AUSTRALIAN CHILD HEALTH AND AIR POLLUTION STUDY

(ACHAPS)

FINAL REPORT

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Format of the report

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Shortened forms

ACHAPS	Australian Child Health and Air Pollution Study
AQM	air quality monitor
BMI	body mass index
Bsp	the measure of back light scattering particles or suspended fine particles measured by nephelometry
CAPS	Childhood Asthma Prevention Study
CI	confidence interval
CO	carbon monoxide
CO_2	carbon dioxide
eNO	nitric oxide in the exhaled breath
EPA	Environmental Protection Agency
EPHC	Environment Protection and Heritage Council
$FEF_{25-75\%}$	average of expired flow over the middle half of forced vital capacity
FEV_1 (litres)	forced expiratory volume in one second
FEV_1/VC	FEV_1 as a percentage of vital capacity or forced vital capacity
FVC (litres)	forced vital capacity
HR	hazard ratio
IQR	interquartile range
ISSAC	International Study of Asthma and Allergies in Childhood
$\mu g/m^3$	micrograms per cubic meter
MMEF	maximal midexpiratory flow
NEPC	National Environment Protection Council
(the) NEPM	National Environment Protection (Ambient Air Quality) Measure
NO	nitric oxide
NO_2	nitrogen dioxide
NO_X	oxides of nitrogen ($NO + NO_2$)
OR	odds ratio
O_3	ozone
PAH	polycyclic aromatic hydrocarbon
PEF	peak expiratory flow
PEFR	peak expiratory flow rate
PM	particulate matter
PM_{10}	particulate matter less than 10 µm in diameter
$PM_{2.5}$	particulate matter less than 2.5 µm in diameter
ppb	parts per billion
ppm	parts per million
RSP	respirable suspended particulate
SCCHS	Southern California Children's Health Study
SO_2	sulphur dioxide
SD	standard deviation
SEIFA	socio-economic indexes for areas
SPFR	standardised peak flow rates
TSP	total suspended particulate matter

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Executive summary

Aims

The study aims were to:

- provide an evidence base of long-term and short-term health effects of air pollutants in Australian children that will contribute to the review of National Environment Protection (Ambient Air Quality) Measure (NEPM) standards
- obtain quantitative effect estimates for the association between children's historical lifetime exposure to the criteria air pollutants contained in the NEPM (O_3, PM_{10}, $PM_{2.5}$, NO_2, CO, SO_2) and (a) the period prevalence of adverse health outcomes such as respiratory symptoms (asthma, cough and wheeze), and (b) lung function
- obtain quantitative estimates of the prospective day-to-day association between the criteria air pollutants and (a) incidence of respiratory symptoms, and (b) lung function in school children with a history of asthma, aged 7–11 years at baseline
- determine whether any effects are modified by other factors, such as socio-economic disadvantage, geographical area, sex, activity patterns and obesity.

Methods

The target population was Australian school children aged 7–11 years whose exposure to the criteria air pollutants was representative of other urban Australian school children of that age. The sampling strategy was based on selecting schools, then whole classes within schools. Children were not excluded on the basis of race, ethnicity or other socio-demographic factors.

Exposures of interest were criteria ambient air pollutants measured using standard NEPM air quality monitoring stations. Schools were selected which:

- were close to NEPM monitors which had been on site for a reasonable number of years
- were considered to be representative of a larger area around the site
- could demonstrate the maximum variability of exposures to the various pollutants.

The cross-sectional study recruited 2,860 children. Air pollution metrics were average exposures over the period of residence of the child near the monitored site. Hierarchical models (with state and school as levels) were used to examine the association between outcome variables such as lung function and respiratory symptom and the air pollutant exposures. These models were fitted separately for each pollutant. Confounding variables (such as age and sex) were added according to their improvement to the overall model fit. Finally, multi pollutant models were explored in order to estimate which pollutants have the strongest independent associations with lung function and asthma.

Within the baseline cross-sectional sample, the nested panel study recruited 270 children with a history of asthma, who each provided up to 36 days of data. Daily air pollution metrics corresponding to the averaging periods used in the NEPM were used. Generalised linear models were used, with a random effects mode (random intercepts) to analyse the panel data, with adjustments for daily mean temperature and number of hours spent outdoors in vigorous physical activity. Interaction between the air pollutant and mean daily temperature and daily number of hours spent outdoors in vigorous physical activity were examined.

Findings from cross-sectional study

The cross-sectional study shows consistent evidence of respiratory adverse effects of nitrogen dioxide (NO_2) for both recent and life-time exposure. These adverse effects are manifested as increased risk of asthma-like symptoms (in particular, wheeze), increased airway inflammation and reduced lung volumes. For current asthma and per ppb recent exposure NO_2, the odds ratio (OR) was 1.06 (1.02, 1.10), with OR per interquartile range (IQR) NO_2 1.26 (1.08, 1.48). For recent wheeze after exercise, the OR was 1.07 (1.03, 1.120) per ppb and 1.32 (1.12, 1.57) per IQR. Airways inflammation as measured by exhaled nitric oxide (NO) increased by 3% (1%-5%) and lung volume as measured by pre-bronchodilator forced expiratory volume (FEV_1) and forced vital capacity (FVC) decreased by 7.1 ml (2.8-11.4) and 6.8 ml (2.7-10.9) per ppb respectively. Effect estimates were slightly smaller for lifetime exposure. Per IQR decreases in lung function measured by FEV1 and FVC pre- and post-bronchodilator ranged from 27.5 to 29 ml.

There was no evidence that the effects were stronger in atopic subjects, apart from sulphur dioxide (SO_2). The absence of a greater effect in atopic subjects, the finding that lung volumes, rather than airway calibre (reflected in FEV_1/FVC ratio), and persistence of the effect after bronchodilator, imply that the consequence of NO_2 exposure is not typical asthma; instead, more non-specific lung effects are implicated.

Particulate matter exposures showed varied results. Lifetime exposure to PM_{10} was associated with decline in FEV_1 post-bronchodilator (decrease of 5.1 ml (0.1-10.1) per $\mu g/m^3$, and 19.3 ml (0.23-38.3) per IQR) and increase in exhaled NO (4% (1%-6%) ppb, and 14% (5%-23%) per IQR), but did not increase current symptoms. Recent exposure to $PM_{2.5}$ was associated with an adverse effect on forced vital capacity (FVC) post-bronchodilator (decrease of 43.4 ml (9.3-77.4) per $\mu g/m^3$ and , and 46.3 ml (9.95-82.7) per IQR and airways inflammation (increase of 2% ppb (2%-3%)) in exhaled NO per $\mu g/m^3$, with no overall effects on current symptoms. In non-atopic children only, recent exposure to $PM_{2.5}$ was associated positively with risk of wheezing, asthma, and asthma medication, and current asthma, use of beta-agonists and itchy rash in non-atopic children.

O_3 showed some effects in a beneficial direction (perhaps due to the NO_2 effects and the negative association between O_3 and NO_2) but these were eliminated in the joint O_3- NO_2 model.

Recent exposure to SO_2, after adjustment for O_3, showed an adverse effect on lung function measures, with a decrease of 30.5 ml (2.2-58.5) per ppb and 24.9 ml (1.79-48.1) per IQR for FEV_1 pre-bronchodilator. SO_2 effects on lung function were modified by atopic status, being more deleterious in atopic children, and non-significant in non-atopic status. Reported history of wheezing, asthma and asthma medication, and recent itchy rash for six months increased with SO_2 in non-atopic children, with no effect in atopic children.

Findings from panel study

Single pollutant models produced only few significant adverse effects of air pollutants on children's respiratory health. In particular significant effects on lung function were few, and those that occurred showed no consistent pattern.

The most consistent adverse effect was that increased NO_2 exposure was associated with an increased risk of cough and wheeze during the day and night, and increased use of bronchodilators for symptom relief. Relationships between NO_2 and night symptoms and

effects were greater for NO_2 24-hr than for NO_2 1-hr and were more consistent. For lag 2 NO_2 1-hr the OR (95% CI) was 1.03 (1.01-1.05) per ppb for the association with night cough. For lag 2 NO_2 24-hr, ORs were 1.06 (1.03-1.09) per ppb for the association with night cough, 1.05 (1.01-1.10) per ppb for the association with night wheeze, and 1.05 (0.99-1.12) per ppb for the association with night shortness of breath. Effects upon symptoms occurring during the day were strongest at lag 0. For lag 0 NO_2 1-hr, the ORs (95% CI) were 1.02 (1.0-1.03), 1.04 (1.01-1.06), and 1.02 (0.99-1.05) per ppb for associations with day cough, wheeze and shortness of breath respectively. For lag 2 NO_2 24-hr, ORs were 1.05 (1.02-1.09), (1.11 (1.07-1.16), and 1.06 (1.01-1.11) per ppb for the association with day cough, wheeze and shortness of breath respectively.

Night symptoms were also adversely associated with 8–hour CO although these effects were not consistent or strong. PM_{10} 24-hr lag 2 was associated with increased risk of night cough: OR = 1.03 (1.01-1.05) per $\mu g/m^3$.

There were protective effects for O_3 and night wheeze and night shortness of breath and this was consistent across all the three metrics for O_3. There was only one significant association between air pollution and the use of reliever medication at night (association between SO_2 1-hr and use of reliever medication at night).

Children were also more likely to use more reliever medications for asthma on days with higher NO_2 concentrations (OR: 1.05 (1.01-1.10) per ppb for daytime use of medication for symptoms and lag 0 NO_2 24-hr). There was one association between air pollution (lag 2 PM_{10} 24-hr) and preventer use for symptoms and a single association where higher O_3 levels (lag 2 O_3 8-hr) were associated with decreased use of preventers for symptoms.

In two pollutant models compared to single pollutant models, the effects of NO_2 on lung function were increased whereas the effects on symptoms slightly decreased. Further, in the two pollutant models compared to single pollutant models, effects on daytime medication use were no longer significant.

Also investigated were the effects of PM_{10} in two pollutant models with each of the gases (O_3, NO_2, SO_2 and CO). Significant negative effects on morning lung function were seen, particularly when SO_2 was included in the models. Associations between PM_{10} and both night and daytime symptoms (cough and wheeze) generally persisted when NO_2 and CO were added to the models. PM_{10} was also associated with runny nose when SO_2 was included in the models. Significant increased use of daytime reliever medications was only observed in two pollutant models with CO. The odds ratios in all models were consistently greater in the two pollutant models compared with single pollutant models especially for lag 1 PM_{10} and lag 2 PM_{10}.

A warm season analysis was conducted for O_3 as O_3 levels are higher in the warmer months. The results were similar to those obtained when the analyses were conducted regardless of the season. There were no adverse associations between warm season O_3 and lung function, symptoms and medication use in this sub-analysis. There were a few positive associations (beneficial effects) with night wheeze; that is, children experienced fewer wheeze symptoms during the night when O_3 levels were high the previous day.

Methodological Issues

Exposure measurement

ACHAPS relied on historical NEPM monitoring for measures of exposure. There have been concerns that the use of such fixed site ambient ozone monitoring stations may not adequately characterise the actual personal exposure to ambient air pollutants especially as people spend a large proportion of their time indoors where the air pollution concentrations can be much lower than ambient concentrations.

While the study differentiated between average lifetime exposure (measured from the time the child began living in the area) and recent exposure (averaged over the last year), it remained difficult to distinguish between long-term and shorter-term effects, due to correlations of effects over time. While ambient pollution measures were available for many sites, gaps in data were left as sites, in general, did not monitor all pollutants over the entire period of the study. This also limited data available to explore multiple-pollutant models.

Sites were chosen according to availability of NEPM monitoring and to maximise variability in the targeted pollutants. A consequence of this choice of sites was that it was difficult to judge the representativeness of the sample of children, in relation to the target population of all urban primary-school aged children. The characteristics of the sample in terms of prevalence of asthma and other conditions appear to correspond to published estimates from national surveys.

Lung function measurement

In the cross-sectional study, lung function was measured, before and after bronchodilator, in accordance with the recommendations of the ATS/ERS Task Force performance criteria for spirometry. This measures flow using a pressure transducer and derives volume by integrating flow over time was attached to a laptop computer running SpiroScore+ V2.6 for immediate data acquisition. These measures have high reliability and validity.

In the panel study, lung function (PEF and FEV_1) was measured using a Mini-Wright Digital electronic peak flow meter. Peak flow meters are widely used in longitudinal studies because they are portable and relatively inexpensive, allowing frequent measures of lung function at low cost. It has been demonstrated that the PEF, as measured by a mini Wright peak flow meter, is both accurate and reproducible and can be used in epidemiological studies to measure lung function. The mini Wright peak flow meter is a convenient and effective tool for characterising changes in PEF associated with exposure to ambient air pollution.

Information bias

A challenge for any spatially-constructed study is that of confounding, particularly by spatial-level confounders. A major contender for confounding is socio-economic status which is spatially distributed, and which may separately relate to both exposure and health outcome. The analyses presented in this report have been adjusted at the cluster level for the SEIFA indices for relative socio-economic advantage and disadvantage, and for education, and at the individual level for parent's education. Sensitivity analyses which incorporated other spatial measures showed, in fact, very few variables (for example, household characteristics) altered estimates of effects once the standard variables (age, sex, socio-economic status - as just described) were included in models.

Questions asking about respiratory symptoms and asthma were derived from existing, widely used questionnaires; these included the International Study of Asthma and Allergies in Childhood and the Southern California Child Health Study. Preference was given to the ISAAC questionnaire as a source document because of its widespread use (over 300,000 respondents) and extensive validation.

Conclusions

Few other studies have been conducted in Australia on the chronic or longer-term health effects of outdoor air pollution on children's health, although a larger number have examined the acute effects.

NO_2 was the pollutant most consistently associated with adverse effects on children's health. These effects were present for both lung function and current symptoms in the cross-sectional study, and for symptoms and medication use in the panel study. The panel study found very little evidence of pollutant effects on lung function. While PM effects on symptoms were seen in both the cross-sectional and panel studies, they were more consistent in the latter.

ACHAPS findings of adverse effects of long-term exposure to NO_2 on asthma, and other respiratory symptoms, are consistent with those of the Southern California Children's Health (SCCHS) Study, although effects are somewhat weaker and apply to current rather than lifetime asthma only. The findings are also consistent in relation to NO_2 and PM effects and lung function, with little consistent evidence of effect modification by gender. ACHAPS found favourable effects of O_3 (contrary to the SCCHS) but these appeared related to negative confounding with NO_2—assuming the effect is null, the O_3 findings are consistent with the SCCHS and the Swiss Study on Childhood Allergy and Respiratory Symptoms with respect to Air Pollution (SCARPOL).

NO_2 is a major constituent of traffic-related pollution and the identified associations are consistent with reports in the literature of adverse associations between proximity to traffic and respiratory symptoms and lung functions. Several studies including SCCHS have found decreased lung growth in children to be associated with NO_2 exposure and proximity to roadways. Unfortunately ACHAPS has no measures of lung function growth, which would require a follow-up of ACHAPS sample of children.

A small number of ecological studies have found adverse health effects related to O_3; this has not been confirmed by large individual studies, including ACHAPS.

The panel study findings of adverse NO_2 effects on symptoms are consistent with several other panel studies conducted in United States on children with asthma. The ACHAPS panel study did not find any adverse short term effects of PM on lung function in single pollution models and a few associations with PM_{10} and symptoms (mainly cough and wheeze with ORs between 1.017 to 1.02 for a 1 ug/m^3 increase in PM_{10}). These effect estimates are much smaller than the pooled estimates from the meta-analysis conducted by Ward and Ayres (Ward and Ayres 2004).

The panel study was not able to demonstrate any adverse effects of ambient O_3 on children's lung function, symptoms or medication use.

Part A

Study background and methods

1. INTRODUCTION

1.1. Purpose

The primary purpose of the Australian Child Health and Air Pollution Study (ACHAPS) project was to obtain quantitative effect estimates for the association between the criteria air pollutants contained in the National Environment Protection (Ambient Air Quality) Measure (ozone (O_3), particulates as PM_{10} and $PM_{2.5}$, nitrogen dioxide (NO_2), carbon monoxide (CO), sulphur dioxide SO_2) and adverse health outcomes such as increases in respiratory symptoms (for example cough and wheeze) and decreases in lung function in school-aged children across Australia. The study examined both cumulative effects in a representative sample of children and day-to-day effects of air pollution in a sub-sample of children with asthma.

The proposed study arose from the scientific needs of the National Environment Protection (Ambient Air Quality) Measure review of Australian air quality standards. Results are critical for two stages of the review, specifically:

- in informing whether the current air quality standards adequately protect the health of Australian children from the effects of air pollution
- to provide quantitative information to inform any amendment of the current standards.

1.2. Background

1.2.1. Australian air quality standards

In recognition of the established relationships between air pollution and human health, the Australian Government has imposed air pollution controls. The National Environment Protection Council (NEPC) is a statutory body, with its members being Ministers from participating jurisdictions (that is, Commonwealth, state and territory governments). The NEPC has two primary functions:

1. to make national environment protection measures (NEPMs)
2. to assess and report on the implementation and effectiveness of NEPMs in participating jurisdictions.

In 1998, the NEPC created the National Environment Protection (Ambient Air Quality) Measure (the NEPM) to protect human health and well-being. This established, for the first time in Australia, air quality standards as maximum ambient concentrations (averaged over certain time periods), as well as the maximum number of exceedances allowed for the six criteria air pollutants — O_3, NO_2, SO_2, CO, particles (as PM_{10}) and lead (

Table 1.1.). The NEPM was varied in 2003 to include standards for particles such as $PM_{2.5}$.

These standards were based on the then available evidence in relation to the adverse effects of air pollution. Any amendment to these standards must, in addition, take account of more recent findings from both Australian and international research. The present report will contribute to this evidence base with a particular contribution being the assessment in Australian school-aged children.

Table 1.1. Australian air quality standards.

POLLUTANT	Averaging period	Concentration	Goals – maximum exceedances per year	WHO recommended standards (2006)
Carbon monoxide (CO)	8-hours	9.0 ppm (10,350 µg/m^3)	1 day	
Nitrogen dioxide (NO_2)	1 hour	0.12 ppm (226 µg/m^3)	1 day	200 µg/m^3
	1 year	0.03 ppm (56.4 µg/m^3)	None	40 µg/m^3
Ozone (O_3)	1 hour	0.10 ppm (196 µg/m^3)	1 day	
	4 hours	0.08 ppm (16 µg/m^3)	1 day	
	8 hours			100 µg/m^3
Sulphur dioxide (SO_2)	10 minutes			500 µg/m^3
	1 hour	0.20 ppm (524 µg/m^3)	1 day	
	24 hours	0.08 ppm (210 µg/m^3)	1 day	20 µg/m^3
	1 year	0.02 ppm (52 µg/m^3)	None	
Lead	1 year	0.5 µg/m^3	None	
Particles as PM_{10}	24 hours	50 µg/m^3	5 days	50 µg/m^3
	1 year			20 µg/m^3
Particles as $PM_{2.5}$	24 hours	25 µg/m^3		25 µg/m^3
	1 year	8 µg/m^3	In review	10 µg/m^3

When creating the NEPM, Ministers agreed to a set of future actions that included a full review of the NEPM. To inform this review, the Environment Protection and Heritage Council (EPHC) (which incorporates the NEPC) have made a determined effort to address gaps in Australian research in this area. Through a consultative process that included national workshops and the release of a discussion paper, a need was identified to conduct studies on more sensitive health indicators, such as decreases in lung function and increases in respiratory symptoms. This was to ensure that the review of the ambient air quality NEPM standards is based on Australian, rather than overseas, information.

