health policies and programs that diminish exposure to air pollution such as $PM_{2.5}$.

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Weight Loss in Individuals with Obesity and Asthma

To the Editor:

We commend Okoniewski and colleagues for their recent systematic review published in *AnnalsATS* (1) on weight loss interventions in obese subjects with asthma, which we read with great interest. Although not cited by the authors, we note a comparable 2012 Cochrane review by Adeniyi and Young (2), which similarly assessed randomized controlled trials of weight loss interventions in asthma.

We draw your attention to the omission in the present review of at least one study eligible for inclusion (3) according to the *a priori* inclusion criteria, which did not restrict studies according to language of publication providing sufficient information in English was available for accurate data collection. This study had been published in Spanish but had been included in the aforementioned Cochrane review, for which the data were extracted and published in English. It is notable that the current review, as published, thus departs from its own protocol, registered in the International Prospective Register of Systematic Reviews (PROSPERO CRD42018085045).

We note also the inclusion of a study (4) of a population that combined subjects deemed to be "at high risk of asthma" with subjects with a diagnosis of asthma, despite no disaggregated data being published for these two groups.

Of 10 studies included in the review by Okoniewski and colleagues (1), only that by Stenius-Aarniala and colleagues (5) was published in full at the time of the Cochrane review, and it is striking that both reviews diverge in their assessment of the risk of bias in that study. The study by Stenius-Aarniala and colleagues is assessed in the current review as having low risk of bias in random sequence allocation but was deemed in the Cochrane review to be at unclear risk of bias, as the method used involved shuffling of cards yet produced equal numbers of participants in both groups, despite a small sample size. Conversely, the authors of the present review deemed the risk of attrition bias and reporting bias in this study to be unclear, whereas the authors of the Cochrane review found the Stenius-Aarniala and colleagues study to be at low risk of bias in these domains.

The current review also overlooks biased estimates in its qualitative analysis when referring to one study (6), which reported "a significant improvement in FVC in liters (P = 0.006 between groups), but not FVC % predicted." It must be noted that the pertinent study used a per-protocol analysis, which did not include those patients randomized to intervention who achieved less than 10% weight loss. The published intent-to-treat analysis included only forced vital capacity (FVC) % predicted, and in this there was no significant between-group difference.

Finally, we must question the decision, in the protocol for the present review, to prioritize "relevant biomarkers (such as leptin, adiponectin, or IL-6)" as a primary outcome, with patient-important outcomes, such as asthma exacerbations, relegated to among the secondary outcomes or not listed at all (e.g., quality of life). These biomarkers were not included as either core or supplemental outcomes by an expert subcommittee convened by the National Institutes of Health and the Agency for Healthcare Research and Quality to propose which biomarkers should be assessed as standardized asthma outcomes in future clinical research studies—neither were they considered to be "emerging" (i.e., requiring validation and standardization) (7).

Notwithstanding these considerations, the review succeeds in highlighting the need for further well-designed randomized controlled trials investigating the effect of weight loss in obese asthma. As more recently approved obesity drugs, including liraglutide and lorcaserin, remain unstudied in this context to date, the time is ripe for such trials.

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