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Ambient Particulate Matter and Paramedic Assessments of Acute Diabetic, Cardiovascular, and Respiratory Conditions

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Background: Ambulance data provide a useful source of population-based and spatiotemporally resolved information for assessing health impacts of air pollution in nonhospital settings. We used the clinical records of paramedics to quantify associations between particulate matter ($PM_{2.5}$) and diabetic, cardiovascular, and respiratory conditions commonly managed by those responding to calls for emergency ambulance services.

Methods: We evaluated 394,217 paramedic assessments from three states in Southeastern Australia (population 13.2 million) and daily $PM_{2.5}$ concentrations modeled at 5 km resolution from 2009 to 2014. We used a time-stratified, case-crossover analysis adjusted for daily meteorology to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for each clinical outcome per 10 μg/m^3 increase in daily $PM_{2.5}$ at lags from 0 to 2 days.

Results: Increased $PM_{2.5}$ was associated with increased odds of paramedic assessments of hypoglycemia (OR = 1.07; 95% CI = 1.02, 1.12, lag 0), arrhythmia (OR = 1.05; 95% CI = 1.02, 1.09, lag 0), heart failure (OR = 1.07; 95% CI = 1.02, 1.12, lag 1), faint (OR = 1.09; 95% CI = 1.04–1.13, lag 0), asthma (OR = 1.06; 95% CI = 1.01, 1.11, lag 1), chronic obstructive pulmonary disease (OR = 1.07; 95% CI = 1.01, 1.13, lag 1), and croup (OR = 1.09; 95% CI = 1.02, 1.17). We did not identify associations with cerebrovascular outcomes.

Conclusions: Ambulance data enable the evaluation of important clinical syndromes that are often initially managed in nonhospital settings. Daily $PM_{2.5}$ was associated with hypoglycemia, faint, and croup in addition to the respiratory and cardiovascular outcomes that are better established.

Keywords: Air pollution; Ambulance dispatches; Cardiovascular; Croup; Diabetes; Faint; Hypoglycemia; Respiratory

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Data access: Access to data is subject to data custodian requirements.

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Exposure to ambient particulate matter (PM) is associated with acute and chronic adverse health outcomes, mediated through pathophysiologic processes including the promotion of inflammation, coagulation, and oxidative stress.[1,2] While impacts on the cardiovascular and respiratory systems have been well characterized, associations with many other health conditions are also emerging, including neurologic, immunologic, and perinatal outcomes.[3–5] In particular, associations between outdoor air pollution and metabolic outcomes have also been recently reported.[4,6] For example, short-term exposure to ambient PM has been associated with increased blood glucose concentrations,[7] hospital admissions for diabetic problems, and admissions for all reasons in people with diabetes.[3,8,9] Further, long-term PM exposure has been associated with increased incidence of diabetes.[6]

Much of the evidence about the population-level health impacts of PM comes from studies of administrative health data, such as hospital emergency room visits, admissions records, and registered deaths. Air quality estimates for these studies are typically referenced to the usual place of residence. Ambulance records are a source of population-level health information that has been less extensively evaluated with respect to air pollution. They can provide information about common clinical syndromes that are less often managed in hospital settings, such as hypoglycemia (low blood glucose) or fainting (brief loss of consciousness that can have many clinical causes). However, the range of clinical information suitable for evaluation is more limited compared with that available from datasets on hospital admissions or emergency room visits. Unlike other sources of administrative data, ambulance records can also provide the precise geolocation of the health event, rather than place of usual residence, and timing of the call to emergency services. This information is especially helpful for short-term air quality studies because atmospheric pollution can exhibit considerable spatial and temporal variation.[10]

Ambulance data are typically categorized at two points in time. The first occurs at the time of the initial call to emergency services, when a dispatch category is assigned to indicate the general problem and degree of urgency. The second occurs when an assessment is made by the attending paramedic following a clinical evaluation, including history, examination and, in some cases, investigations such as blood or urine testing. Dispatch categories are assigned according to standardized over-the-phone protocols,[11] so the cases included in each category can have considerable clinical heterogeneity and diagnostic uncertainty.[12] In comparison, paramedics follow standardized in-person protocols for identifying and managing a range of important medical conditions, which makes their patient records more clinically informative.[13] Paramedic assessments have been understudied in the environmental health literature compared with dispatch data, which are more readily available. Paramedic assessments of cardiac arrest have been associated with ambient air quality,[14] but studies on assessments for other conditions are limited.[15] Here, we aimed to assess the association between $PM_{2.5}$ (PM less than 2.5 μm in aerodynamic diameter) and primary paramedic assessments of selected diabetic, cardiovascular, and respiratory conditions. We hypothesized that by examining data collected in ambulance settings, we would identify new plausible clinical manifestations of reduced air quality.