A priority of these standards is to ensure that sensitive groups within the Australian population, including children, are protected and their quality of life is not impacted by air pollution. One key area that was identified and supported through the national consultation process was a study into the effects of air pollution on children.

A full review of standards started in 2005. It was essential that this review take account of international developments in standard setting - for example, the increasing focus on protecting vulnerable groups - but also have access to an Australian evidence base for the standards. Noting the importance of this study, EPHC Ministers committed $300,000 toward the conduct of this study.

1.2.2. Relevance of standards to Australia

The current Australian evidence base for long-term health effects of air pollution in children is weak, since very few studies have been conducted here. Australia is different from the overseas countries that have provided most of the current evidence base in a number of factors that may affect the associations between air pollution and child respiratory health. Factors such as pollutant exposure levels, pollutant compositions, possible higher individual exposures due to a different, more outdoor-based lifestyle, and differences in housing and road infrastructure (National Heritage Trust, 2003) are likely to be different to overseas countries. Asthma is the leading cause of burden of disease in children aged 0–14 years in Australia, accounting for 17.9% of the total burden in boys and 18.6% in girls (AIHW Australian Centre for Asthma Monitoring, 2005).

1.2.3. Mechanisms affecting human health

Air pollution is a complex mixture of chemicals that has different implications for the atmosphere and human health depending on the type and levels of human exposure. CO binds with haemoglobin in the blood and reduces the capacity of haemoglobin to transport oxygen in the blood stream (Maynard and Waller, 1999). NO_X (oxides of nitrogen: NO + NO_2) has the capacity to impair the function of the alveolar macrophages and epithelial cells, thereby increasing the risk of lung infection (Brunekreef and Holgate, 2002). SO_2 is not lethal at levels of ambient exposure, but is a chemical irritant, and exposure for more than a few minutes will result in irritation of the eyes, mucous membranes, and throat (Schlesinger, 1999). People with asthma are uniquely susceptible to the adverse effects of SO_2 exposure. Brief exposure to concentrations as low as 0.25 ppm cause bronchoconstriction (airway narrowing) with resultant symptoms of wheezing, chest tightness and/or shortness of breath (Schlesinger, 1999). Particulate matter (PM) is divided into two categories: PM_{10} — coarse particles having an aerodynamic diameter less than 10 μm, and $PM_{2.5}$ — fine particles with a diameter less than 2.5 μm. Exposure to PM is through inhalation and size is relevant to effect. Particles with a diameter of greater than 5 μm are often deposited in the upper airways, whereas smaller particles reach the small airways (bronchioli) and alveoli, with fine particles able to permeate the airway epithelium and vascular walls (Jeffery, 1999). Particles from diesel exhaust have a carbonaceous core to which various hydrocarbons are absorbed, including carcinogenic polycyclic aromatic hydrocarbons (PAHs) and nitro-PAHs. Diesel emissions have also been associated with an increased response to allergens (Bates and Vedal, 2002) and it has been suggested that this is the link between exposure to traffic and asthma prevalence (Brauer et al., 2002). O_3 has been shown experimentally to induce inflammation of mucous membranes and, in some individuals, induces bronchoconstriction (Chan-Yeung, 2000; Schwela, 2000; Thurston and Ito, 1999).

1.2.4. Exposure measurement

Assessment of exposure may be direct or indirect. Direct methods are costly, cumbersome for the participant, and are usually tolerated only for a short time (especially in children, if feasible

at all) so may not be useful as measures of long-term exposures. Indirect measures are obviously not precise measures of actual exposure at a particular point in time, but may be obtainable for longer time periods, and therefore more appropriate for long-term exposures. Ethical reasons may preclude specimens from children for biomarkers which, in any case, may be mainly sensitive to short-term exposures.

1.2.5. Children are not 'little adults'

Children represent a large sub-population susceptible to the adverse health effects of air pollution. They inhale and retain larger amounts of air pollution per unit of body weight than adults, and have narrower bronchioles more likely to be constricted in response to environmental irritants. Children's developing organ systems may be more vulnerable when exposed to pollutants at critical periods (Mathieu-Nolf, 2002).

Children tend to spend more time outdoors than adults, as they participate in more physical play and sports activities, perhaps by a three-fold factor (California Air Resources Board, 1991). Levels of O_3 tend to be higher in the afternoon when school children may be most exposed whilst playing or walking home after school (Bates, 1995; Mathieu-Nolf, 2002).

1.2.6. Effects of air pollution on child health

A review of 50 publications over the last 20 years (to 2008) examining long-term health effects of ambient air pollution on all ages (Gotschi et al., 2008) concluded that

> there is strong support for air pollution effects on the development of lung function in children and adolescents. It remains unclear whether subjects with slower development of lung function compensate by prolonging the growth phase, or whether they end their development at a lower plateau, thus entering the decline phase with a reduced lung function.

The review further concluded that

> [t]here is great diversity in study designs, markers of air pollution, approaches to the measurement of exposure, and choices in lung function measures. These limit the comparability of studies and impede quantitative summaries. New studies should use individual-level exposure assessment to clarify the role of traffic and to preclude potential community-level confounding. Further research is needed on the relevance of specific pollution sources, particularly with regard to susceptible populations and relevant exposure periods throughout life.

Cohort studies evaluating the relationship between traffic exposure and respiratory health and published between 2002 and October 2008 were reviewed (Braback et al., 2009). All surveys reported associations with at least some of the studied respiratory symptoms. They concluded that '...traffic exhaust contributes to the development of respiratory symptoms in healthy children' and that '[f]uture studies should also evaluate effects of traffic exhaust on the development and long-term outcome of different phenotypes of asthma and wheezing symptoms'.

PUBMED, MEDLINE and EMBASE databases were searched for epidemiological studies, published between January 1989 and December 2004, on the adverse health effects of criteria air pollutants among Canadian children. The researchers concluded that '[d]espite inconsistencies among study results and data from elsewhere, evidence from Canadian studies suggest that air pollution may cause adverse respiratory health effects in children...' (Koranteng et al., 2007).

The World Health Organisation has published air quality guidelines (WHO, 2008) for air quality targets to protect human health. These guidelines represent the widely agreed and up-

to-date assessment of health effects of air pollution, recommending targets for air quality at which health risks are significantly reduced. No specific targets in relation to effects on child health have been set, however.

Research distinguishes long-term effects (resulting from chronic exposure to high levels) from short-term effects (within days of an unusually high exposure). Time series studies of the latter have found associations between daily changes in levels of ambient air pollution and increased childhood hospital admissions (Braga et al., 1999; Chew et al., 1999; Barnett et al, 2005), exacerbation of respiratory symptoms (Lee et al., 2002), and increased infant mortality (Ha et al., 2003; Loomis et al., 1999; Woodruff et al., 1997). Panel studies have found associations between daily levels of SO_2, PM_{10} and daily decreased lung function (Timonen and Pekkanen, 1997; van der Zee et al., 1999) as well as daily CO, PM and daily exacerbation of asthma symptoms (Yu et al., 2000).

The Harvard Six Cities Study of 10,000 children during 1974–1977 involved six cities throughout North America, and found a 10 $\mu g/m^3$ increase in TSP (total suspended particulate matter) elevated the risk of chronic cough, bronchitis and lower respiratory illnesses in the previous year (Ware et al., 1986), and significant positive associations between PM_{10} and bronchitis and chronic cough, and a positive association between O_3 and asthma (Dockery et al., 1989).

The ongoing Southern California Children's Health Study (SCCHS) (Peters, 1997) of 3,600 school children from 12 communities in Southern California provided early information on possible chronic effects of air pollution. Cross-sectional results from the SCCHS show prevalence of wheeze and lung function in children were associated with various pollutants (Peters et al., 1999a, 1999b). Sub-cohort analyses of the SCCHS have demonstrated that children who moved to areas of lower PM_{10} showed increased growth in lung function and vice versa for children who moved to areas of higher PM_{10} (Avol et al., 2001). O_3 was strongly associated with an increase in respiratory illness-related absences (Gilliland et al., 2001). Repeated follow-up data have shown adverse effects of air pollutants on lung function growth (Gauderman 2000, 2002, 2004, 2007).

A number of other, mostly European, studies have also shown that relatively low levels of air pollution are responsible for increased morbidity and mortality in children (Bates, 1995; Mathieu-Nolf, 2002; Nicolai, 1999; Segala, 1999).

1.2.7. Australian evidence

Very limited research has been performed to establish the long-term effects of ambient air pollution on the health of Australian children. Somewhat more has been done in relation to short-term effects but this has, for the most part, been confined to small localised studies. An exception is a time series case-crossover study which examined the association between monitored air pollutants and hospital respiratory admissions by children in five Australian (and two New Zealand) cities (Barnett et al., 2005). Increases were found in relation to $PM_{2.5}$, PM_{10}, nephelometry, NO_2, and SO_2. The largest association found was a 6.0% increase in asthma admissions for children aged 5-14 years old in relation to a 5.1-ppb increase in 24-hour NO_2.

An Australian cross-sectional survey on the respiratory health of 3,023 children from industrial and non-industrial sites in the Hunter-Illawarra region found a positive association between PM_{10} and both night cough and chest colds in children (Lewis et al., 1998).

Short-term effects have been demonstrated in an Australian panel in 148 children from six primary schools in western and south-western Sydney. A significant negative association

between peak expiratory flow rate (PEFR) and same-day mean daytime O_3 concentration was shown (Jalaludin et al., 2000). These findings need to be replicated on a national sample.

2. STUDY AIMS AND APPROACH

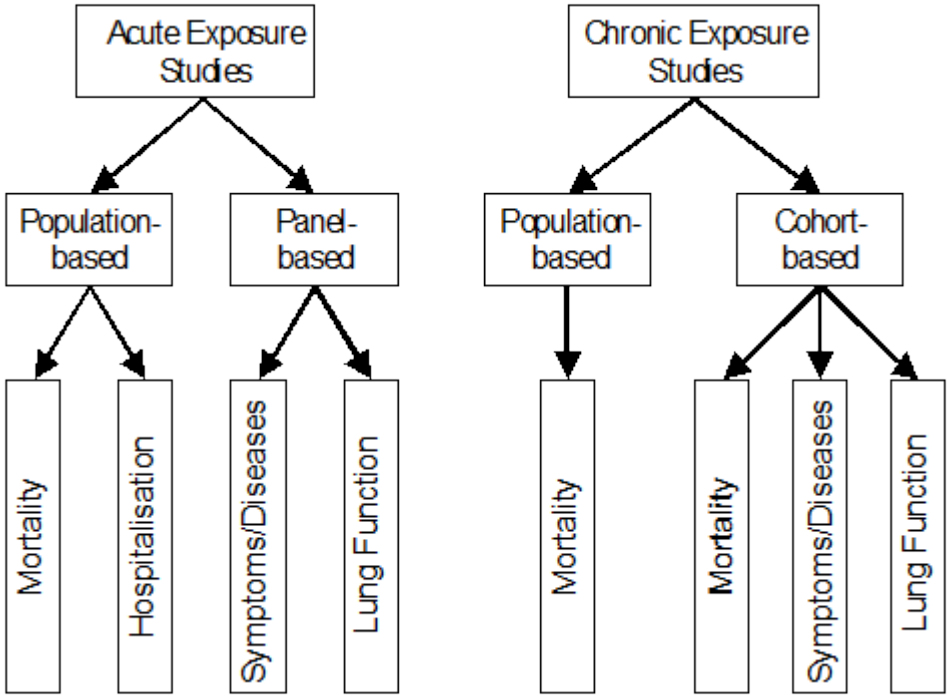
2.1. Background

Epidemiological studies of the health effects of air pollution can be classified as investigating acute effects or chronic effects (Figure 2.1). Studies of acute exposure effects assess relationships between day-to-day changes in mortality and morbidity and same day or previous day/s air pollution level. Such studies have found associations between air pollution and acute health effects ranging in severity from death, hospital usage, restricted activity days, exacerbations of asthma, occurrence of respiratory and other symptoms, and changes in lung function. Acute effects should be distinguished from the way in which *long-term exposure* to ambient levels of air pollution may initiate or promote development of chronic disease. Such chronic effects may eventually lead to increased or earlier hospital usage or to premature death, irrespective of whether higher air pollution levels on preceding days had a role in triggering acute health effects.

Cross-sectional and cohort studies have been used to examine long- to medium-term exposure effects on health. In cross-sectional studies, current exposure may be measured (for example, ambient levels, proximity to roads, indoor sources of pollutants) but is assumed to represent the exposure over a significant period in the past (new arrivals to an area may be excluded). Alternatively, exposure may be retrospectively estimated by gathering a history of previous residences and exposures. Current health outcomes are measured, and a history of development of respiratory symptoms and conditions obtained. Cohort studies may gather both exposures and health outcomes prospectively. Cohort studies would generally be considered more powerful studies since they have the opportunity to gather more accurate and detailed data, the temporal sequence between exposure and outcome is clear, and it is possible to study changes within individuals as changes in exposure occur. The chief weakness of cross-sectional studies in this context is that they may be affected by confounding; for example, socio-economic class may be related both to exposure (higher socio-economic classes may be able to choose to live in lower pollution environments) and exposure (higher socio-economic classes may be able to obtain more effective treatment for a child's early symptoms, therefore preventing disease progression). However, with careful design and analysis, cross-sectional studies can provide useful information on the health effects of air pollutants. Cross-sectional and cohort designs have been combined effectively; for example, in the Southern California Study of Child Health (Peters et al., 1999a, 199b), with a cross-sectional study providing information in its own right as well as being used to identify a cohort of children to be followed up over a longer period to provide prospective data.

Ecological studies are population studies where both the risk factor and the outcome factor are measured at the population level. Therefore, groups of people rather than individuals are the units of analysis. For each group of people, aggregate measures for the risk factors and health outcomes are determined and then examined for associations. In ecological studies, groups of people are often defined by geographical areas or administrative boundaries. Ecological study designs are widely used in environmental epidemiology because environmental factors expose large numbers of the population in a similar manner.

Figure 2.1 Basic study designs of most epidemiological studies of air pollution (Source: Pope and Dockery, 1999).



Two common study designs used in air pollution studies— the time series study and the panel study— are types of ecological studies.

In air pollution time series studies, data (both exposures and health outcomes) are aggregated over a short period of time (usually one day) and are useful for investigating the acute or short-term effects of air pollution. Common outcome measures are deaths, hospital admissions, emergency department visits and general practitioner visits. In these instances, the exposure factor will consist of daily air pollution concentrations and the outcome factor will be the daily number of deaths (or any of the other health outcomes mentioned above) for a defined population. Time series studies often rely on routinely collected administrative datasets (for example, health datasets from health agencies and air pollution data from environmental agencies) for analysis.

In panel studies, the air pollution exposure is usually measured at the population or geographic level whereas the outcome factor (lung function, respiratory symptoms) is measured at the individual level. Hence, panel studies are also known as semi-ecological studies. Panel studies take a group of subjects and follow them prospectively for a period of time (typically weeks or months). The subjects keep a daily record of their lung function, symptoms and medication use in a diary (and therefore panel studies are also often called *diary studies*). At the end of the study period, data are analysed to determine associations between daily air pollution levels and daily measures of symptoms or lung function. Panel studies are useful for investigating the acute or short-term effects of air pollution.

2.2. Overall aims of this study

1) To provide an evidence base of long-term and short-term health effects of air pollutants in Australian children that will support the review of the NEPM standards
2) To obtain quantitative effect estimates for the association between children's historical lifetime exposure to the criteria air pollutants contained in the NEPM (O_3, PM_{10}, $PM_{2.5}$, NO_2, CO, SO_2) and (a) the period prevalence of adverse health outcomes such as respiratory symptoms (asthma, cough and wheeze), and (b) lung function
3) To obtain quantitative estimates of the prospective day-to-day association between the criteria air pollutants and (a) incidence of respiratory symptoms, and (b) lung function, in school children with a history of asthma, aged 7–11 years at baseline
4) To determine whether the effects described in **2)** and **3)** are modified by other factors, such as socio-economic disadvantage, geographical area, sex, activity patterns and obesity.

2.3. Approach

The target population was Australian school children aged 7–11 years whose exposure to the criteria air pollutants was representative of other urban Australian school children of that age. The sampling strategy was based on selecting schools, then whole classes within schools. Children were not excluded on the basis of race, ethnicity or other socio-demographic factors.

Exposures of interest were criteria ambient air pollutants measured using standard NEPM air quality monitoring stations. It was important to select schools which:

- were close to NEPM monitors which had been on site for a reasonable number of years
- were considered to be representative of a larger area around the site
- could demonstrate the maximum variability of exposures to the various pollutants.

For Aim 2 (see above in 2.2), the approach used was a cross-sectional study. Air pollution metrics were average exposures over the period of residence of the child near the monitored site. Analyses took into account appropriate confounding variables (other site-specific or individual factors) and effect modifiers (for example, gender).

For Aim 3 (see above in 2.2), the approach used was a nested panel study, which selected a vulnerable cohort within the baseline sample. Daily air pollution metrics corresponding to the averaging periods used in the NEPM were used. Analyses took into account appropriate time-dependent confounding variables (meteorology, physical activity and effect modifiers (for example, gender).

3. REVIEWS AND CLEARANCES

Ethical and administrative reviews were obtained from the universities of Queensland and Sydney, departments of education in the Australian Capital Territory (ACT), New South Wales (NSW), Queensland (Qld), South Australia (SA), Victoria (Vic) and Western Australia (WA), and the Catholic Education Office of Victoria. Project staff obtained Working with Children Checks, and National Police Clearances.

3.1. University ethics approvals

Approval was sought and given by the University of Queensland's Human Research Ethics Committee on 11 October 2006 (Ref no. 2006000592) as well as the University of Sydney's Human Research Ethics Committee on 18 April 2007 (Ref no. 10050). The ethics committees reviewed study information documents: the letter to school principals (Appendix 1), the explanatory letter, information statement and consent form for parents (Appendices 2-4), the children's questionnaire and privacy statement (Appendices 5,6), the diary study consent from and information sheet (Appendices 7,8), the peak flow and symptom diary and the time activity diary (Appendices 9,10) and the diary study calendar and tracking form (Appendices 11,12).

3.2. Departments of education approval

The departments of education that were approached by the research team gave approval for the study to be conducted. Details of the relevant state or territory department of education and dates of submission and approval to conduct the study are shown in Table 3.1.

Table 3.1. Departments of education submission and approval dates.

Department of education	Date of submission	Date of approval
Victorian Department of Education and Training	24 October 2006	9 January 2007
South Australian Department of Education and Children's Services	23 November 2006	6 March 2007
Western Australian Department of Education and Training	5 December 2006	15 December 2006
ACT Department of Education and Training	6 December 2006	4 January 2007
Queensland Department of Education, Training and the Arts	6 December 2006	12 March 2007
New South Wales Department of Education and Training	20 March 2007	14 December 2007

The departments of education in Victoria and New South Wales had special requirements about some of the study research forms and therefore they had to be slightly modified. The New

South Wales Department of Education also requested clarification, mostly about general testing issues, such as potential risk of the tests, safety measures and confidentiality arrangements. Questions about these and other topics were answered by the co-investigators and approval was granted after the amendments requested were submitted.

In Victoria, the main consent form was modified allowing parents to choose if they wanted their children to have the breathing tests and/or the allergy test. These changes were implemented across the study. This modification was submitted to the Victorian Department of Education and Training on 19 December 2006.

In NSW, modifications were submitted to the New South Wales Department of Education and Training on the 2 December 2007. For the main consent form, a statement was inserted in order to give parents the option to request a copy of the website information, in case of no access to the internet. In the main information statement, the sentence, 'The success of the study depends on the participation of as many children as possible', was deleted as requested. The statement, 'We ask for your contact details to discuss results, complete missing information or discuss further involvement in the study', was included as a way to explain the reasons for collecting contact information. In the letter to principals, the statement, '…it is important that we try to get information on as many people as possible to improve the accuracy of the study results so…', was deleted.

3.3. Amendments to ethics approval

After the approval of these modifications by the departments of education in Victoria and New South Wales, three amendments were submitted to the University of Queensland's Human Research Ethics Committee: the first one (submission date: 26 February 2007, approval date: 5 March 2007) included minor changes made to the principals' letter, information statement, consent form and peak flow and symptom diary. In addition, some new forms were submitted for approval, including an explanatory letter, explanatory form for teachers, school characteristics form, time-activity diary, calendar for participants of the panel study, and the study website structure.

The second amendment (submission date: 20 December 2007, approval date: 29 April 2008) consisted of slight changes made to the principals' letter, information statement and main consent form. The last amendment (submission date: 7 February 2008, approval date: 29 April 2008) incorporated slight changes made to the result sheet.

3.4. Application to the Catholic Education Office

The Catholic Education Office of Victoria was approached in order to seek approval to conduct the study at selected Victorian Catholic primary schools. This was necessary because of the limited number of eligible state government schools at some monitoring sites. One Catholic school from each of these sites was recruited in the study.

3.5. Working with Children Check

A Working with Children Check was obtained by all research staff involved in the study fieldwork in the Australian Capital Territory, Victoria, Queensland, Western Australia, South Australia and New South Wales.

4. OVERALL STUDY DESIGN

4.1. Site selection

Data for 2004–5 were obtained for all NEPM monitors in the ACT, New South Wales, Queensland, South Australia, Victoria and Western Australia from the relevant jurisdictions. The Northern Territory and Tasmania were excluded due to lack of sufficient monitored air pollution data.

The first stage of the study involved the selection of potentially useful sites according to the following inclusion criteria:

(i) existence of a NEPM monitor, with at least a five-year history of measurement of criteria air pollutants

(ii) at least three eligible (see later) primary schools within the monitored area, and

(iii) not considered by the relevant environmental protection agency (EPA) jurisdiction to be an 'unrepresentative site' (such as proximal to a roadway).

The second stage involved the ranking of selected sites according to average measured pollutant levels for each pollutant. A quota (around six) of the highest and lowest ranked sites for each pollutant were then selected so that (allowing for overlap) finally 30 sites were selected. This ensured that the study covered maximum variability in air pollution exposures as well as diversity of air pollution scenarios (that is, air pollution mixtures/gradients), critical to study power and generalisability. This procedure resulted in at least two sites per jurisdiction being chosen to ensure national coverage and relevance.

4.2. Air pollution exposures

Hourly air pollution data (O_3, PM_{10}, $PM_{2.5}$, CO_2 (carbon dioxide), NO_2, $SO_{2)}$ from 1995 to 2007 (2008 for NSW), for all available pollutants, were supplied by the various jurisdictions for each of the selected sites.

Monitoring sites were linked to school sites and, in turn, to children. For the cross-sectional study, exposure metrics based on the number of years of residence of the child in that area or at each school were developed. For the panel study, daily air pollutant levels, corresponding to the averaging periods used in the NEPM, were used.

4.3. Sample size and power

Spatial variability in prevalence of respiratory conditions is evident across cities: a lifetime self-report of asthma history (not necessarily doctor-diagnosed) varied from 24.9% in Sydney to 30.4% in Adelaide (AIHW Australian Centre for Asthma Monitoring, 2003).

Available data on the variability among pollutants across 27 NEPM monitoring stations in Brisbane, Melbourne, Perth and Sydney for 1998 to 2001 was examined. Average 24-hour PM_{10} had a mean of 16.4 $\mu g/m^3$, a between-station standard deviation (SD) of 1.6 $\mu g/m^3$ and a range 13.3–19.8 $\mu g/m^3$. Power calculations were based on a 30 cluster regression analysis. Setting power to 80% and significance level at 5% (two-sided) a net sample of 1,600 would be able to detect an increase of 1.8% in rates of asthma or respiratory symptoms per unit PM_{10}; that is, a total increase in prevalence of 13.8% to 15.7% (four capital cities). A similar calculation based

on O_3 levels showed that the study is able to detect an increase of 14.0% to 15.8% in prevalence of asthma per unit O_3.

Power calculations used the POWER procedure within SAS statistical software.

The consent rate was expected to be 50–70% based on earlier research on school children conducted by the Woolcock Institute of Medical Research. Thus, the sample size required was calculated to be approximately 3,200. Health outcomes based on continuous measures (peak flow) were associated with power exceeding 80%, for the proposed sample size.

Assuming 15% prevalence of current asthma, and a further consent rate of 70%, the panel study was to comprise around 330 participants, or 9,900 person-days. Examination of variability within the four capital cities and over the time period above gives a day-to-day SD of PM_{10} of 6 $\mu g/m^3$. With a total of 330 persons, and a random effects model, the study was expected to have 80% power to detect a decline in standardised peak flow rates (SPFR) of 0.025 per unit PM_{10}. Inter-quartile ranges for daily PM_{10} in Brisbane and Melbourne respectively were 7.3 and 8.4 $\mu g/m^3$ in 2001; other cities would be expected to be similar. Thus, the panel study could detect a decline of at least 0.18 in SPFR at the individual level. By definition, the SD of an individual's SPFR is unity, yielding a 95% range of 4; thus, the study has the capacity to decline a decline of 4.5% of the individual's range of lung function.

5. LOGISTICS

5.1. Fieldwork planning

Planning of the study fieldwork began in November 2006 at the Woolcock Institute of Medical Research. The last versions of the forms to be used with participants were created and, along with applications to conduct the study, submitted to the departments of education in each state and territory. During this time, fieldwork for 2007 and 2008 was planned and plotted into a calendar.

In February 2007, the project management committee and study staff reached an agreement about the times of the year when the study was to be conducted in each state. At this time, it was also decided that the EPA in each jurisdiction would provide local staff members to support fieldwork activities as part of the in-kind contribution of the EPHC to the study.

A weekly calendar was created which specified the tasks to be completed in each state in order to run both the cross-sectional and panel components of the study. These tasks included recruitment of the schools, distribution of the questionnaires, processing of data, testing of children and recruitment of panel study participants and, finally, completion of follow-up of the panel study.

5.2. EPA staff support

Local EPA staff members assisted with the activities during fieldwork. A final agreement was reached about the tasks to be undertaken and included the following:

- training for one hour with the study project manager as preparation for fieldwork
- picking up the sealed envelopes after parents returned completed questionnaires to the school, and arranging to courier these bundles back to the Woolcock Institute of Medical Research in Sydney

- assisting on the testing day with collection of children from classes, measurement of height and weight, and crowd control of the testing room.
- assisting with any panel study home visits.

5.3. Time frame for cross-sectional and panel study

The study fieldwork started in February 2007 and was completed in June 2008. Victoria and New South Wales fieldwork was divided into different stages since they had the greater number of air quality monitoring stations. Table 5.1. and Table 5.2. show details of data collection dates across Australia**:** 'Prep' refers to preparation phase (weeks 1 to 8), 'T' refers to testing period (weeks 9 and 10) and 'Panel' refers to follow-up of panel study (weeks 11 to 15).

Table 5.1. Fieldwork dates for 2007.

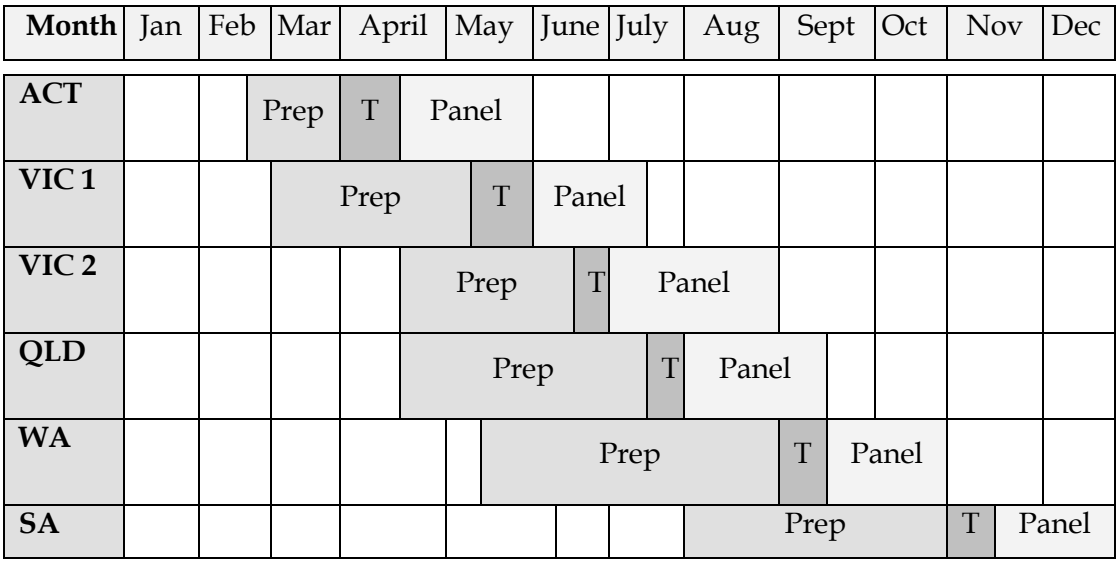
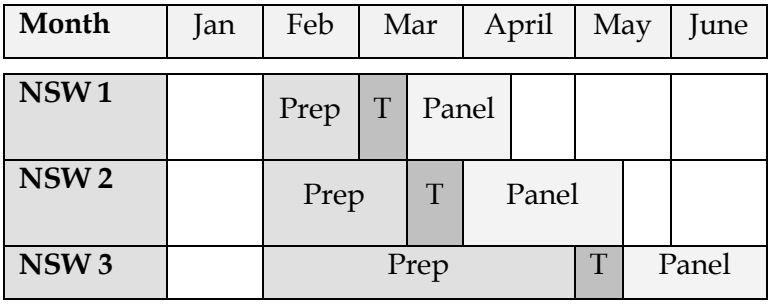


Table 5.2. Fieldwork dates for 2008.



The panel study in each monitoring station started from the testing day and lasted for four weeks. Weeks were considered as calendar weeks (Monday to Sunday) and the remaining days of the first week were also included for data collection. For example, if a child was tested on a Wednesday, the remaining days of that week were included in the study in addition to the next four weeks counting from the next Monday.

The Australian school year is divided into four terms. Exact dates for these vary according to State/Territory jurisdiction. The school year itself runs from late January/early February until December. There is a short holiday between terms and a long summer holiday in December and January.

The panel study took place only during school terms and not in school holidays since children would not be exposed to the air quality in the school area. The only states and territory that had school holidays in the middle of panel study were the ACT, Victoria and Western Australia.

Part B

The cross-sectional study:

chronic exposure to air pollution: effects upon children's health

1. STUDY DESIGN AND MEASUREMENT

1.1. Aims

This section addresses the following aims of the study:

- to obtain quantitative effect estimates for the association between children's historical lifetime exposure to the criteria air pollutants contained in the NEPM (O_3, PM_{10}, $PM_{2.5}$, NO_2, CO, SO_2) and (a) the period prevalence of adverse health outcomes such as respiratory symptoms (asthma, cough and wheeze), and (b) lung function
- to determine whether the effects are modified by other factors, such as socio-economic disadvantage, geographical area, sex, activity patterns and obesity.

1.2. Data collection

Children were tested on school premises during school hours, and parents were asked to complete a questionnaire and return it to the project office.

1.2.1. Questionnaire

The questionnaire was designed to include information on relevant respiratory outcomes, household sources of pollutants, and covariates. The sources for items from the questionnaire included the International Study of Asthma and Allergies in Childhood (ISAAC) (ISSAC Steering Committee and ISAAC Phase Three Study Group, 2000), the SCCHS (Peters et al., 1999a,b), the Belmont Schoolchildren Study (Toelle et al., 2004), the Childhood Asthma Prevention Study (CAPS) (Marks et al., 2006) and the NSW Health Survey (Centre for Epidemiology and Research, 2003). Preference was given to the ISAAC questionnaire as a source document because of its widespread use (over 300,000 respondents) and extensive validation. The selection was decided by the investigator team and decisions about each item were recorded. The final questionnaire included 70 items (Appendix 5).

Questions asking about respiratory symptoms and asthma were derived from existing, widely used questionnaires; that is, the ISAAC and the SCCHS.

The questionnaire also collected information about eczema, hay fever, upper and lower respiratory tract conditions, birth history, parental history of respiratory problems (including asthma and atopic diseases), parent smoking history, transport, children's time-activity patterns, past addresses the child has lived, socio-economic factors, and other variables. These questions were derived from questionnaires used in other studies such as the Belmont Schoolchildren Study, CAPS, and the NSW Health Survey.

The home environment characteristics (only indoor sources of air pollutants) were collected.

The indoor pollutant levels induced by ambient sources lie in the causal pathway, and do not confound the outdoor-health effect association.

Information about school absenteeism in relation to the presence of respiratory symptoms was also collected by parent self-report in the questionnaire.

1.2.2. Clinical assessments

The main health outcomes for the cross-sectional study included objective lung function measurements and, additionally, assessment of exhaled NO and of atopic status. Collection of these measurements occurred at fieldwork in each of the schools. One day of testing was conducted at each school. These tests were performed if *all* of the following criteria were met:

- the consent form was properly completed
- the child was present at the school at the day of testing
- the child consented to be tested or the researcher considered it appropriate to carry out the tests on the child (that is, tests were not performed where any signs of anxiety were present)
- the child was physically able to perform the tests
- the testing equipment was functioning properly.

Children who had a recent absence from school and reported having had a respiratory illness or who showed signs of respiratory illness did not have spirometry measured.

A brief description of the tests is provided below.

Spirometric lung function

Spirometric function was measured, before and after bronchodilator, in accordance with the recommendations of the ATS/ERS Task Force performance criteria for spirometry (Miller et al., 2005). A Spirocard spirometer (QRZ-7000-5636C.1 SpiroCard PC Card, QRS Diagnostics, LLC, Plymouth, Minnesota, USA) that measures flow using a pressure transducer and derives volume by integrating flow over time was attached to a laptop computer running SpiroScore+ V2.6 (supplied by Bird Healthcare, Melbourne, Australia) for immediate data acquisition.

Participants were requested to withhold short-acting bronchodilators for six hours and long-acting bronchodilators for 12 hours prior to the baseline measurements. The procedure was explained to the children by the research assistant observing the test. They stood upright during the procedure, which was performed without a nose clip. Children took a full breath in and, with their lips placed around the mouthpiece for sealing, were instructed to blast the air out 'as fast and as far as you can'. They were encouraged to continue expiration as long as possible, while ensuring that they did not bend over during the manoeuvre.

The procedure was repeated at least three times, or more as required to achieve reproducibility of ≤ 100 ml between the best and the second-best FEV_1. The procedure was repeated a maximum of 8 times.

Immediately after the baseline spirometry was completed, participants received salbutamol 200 µg (Ventolin® 100 µg x 2), administered by a tube spacer, with one minute between doses. Post-bronchodilator measurements were made 10 minutes later using the same procedure.

The following parameters were derived from the spirometric measurements:

- **FVC** (forced vital capacity) is the maximum volume of air which can be exhaled during a forced manoeuvre
- **FEV_1**(forced expired volume in one second) is the volume expired in the first second of maximal expiration after a maximal inspiration and is a useful measure of airway calibre

- **FEV_1/FVC** is the FEV_1 expressed as a percentage of the FVC and gives a clinically useful index of airflow limitation
- **$FEF_{25-75\%}$** is the average expired flow between 25% and 75% of FVC and is regarded as a more sensitive measure of small airways narrowing than FEV_1 , but is less reproducible.
- **PEF** (peak expiratory flow) is the maximal expiratory flow rate achieved and this occurs very early in the forced expiratory manoeuvre.

Predicted lung function, for give sex and height were calculated for each child, based on NHANES III predicted equations for Caucasians males <20 and females <18 (Hankinson et al 1999). Percent predicted lung function was calculated as the percentaged ratio of measured lung function to predicted lung function.

Exhaled nitric oxide

NO is produced in the airways by a number of different cell types. Levels of NO in the exhaled breath (eNO) are believed to be an indicator of the severity of airway inflammation (Barnes and Belvisi, 1993). In many, but not all, studies, eNO correlates with the number of eosinophils in sputum and bronchoalveolar lavage and with the severity of airway hyperresponsiveness. Levels of eNO are increased in asthmatic subjects and in many atopic non-asthmatic subjects. They are increased following allergen challenge and reduced following treatment with inhaled corticosteroids.

NO can be measured in exhaled breath and is a highly reliable measurement in population studies (Salome et al., 1999). A sample of expired air for this study was collected to measure NO levels using an offline technique (Massaro and Gaston, 1995; Salome et al., 1999). Before collection, children took three breaths with a scrubber to filter ambient NO. After filling their lungs with air they breathed out against a small resistance to residual volume into an NO impermeable polyethylene bag (supplied by Scholle Industries Pty Ltd, SA, Australia) at an exhaled flow of 12 litres/min. The first 2 seconds of the exhalation were diverted from the collection bag, using a three-way tap, to exclude dead space air (Paredi and Loukides, 1998). The procedure was repeated until there was enough air in the bag to measure.

The exhaled gas from multiple breaths was analysed within six hours of collection using a chemiluminescence analyser (supplied by Thermo Environmental Instruments Model 42i, Lear Siegler, Australia) and values for NO, NO_X and NO_2 were recorded for each participant.

Skin prick tests

Skin testing is a long-established, quick, safe and easy procedure used to diagnose allergies. It has been in use since Charles Blackley performed the first scratch test in 1873. The four main types of skin testing procedures are the intracutaneous (intradermal) (ICT), scratch, puncture and prick methods. In this study, as in previous Australian epidemiological studies, the prick method was used, it having an excellent safety record.