METHODS

Study Population

The study included 394,217 ambulance dispatches with paramedic records in the Southeastern Australian States of Victoria, New South Wales (NSW), and Tasmania for the period 2009–2014 (Figure 1). The 2012 combined population of this areas was 13.2 million people, approximately half of the total Australian population. Of the 7.3 million people in NSW, more than half are in the greater Sydney area.[16] Similarly, Victoria has a population of 5.6 million, most of which is in the greater Melbourne area. In contrast, Tasmania has a smaller, more dispersed population of 512,000.[16]

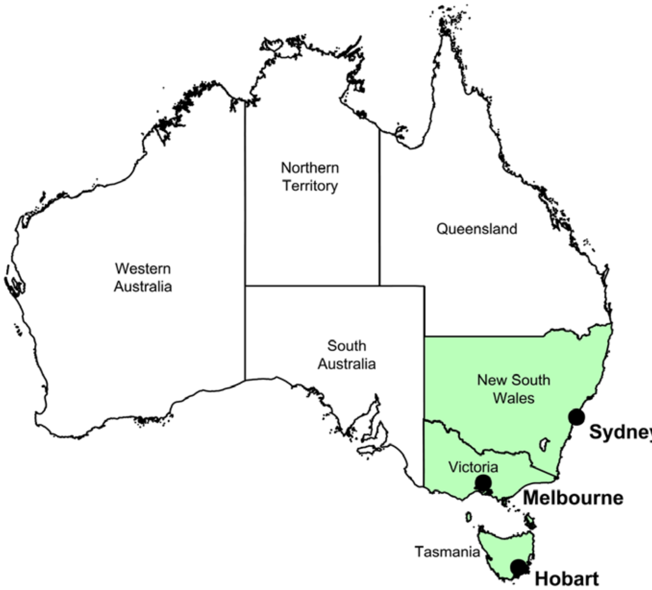

FIGURE 1. Map of Australia illustrating the states of New South Wales, Victoria, and Tasmania. More than half the population of Australia reside in these three states, the majority in, or close to, the major cities of Sydney and Melbourne.

Outcome Data

A standard clinical information system was used by all jurisdictions participating in this study. Data are entered directly by paramedics at the scene of the incident or after patient handover at hospital. We selected primary paramedic assessments of hyperglycemia and hypoglycemia for the diabetes-related outcomes. Cardiovascular outcomes included arrhythmia, heart failure, faint, acute coronary syndrome, angina, stroke, and transient ischemic attack. Heart failure was a combined category that included assessments of both cardiac failure and acute pulmonary edema. Respiratory outcomes included asthma, chronic obstructive pulmonary disease (COPD), lower respiratory infections, and croup, a common upper airway infection in young children. Lower respiratory infections were a combined category that included assessments of chest infection and pneumonia. Later introduction of the electronic information system in NSW meant that only 18 months of paramedic assessment data were available in this state (eFigure 1; http://links.lww.com/EDE/B415). The ambulance dispatch date, time, and location were recorded for all cases. We excluded elective (nonurgent) dispatches, which mainly comprised patient transfers for prearranged appointments.

Exposure Data

Gridded daily average exposure estimates for $PM_{2.5}$ were produced at a resolution of 5×5 km by adapting the general approach of Yao and Henderson[10] to the Australian study region using an empirical Random Forest model and more environmental covariates.[17] The model domain included the Southeastern states and territories of Australia (Victoria, NSW, Tasmania, and the Australian Capital Territory) from October

2009 to April 2015. Model inputs were remotely sensed aerosol optical depth and fire radiative power from the Moderate Resolution Imaging Spectroradiometer instruments. Aerosol optical depth is a measure of aerosol in the entire atmospheric column that correlates with on-ground particulate concentrations, while fire radiative power measures the intensity of landscape fire points and is proportional to their aerosol emissions.[18] We obtained daily $PM_{2.5}$ data from state Environmental Protection Agencies for the nearest available surface monitor, and the atmospheric venting index was interpolated from nearest available weather station.[19] In addition, we included the C-Haines index of atmospheric stability, a driver of air pollution dispersion,[20] and ozone data from the Aura satellite. Gridded daily average temperature and relative humidity were provided by the Australian Bureau of Meteorology in each state.[19]

The $PM_{2.5}$ model was constructed to tolerate missing data. For example, if satellite or monitor data were missing for given day and location, a simpler form of the model was run using the available variables.[17] A leave-one-out cross-validation of the model produced a Pearson correlation coefficient of 0.82 with the observed ground-based measurements and a root mean square error (RMSE) of 5.7 $\mu g \cdot m^{-3}$. Additionally, we cross-validated the model by leaving out individual monitoring stations and predicting those points using remaining stations to assess the spatial stability of the model, which resulted in a mean Pearson correlation coefficient 0.82 mean RMSE of 4.13 $\mu g \cdot m^{-3}$.