For this study, eight common aeroallergens were tested by skin prick test: *Dermatophagoidies pteronyssinuss* (Der p 1), *Dermatophagoidies farinae*, ryegrass, grass mix, cockroach, cat, Alternaria and Aspergillius.

The participants were asked whether they had taken any antihistamines within the last 48 hours and if they were allergic to anything (and, if so, the reaction they experienced). With their arm facing upwards, a stamp was placed and a tiny droplet (2 mm diameter) of each of the allergens

was positioned. For each allergen / control, a lancet was passed through the drop just catching the skin at anywhere from a 20° to an 80° angle. The lancet was then lifted (skin pricked), creating a small break in the epidermis so the allergen could enter the dermis.

The wheal size was measured, 15 minutes after the skin prick test was performed, at the largest diameter of the wheal. Measurements were made to the nearest 1 mm. The mean wheal size was calculated as the average of these two diameters and this result was rounded down. A mean wheal size ≥ 3 mm was classified as positive.

Height and weight

Anthropometric measurements were made with shoes removed. Standing height and sitting height were measured with the participants standing or sitting on a firm, horizontal surface on the floor. The stadiometer (measuring rod) was placed perpendicular (at a 90^{o} angle) to this surface. Weight was measured using digital scales.

Environmental measures

Daily average hourly levels of each air pollutant were averaged over the period of residence of the child at the current residence to provide an aggregated measure of exposure. Period of residence was defined as the time between the child's birth and the date of the child's assessment if the child had lived at that address all his/her life, or if s/he had not the time between the midpoint of the year the child had moved to that address (ascertained in the questionnaire) and the date of the child's assessment. In addition, annual average exposures were calculated, as well as average exposures in the last 12 months prior to assessment.

The following information about classroom and school characteristics was collected: building type, proximity to roads, type of heating and cooling, and type of flooring. Latitude and longitude was recorded in each of the classrooms. The ambient NO of the testing room was collected twice in the day and measured no more than six hours later by the chemiluminescence analyser. The room temperature and barometric pressure were measured twice daily.

1.3. Statistical analysis

Standard statistical measures are used to describe the characteristics of the children, their respiratory history and the results of clinical tests.

Hierarchical models (with state and school as levels) were used to examine the association between outcome variables such as lung function and respiratory symptom and the air pollutant exposures. These models were fitted separately for each pollutant. Models involving lung function also included height and sex. Confounding variables (such as age, parental employment and education, and household variables) were added according to their improvement to the overall model fit. Non-linearity was assessed by incorporating quadratic and cubic polynomial terms for the pollutants (after centring), as well as generalised additive models. Multi pollutant models were explored in order to estimate which pollutants have the strongest independent associations with lung function and asthma. The analyses were carried out using SAS 9.2 and the procedures SURVEYREG and SURVEYLOGISTIC.

Sensitivity analyses were carried out for two-pollutant models involving NO_2 and O_3, related to the high correlation between these pollutants. Owing to the presence of one site with high SO_2 values, sensitivity analyses were performed excluding this site from models involving SO_2.

Interaction terms were added to the models to examine possible effect modification. Criteria for establishing effect modification were the significance of an interaction test (at the 5% level) and the existence of one or more significant effects across the levels of the interacting variable.

2. RECRUITMENT

2.1. School recruitment

After the schools were approached, they were classified into different categories:

- agreed to participate in the study
- refused to participate in the study
- ineligible for different reasons, e.g. most parents from non-English speaking background and/or not enough children to approach for the study.

The overall response rate was 64% for schools (55 out of 86 eligible schools approached). Most of the recruited schools were within 2.5 km of the air quality monitoring station. One school was 2.8 km from the relevant air quality monitoring station.

2.2. Participant recruitment

Around 100 to 120 questionnaires were distributed per school in the ACT and Victoria. The participant response rate in these jurisdictions was lower than expected. As a result, it was decided to increase the number of children approached from 100 to 150 in order to recruit the required number of children in the rest of the states. In total, 7,618 packages of study materials were distributed to the 55 participating schools and 2,880 completed questionnaires were returned. At fieldwork, 2,653 children underwent at least one of the tests and 2,603 completed post-bronchodilator spirometry. Finally, 34% of those approached to participate in the study completed post-bronchodilator spirometry.

Reasons for not completing any or all tests on a child for whom a questionnaire was received included:

- no parental consent
- absent on the day of testing
- other reason on the moment of testing, e.g. child did not consent or researcher considered it not appropriate to conduct the test
- test was technically unsatisfactory
- testing equipment malfunction at fieldwork.

Table 2.1. shows the number of tests completed and not completed for each specific test and Table 2.2. shows the reason why the tests were not completed.

A substantial number of participants did not have valid results for exhaled NO measurements (35.1%). This was mainly due to equipment malfunction or the test being technically unsatisfactory. At the beginning of the study, an electronic, automated exhaled breath collection device was used. There was a number of technical problems with this device. After several days of testing, it was evident that the device could not be used for this study. At this time, it was decided to change to the manual rotameter exhaled breath collection device. This was used from the time of the Queensland fieldwork. A substantial number of samples that were collected could not be analysed due to malfunction of the NO chemiluminescence

analyser. This affected some sites in South Australia and Newcastle. While regrettable, these lost measurements merely limit the statistical power of the study, since these losses were unrelated to the true level of exhaled NO.

Table 2.1. Description of test completion in ACHAPS.

TEST	Spirometry Pre-Bronchodilator		Spirometry Post-Bronchodilator		Exhaled NO		Skin prick test	
	N	%	N	%	N	%	N	%
Tests completed	2628	**91.3**	2603	**90.4**	1868	**64.9**	2414	**83.8**
Tests NOT completed	252	**8.8**	277	**9.6**	1012	**35.1**	466	**16.2**
TOTAL	**2880**	**100**	**2880**	**100**	**2880**	**100**	**2880**	**100**

Table 2.2. Reasons for tests not completed in ACHAPS.

TEST	Spirometry Pre-Bronchodilator		Spirometry Post-Bronchodilator		Exhaled NO		Skin prick test	
	N	%	N	%	N	%	N	%
No consent	79	**31.3**	83	**30.0**	79	**7.8**	164	**35.2**
Absent on testing day	158	**62.7**	158	**57.0**	158	**15.6**	157	**33.7**
Another reason	7	**2.8**	19	**6.9**	10	**1.0**	136	**29.2**
Technically unsatisfactory	8	**3.2**	17	**6.1**	209	**20.7**	8	**1.7**
Equipment malfunction	0	**0.0**	0	**0.0**	556	**54.9**	1	**0.2**
TOTAL NOT TESTED	**252**	**100**	**277**	**100**	**1012***	**100**	**466**	**100**

* This large number of tests missed does not affect primary study outcomes

There were some adverse events due to the skin prick test. Three children experienced a vaso-vagal syncopal episode after skin prick tests were performed. This was attributed to anxiety and associated hyperventilation. At the time of the event, first aid was provided to the children. No other serious adverse events occurred. In particular, there were no systemic allergic reactions. After the three episodes of syncope, which occurred in Victoria and Queensland, procedures were changed to safeguard against this event. In particular, children with any evidence of anxiety prior to performing the skin prick test did not have this procedure.

3. RESULTS

3.1. Demographic characteristics of cross-sectional study participants

The mean age of the sample was 10 years (SD=1.2, 7–12 years); 48.5% were boys. Most (90%) children were born in Australia; 17.7% spoke a language other than English at home. Most parents (72% mothers, 73% fathers) had completed high school education (Table 3.1).

Table 3.1.Child characteristics (N = 2,860); numbers and per cent unless otherwise specified.

Characteristic	
Age (years)	
Mean (SD)	9.6 (1.2)
Range	7-12
Gender	
Female	1462 (51.5)
Male	1378 (48.5)
Born in Australia	
No	283 (10.1)
Yes	2534 (89.9)
Speak language other than English at home	
No	2308 (82.3)
Yes	495 (17.7)
Mother's educational qualification	
Completed primary school	12 (0.4)
Completed 7-9 years	114 (4.1)
Completed 10 years	525 (18.8)
Completed 12 years	407 (14.6)
TAFE Certificate/Diploma	706 (25.3)
Tertiary	924 (33.1)
Other	100 (3.6)
Father's educational qualification	
Completed primary school	22 (0.4)
Completed 7-9 years	115 (4.4)
Completed 10 years	466 (17.6)
Completed 12 years	367 (13.9)
TAFE Certificate/Diploma	682 (25.8)
Tertiary	882 (33.3)
Other	105 (4.4)
Mother's employment (last week)	
Worked for payment/profit	1820 (66.2)
Usually work for payment, but absent last week	67 (2.4)
Unpaid work in family business	72 (2.6)
Other unpaid work	127 (4.6)
No job	471 (17.1)
Other	193 (7.0)
Father's employment (last week)	
Worked for payment/profit	2307 (88.8)
Usually work for payment, but absent last week	70 (2.7)
Unpaid work in family business	22 (0.9)
Other unpaid work	14 (0.5)

No job	114 (4.4)
Other	72 (2.8)

3.2. Respiratory conditions of cross-sectional study participants

Twenty-seven per cent of children had a history of asthma, which is consistent with Australian estimates for this age group and 14% stated that they still had asthma (Table 3.2.). Rather more (38%) had used medication for asthma, 22% in the last year. Predominant medications used were short-acting beta-agonists (21%) followed by inhaled steroids (9%).

Table 3.2. History of asthma; numbers (n) and per cent (%).

Item	N	n	%
Diagnosis and treatment			
Ever had asthma diagnosis	2840	781	27.5
Current asthma	2829	405	14.3
Medical attention for asthma last 12 months	2591	351	13.5
General Practitioner		341	13.1
Emergency Department		45	1.8
Hospital admission		14	0.5
Hospital admitted for breathing problems ever	2830	386	13.6
Asthma/wheezing caused child to miss school last 12 months	2622	227	8.6
Asthma medication use			
Ever used medication for asthma/wheezing	2703	1,042	38.5
Any asthma medication in the last 12 months	2704	250	22.5
Short-acting beta-agonist (SABA)	2693	572	21.2
Long-acting beta-agonist (LABA) alone	2651	12	0.5
All Inhaled steroids	2703	250	9.2
Inhaled steroids alone	2656	130	4.9
Combined inhaled steroid and LABA	2659	141	5.3
Leukotriene receptor antagonist	2651	24	0.9
Oral steroids	2654	609	22.5

Over one-third (34%) of children had has a wheezing episode at some time in their lives with about half (16%) in the last 12 months (Table 3.3.). Seventy-two per cent of children had experienced a cough in the last year, with 23% experiencing a dry cough at night (Table 3.4.).

Table 3.3. History of wheezing; numbers (n) and per cent (%).

Item	N	n	%
Ever had wheezing	2840	987	34.8
Wheezing in last 12 months	2839	463	16.3
After exercise		324	13.2
After crying		310	12.6
Limiting speech		70	2.8

Table 3.4. History of cough in the last 12 months; numbers (n) and per cent (%).

Item	N	n	%
Cough	2860	2,048	71.6

Dry cough at night	2851	658	23.1
Dry cough at night, for more than 2 weeks	2846	160	5.6

Twenty-three per cent of children's were reported to have experienced an itchy rash for at least six months, 29% itchy eyes and 33% problems with sneezing or blocked nose (in the absence of a cold) (Table 3.5.).

Table 3.5. History of itchy rash/eyes or rhinitis; numbers (n) and per cent (%).

Item	N	n	%
Itchy rash			
For 6 months ever	2859	662	23.2
For 6 months, in the last 12 months	2855	471	16.5
Medication in last 12 months	2851	447	15.7
Itchy eyes			
Ever	2849	830	29.1
In the last 12 months	2847	762	26.8
Medication in last 12 months	2848	415	14.6
Rhinitis			
Ever	2857	955	33.4
In the last 12 months	2856	886	31.0
Medication in last 12 months	2856	558	19.5

The most common respiratory or allergic condition diagnosed was otitis media (39%), followed by tonsillitis (26%) and eczema or atopic dermatitis (23%) (Table 3.6.).

Table 3.6. History of diagnosed illnesses ever; numbers (n) and per cent (%)

Item	N	n	%
Otitis media	2783	1097	39.4
Tonsillitis	2784	736	26.4
Eczema/atopic dermatitis	2794	645	23.1
Croup	2770	518	18.7
Allergic rhinitis/hay fever	2775	409	14.7
Bronchitis	2775	361	13.0
Bronchiolitis	2774	250	9.0
Pneumonia	2774	169	6.1
Whooping cough	2758	83	3.0

Twenty-four per cent of parents reported the child had had an allergic reaction, and 48% of those tested had a positive skin prick test (Table 3.7.). In all, 59% of children either had a reported allergic reaction or a positive skin prick test. The most common parental history of allergic conditions was hay fever (48% mothers, 38% fathers), with 21% of mothers and 18% of fathers reporting a history of asthma (Table 3.8).

Table 3.7. Child allergies; numbers (n) and per cent (%).

Item	N	n	%
History of allergic reaction (reported by parent)	2444	594	24.3
Positive response to skin prick test	2084	993	47.6

House dust mite allergy (skin prick test)	2084	807	38.7
Positive skin prick test or history of allergic reaction	2174	1285	59.1

Table 3.8. Family history of asthma or allergies; numbers (n) and per cent (%).

Item	N	n	%
Mother			
Hay fever	2749	1308	47.6
Wheezing	2700	617	22.9
Asthma	2733	582	21.3
Eczema	2695	567	21.0
Father			
Hay fever	2580	970	37.6
Wheezing	2557	494	19.3
Asthma	2593	460	17.7
Eczema	2523	276	10.9

Mean BMI was 19 kgm^{-2} (12-38) and mean birthweight was 3.6 kg (0.8-5.8) (Table 3.9).

Table 3.9. Child anthropometry; mean, standard deviation (SD), and range.

Item	N	Mean	SD	Range
Birth				
Birthweight (kg)	2594	3.6	0.6	0.8 - 5.8
Born premature (%)	2834	6.5%		
Measured at time of survey				
Weight (kg)	2646	37.6	9.9	20 - 91
Height (cm)	2648	141.1	9.1	113 -
Body mass index (BMI) kgm^{-2}	2645	18.7	3.3	12 - 38

3.3. Lung function

Children's lung function measures were consistent with population values (Table 3.10).

Table 3.10. Child lung function tests; mean, standard deviation (SD), and range.

Item	N	Mean	SD	Range
FEV_1	2631			
Pre-bronchodilator (l)		2.0	0.4	0.8 - 4.1
Post-bronchodilator (l)		2.1	0.4	0.8 - 4.0
% change: Pre- to post- bronchodilator		3.6	5.3	-50 - 43
% predicted: Pre-bronchodilator		97.1	10.8	44 - 147
% predicted: Post-bronchodilator		100.5	10.9	41 - 152
FVC	2498			
Pre-bronchodilator (l)		2.3	0.5	0.9 - 4.7
Post-bronchodilator (l)		2.3	0.5	1.2 - 4.5
% predicted: Pre-bronchodilator		110.7	12.6	50 - 164
% predicted: Post-bronchodilator		112.0	12.6	52 - 164
FEV_1/FVC ratio	2498			
Pre-bronchodilator (%)		87.9	6.5	63 - 176
Post-bronchodilator (%)		90.0	5.4	56 - 119
Exhaled NO	1823			
In ppb		9.4 (7.2*)	7.2	0.1 - 67

* Geometric mean

3.4. Household environment

A high percentage of homes used gas for cooking, either in the child's first year of life (62%) or currently (67%) (Table 3.11.). Thirty-three per cent of homes used gas for heating, about half of these unflued. Sixty-five per cent of homes were air conditioned, largely room air conditioners. Eighteen per cent of homes had an internal garage accessible from the home.

Table 3.11. Household exposures; numbers (n) and per cent (%).

Item	N	n	%
Use gas for cooking			
In child's first year of life	2774	1732	62.4
At present	2840	1904	67.0
Heating at home in child's first year of life	2859		
None		208	7.2
Gas		946	32.7
Unflued gas heater		448	15.5
Electric		872	30.1
Central		513	17.7
Open fire		261	9.0
Stove		258	8.9
Other		95	3.3
Heating at home at present	2859		
None		232	8.0
Gas		955	33.0
Unflued gas heater		455	15.7
Electric		679	23.5
Central		605	20.9
Open fire		234	8.0
Stove		194	6.7
Other		106	3.7
Air conditioning			
Home air conditioned	2814	1842	65.5
Use of air conditioning last summer when child home	1801		
Never used		51	2.8
Used less than 10 days		326	18.1
Used 10-20 days		557	30.9
Used 21-40 days		457	25.4
Used 41 or more days		410	22.8
Type of air conditioning	1802		
Room		1131	62.8
Ducted		369	20.5
Evaporative		302	16.8
Garage			
No garage	2734	945	34.6
Separate garage		933	34.1
Attached garage, no internal access		460	16.8
Garage is accessed internally from house		499	18.2
Internal garage in child's first year		351	12.6

Ninety-one per cent of children lived in a smoking-free house (Table 3.12.), although 19% of mothers currently smoked; 15% of mothers reported smoking during pregnancy.

Table 3.12. Smoking exposure of child; numbers (n) and per cent (%).

Item	N	n	%
Mother smoked during pregnancy	2724	397	14.6
Mother smoked during child's first year	2728	566	20.7
Mother smokes regularly at present	2820	546	19.4
Smoking in house	2854		
Home is smoke free		2594	90.9
People occasionally smoke		177	6.2
People frequently smoke		83	2.9
Number of cigarettes smoked per day in house	2224		
None		1963	88.3
1-10		182	8.2
11-20		46	2.0
21-40		26	1.2
40 or more		7	0.3

Sixty-one per cent of homes had a dog and 36% a cat (Table 3.13).

Table 3.13. Other exposures: numbers (n) and per cent (%).

Item	N	n	%
Pets	2830		
Ever had a cat or dog since child born		2140	75.6
Have a cat at present		812	35.5
Have a dog at present		1385	60.5
Have a cat during child's first year		761	33.8
Have a dog during child's first year		1138	50.4
Child care			
Attend day care in first year	2825	690	24.4
Attend day care for more than 20 hrs/week in first year	2789	296	10.6

3.5. Air pollutant exposures

Not all selected sites monitored all pollutants. The numbers of sites available for each pollutant measure, and pairwise combinations, is shown in Table 3.14.

Table 3.14. Numbers of sites available for pollutant measures.

	Bsp	$PM_{2.5}$	PM_{10}	NO_2	O_3	CO	SO_2
Bsp	46	45	44	46	41	29	24
$PM_{2.5}$	45	55	53	55	47	32	32
PM_{10}	44	53	54	54	45	33	32
NO_2	46	55	54	56	47	33	32
O_3	41	47	45	47	47	26	30
CO	29	32	33	33	26	33	17
SO_2	24	32	32	32	30	17	32

For each pollutant, distributions of lifetime exposures (lifetime = time from first residence in area to date of survey) and recent exposures (last year, or lifetime if residence less than one year) are shown in Table 3.15. and Table 3.16. respectively. Correlations among lifetime exposures are shown in (Table 3.17.).

The distributions of lifetime exposures are shown in Figure 3.1. The outlier for SO2 occurred at the Port Pirie site, which hosts the largest lead refinery in the southern hemisphere.

Table 3.15. Mean and variability of lifetime child exposures.

Pollutant	N	Mean	SD	Median	Lower quartile	Upper quartile	Range	Inter-quartile range
Bsp 10^{-4} m^{-1}	2110	0.27	0.09	0.25	0.20	0.28	0.13 - 0.55	0.08
$PM_{2.5}$ μg/m^3	1486	8.04	1.51	7.76	6.75	8.92	4.90 -13.52	2.16
PM_{10} μg/m^3	2545	18.47	2.14	18.38	16.59	20.39	13.68 - 25.86	3.80
NO_2 ppb	2620	9.31	3.34	8.83	7.25	11.57	2.83 - 18.30	4.31
O_3 ppb	2226	15.88	2.98	15.20	13.87	16.99	10.96 - 22.42	3.12
CO ppm	1641	0.30	0.13	0.29	0.24	0.35	0.03 - 1.04	0.11
SO_2 ppb	1463	1.39	1.43	1.11	0.75	1.49	0 - 8.86	0.74

Table 3.16. Mean and variability of recent child exposures.

Pollutant	N	Mean	SD	Median	Lower quartile	Upper quartile	Range	Inter-quartile range
Bsp 10^{-4} m^{-1}	1744	0.29	0.12	0.23	0.18	0.40	0.13 - 0.53	0.22
$PM_{2.5}$ μg/m^3	1237	7.42	0.75	7.55	6.85	7.92	4.90 - 8.70	1.07
PM_{10} μg/m^3	2437	18.94	2.73	18.75	16.83	20.97	13.68 - 25.86	4.13
NO_2 ppb	2511	8.78	2.98	7.85	7.11	11.14	3.36 - 15.60	4.03
O_3 ppb	2120	16.99	2.84	16.66	14.46	17.94	12.19 - 22.78	3.48
CO ppm	1632	0.24	0.10	0.24	0.18	0.29	0.03 - 0.47	0.12
SO_2 ppb	1249	1.53	1.63	1.06	0.77	1.59	0.37 - 8.96	0.82

Table 3.17. Pearson correlations among lifetime child exposures (above diagonal) and among recent exposures (below diagonal). Correlations between lifetime and recent exposures for the same pollutant are shown on the diagonal. Correlations above 0.5 in bold.

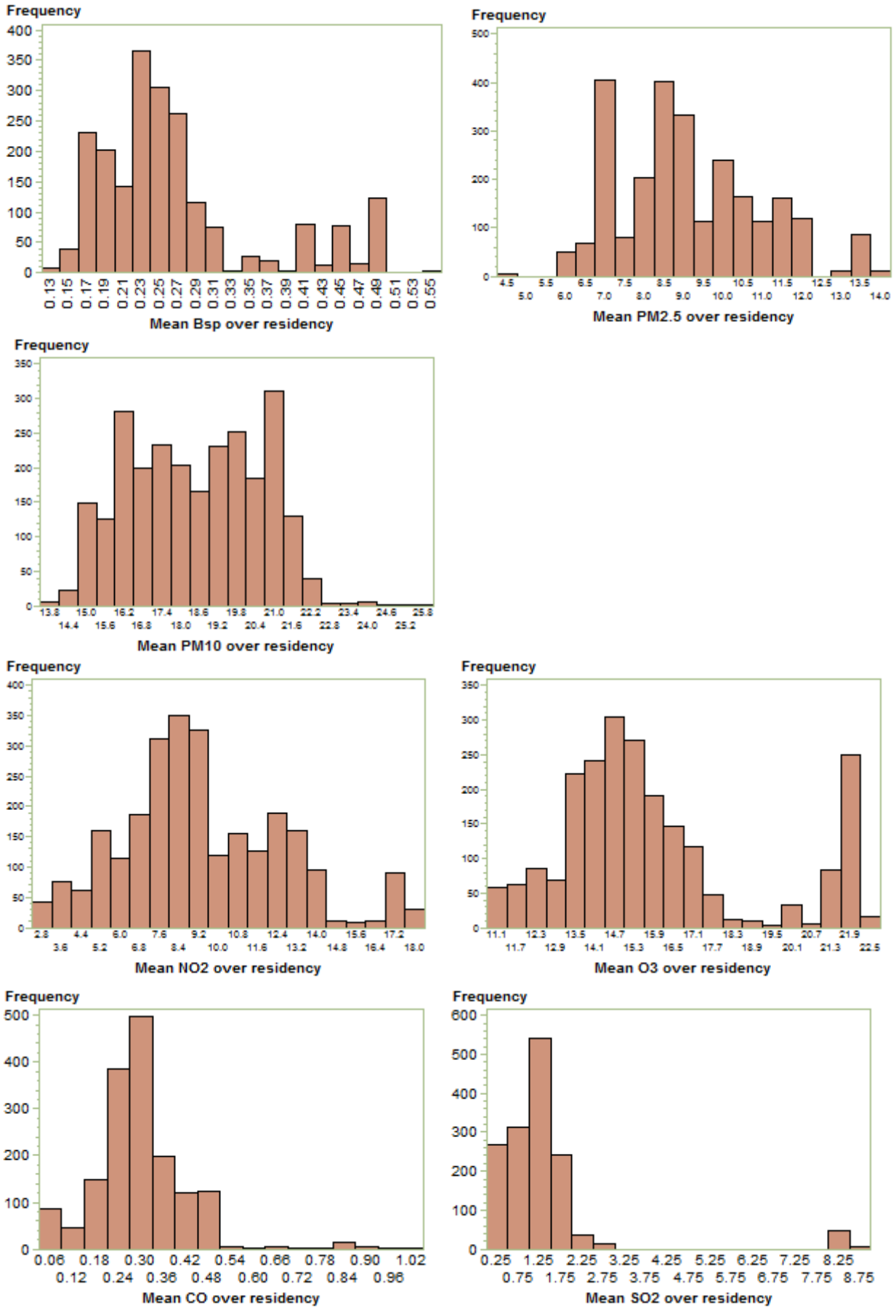
	Bsp	$PM_{2.5}$	PM_{10}	NO_2	O_3	CO	SO_2

Bsp	**0.770**	0.271	0.251	0.082	0.002	0.005	-0.023
$PM_{2.5}$	0.140	**0.691**	**0.520**	0.328	-0.235	0.154	**0.592**
PM_{10}	**0.651**	0.431	**0.762**	0.379	-0.393	0.131	0.194
NO_2	0.212	0.280	0.232	**0.963**	**-0.777**	**0.692**	-0.438
O_3	0.245	-0.426	-0.216	**-0.761**	**0.858**	**-0.729**	0.305
CO	0.344	0.292	0.185	**0.510**	-0.453	**0.763**	**-0.501**
SO_2	-0.255	0.287	0.227	-0.166	-0.380	-0.189	**0.989**

Table 3.18. Summary of correlations among child exposures. Correlations above 0.5 in bold.

Lifetime exposure	**Positively correlated with:**	**Negatively correlated with:**
Bsp	$PM_{2.5}$, PM_{10}, NO_2	
$PM_{2.5}$	Bsp, **PM_{10}**, NO_2, CO, **SO_2**	O_3
PM_{10}	Bsp, **$PM_{2.5}$**, NO_2, CO, SO_2	O_3
NO_2	Bsp, $PM_{2.5}$, PM_{10}, **CO**	**O_3**, SO_2
O_3	SO_2	$PM_{2.5}$, PM_{10}, **NO_2**, **CO**
CO	$PM_{2.5}$, PM_{10}, **NO_2**	**O_3**, **SO_2**
SO_2	**$PM_{2.5}$**, PM_{10}, O_3	NO_2, **CO**
Recent exposure	**Positively correlated with:**	**Negatively correlated with:**
Bsp	$PM_{2.5}$, **PM_{10}**, NO_2, O_3, CO	SO_2
$PM_{2.5}$	Bsp, PM_{10}, NO_2, CO, SO_2	O_3
PM_{10}	**Bsp**, $PM_{2.5}$, NO_2, CO, SO_2	**O_3**, SO_2
NO_2	Bsp, $PM_{2.5}$, PM_{10}, **CO**	$PM_{2.5}$, PM_{10}, **NO_2**, CO, SO_2
O_3	Bsp	$PM_{2.5}$, PM_{10}, **NO_2**, CO, SO_2
CO	Bsp, $PM_{2.5}$, PM_{10}, **NO_2**	O_3, SO_2
SO_2	$PM_{2.5}$, PM_{10}	Bsp, NO_2, O_3, CO

Figure 3.1. Distributions of child-based exposures.



3.6. SEIFA characteristics

Socio-economic indexes for areas (SEIFA) of the child's postcode of residence were obtained. Each of the four indexes summarises different aspects of the socio-economic conditions of people living in an area; each is based upon a different set of social and economic information from the 2006 Census (Australian Bureau of Statistics, 2010). The four indexes in SEIFA 2006 are:

- **Index of relative socio-economic disadvantage (IRSED)**: is derived from Census variables related to disadvantage, such as low income, low educational attainment, unemployment, and dwellings without motor vehicles.
- **Index of relative socio-economic advantage and disadvantage (IRSEAD)**: a continuum of advantage (high values) to disadvantage (low values) which is derived from Census variables related to both advantage and disadvantage, like household with low income and people with a tertiary education.
- **Index of economic resources (IER)**: focuses on Census variables like the income, housing expenditure and assets of households.
- **Index of education and occupation (IEO)**: includes Census variables relating to the educational and occupational characteristics of communities, like the proportion of people with a higher qualification or those employed in a skilled occupation.

The mean and variability of these, over all children, is shown in Table 3.19.

SEIFA indices are standardised to a mean of 1000 and a standard deviation of 100. The means of the sample are slightly above average (by about one-quarter of a standard deviation) on IRSEAD, IRSED and IEO, and are somewhat more homogeneous than the Australian population (SDs range from 64 to 90). The latter possibly reflects the urban nature of the sample.

Table 3.19. Mean and variability of SEIFA indices of child's postcode of residence.

Index	N	Mean	SD	Median	Lower quartile	Upper quartile	Range	Inter-quartile range
IRSEAD	2856	1022	76	1027	788	980	1075-1213	95.14
IRSED	2856	1013	66	1018	781	992	1059-1149	66.50
IER	2856	1005	64	1001	808	970	1048-1187	78.34
IEO	2856	1023	90	1027	800	962	1094-1201	131.78

IRSEAD: Index of relative socio-economic advantage and disadvantage
IRSED: Index of relative socio-economic disadvantage
IER: Index of economic resources
IEO: Index of education and occupation

Correlations appear strongest between pollutants and the IRSEAD and IEO indices, with higher scores associated with higher NO_2 and CO, and lower scores associated with higher SO_2, and to some extent, O_3, $PM_{2.5}$, and PM_{10} (

Table 3.20.).

Association between selected respiratory conditions (lifetime or recent asthma or wheeze, cough) and SEIFA indices were generally weak. Statistically significant correlation coefficients ranged from -0.04 to -0.09; the lower the SEIFA, the more likely the condition present. Lung function was generally not significantly associated with SEIFA codes. Exhaled NO was significantly correlated with SEIFA indices (correlation coefficients: -0.05 to -0.09).

Table 3.20. Correlations among child exposures (Pearson coefficients) and SEIFA indices. Correlations above 0.3 in bold.

	Bsp	**$PM_{2.5}$**	**PM_{10}**	**NO_2**	**O_3**	**CO**	**SO_2**
IRSEAD	0.062	-0.226	-0.152	**0.340**	-0.184	**0.361**	**-0.475**
IRSED	0.149	-0.185	-0.221	0.165	-0.115	0.262	**-0.408**
IER	0.160	-0.164	-0.246	0.057	-0.084	0.144	**-0.389**
IEO	-0.006	-0.239	-0.120	**0.433**	-0.171	**0.443**	**-0.441**

IRSEAD: Index of relative socio-economic advantage and disadvantage
IRSED: Index of relative socio-economic disadvantage
IER: Index of economic resources
IEO: Index of education and occupation

3.7. Pollutants and lung function

3.7.1. Single pollutant models

Results of all single pollutant models and outcomes considered of clinical importance are shown in Table 3.21. and Table 3.22. These are adjusted for age, gender, height (where appropriate), parental education and two SEIFA indices: relative socio-economic advantage and disadvantage, and education and occupation. Effect estimates per unit for the pollutant exposures are shown, with 95% confidence intervals (CIs), and P-values. In this section, findings are summarised, by pollutant, for outcomes considered to be of major clinical significance.

Bsp

No significant effects were seen for the outcomes considered in Table 3.21 and 3.22.

$PM_{2.5}$

Small but significant increases in FEV_1/FVC ratio pre- and post-bronchodilator were found for lifetime exposure to $PM_{2.5}$. For recent exposure, both FEV_1 and FVC post-bronchodilator decreased: 0.18 ml (0.00, 0.35) per $\mu g/m^3$ and 0.16 ml (0.03, 0.28) per $\mu g/m^3$ respectively. Per interquartile range (IQR) effects were -24.0 ml (-48.4, 0.33) and 46.3 ml (-82.7, -9.95) respectively. FEV_1/FVC ratio post-bronchodilator increased with recent exposure, somewhat more strongly than the effect seen with lifetime exposure: 0.58 (0.07, 1.10) per $\mu g/m^3$ and 0.62 (0.07, 1.17) per IQR. Exhaled NO increased significantly with recent exposure, by about 2% per $\mu g/m^3$ and 2% per IQR.

PM_{10}

Post-bronchodilator FEV_1 and FVC decreased with increasing lifetime PM_{10}, although only the FEV_1 effect was statistically significant: effect estimates were -5.1 ml (-10.1, -0.1) and -7.1 ml (-4.4, 0.3) per $\mu g/m^3$, respectively. Per IQR effect estimates were 19.3 ml (-38.3,-0.23) and -26.8 ml (-54.7, 1.07) respectively.

Exhaled NO significantly increased with PM_{10}, but this association was statistically significant for lifetime exposure only: increases of 4% per $\mu g/m^3$ (1%, 6%) for lifetime exposure and 2% per $\mu g/m^3$ (0%, 3%) for recent exposure. Per IQR effects were 15% (5%, 26%) and 7% (-1%, 15%), respectively.

NO_2

FEV_1 and FVC significantly decreased, both before and after bronchodilator use, ranging from 5.9 to 6.1 ml per ppb, or 25.3 to 26.4 ml per IQR (about 1.3% drop in mean lung function) for lifetime exposure. Effect estimates were somewhat larger for recent exposure, ranging from 6.8 to 7. 3ml per ppb, or 27.5 to 29.6 ml per IQR.

Exhaled NO significantly increased with increasing NO_2 by 3% (1%, 5%) per ppb for lifetime exposure and 2% (1%, 3%) ppb for recent exposure. Per IQR, these increases are 13% (5%, 21%) and 14% (6%, 23%), respectively.

All effects of NO_2 were clearly linear with the exception of exhaled NO which increased linearly up till about 12 ppb NO_2 (approximately the third quartile of NO_2 exposure) when the effects reached a peak (of about 7 ppb exhaled NO) for both lifetime and recent exposure, and decreased somewhat over the remaining range.

O_3

Findings for O_3 were generally in a 'protective' direction, which might be related to (a) a true protective effect of O_3, (b) the effects found for NO_2 and strong negative correlation between NO_2 and O_3, or (c) other confounding variables. For FEV_1 post-bronchodilator, O_3 showed a significant positive effect; 5.2 ml (1.2, 9.1) per ppb for lifetime exposure. Statistically significant and positive effects also existed for recent O_3 exposure and FEV_1 and FVC post-bronchodilator. For exhaled NO, O_3 showed significant protective effects.

CO

CO showed no impact on lung function measures for lifetime exposure, and increasing effects on FEV_1 and FEV_1/FVC ratio pre-bronchodilator for recent exposure.

SO_2

For exhaled NO, SO_2 showed a significant negative effect for both lifetime and recent exposure. This effect became non-significant with the exclusion of Port Pirie from the analyses. Exclusion of Port Pirie from the recent SO_2 exposure models showed significant decrease in FVC pre-bronchodilator: -32.9 ml (--61.5, -4.2) per ppb. A similar but non-significant decrease occurred for FVC post-bronchodilator: -35.0 ml (-78.1, 8.0) per ppb.

In summary, the most important findings from the single pollutant models are the adverse effects of NO_2, PM_{10} and $PM_{2.5}$ on lung volumes (FEV_1 and FVC), which was not reversible with bronchodilator, and on airway inflammation (measured as exhaled NO).

Table 3.21. Lung function: single pollutant models. Lifetime exposure; effects per unit pollutant. Bolded entries represent effects significant at the p=0.05 level.

Measure	Bsp 10^{-4} m^{-1}	$PM_{2.5}$ $\mu g/m^3$	PM_{10} $\mu g/m^3$	NO_2 ppb	O_3 ppb	CO ppm	SO_2 ppb
FEV_1 Pre-bronchodilator/ml	51.3 (-54.0, 156.6) P = 0.33	2.1 (-4.8, 8.9) P = 0.55	-4.4 (-9.8, 1.0) P = 0.11	**-6.1** **(-9.8, -2.3)** **P = 0.001**	3.2 (-1.4, 7.8) P = 0.16	44.4 (-88.5, 177.3) P = 0.49	-1.0 (-10.7, 8.6) P = 0.82
FEV_1 Post-bronchodilator/ml	-58.0 (-190.7, 74.6) P = 0.38	1.7 (-5.3, 8.7) P = 0.63	**-5.1** **(-10.1, -0.1)** **P = 0.047**	**-6.0** **(-9.6, -2.4)** **P = 0.001**	**5.2** **(1.2, 9.1)** **P = 0.011**	-23.7 (-141.9, 94.5) P = 0.68	-2.0 (-9.2, 5.1) P = 0.56
FVC Pre-bronchodilator	11.6 (-126.2, 149.3) P = 0.86	-1.4 (-7.7, 5.0) P = 0.66	-3.5 (-9.5, 2.5) P = 0.24	**-5.9** **(-9.4, -2.3)** **P = 0.001**	2.7 (-2.0, 7.5) P = 0.24	-33.6 (-159.7, 92.5) P = 0.58	-4.1 (-16.1, 7.9) P = 0.49
FVC Post-bronchodilator/ml	-109.4 (-275.6, 56.7) P = 0.19	-1.8 (-10.3, 6.7) P = 0.67	-7.1 (-14.4, 0.3) P = 0.05	**-5.9** **(-10.3, -1.6)** **P = 0.008**	3.9 (-2.3, 10.1) P = 0.21	-79.4 (-220.2, 61.3) P = 0.25	-7.0 (-18.6, 4.7) P = 0.22
FEV_1/FVC Ratio Pre-bronchodilator (%)	1.42 (-1.25, 4.08) P = 0.28	**0.18** **(0.00, 0.35)** **P = 0.046**	-0.05 (-0.27, 0.16) P = 0.63	**-0.05** **(-0.17, 0.08)** **P = 0.46**	0.03 (-0.11, 0.17) P = 0.66	2.62 (-1.94, 7.18) P = 0.24	0.11 (-0.22, 0.45) P = 0.49
FEV_1/FVC Ratio Post-bronchodilator (%)	0.68 (-2.09, 3.44) P = 0.62	**0.16** **(0.03, 0.28)** **P = 0.015**	0.08 (-0.10, 0.26) P = 0.35	-0.01 (-0.10, 0.08) P = 0.87	0.06 (-0.05, 0.16) P = 0.27	2.19 (-0.78, 5.16) P = 0.14	0.08 (-0.25, 0.41) P = 0.63
Exhaled NO*	1.02 (0.59, 1.77) P = 0.92	0.99 (0.96, 1.01) P = 0.35	**1.04** **(1.01, 1.06)** **P = 0.004**	**1.03** **(1.01, 1.05)** **P = 0.002**	**0.96** **(0.94, 0.98)** **P < 0.0001**	0.74 (0.50, 1.11) P = 0.13	**0.98** **(0.96, 0.99)** **P = 0.009**

* Coefficient represents relative increase in exhaled NO, per unit pollutant

Table 3.22. Lung function: single pollutant models. Recent exposure; effects per unit pollutant. Bolded entries represent effects significant at the p=0.05 level.