Statistical Analysis

A time-stratified case-crossover design[21] was used to estimate the association between exposure to $PM_{2.5}$ and the paramedic assessments. Our design controlled for day of the week, monthly, seasonal, and long-term trends. The daily average of modeled $PM_{2.5}$ on the day of the dispatch and at the location of the dispatch (case exposure) was compared with $PM_{2.5}$ estimates at the same 5×5 km grid cell for all other occurrences of the same weekday in the same calendar month and year (control exposures). Control exposure data thus contrast temporal rather than spatial variations in air quality. Because each case is their own control, it accounts for individual factors that do not vary meaningfully within 1 month, such as age, sex, socioeconomic position, residential location, and smoking status. The following conditional logistic model was used to estimate the association between $PM_{2.5}$ and the paramedic assessment as an odds ratio (equation 1):

$$\text{Paramedicassessment}|\text{UID} \sim \text{PM}_{2.5} + s(T_t, 2) + s(T_{\text{lag}(t,1-3)}, 2) + s(\text{RH}_t, 2) + s(\text{RH}_{\text{lag}(t,1-3)}, 2),$$

where the paramedic assessment is 1 for the case day and 0 for control days, conditioned on the unique identifier of the study subject; $PM_{2.5}$ is the daily concentration at the dispatch incident location of each subject; s (T, 2) is a natural cubic spline of the average temperature with two degrees of freedom (df) and the lag (1–3) is the average for the previous 3 days; and RH is the average relative humidity with the same degrees of freedom and lag structure.

We ran models for the combined dataset and separately for each state. Individual models were run for $PM_{2.5}$ concentrations on the same day (lag 0), the previous day (lag 1), and 2 days (lag 2) before the health outcome to assess temporal relationships. The combined dataset was used to evaluate differences by sex and age group (0–15, 16–50, 51–65, and above 65 years old). The significance of the statistical difference between effect estimates within subgroups (e.g., males versus females) was tested using meta-regression.[22,23] All analyses were performed in R statistical software.[24] The research was approved by the Health and Medical Research Ethics Committee of the University of Tasmania (Reference H0013521).

RESULTS

Air quality was generally good over the study period, with a mean (standard deviation) daily $PM_{2.5}$ concentration of 8.4 (4.1) $\mu g/m^3$, though there were some highly exposed days (Table 1). Lower respiratory infections (N = 67,952) and acute coronary syndrome (N = 66,231) were the most common paramedic assessments recorded (Table 1).

Paramedic Assessments and $PM_{2.5}$

In the analysis of diabetic outcomes, we found that increased $PM_{2.5}$ was associated with paramedic assessments of hypoglycemia. In the combined analysis, there was an approximate 7% increase in the odds of this outcome for each 10 $\mu g/m^3$ increase in $PM_{2.5}$ (odds ratio [OR] = 1.07; 95% confidence interval [CI] = 1.02, 1.12, lag 0) (Figure 2). We also observed positive associations in each individual state (Table 2). In contrast, there was no association with hyperglycemia in the combined analysis, but results from the state of Tasmania alone showed a strong association (Table 2).

In the analyses of cardiovascular conditions, paramedic assessments of arrhythmia, heart failure, and faint were all associated with increased $PM_{2.5.}$ For each 10 $\mu g/m^3$ increase in same-day $PM_{2.5}$, the odds of assessments for faint increased by approximately 9% (OR = 1.09; 95% CI = 1.04, 1.13, lag 0) and the odds of arrhythmia increased by 5% (OR = 1.05; 95% CI = 1.02, 1.09, lag 0). In contrast, associations with heart failure increased with increasing lags and were greatest at the maximum lag of 2 days (OR = 1.07; 95% CI = 1.02, 1.12, lag 2). Associations with acute coronary syndrome (OR = 1.02; 95% CI = 0.99, 1.05, lag 0) and angina (OR = 1.04; 95% CI = 0.99, 1.09, lag 0) were imprecisely elevated (Table 2; Figure 2). We did not find any associations with assessments stroke or transient ischemic attack.