Measure	Bsp 10^{-4} m^{-1}	$PM_{2.5}$ $\mu g/m^3$	PM_{10} $\mu g/m^3$	NO_2 ppb	O_3 ppb	CO ppm	SO_2 ppb
FEV_1 Pre-bronchodilator/ml	55.1 (-38.7, 148.9) P = 0.23	6.6 (-7.9, 21.1) P = 0.35	-1.1 (-4.8, 2.7) P = 0.57	**-7.1** **(-11.4, -2.8)** **P = 0.001**	4.1 (-0.9, 9.2) P = 0.10	**181.6** **(43.8, 319.5)** **P = 0.011**	-3.4 (-16.1, 9.3) P = 0.58
FEV_1 Post-bronchodilator/ml	-43.2 (-164.1, 77.7) P = 0.47	-22.5 (-45.2, 0.3) P = 0.05	-3.0 (-6.9, 0.8) P = 0.11	**-7.3** **(-11.4, -3.3)** **P = 0.0007**	**5.8** **(1.8, 9.8)** **P = 0.005**	74.7 (-106.6, 256.0) P = 0.40	-5.0 (-14.9, 4.8) P = 0.29
FVC Pre-bronchodilator	39.2 (-89.7, 168.0) P = 0.53	-12.4 (-36.1, 11.3) P = 0.28	-0.5 (-4.1, 3.1) P = 0.78	**-6.8** **(-10.9, -2.7)** **P = 0.001**	4.6 (-0.6, 9.8) P = 0.08	59.9 (-101.8, 221.7) P = 0.45	-7.0 (-20.4, 6.5) P = 0.29
FVC Post-bronchodilator/ml	-34.4 (-196.3, 127.5) P = 0.66	**-43.4** **(-77.4, -9.3)** **P = 0.015**	-3.1 (-8.1, 1.8) P = 0.20	**-6.9** **(-12.1, -1.6)** **P = 0.011**	**6.6** **(0.9, 12.3)** **P = 0.024**	45.3 (-181.1, 271.6) P = 0.68	-8.8 (-22.5, 5.0) P = 0.19
FEV_1/FVC Ratio Pre-bronchodilator (%)	0.27 (-2.45, 2.99) P = 0.84	0.68 (-0.16, 1.52) P = 0.10	-0.03 (-0.18, 0.12) P = 0.67	-0.06 (-0.19, 0.08) P = 0.42	-0.00 (-0.14, 0.14) P = 0.97	**5.40** **(0.85, 9.94)** **P = 0.021*I**	0.12 (-0.26, 0.50) P = 0.50
FEV_1/FVC Ratio Post-bronchodilator (%)	-1.32 (-4.63, 1.99) P = 0.42	**0.58** **(0.07, 1.10)** **P = 0.027**	-0.01 (-0.14, 0.11) P = 0.82	-0.05 (-0.14, 0.05) P = 0.32	-0.02 (-0.13, 0.08) P = 0.64	0.95 (-3.40, 5.29) P = 0.65	0.03 (-0.35, 0.42) P = 0.85
Exhaled NO	1.25 (0.97, 1.62) P = 0.08	**1.02** **(1.02, 1.02)** **P < 0.0001**	1.02 (1.00, 1.03) P = 0.07	**1.03** **(1.01, 1.05)** **P = 0.0008**	**0.96** **(0.94, 0.98)** **P = 0.0001**	0.89 (0.48, 1.66) P = 0.70	**0.98** **(0.96, 0.99)** **P = 0.011**

* Coefficient represents relative increase in exhaled NO, per unit pollutant

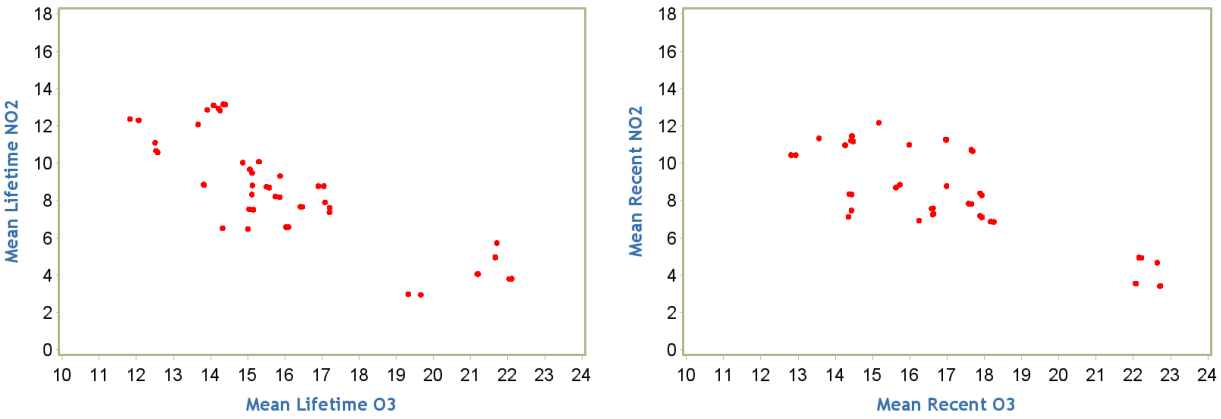
3.7.2. Joint pollutant models

Detailed results are given in Appendices - Part B.

Joint NO_2 - O_3 model

NO_2 and O_3 are strongly negatively correlated (r = -0.78 and -0.76 for lifetime and recent respectively) and where effects on lung function are demonstrated these are in opposite directions. A joint pollutant model was therefore fitted to health outcomes for these pollutants. The difficulty of separating effects of NO_2 and O_3 is illustrated in Figure 3.2., showing mean exposures, by school, for NO_2 and O_3. The small number of schools in locations with high mean O_3 levels for lifetime and recent exposures were in locations with the lowest NO_2 levels.

Figure 3.2. Scatter plots of NO_2 and O_3 exposures.



To minimise the influence of the high-ozone sites, a sensitivity analysis examined single and joint pollutant models, restricting analyses to sites with mean exposure less than 20 ppb. This resulted in the omission of 10 schools (one in Queensland, two at one site in South Australia and seven at three sites in Western Australia)

Joint pollutant NO_2-O_3 model including all sites (Table 3.23., Table 3.24.): Effects of NO_2 noted above reduced only slightly in magnitude (some effects becoming just non-significant) or strengthened. Effects of O_3 reduced considerably, to non-significance in most cases, with only exhaled NO remaining a significant effect.

Joint pollutant NO_2-O_3 model excluding high-ozone schools (Table 3.25., Table 3.26.): These analyses largely confirmed the NO_2 effects. While effect sizes remained consistent with the unrestricted analyses, in some cases significance was reduced, perhaps due to the smaller sample size. O_3 effects for FEV_1/FVC ratio post-bronchodilator and exhaled NO were consistent with the unrestricted model. Other spirometry measures were either non-significant or showed a significant decline with increasing O_3 (FVC post-bronchodilator - lifetime exposure - and percent change in FEV_1 - recent exposure).

In summary, joint pollutant and restricted O_3 models largely confirmed the NO_2 findings with (from the joint model) decreases in lung volume of 6.3 to 10 ml per ppb of NO_2 in FEV_1 and FVC pre- and post-bronchodilator and 26.3 to 43.1 ml per IQR. These effects showed no evidence of non-linearity in either the polynomial or nonparametric models. The significant protective O_3 effects seen in the single pollutant unrestricted analysis appear related to the large negative correlation with NO_2. A 'paradoxical' effect remains for O_3, however, for exhaled NO.

Table 3.23. Lifetime exposure: effects per unit pollutant, all schools. Bolded entries represent effects significant at the p=0.05 level.

	NO2 (ppb): One pollutant model	NO_2 (ppb): Joint pollutant model	O_3 (ppb): One pollutant model	O_3 (ppb): Joint pollutant model
FEV_1 Pre-bronchodilator (ml)	**-6.1 (-9.8, -2.3) P = 0.001**	-6.3 (-13.2, 0.7) P = 0.07	3.2 (-1.4, 7.8) P = 0.16	-1.2 (-7.9, 5.6) P = 0.72
FEV_1 Post-bronchodilator (ml)	**-6.0 (-9.6, -2.4) P = 0.001**	-6.1 (-13.1, 0.9) P = 0.08	**5.2 (1.2, 9.1) P = 0.011**	0.9 (-6.1, 7.9) P = 0.79
FVC Pre-bronchodilator (ml)	**-5.9 (-9.4, -2.3) P = 0.001**	**-10.0 (-16.7, -3.3) P = 0.004**	2.7 (-2.0, 7.5) P = 0.24	-4.3 (-11.1, 2.6) P = 0.21
FVC Post-bronchodilator (ml)	**-5.9 (-10.3, -1.6) P = 0.008**	**-9.8 (-17.5, -2.1) P = 0.013**	3.9 (-2.3, 10.1) P = 0.21	-3.0 (-13.1, 7.1) P = 0.55
FEV_1/FVC Ratio - Pre-bronchodilator	-0.05 (-0.17, 0.08) P = 0.46	0.07 (-0.20, 0.33) P = 0.60	0.03 (-0.11, 0.17) P = 0.66	0.08 (-0.16, 0.32) P = 0.51
FEV_1/FVC Ratio - Post-bronchodilator	-0.01 (-0.10, 0.08) P = 0.87	0.14 (-0.08, 0.37) P = 0.20	0.06 (-0.05, 0.16) P = 0.27	0.16 (-0.05, 0.36) P = 0.13
Exhaled NO (ppb)	**1.03 (1.01, 1.05) P = 0.002**	**1.02 (1.00, 1.04) P = 0.046**	**0.96 (0.94, 0.98) P < 0.0001**	**0.97 (0.95, 0.99) P = 0.003**

Table 3.24. Recent exposure: effects per unit pollutant, all schools. Bolded entries represent effects significant at the p=0.05 level.

	NO2 (ppb): One pollutant model	NO_2 (ppb): Joint pollutant model	O_3 (ppb): One pollutant model	O_3 (ppb): Joint pollutant model
FEV_1 Pre-bronchodilator (ml)	**-7.1 (-11.4, -2.8) P = 0.001**	-6.0 (-14.4, 2.4) P = 0.15	4.1 (-0.9, 9.2) P = 0.10	0.2 (-7.4, 7.7) P = 0.96
FEV_1 Post-bronchodilator (ml)	**-7.3 (-11.4, -3.3) P = 0.0007**	**-8.6 (-17.0, -0.2) P = 0.045**	5.8 (1.8, 9.8) P = 0.005*I	0.2 (-6.2, 6.5) P = 0.96
FVC Pre-bronchodilator (ml)	**-6.8 (-10.9, -2.7) P = 0.001**	-7.5 (-17.0, 2.0) P = 0.11	4.6 (-0.6, 9.8) P = 0.08	-0.4 (-8.5, 7.7) P = 0.92
FVC Post-bronchodilator (ml)	**-6.9 (-12.1, -1.6) P = 0.011**	-6.7 (-16.7, 3.4) P = 0.18	6.6 (0.9, 12.3) P = 0.024*I	2.2 (-6.5, 10.8) P = 0.61
FEV_1/FVC Ratio - Pre-bronchodilator	-0.06 (-0.19, 0.08) P = 0.42	-0.03 (-0.24, 0.18) P = 0.74	-0.00 (-0.14, 0.14) P = 0.97	-0.02 (-0.19, 0.15) P = 0.77
FEV_1/FVC Ratio - Post-bronchodilator	-0.05 (-0.14, 0.05) P = 0.32	-0.15 (-0.37, 0.07) P = 0.16	-0.02 (-0.13, 0.08) P = 0.64	-0.12 (-0.30, 0.06) P = 0.17
Exhaled NO (ppb)	**1.03 (1.01, 1.05) P = 0.0008*I**	**1.02 (1.00, 1.05) P = 0.05**	**0.96 (0.94, 0.98) P = 0.0001**	**0.98 (0.95, 1.00) P = 0.026**

Table 3.25. Lifetime exposure: effects per unit pollutant, 10 high-O_3 schools omitted. Bolded entries represent effects significant at the p=0.05 level.

	NO_2 (ppb): One pollutant model	NO_2(ppb): Joint pollutant model	O_3 (ppb): One pollutant model	O_3 (ppb): Joint pollutant model
FEV_1 Pre-bronchodilator (ml)	**-6.6 (-11.2, -2.0) P = 0.005**	-7.1 (-14.5, 0.4) P = 0.06	1.0 (-7.1, 9.1) P = 0.80	-4.0 (-14.6, 6.6) P = 0.44
FEV_1 Post-bronchodilator (ml)	**-5.2 (-9.9, -0.6) P = 0.028**	**-8.6 (-15.6, -1.5) P = 0.019**	0.1 (-8.9, 9.1) P = 0.98	-5.9 (-17.0, 5.2) P = 0.28
FVC Pre-bronchodilator (ml)	**-7.4 (-11.8, -3.0) P = 0.001**	**-11.9 (-19.1, -4.7) P = 0.002**	0.0 (-11.0, 11.1) P = 0.99	-8.3 (-21.2, 4.6) P = 0.19
FVC Post-bronchodilator (ml)	**-5.7 (-10.9, -0.5) P = 0.032**	**-13.4 (-20.6, -6.3) P = 0.0005**	-5.7 (-17.9, 6.6) P = 0.35	**-15.1 (-29.1, -1.0) P = 0.036**
FEV_1/FVC Ratio - Pre-bronchodilator	-0.04 (-0.19, 0.11) P = 0.56	0.11 (-0.17, 0.39) P = 0.44	0.11 (-0.12, 0.34) P = 0.32	0.19 (-0.12, 0.49) P = 0.21
FEV_1/FVC Ratio - Post-bronchodilator	0.00 (-0.12, 0.12) P = 0.98	0.16 (-0.07, 0.40) P = 0.17	**0.23 (0.06, 0.40) P = 0.008**	**0.35 (0.11, 0.58) P = 0.004**
Exhaled NO (ppb)	1.01 (1.00, 1.03) P = 0.14	1.01 (1.00, 1.03) P = 0.13	**0.95 (0.92, 0.98) P = 0.005**	**0.96 (0.93, 1.00) P = 0.037**

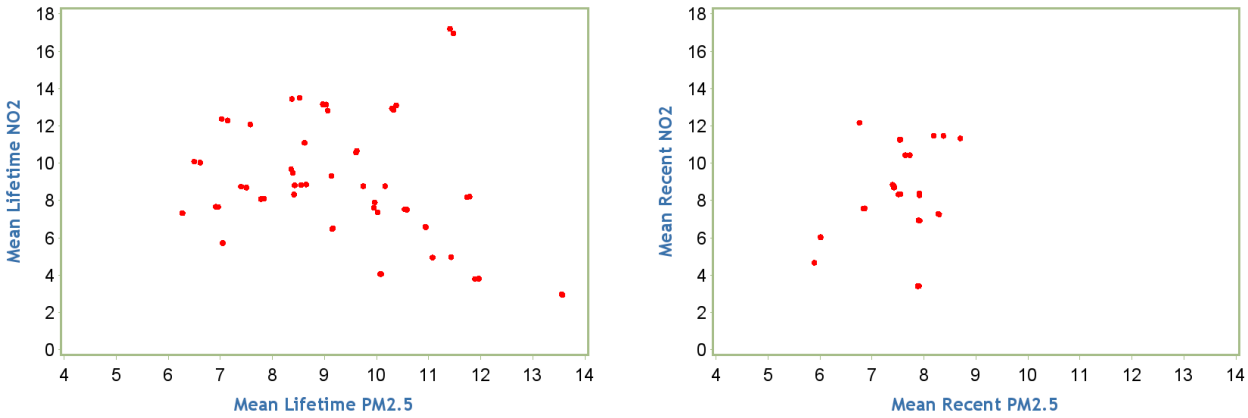
Table 3.26. Recent exposure: effects per unit pollutant, 10 high-O_3 schools omitted. Bolded entries represent effects significant at the p=0.05 level.

	NO_2(ppb): One pollutant model	NO_2 (ppb) Joint pollutant model	O_3(ppb): One pollutant model	O_3(ppb) Joint pollutant model
FEV_1 Pre-bronchodilator (ml)	**-7.3 (-12.6, -1.9) P = 0.008**	-5.0 (-12.8, 2.8) P = 0.20	4.3 (-2.9, 11.4) P = 0.23	1.6 (-6.9, 10.1) P = 0.70
FEV_1 Post-bronchodilator (ml)	**-5.6 (-10.8, -0.4) P = 0.036**	**-8.1 (-16.6, 0.3) P = 0.05**	1.0 (-6.3, 8.3) P = 0.77	-3.3 (-11.5, 4.8) P = 0.41
FVC Pre-bronchodilator (ml)	**-7.7 (-12.9, -2.5) P = 0.004**	-7.7 (-17.1, 1.7) P = 0.10	5.5 (-3.6, 14.6) P = 0.22	1.4 (-9.4, 12.1) P = 0.79
FVC Post-bronchodilator (ml)	-4.9 (-11.0, 1.2) P = 0.11	-7.2 (-17.4, 3.1) P = 0.16	2.0 (-7.1, 11.1) P = 0.65	-1.8 (-12.5, 8.9) P = 0.72
FEV_1/FVC Ratio - Pre-bronchodilator	-0.06 (-0.21, 0.1) P = 0.40	-0.00 (-0.22, 0.21) P = 0.96	0.01 (-0.22, 0.23) P = 0.94	0.01 (-0.21, 0.22) P = 0.95
FEV_1/FVC Ratio - Post-bronchodilator	-0.06 (-0.18, 0.1) P = 0.30	-0.13 (-0.35, 0.1) P = 0.26	-0.08 (-0.31, 0.1) P = 0.48	-0.14 (-0.41, 0.12) P = 0.26
Exhaled NO (ppb)	1.02 (1.00, 1.04) P = 0.05	1.02 (1.00, 1.04) P = 0.10	**0.97 (0.94, 0.99) P = 0.020**	0.98 (0.95, 1.01) P = 0.19

Joint NO_2-$PM_{2.5}$ model

NO_2 and $PM_{2.5}$ exposures are positively correlated, more strongly for lifetime exposure than recent exposure (Figure 3.3).

Figure 3.3. Scatterplot of NO_2 and $PM_{2.5}$ exposures.



A joint-NO_2-$PM_{2.5}$ model (Table 3.27.,

Table 3.28.) provided very similar estimates to the respective single pollutant models, providing some evidence of independent effects of these two pollutants.

Table 3.27. Lifetime exposure: effects per unit pollutant. Bolded entries represent effects significant at the p=0.05 level.

	NO_2 (ppb): One pollutant model	**NO_2(ppb): Joint pollutant model**	**$PM_{2.5}$(μg/m3): One pollutant model**	**$PM_{2.5}$ (μg/m3): Joint pollutant model**
FEV_1 Pre-bronchodilator (ml)	**-6.1 (-9.8, -2.3) P = 0.001**	**-6.2 (-10.2, -2.3) P = 0.002**	2.1 (-4.8, 8.9) P = 0.55	0.4 (-5.8, 6.7) P = 0.88
FEV_1 Post-bronchodilator (ml)	**-6.0 (-9.6, -2.4) P = 0.001**	**-6.1 (-10.1, -2.2) P = 0.003**	1.7 (-5.3, 8.7) P = 0.63	0.2 (-6.5, 7.0) P = 0.94
FVC Pre-bronchodilator (ml)	**-5.9 (-9.4, -2.3) P = 0.001**	**-6.2 (-9.9, -2.4) P = 0.001**	-1.4 (-7.7, 5.0) P = 0.66	-3.0 (-9.0, 2.9) P = 0.30
FVC Post-bronchodilator (ml)	**-5.9 (-10.3, -1.6) P = 0.008**	**-6.2 (-11.0, -1.4) P = 0.013**	-1.8 (-10.3, 6.7) P = 0.67	-3.4 (-11.8, 5.0) P = 0.42
FEV_1/FVC Ratio - Pre-bronchodilator	-0.05 (-0.17, 0.08) P = 0.46	-0.03 (-0.2, 0.10) P = 0.65	**0.18 (0.00, 0.35) P = 0.046**	0.17 (-0.01, 0.35) P = 0.06
FEV_1/FVC Ratio - Post-bronchodilator	-0.01 (-0.10, 0.08) P = 0.87	-0.00 (-0.09, 0.08) P = 0.96	**0.16 (0.03, 0.28) P = 0.015**	**0.16 (0.03, 0.29) P = 0.019**
Exhaled NO	**1.03 (1.01, 1.05) P = 0.002**	**1.03 (1.02, 1.05) P < 0.0001**	0.99 (0.96, 1.01) P = 0.35	0.99 (0.96, 1.01) P = 0.17

Table 3.28. Recent exposure: effects per unit pollutant. Bolded entries represent effects significant at the p=0.05 level.

	NO_2 (ppb): One pollutant model	NO_2 (ppb): Joint pollutant model	$PM_{2.5}$(µg/m3): One pollutant model	$PM_{2.5}$(µg/m3): Joint pollutant model
FEV_1 Pre-bronchodilator (ml)	**-7.1 (-11.4, -2.8) P = 0.001**	-4.8 (-10.8, 1.2) P = 0.11	6.6 (-7.9, 21.1) P = 0.35	11.8 (-4.9, 28.6) P = 0.15
FEV_1 Post-bronchodilator (ml)	**-7.3 (-11.4, -3.3) P = 0.0007**	**-7.2 (-13.2, -1.2) P = 0.020**	-22.5 (-45.2, 0.3) P = 0.05	-14.5 (-34.4, 5.4) P = 0.14
FVC Pre-bronchodilator (ml)	**-6.8 (-10.9, -2.7) P = 0.001**	**-7.4 (-14.6, -0.3) P = 0.042**	-12.4 (-36, 11.3) P = 0.28	-4.2 (-26.9, 18.6) P = 0.70
FVC Post-bronchodilator (ml)	**-6.9 (-12.1, -1.6) P = 0.011**	-6.9 (-14.2, 0.5) P = 0.06	**-43.4 (-77.4, -9.3) P = 0.015**	**-35.8 (-65.2, -6.3) P = 0.019**
FEV_1/FVC Ratio - Pre-bronchodilator	-0.06 (-0.19, 0.1) P = 0.42	0.05 (-0.11, 0.21) P = 0.54	0.68 (-0.16, 1.52) P = 0.10	0.63 (-0.17, 1.42) P = 0.11
FEV_1/FVC Ratio - Post-bronchodilator	-0.05 (-0.14, 0.05) P = 0.32	-0.06 (-0.2, 0.03) P = 0.18	**0.58 (0.07, 1.10) P = 0.027**	**0.66 (0.15, 1.16) P = 0.013**
Exhaled NO (ppb)	**1.03 (1.01, 1.05) P = 0.0008**	**1.05 (1.05, 1.05) P < 0.0001**	**1.02 (1.02, 1.02) P < 0.0001**	**0.94 (0.94, 0.94) P < 0.0001**

Joint SO_2-O_3 Model

SO_2 and O_3 were negatively correlated for lifetime exposure, but positively correlated for recent exposure (Figure 3.4. Scatterplot of SO2 and O3 exposures.). A joint SO_2 - O_3 model (Table 3.30. Recent exposure) showed declining effects in FEV_1 and FVC pre- and post-bronchodilator with increasing lifetime SO_2 and no effects for these lung function measures with lifetime O_3. For recent exposures, effects of SO_2 were similar, although only the pre-bronchodilator effects were statistically significant; additionally, FEV_1/FVC ratio post-bronchodilator significantly increased with recent SO_2. FEV_1 and FVC post-bronchodilator decreased significantly with recent O_3, reversing the increasing effects seen in the single pollutant O_3 model.

Figure 3.4. Scatterplot of SO_2 and O_3 exposures.

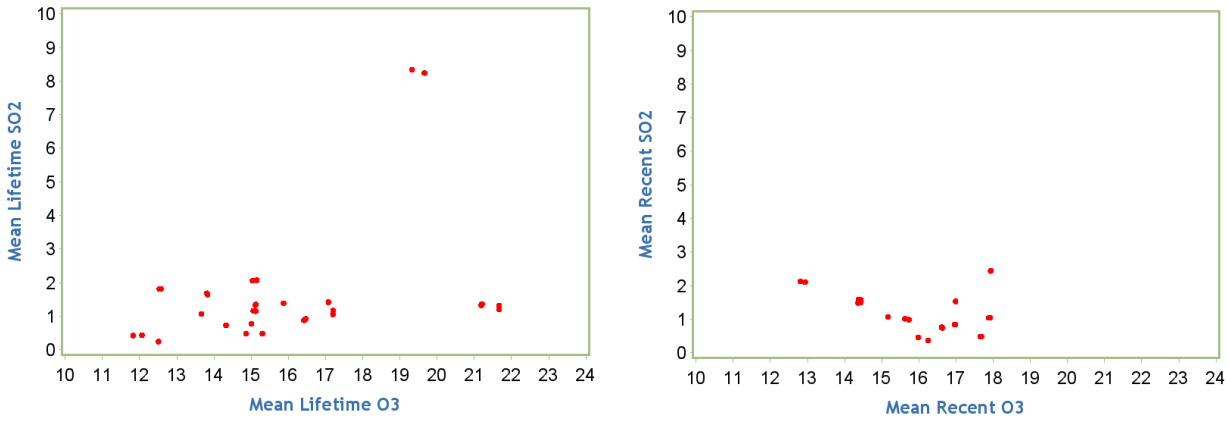


Table 3.29. Lifetime exposure: effects per unit pollutant. Bolded entries represent effects significant at the p=0.05 level.

	SO_2 (ppb): One pollutant model	SO_2 (ppb): Joint pollutant model	O_3 (ppb): One pollutant model	O_3 (ppb): Joint pollutant model
FEV_1 Pre-bronchodilator (ml)	-1.0 (-10.7, 8.6) P = 0.82	**-8.9 (-16.5, -1.3) P = 0.023**	3.2 (-1.4, 7.8) P = 0.16	2.9 (-2.8, 8.6) P = 0.29
FEV_1 Post-bronchodilator (ml)	-2.0 (-9.2, 5.1) P = 0.56	**-8.3 (-15.2, -1.5) P = 0.019**	**5.2 (1.2, 9.1) P = 0.011**	2.6 (-3.0, 8.1) P = 0.35
FVC Pre-bronchodilator (ml)	-4.1 (-16.1, 7.9) P = 0.49	**-11.3 (-21.7, -0.9) P = 0.034**	2.7 (-2.0, 7.5) P = 0.24	0.7 (-7.0, 8.3) P = 0.86
FVC Post-bronchodilator (ml)	-7.0 (-18.6, 4.7) P = 0.22	**-12.5 (-21.9, -3.1) P = 0.011**	3.9 (-2.3, 10.1) P = 0.21	-0.2 (-7.3, 6.9) P = 0.95
FEV_1/FVC Ratio - Pre-bronchodilator	0.11 (-0.22, 0.45) P = 0.49	0.06 (-0.33, 0.45) P = 0.75	0.03 (-0.11, 0.17) P = 0.66	0.11 (-0.05, 0.27) P = 0.18
FEV_1/FVC Ratio - Post-bronchodilator	0.08 (-0.25, 0.41) P = 0.63	0.04 (-0.34, 0.43) P = 0.81	0.06 (-0.05, 0.16) P = 0.27	0.08 (-0.03, 0.20) P = 0.14
Exhaled NO (ppb)	**0.98 (0.96, 0.99) P = 0.009**	0.99 (0.98, 1.01) P = 0.32	**0.96 (0.94, 0.98) P < 0.0001**	**0.95 (0.93, 0.97) P < 0.0001**

Table 3.30. Recent exposure: effects per unit pollutant. Bolded entries represent effects significant at the p=0.05 level.

	SO_2 (ppb): One pollutant model	SO_2 (ppb): Joint pollutant model	O_3 (ppb): One pollutant model	O_3 (ppb): Joint pollutant model
FEV_1 Pre-bronchodilator (ml)	-3.4 (-16.1, 9.3) P = 0.58	**-30.5 (-58.7, -2.2) P = 0.036**	4.1 (-0.9, 9.2) P = 0.10	-6.2 (-16.4, 4.1) P = 0.22
FEV_1 Post-bronchodilator (ml)	-5.0 (-14.9, 4.8) P = 0.29	-25.4 (-66, 15.2) P = 0.20	**5.8 (1.8, 9.8) P = 0.005**	**-10.7 (-19.6, -1.8) P = 0.021**
FVC Pre-bronchodilator (ml)	-7.0 (-20.4, 6.5) P = 0.29	**-46.8 (-78, -15.1) P = 0.006**	4.6 (-0.6, 9.8) P = 0.08	-3.8 (-12.6, 5.0) P = 0.37
FVC Post-bronchodilator (ml)	-8.8 (-22.5, 5.0) P = 0.19	-46.7 (-97.2, 3.9) P = 0.06	**6.6 (0.9, 12.3) P = 0.024**	**-9.7 (-17.5, -1.9) P = 0.018**
FEV_1/FVC Ratio - Pre-bronchodilator	0.12 (-0.26, 0.50) P = 0.50	0.54 (-0.32, 1.40) P = 0.20	-0.0 (-0.14, 0.14) P = 0.97	-0.1 (-0.41, 0.19) P = 0.46
FEV_1/FVC Ratio - Post-bronchodilator	0.03 (-0.35, 0.42) P = 0.85	**0.93 (0.30, 1.56) P = 0.006**	-0.0 (-0.13, 0.08) P = 0.64	-0.1 (-0.37, 0.19) P = 0.51
Exhaled NO (ppb)	**0.98 (0.96, 0.99) P = 0.011**	1.01 (0.92, 1.11) P = 0.76	**0.96 (0.94, 0.98) P = 0.0001**	1.00 (0.98, 1.02) P = 0.89

3.7.3. Interaction models

Models were extended to incorporate interaction terms to allow for the detection of modification of pollutant effects by atopy (a positive response to one or more of the eight allergens tested), current asthma and gender. Evidence of an interactive effect was assumed when the interaction was significant and at least one subgroup effect was significant at the 5% level.

Atopy

No significant effect modification was found in relation to Bsp, NO_2, and O_3. Effect modification was most marked for SO_2 (Table 3.31.), with atopic children having significant decreases in lung function on many measures, and non-atopic children showing no effects, for both lifetime and recent exposure. Effects persisted when Port Pirie was excluded.

Other pollutants showed evidence of interactive effects, but these were somewhat inconsistent. For recent exposure, the increase in exhaled NO with Bsp and PM_{10} was significantly greater in atopic children, and non-significant within non-atopic children. Exhaled NO increased by 2% (1%, 3%) per μg/m3 recent PM_{10} exposure in atopic children, with virtually no effect in non-atopic children, with P = 0.003 for interaction). The relationship between exhaled NO and recent Bsp exposure was consistent with this pattern (effect estimate 28% per 10^{-4} m^{-1} (1%, 65%) in atopic children, and no effect in non-atopic children, with P = 0.014 for interaction), but the effect in atopic children fell just short of significance (P=0.053).

Conversely, adverse effects of lifetime CO on FVC post-bronchodilator were greater in non-atopic children and non-significant in atopic children (decrease of 12.3 ml per ppm (-142, 166) for atopic children, and -172 ml per ppm (-305, -40) for non-atopic children, with P = 0.01 for interaction). No effect modification of CO effects was seen for recent exposure.

FEV_1/FVC ratio post-bronchodilator was not significantly related to recent $PM_{2.5}$ in atopic children but increased significantly with $PM_{2.5}$ in non-atopic children (effect estimate 0.03 per μg/m3 $PM_{2.5}$ (-0.47, 1.08) in atopic children, 1.28 (0.83, 1.73) for non-atopic children, with P = 0.036 for interaction).

Gender

Atopic status was included in the interaction models for gender.

No significant effect modification by gender was found in relation to CO. Where evidence of effect modification occurred, it was predominantly males who showed the greater (or only) effects. The evidence for male specific effects (in terms of interaction tests) was stronger than that for the female specific effects.

Females showed some specific effects for particulate matter and O_3; males showed specific effects for NO_2 and SO_2.

For FEV_1 post-bronchodilator, the effect estimates for lifetime NO_2 were -7.0 ml (-11.6, -2.4) per ppb for males, -3.4 ml (-8.5, 1.8) per ppb for females, with P =0.057 for interaction, and for recent NO_2, were -9.6 ml (-14.7, -4.4) per ppb for males, -4.7 ml (-10.2, 0.8) per ppb for females, with P =0.018 for interaction.

FVC pre- and post-bronchodilator decreased with lifetime and recent SO_2, for males only (Table 3.32.). For FVC post-bronchodilator, effect estimates for lifetime SO_2 were -16.1 (-25.2,--7.0) for males, -2.7 (-18.1, 12.6) for females, with P =0.012 for interaction, and for recent SO_2, were --16.3 (-26.3,-6.3) for males, -2.4 (-19.6, 14.9) for females, with P =0.019 for interaction. For FVC pre-bronchodilator, effect estimates were consistent with this pattern, but effect estimates were not quite significant.

Table 3.31. Modification of SO_2 (ppb) effects by atopic status. Bolded entries represent effects significant at the p=0.05 level.

Outcome	Lifetime exposure	P	Recent exposure	P
FEV_1 Pre-bronchodilator (ml)				
Atopic	**-17.0 (-30.3, -3.6)**	**0.014**	**-20.0 (-35.11, -4.89)**	**0.012**
Non-atopic	**-1.0 (-9.5, 7.4)**	**0.80**	**-2.0 (-14.00, 10.01)**	**0.73**
Interaction	**16.0 (6.9, 25.1)**	**0.001**	**18.0 (10.04, 25.96)**	**0.0001**
FEV_1 Post-bronchodilator (ml)				
Atopic	**-19.4 (-29.5, -9.3)**	**0.0006**	**-23.1 (-34.83, -11.45)**	**0.0005**
Non-atopic	**-0.2 (-6.7, 6.3)**	**0.95**	**-2.2 (-11.29, 6.82)**	**0.61**
Interaction	**19.2 (11.0, 27.4)**	**< 0.0001**	**20.9 (14.27, 27.54)**	**< 0.0001**
FVC Pre-bronchodilator (ml)				
Atopic	**-33.8 (-56.3, -11.3)**	**0.005**	**-38.0 (-61.98, -14.06)**	**0.003**
Non-atopic	**2.1 (-6.0, 10.1)**	**0.60**	**-1.6 (-9.86, 6.58)**	**0.68**
Interaction	**35.9 (15.9, 55.8)**	**0.001**	**36.4 (15.10, 57.66)**	**0.002**
FVC Post-bronchodilator (ml)				
Atopic	**-27.7 (-49.4, -6.0)**	**0.014**	**-27.8 (-51.3, -4.2)**	**0.023**
Non-atopic	**1.25 (-4.7, 7.2)**	**0.66**	**1.33 (-4.6, 7.3)**	**0.64**
Interaction	**29.0 (10.0, 47.9)**	**0.004**	**29.1 (9.0, 49.2)**	**0.006**
FEV_1/FVC Ratio Pre-bronchodilator (%)				
Atopic	**0.62 (0.15, 1.09)**	**0.011**	**0.66 (0.18, 1.14)**	**0.009**
Non-atopic	**-0.15 (-0.46, 0.15)**	**0.31**	**-0.05 (-0.36, 0.26)**	**0.72**
Interaction	**-0.77 (-1.17, -0.37)**	**0.0005**	**-0.71 (-1.05, -0.37)**	**0.0003**
FEV_1/FVC Ratio Post-bronchodilator (%)				
Atopic	0.31 (-0.30, 0.92)	0.29	0.26 (-0.44, 0.96)	0.44
Non-atopic	-0.06 (-0.31, 0.18)	0.58	-0.04 (-0.33, 0.25)	0.76
Interaction	-0.38 (-0.91, 0.16)	0.15	-0.30 (-0.91, 0.31)	0.31
Exhaled NO (ppb)				
Atopic	0.99 (0.96, 1.01)	0.26	0.99 (0.96, 1.01)	0.28
Non-atopic	0.98 (0.96, 1.00)	0.044	0.98 (0.96, 1.00)	0.038
Interaction	-0.01 (-0.04, 0.03)	0.67	-0.01 (-0.04, 0.03)	0.68

Table 3.32. Modification of SO_2 (ppb) effects by gender. Bolded entries represent effects significant at the p=0.05 level.