In the analyses of respiratory conditions, paramedic assessments of asthma, COPD, and croup were associated with elevated $PM_{2.5}$ (Figure 2). The magnitude of the association was greatest for croup, for which the odds were increased by 8%–9% per 10 $\mu g/m^3$ increase in $PM_{2.5}$ at lags of 0 and

TABLE 1. Total Number, Mean, Standard Deviation, Quartiles, and Range of Daily Average $PM_{2.5}$, Relative Humidity, Temperature, and Health Outcomes for Study Participants, South Eastern Australia 2009–2014

	N	Mean	Standard Deviation	Min	First Quartile	Median	Third Quartile	Max
Environmental exposures								
Daily average $PM_{2.5}$ (μg/m^3)	394,217	8.4	4.1	0.3	5.5	7.9	10.8	141.3
Daily average relative humidity (%)	394,217	67.6	15.1	8.0	57.5	68	78.5	103
Daily average temperature (°C)	394,217	14.8	5.1	−4.0	10.9	14.2	18.4	35.5
Diabetes-related outcomes								
Hypoglycemia	24,795	17.7	4.7	5	14.8	17	20	34
Hyperglycemia	10,332	7.8	2.8	1	6	8	10	18
Cardiovascular outcomes								
Arrhythmia	48,387	31.8	6.4	18	27	32	36	54
Heart failure	21,381	13.5	4.6	4	10	13	17	27
Faint	29,612	24.0	6.0	8	20	23	28	56
Acute coronary syndrome	66,231	59.6	10.6	24	52	59	66	93
Angina	26,612	14.1	4.2	5	11	14	17	30
Stroke	25,651	19.6	4.5	6	16	20	23	35
Transient ischemic attack	15,793	10.3	3.3	1	8	10	13	21
Respiratory outcomes								
Asthma	25,746	20.0	5.7	7	16	20	24	37
Chronic obstructive pulmonary disease	18,851	13.4	4.2	4	10	13	16	27
Lower respiratory infections	67,952	41.7	13.0	16	32	39.5	50	86
Croup	12,874	9.8	5.2	0	6	9	13	25

1 days (OR = 1.09; 95% CI = 1.02%, 1.17%, lag 1; Table 2; Figure 2). For the other respiratory outcomes, there was some heterogeneity in the results from individual states, especially for the overlapping clinical conditions of asthma, COPD, and lower respiratory infections.

Differences by Age and Sex

Most outcomes were more frequent in older age groups, apart from the childhood disease of croup, and the number of cases was similar between sexes (Supplemental digital information eTable1; http://links.lww.com/EDE/B415). The pattern of association with $PM_{2.5}$ was similar for males and females, with the exception of acute coronary syndrome. The same-day odds of this outcome was increased by 5% per 10 μg/m^3 increase in $PM_{2.5}$ (OR = 1.05; 95% CI = 1.01, 1.09, lag 0) for males, while no association was observed in females (OR = 0.99; 95% CI = 0.94, 1.03, lag 0). This difference was confirmed by meta-regression comparing results by sex (P = 0.03). The pattern of associations by age groups generally reflected the expected population distribution of each outcome with most associations observed in people aged over 65 years (Supplemental digital information eTable 2; http://links.lww.com/EDE/B415).

DISCUSSION

We have identified associations between paramedic assessments and daily ambient $PM_{2.5}$ for a wide range of outcomes. While many of these outcomes have been previously associated with air pollution, our finding of clear associations with hypoglycemia and faint appears to be novel and the association with croup has not been widely reported.

Diabetic Outcomes

When evaluating diabetic outcomes in association with air pollution, it can be difficult to disentangle direct effects from indirect associations. Poor air quality directly affects diabetic control, but also affects many of the chronic conditions that are more common in people with diabetes, such as heart disease.[3] Tasmania was the only state in which an association with paramedic assessments of hyperglycemia was observed. One explanation for this regional difference could be the higher prevalence of self-reported diabetes in Tasmania compared with the national average (9.9% vs. 4.7%)[25,26] and the higher rate of diabetes mortality in Tasmania compared with all of Australia (24.7 vs. 15.6 deaths per 100 000 population).[26] Another reason for the discrepancy between states could be differences in paramedic coding conventions for determining the primary assessment when more than one condition is present. For example, a person with diabetes who develops a respiratory infection might have raised blood glucose levels in addition to respiratory symptoms, and the primary paramedic assessment could reflect either condition.

The association between hypoglycemia and $PM_{2.5}$ was more consistent in our study. This is, to the best of our knowledge, the first time that a potential association between air pollution and low blood glucose has been reported. While the precise

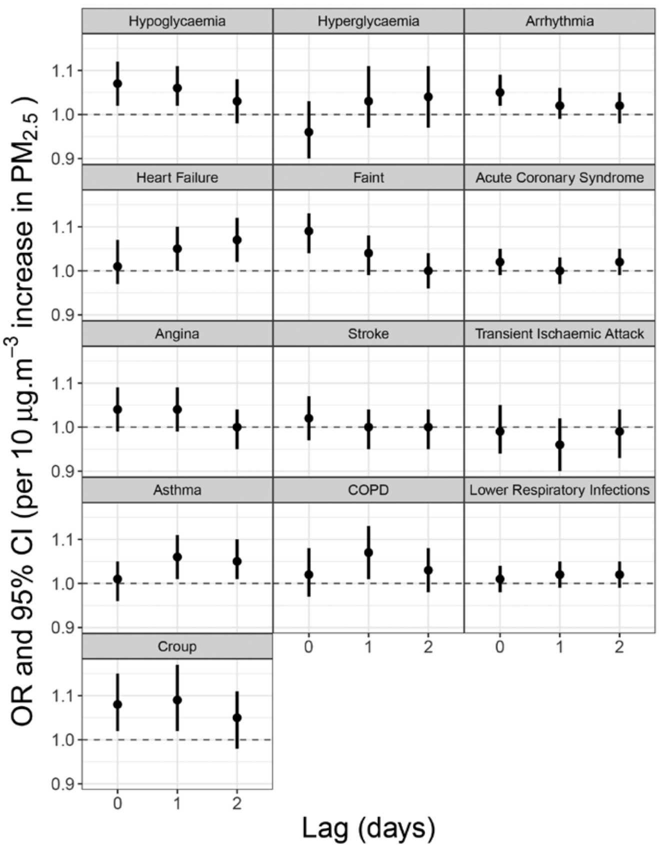

FIGURE 2. Odds ratio and 95% confidence intervals for paramedic assessments per 10-µg/m^3 increase in $PM_{2.5}$, for same-day associations (lag 0) and at lags of 1 and 2 days.

relationship between air pollution and glucose homeostasis is unknown, it has been hypothetically linked with an inflammatory response in the context of insulin resistance.[27] Further, positive associations between PM and elevated blood glucose have been observed in people with and without impaired glucose metabolism.[27] While the association we observed with hypoglycemia could be a chance finding, the effect was consistent at different lags in all three states. A speculative mechanism might be that increased air pollution leads to decreased glycemic control, such that some individuals increase use of insulin or other medications, which can lead to increased risk of hypoglycemia. However, we could not find any empirical evidence for this association. Previous studies have shown that cases of hypoglycemia attended by ambulance services are often successfully treated at the scene and not transported to hospital,[28,29] which might explain why hypoglycemia has not been identified in air quality studies of diabetic outcomes based on ER or hospital admissions datasets. We were unable to explore this observation further because we did not have information about the use of insulin or other medications.

Cardiovascular Outcomes

The pattern of observed associations between $PM_{2.5}$ and paramedic assessments of cardiovascular conditions was partially consistent with the wider evidence.[30] This includes the positive associations observed for arrhythmia, heart failure, and acute coronary syndrome in males. In contrast, we did not observe associations with assessments of angina, stroke, or transient ischemic attack, all of which were expected based on the available evidence.[31] Although ambulance dispatches for cardiac arrest have been associated with ambient PM in a handful of studies from the United States, Italy, Japan, and Australia,[12,32–34] we were not able to evaluate this outcome because arrest data were not consistently recorded.

There is very little research evaluating the association between air quality and fainting. The only other study we identified also observed associations between ambient $PM_{2.5}$ and assessment of fainting by an emergency responder.[15] Fainting can be symptomatic of different medical problems, and the assessment is only made by paramedics after possible alternative causes have been excluded. These typically include seizures, serious cardiac arrhythmias, or low blood glucose, which are excluded by history, examination, electrocardiogram, and blood glucose testing. Fainting can have a number of precipitants including dehydration, prolonged standing, instability of the autonomic nervous system, a neuronal reflex, or transient abnormalities of cardiac rhythm.[35] An association with air pollution could be plausible, given that cardiac arrhythmias and alterations in heart rate variability have been associated both with air pollution and with clinical syndromes of fainting.[2,36]

Respiratory Outcomes

The literature on air pollution and respiratory outcomes has demonstrated that short-term exposure to $PM_{2.5}$ is associated with exacerbations of respiratory illnesses including asthma, COPD, and infections. Increasing $PM_{2.5}$ is associated with measurable increases in respiratory symptoms, emergency presentations, hospital admissions, and mortality.[1,37] However, studies of ambulance dispatches are more limited. In Fukuoka, Japan, a 10-µg/m^3 increase in $PM_{2.5}$ was associated with ambulance dispatches that were later verified as respiratory diagnoses (odds ratio = 1.03; 95% CI = 1.01, 1.05).[33] A study of dispatch codes in Italy found positive associations between increased PM and dispatches for all nontraumatic causes, but not the dispatch categories most associated with respiratory and cardiovascular causes.[38] A previous study in Sydney, Australia, found a clear association between increased $PM_{2.5}$ (10 µg/m^3) and ambulances dispatched for breathing problems (relative risk (RR) = 1.03; 95% CI = 1.02, 1.04), while noting that this could reflect many possible clinical conditions.[12]

Our findings of associations between air quality and both asthma and COPD are consistent with the wider literature, even though a limited number of studies have analyzed ambulance data. The lagged associations we observed are consistent with the mechanisms of airway inflammation.

TABLE 2. Associations Between Paramedic Assessments and 10 μg/m^{-3} Increase in $PM_{2.5}$ for Same Day (Lag 0) and Lags of 1 and 2 Days

Paramedic Assessment	Lag	All States Combined OR (95% CI)	Tasmania OR (95% CI)	Victoria OR (95% CI)	New South Wales OR (95% CI)
Diabetes-related outcomes					
Hypoglycemia	0	1.07 (1.02, 1.12)	1.20 (1.00, 1.44)	1.03 (0.98, 1.09)	1.22 (1.07, 1.38)
	1	1.06 (1.02, 1.11)	1.04 (0.87, 1.25)	1.05 (1.00, 1.11)	1.12 (0.99, 1.27)
	2	1.03 (0.98, 1.08)	1.04 (0.87, 1.24)	1.02 (0.97, 1.08)	1.06 (0.94, 1.20)
Hyperglycemia	0	0.96 (0.90, 1.03)	1.19 (0.95, 1.50)	0.93 (0.86, 1.01)	0.94 (0.74, 1.18)
	1	1.03 (0.97, 1.11)	1.35 (1.11, 1.66)	1.00 (0.92, 1.08)	0.92 (0.73, 1.16)
	2	1.04 (0.97, 1.11)	1.27 (1.04, 1.56)	1.00 (0.92, 1.08)	1.02 (0.83, 1.26)
Cardiovascular outcomes					
Arrhythmia	0	1.05 (1.02, 1.09)	1.04 (0.93, 1.17)	1.07 (1.03, 1.10)	0.99 (0.87, 1.12)
	1	1.02 (0.99, 1.06)	1.02 (0.92, 1.14)	1.03 (0.99, 1.07)	1.00 (0.88, 1.14)
	2	1.02 (0.98, 1.05)	1.06 (0.95, 1.18)	1.02 (0.99, 1.06)	0.97 (0.85, 1.10)
Heart failure	0	1.01 (0.97, 1.07)	1.04 (0.88, 1.23)	1.01 (0.95, 1.07)	1.00 (0.85, 1.18)
	1	1.05 (1.00, 1.10)	1.04 (0.87, 1.24)	1.04 (0.99, 1.10)	1.09 (0.92, 1.28)
	2	1.07 (1.02, 1.12)	1.11 (0.94, 1.32)	1.06 (1.01, 1.12)	1.01 (0.86, 1.18)
Faint	0	1.09 (1.04, 1.13)	1.11 (0.97, 1.27)	1.10 (1.05, 1.15)	1.06 (0.95, 1.18)
	1	1.04 (0.99, 1.08)	1.08 (0.94, 1.24)	1.03 (0.98, 1.08)	1.08 (0.97, 1.20)
	2	1.00 (0.96, 1.04)	1.03 (0.90, 1.18)	0.98 (0.94, 1.03)	1.03 (0.93, 1.14)
Acute coronary syndrome	0	1.02 (0.99, 1.05)	1.05 (0.94, 1.17)	1.03 (0.99, 1.06)	0.99 (0.93, 1.05)
	1	1.00 (0.97, 1.03)	1.02 (0.92, 1.13)	1.01 (0.98, 1.04)	0.98 (0.92, 1.04)
	2	1.02 (0.99, 1.05)	1.04 (0.94, 1.16)	1.04 (1.00, 1.07)	0.96 (0.90, 1.02)
Angina	0	1.04 (0.99, 1.09)	1.03 (0.92, 1.16)	1.04 (0.98, 1.09)	0.95 (0.79, 1.14)
	1	1.04 (0.99, 1.09)	1.05 (0.94, 1.17)	1.04 (0.99, 1.10)	0.93 (0.78, 1.11)
	2	1.00 (0.95, 1.04)	1.06 (0.95, 1.18)	0.99 (0.93, 1.04)	0.91 (0.76, 1.10)
Stroke	0	1.02 (0.97, 1.07)	1.05 (0.90, 1.22)	1.00 (0.95, 1.06)	1.11 (0.97, 1.25)
	1	1.00 (0.95, 1.04)	1.02 (0.88, 1.18)	0.98 (0.93, 1.03)	1.08 (0.95, 1.22)
	2	1.00 (0.95, 1.04)	0.96 (0.83, 1.11)	0.98 (0.93, 1.03)	1.13 (1.00, 1.27)
Transient ischemic attack	0	0.99 (0.94, 1.05)	0.88 (0.71, 1.08)	1.02 (0.96, 1.08)	0.87 (0.70, 1.08)
	1	0.96 (0.90, 1.02)	0.99 (0.81, 1.22)	0.96 (0.90, 1.03)	0.95 (0.77, 1.18)
	2	0.99 (0.93, 1.04)	0.99 (0.81, 1.21)	0.98 (0.92, 1.05)	1.08 (0.88, 1.32)
Respiratory outcomes					
Asthma	0	1.01 (0.96, 1.05)	0.96 (0.80, 1.15)	0.98 (0.93, 1.03)	1.17 (1.05, 1.29)
	1	1.06 (1.01, 1.11)	1.13 (0.95, 1.35)	1.05 (1.00, 1.11)	1.09 (0.99, 1.20)
	2	1.05 (1.01, 1.10)	1.25 (1.05, 1.48)	1.06 (1.00, 1.11)	0.99 (0.89, 1.09)
Chronic obstructive pulmonary disease	0	1.02 (0.97, 1.08)	0.95 (0.78, 1.15)	1.03 (0.97, 1.10)	1.05 (0.88, 1.24)
	1	1.07 (1.01, 1.13)	0.91 (0.75, 1.10)	1.10 (1.04, 1.17)	1.01 (0.84, 1.20)
	2	1.03 (0.98, 1.08)	0.95 (0.79, 1.15)	1.04 (0.98, 1.11)	1.01 (0.85, 1.19)
Lower respiratory infections	0	1.01 (0.98, 1.04)	1.08 (0.99, 1.18)	1.01 (0.98, 1.04)	0.98 (0.88, 1.10)
	1	1.02 (0.99, 1.05)	1.18 (1.08, 1.29)	1.01 (0.98, 1.04)	0.99 (0.89, 1.10)
	2	1.02 (0.99, 1.05)	1.15 (1.05, 1.26)	0.99 (0.96, 1.03)	1.09 (0.98, 1.20)
Croup	0	1.08 (1.02, 1.15)	1.09 (0.84, 1.41)	1.09 (1.02, 1.16)	1.08 (0.87, 1.35)
	1	1.09 (1.02, 1.17)	1.19 (0.91, 1.55)	1.09 (1.02, 1.17)	1.11 (0.89, 1.37)
	2	1.05 (0.98, 1.11)	1.09 (0.83, 1.41)	1.05 (0.98, 1.12)	1.07 (0.88, 1.31)

Croup is a viral infection that typically affects pre-school-aged children and causes inflammation and swelling of the larynx and larger airways to produce a characteristic cough and stridor.[39] It has been less extensively studied than asthma and COPD as an outcome related to air pollution. Our finding of an association was consistent with the results of two early studies from Germany.[40,41] More recent cohort studies of long-term exposure to air pollution and croup have not found associations.[42] This suggests that short-term exposure to air pollution is more important as a risk factor for acute exacerbations of croup, rather than long-term exposure contributing to underlying incidence of the infection.

Strengths and Limitations

Most previous studies of ambulance callouts and air quality have relied on dispatch data, which have limited clinical value because their purpose is to assess urgency and enable allocation of appropriate resources. They are solely based on telephone interviews with the patient, a caregiver, or bystander, who rarely have medical training. However, these data do provide information about ambulance workloads and some dispatch categories have been shown to be sensitive to air quality.[43,44] One strength of our study was the use of paramedic assessments, which are conducted according to standard protocols involving clinical history, physical examination, and diagnostic tests. They are much more likely than dispatch data to accurately reflect the clinical problem. Another strength is that ambulance data provide the opportunity to evaluate clinical syndromes such as croup, faint, and hypoglycemia, which are more commonly managed in community than in hospital settings.[29,39,45] Further, the data are population based, enabling large, geographically dispersed populations to be included.

Relative humidity exhibits temperature-dependent daily and seasonal variation. By including daily temperature and seasonal adjustment in our models, we addressed the potential limitations of using a relative, rather than an absolute measure of atmospheric moisture such as dew point.[46] Geospatially resolved $PM_{2.5}$ estimates that integrate surface air quality measurements with remote sensing measurements reduce the likelihood of exposure misclassification when compared with studies that derive exposures by averaging data from fixed-site monitoring stations.[47] Our approach of integrating data from multiple sources enabled us to generate exposure surfaces across wide geographic areas, including those places that do not have routine air quality monitoring.[10] Another strength was our ability to link air quality data with the timing and location of the clinical event, information that is not readily available from administrative hospital and mortality datasets.

Limitations of this study include the potential for both exposure and outcome misclassification. Air pollution can have considerable spatial variation within a 5×5 km area, which cannot be captured in our exposure model. Further, when the paramedic attendance occurred in the early morning, a large proportion of the estimated same-day exposure (but not the lagged exposures) followed the health outcome. These limitations are common to population-based studies of acute health outcomes associated with short-term air pollution exposures when individual exposure measurements are not possible.[48]

Exposure misclassification also occurs when the case has a lengthy hospital admission. Such individuals will not be at the same location on control days that follow the case day. However, in situations where individual events do not affect the distribution of future exposure in the overall study population, selecting postevent control windows is acceptable.[49] Indeed, postevent control days are essential to minimize the risk of bias by long-term trends and seasonal changes in air quality.[50] Both spatial and temporal exposure misclassification introduce nondifferential measurement error, which would bias any true association toward the null.

Like other administrative health datasets, records of paramedic assessments rely on documentation of a clinical judgement made by a trained professional based on the patient history, physical examination, and results of diagnostic tests. There is relatively high potential for outcome misclassification, although this varies by outcome. Ambulances carry blood glucose analyzers and electrocardiograms, meaning that paramedics can diagnostically test for hypoglycemia and hyperglycemia, arrhythmia, and acute coronary syndrome.[13] Uncertainty is greater for outcomes that rely on clinical identification based on symptoms. For example, COPD and asthma can be especially difficult to distinguish by paramedics and doctors who do not have access to pulmonary function testing.[51,52] Inconsistencies can also arise when patients have coexisting conditions, but one must be recorded as the primary assessment.

More than 80% of patients in the Tasmanian data were transferred to hospital for most outcomes we evaluated (Supplemental digital information eTable 3; http://links.lww.com/EDE/B415), with the exceptions of hypoglycemia and faint. While we did not have access to linked data, other studies have demonstrated agreement between the paramedic assessment and hospital medical assessments for particular conditions ranging from 45% to 70% for stroke up to 100% for acute anaphylaxis.[53–55] In Australia, where all paramedics hold degree qualifications, a study of outcomes following acute myocardial infarction found that 75% of paramedic assessments of myocardial infarction were later verified in hospital.[56] Given the more limited access to specialist clinicians and diagnostic testing in ambulances compared with hospitals, it is probable that paramedic assessments have greater misclassification than hospital admission diagnoses. This means more noise in the outcome data and likely bias of the results toward the null. This could be a factor contributing to our null result for cerebrovascular outcomes, when the weight of existing evidence supports an association between short-term fluctuations in air quality and cerebrovascular outcomes such as stroke.[31]

Our main results include 13 primary health end points at three different lags (Figure 1) to characterize the temporal patterns of any observed associations, for a total of 39 models. We expect that 5% of these models (N = 2) would be statistically significant by chance alone (type 1 error). By presenting the same models for each individual state (Table 2) in addition to the combined analysis, the expected number of models affected by type 1 error increases (N = 8). However, the information gained by the ability to compare results from three different ambulance services in different geographical settings remains useful. Where we see a consistent pattern of associations across the three states, our confidence in the primary association is strengthened. Such consistency was particularly notable for the outcomes of hypoglycemia and asthma.

People who use ambulance services for transport to hospital are typically older and of lower socioeconomic status than those who use alternative means of transport to hospital.[57] These characteristics are also well-recognized risk factors for increased susceptibility to the adverse impacts of air pollution.[1,58,59] Therefore, the effect estimates we report may be higher than if the sample had been completely representative of the population. While this does not affect the internal validity of the study, it limits the generalizability of our results. For example, our results are not generalizable to people who do not seek health care at all for their symptoms, who use other primary health facilities for similar problems or who chose use other means of transport to hospital.

CONCLUSIONS

Our findings generally fit with the known associations of air pollution with metabolic, cardiovascular respiratory systems adding coherence to evidence derived from other sources of administrative health data such as hospital admissions or mortality. We have further identified some health problems that been less conclusively associated with changes in air quality. These included hypoglycemia, fainting, and croup, which are all relatively common health problems in the community. The association with hypoglycemia was unexpected and warrants further investigation.

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