Outcome	Lifetime exposure	P	Recent exposure	P
FEV_1 Pre-bronchodilator (ml)				
Males	-7.7 (-16.5, 1.1)	0.08	-10.6 (-23.1, 1.8)	0.09
Females	-6.0 (-19.4, 7.5)	0.36	-6.4 (-22.9, 10.0)	0.42
Interaction	1.7 (-10.5, 13.9)	0.77	4.2 (-9.3, 17.6)	0.52
FEV_1 Post-bronchodilator (ml)				
Males	-9.4 (-16.0, -2.73)	0.007	-13.0 (-22.9, -3.1)	0.0126
Females	-4.9 (-15.6, 5.7)	0.34	-6.7 (-19.4, 6.0)	0.284
Interaction	4.4 (-6.3, 15.1)	0.4	6.3 (-5.3, 17.9)	0.2709
FVC Pre-bronchodilator (ml)				
Males	-16.7 (-26.5, -6.9)	0.001	-20.8 (-31.7, -9.8)	0.0008
Females	-6.3 (-24.2, 11.5)	0.46	-10.1 (-29.3, 9.2)	0.28
Interaction	10.4 (-0.9, 21.6)	0.06	10.7 (-0.7, 22.0)	0.06
FVC Post-bronchodilator (ml)				
Males	**-16.1 (-25.2, -7.0)**	**0.001**	**-16.3 (-26.3, -6.3)**	**0.003**
Females	**-2.7 (-18.1, 12.6)**	**0.71**	**-2.4 (-19.6, 14.9)**	**0.77**
Interaction	**13.4 (3.2, 23.5)**	**0.011**	**13.9 (2.5, 25.3)**	**0.019**
FEV_1/FVC Ratio Pre-bronchodilator (%)				
Males	**0.41 (0.03, 0.79)**	**0.036**	0.43 (-0.01, 0.87)	0.05
Females	**-0.12 (-0.49, 0.25)**	**0.5**	0.02 (-0.35, 0.38)	0.93
Interaction	**-0.53 (-0.75, -0.31)**	**< 0.0001**	-0.41 (-0.63, -0.19)	0.0008
FEV_1/FVC Ratio Post-bronchodilator (%)				
Males	0.30 (-0.05, 0.65)	0.08	0.25 (-0.17, 0.67)	0.2274
Females	-0.15 (-0.53, 0.24)	0.43	-0.10 (-0.53, 0.32)	0.614
Interaction	-0.45 (-0.61, -0.28)	< 0.0001	-0.36 (-0.53, -0.18)	0.0003
Expired NO (ppb)				
Males	0.98 (0.97, 1.00)	0.016	0.98 (0.97, 1.00)	0.024
Females	0.98 (0.97, 1.00)	0.035	0.98 (0.96, 1.00)	0.037
Interaction	-0.00 (-0.01, 0.01)	0.87	-0.00 (-0.01, 0.01)	0.81

FEV_1/FVC ratio pre- and post-bronchodilator decreased with lifetime O_3 in females, but not in males.

Females showed a significant increase in FEV_1 pre-bronchodilator and FEV_1/FVC ratio pre-bronchodilator with lifetime Bsp: FEV_1 pre-bronchodilator effect estimates were -28.3 ml (-180, 123) per 10^{-4} m^{-1} for males, 138 (0.1, 276) per 10^{-4} m^{-1} for females, with P =0.041 for interaction and for FEV_1/FVC ratio pre-bronchodilator were -0.94 ml (-5.0, 3.1) per 10^{-4} m^{-1} for males 7.6 (3.4,11.7) per 10^{-4} m^{-1} for females, with P =0.0008 for interaction. The pattern for FEV_1/FVC ratio pre-bronchodilator was similar for recent exposure, and held for Bsp, $PM_{2.5}$ and PM_{10}.

3.8. Pollutants and respiratory symptoms

3.8.1. Single pollutant models

Results of all single pollutant models and outcomes considered of clinical importance are shown in Table 3.33 and Table 3.34. These are adjusted for age and gender, parental education and two SEIFA indices: relative socio-economic advantage and disadvantage, and education and occupation. Effect estimates per unit pollutant exposures are shown, with 95% CIs, and P-values. Findings are summarised in this section.

Bsp

The only symptom which was significantly linearly related to Bsp (recent exposure only) was recent wheeze after exercise which showed an increased risk: odds ratio (OR) and 95% CI: 5.88 (1.56, 22.2) per 10^{-4} m^{-1} and 1.45 (1.10, 1.91) per inter-quartile range (IQR) .

$PM_{2.5}$

No symptoms showed any linear association with lifetime or recent $PM_{2.5}$.

PM_{10}

Recent cough significantly declined with both lifetime and recent exposure to PM_{10}.

NO_2

Current asthma, recent wheeze, and recent wheeze after exercise were associated with increasing NO_2, for both lifetime and recent exposure, with effects slightly greater for recent exposure. For current asthma and per ppb recent exposure NO_2, the OR was 1.06 (1.02, 1.10), with OR per IQR NO_2 1.26 (1.08, 1.48). For recent wheeze after exercise, the OR was 1.07 (1.03, 1.120) per ppb and 1.32 (1.12, 1.57) per IQR.

O_3

Symptom prevalence for wheezing and asthma decreased with lifetime exposure to O_3. No significant associations were found for recent exposure, except for an increase in prevalence of recent cough with increasing O_3.

CO

No associations between CO and symptoms were detected.

SO_2

Recent wheeze after exercise, and use of beta-agonists declined with increasing SO_2, for both lifetime and recent measures. These effects became non-significant with the exclusion of Port Pirie from the models.

In summary, the most important adverse effects noted in these single pollutant models were the effects of NO_2 exposure on risk of asthma-related symptoms.

Table 3.33. Symptoms: single pollutant models, lifetime exposure; effects per unit pollutant. Bolded entries represent effects significant at the p=0.05 level.

Symptom	Bsp 10^{-4} m^{-1}	$PM_{2.5}$ $\mu g/m^3$	PM_{10} $\mu g/m^3$	NO_2 ppb	O_3 ppb	CO ppm	SO_2 ppb
Ever had wheezing	0.93 (0.25, 3.50) P = 0.91	1.02 (0.96, 1.08) P = 0.54	0.98 (0.94, 1.02) P = 0.35	1.02 (0.99, 1.05) P = 0.13	**0.97 (0.95, 1.00) P = 0.047**	0.81 (0.25, 2.65) P = 0.73	0.97 (0.91, 1.03) P = 0.32
Ever had asthma	1.60 (0.51, 5.05) P = 0.42	1.00 (0.95, 1.06) P = 0.95	0.99 (0.95, 1.03) P = 0.54	1.02 (1.00, 1.04) P = 0.08	**0.97 (0.95, 1.00) P = 0.021**	1.11 (0.33, 3.68) P = 0.86	0.96 (0.89, 1.02) P = 0.19
Ever had medication for asthma/wheezing	1.05 (0.19, 5.68) P = 0.95	1.02 (0.96, 1.08) P = 0.53	0.99 (0.94, 1.04) P = 0.58	1.02 (0.99, 1.05) P = 0.20	0.98 (0.96, 1.01) P = 0.13	0.60 (0.19, 1.89) P = 0.37	1.00 (0.94, 1.05) P = 0.87
Ever had rhinitis	1.23 (0.26, 5.86) P = 0.79	1.03 (0.96, 1.11) P = 0.36	0.99 (0.94, 1.04) P = 0.72	0.99 (0.95, 1.03) P = 0.60	1.00 (0.97, 1.04) P = 0.85	0.66 (0.25, 1.73) P = 0.39	0.97 (0.90, 1.05) P = 0.48
Recent wheeze	1.34 (0.34, 5.24) P = 0.67	0.98 (0.91, 1.04) P = 0.50	0.99 (0.94, 1.04) P = 0.65	**1.03 (1.00, 1.07) P = 0.042**	**0.96 (0.92, 1.00) P = 0.031**	0.66 (0.21, 2.10) P = 0.48	0.97 (0.92, 1.02) P = 0.26
Recent wheeze after exercise	3.25 (0.58,18.11) P = 0.17	1.00 (0.92, 1.08) P = 0.94	1.01 (0.95, 1.08) P = 0.74	**1.06 (1.02, 1.09) P = 0.001**	**0.94 (0.89, 0.99) P = 0.012**	0.73 (0.22, 2.36) P = 0.59	**0.81 (0.74, 0.89) P < 0.0001**
Current asthma	1.56 (0.33, 7.33) P = 0.57	0.97 (0.90, 1.05) P = 0.43	0.99 (0.94, 1.04) P = 0.75	**1.05 (1.01, 1.09) P = 0.010**	**0.94 (0.90, 0.98) P = 0.001**	1.68 (0.40, 7.15) P = 0.48	0.91 (0.82, 1.00) P = 0.059
Recent visit to GP/ED/hospital	0.91 (0.31, 2.70) P = 0.86	0.99 (0.92, 1.06) P = 0.68	0.96 (0.90, 1.03) P = 0.29	1.03 (0.98, 1.08) P = 0.24	0.99 (0.94, 1.05) P = 0.84	0.22 (0.04, 1.22) P = 0.08	0.96 (0.83, 1.12) P = 0.63
Recent use of beta-agonist (short-term)	1.58 (0.42, 5.91) P = 0.49	0.97 (0.92, 1.03) P = 0.32	0.99 (0.94, 1.03) P = 0.61	1.02 (0.99, 1.06) P = 0.15	**0.97 (0.95, 1.00) P = 0.038**	0.68 (0.25, 1.86) P = 0.45	**0.93 (0.88, 0.97) P = 0.003**
Recent cough	0.61 (0.13, 2.79) P = 0.52	0.98 (0.92, 1.05) P = 0.61	**0.93 (0.88, 0.98) P = 0.008**	1.00 (0.96, 1.03) P = 0.89	**1.04 (1.00, 1.08) P = 0.038**	0.50 (0.09, 2.85) P = 0.43	1.02 (0.95, 1.11) P = 0.53
Recent rhinitis	1.52 (0.30, 7.65) P = 0.61	1.05 (0.97, 1.12) P = 0.21	0.99 (0.94, 1.05) P = 0.79	0.99 (0.95, 1.03) P = 0.67	1.00 (0.96, 1.04) P = 0.96	0.87 (0.32, 2.36) P = 0.78	0.98 (0.92, 1.05) P = 0.53
Recent itchy rash for 6 months	1.18 (0.22, 6.36) P = 0.84	1.01 (0.93, 1.10) P = 0.76	0.99 (0.94, 1.05) P = 0.83	1.00 (0.96, 1.04) P = 0.96	1.00 (0.96, 1.04) P = 0.88	0.81 (0.36, 1.81) P = 0.61	1.04 (0.95, 1.14) P = 0.44

Table 3.34. Symptoms: single pollutant models, recent exposure; effects per unit pollutant. Bolded entries represent effects significant at the p=0.05 level.

Symptom	Bsp 10^{-4} m^{-1}	$PM_{2.5}$ $\mu g/m^3$	PM_{10} $\mu g/m^3$	NO_2 ppb	O_3 ppb	CO ppm	SO_2 ppb
Recent wheeze	2.22 (0.78, 6.32) P = 0.13	0.96 (0.72, 1.28) P = 0.78	1.00 (0.96, 1.04) P = 0.99	**1.04 (1.01, 1.08)** **P = 0.013**	0.97 (0.93, 1.01) P = 0.14	0.68 (0.15, 3.06) P = 0.61	0.95 (0.89, 1.02) P = 0.18
Recent wheeze after exercise	**5.88 (1.56,22.19)** **P = 0.008**	0.97 (0.65, 1.45) P = 0.88	1.03 (0.98, 1.09) P = 0.20	**1.07 (1.03, 1.12)** **P = 0.001**	0.96 (0.91, 1.02) P = 0.20	1.22 (0.16, 9.57) P = 0.84	**0.81 (0.75, 0.89)** **P < 0.0001**
Current asthma	3.33 (0.85,13.01) P = 0.08	1.04 (0.76, 1.41) P = 0.82	1.01 (0.97, 1.06) P = 0.56	**1.06 (1.02, 1.10)** **P = 0.003**	0.96 (0.92, 1.00) P = 0.07	2.77 (0.54,14.36) P = 0.22	0.92 (0.83, 1.03) P = 0.14
Recent visit to GP/ED/hospital	1.80 (0.45, 7.09) P = 0.40	1.00 (0.79, 1.26) P = 0.97	0.97 (0.92, 1.02) P = 0.21	1.04 (0.99, 1.10) P = 0.15	1.01 (0.95, 1.06) P = 0.85	0.20 (0.02, 1.92) P = 0.16	0.97 (0.81, 1.16) P = 0.72
Recent use of beta-agonist (short-term)	1.64 (0.58, 4.67) P = 0.35	0.97 (0.75, 1.25) P = 0.79	1.00 (0.97, 1.04) P = 0.84	1.03 (1.00, 1.06) P = 0.08	0.98 (0.96, 1.01) P = 0.30	0.69 (0.21, 2.23) P = 0.53	**0.92 (0.86, 0.97)** **P = 0.004**
Recent cough	0.54 (0.17, 1.74) P = 0.30	0.84 (0.61, 1.17) P = 0.30	**0.93 (0.89, 0.97)** **P = 0.001**	1.00 (0.96, 1.04) P = 0.97	1.05 (1.00, 1.10) P = 0.059	0.16 (0.02, 1.23) P = 0.07	1.05 (0.96, 1.14) P = 0.30
Recent rhinitis	1.43 (0.47, 4.40) P = 0.52	1.08 (0.75, 1.56) P = 0.67	0.99 (0.94, 1.04) P = 0.66	0.99 (0.94, 1.03) P = 0.50	1.00 (0.96, 1.05) P = 0.89	0.99 (0.27, 3.67) P = 0.99	0.98 (0.89, 1.07) P = 0.61
Recent itchy rash for 6 months	2.12 (0.50, 8.97) P = 0.30	0.83 (0.64, 1.09) P = 0.18	1.01 (0.96, 1.07) P = 0.63	1.00 (0.96, 1.05) P = 0.87	1.02 (0.97, 1.06) P = 0.47	0.99 (0.22, 4.45) P = 0.99	1.08 (0.96, 1.21) P = 0.22

3.8.2. Joint pollutant models

More details are given in Appendices - Part B

NO_2 and O_3 joint model

Joint pollutant model including all sites (Table 3.35. and Table 3.36.): Effects of lifetime NO_2 were generally reduced in the joint pollutant model, although a significant increase in urgent asthma care was identified. However, effects of recent NO_2 were increased in magnitude with increased risks for recent wheeze, wheeze after exercise, current asthma, and urgent asthma care. O_3 effects were largely unchanged in the joint pollutant models, with the exception of an increased risk of urgent medical care with recent O_3 exposure.

Joint pollutant model excluding high-ozone schools (
Table 3.37. and Table 3.38.): No effects of lifetime exposures were identified, except for a protective effect of O_3 on current asthma, in both single and joint pollutant models. Recent NO_2 effects were reduced compared to the unrestricted models, with recent wheeze after exercise and urgent asthma care remaining significant in the restricted two pollutant model. Recent O_3 exposure was associated with increased risk of recent wheeze after exercise and recent rhinitis.

Table 3.35. Lifetime exposure: effects per unit pollutant; unrestricted O_3. Bolded entries represent effects significant at the p=0.05 level.

Measure	NO_2 (ppb): One pollutant model	NO_2 (ppb): Two pollutant model	O_3 (ppb): One pollutant model	O_3 (ppb): Two pollutant model
Recent wheeze	**1.03 (1.00, 1.07) P = 0.042**	1.01 (0.95, 1.08) P = 0.66	**0.96 (0.92, 1.00) P = 0.031**	0.97 (0.91, 1.03) P = 0.28
Recent wheeze after exercise	**1.06 (1.02, 1.09) P = 0.001**	1.02 (0.95, 1.10) P = 0.51	**0.94 (0.89, 0.99) P = 0.012**	0.95 (0.88, 1.03) P = 0.21
Current asthma	**1.05 (1.01, 1.09) P = 0.010**	0.98 (0.92, 1.05) P = 0.57	**0.94 (0.90, 0.98) P = 0.001**	**0.92 (0.87, 0.98) P = 0.013**
Recent visit to GP/ED/hospital	1.03 (0.98, 1.08) P = 0.24	**1.10 (1.01, 1.20) P = 0.028**	0.99 (0.94, 1.05) P = 0.84	1.06 (0.98, 1.15) P = 0.12
Recent use of beta-agonist (short-term)	1.02 (0.99, 1.06) P = 0.15	1.00 (0.94, 1.06) P = 0.92	**0.97 (0.95, 1.00) P = 0.038**	0.97 (0.92, 1.02) P = 0.23
Recent cough	1.00 (0.96, 1.03) P = 0.89	1.03 (0.97, 1.08) P = 0.32	**1.04 (1.00, 1.08) P = 0.038**	**1.06 (1.00, 1.12) P = 0.034**
Recent rhinitis	0.99 (0.95, 1.03) P = 0.67	1.02 (0.96, 1.09) P = 0.45	1.00 (0.96, 1.04) P = 0.96	1.02 (0.96, 1.08) P = 0.54
Recent itchy rash for 6 months	1.00 (0.96, 1.04) P = 0.96	1.04 (0.97, 1.12) P = 0.28	1.00 (0.96, 1.04) P = 0.88	1.03 (0.96, 1.11) P = 0.37

Table 3.36. Recent exposure: effects per unit pollutant: unrestricted O_3. Bolded entries represent effects significant at the p=0.05 level.

Measure	NO_2 (ppb): One pollutant model	NO_2 (ppb): Two pollutant model	O_3 (ppb): One pollutant model	O_3 (ppb): Two pollutant model
Recent wheeze	**1.04 (1.01, 1.08) P = 0.013**	**1.08 (1.00, 1.17) P = 0.048I**	0.90 (0.79, 1.04) P = 0.1463	1.02 (0.96, 1.09) P = 0.47
Recent wheeze after exercise	**1.07 (1.03, 1.12) P = 0.001**	**1.15 (1.08, 1.22) P < 0.0001**	0.88 (0.73, 1.07) P = 0.2074	1.06 (0.98, 1.14) P = 0.13
Current asthma	**1.06 (1.02, 1.10) P = 0.003**	1.06 (0.98, 1.16) P = 0.14	0.87 (0.75, 1.01) P = 0.0717	1.00 (0.94, 1.07) P = 0.94
Recent visit to GP/ED/hospital	1.04 (0.99, 1.10) P = 0.15	**1.18 (1.04, 1.33) P = 0.008**	1.02 (0.85, 1.22) P = 0.8529	**1.12 (1.03, 1.23) P = 0.012**
Recent use of beta-agonist (short-term)	1.03 (1.00, 1.06) P = 0.08	1.03 (0.97, 1.10) P = 0.29	0.95 (0.85, 1.05) P = 0.3077	1.01 (0.96, 1.05) P = 0.81
Recent cough	1.00 (0.96, 1.04) P = 0.97	1.03 (0.97, 1.09) P = 0.29	1.17 (0.99, 1.37) P = 0.0598	1.07 (1.00, 1.14) P = 0.052
Recent rhinitis	0.99 (0.94, 1.03) P = 0.50	1.01 (0.95, 1.08) P = 0.71	1.01 (0.87, 1.17) P = 0.8998	1.01 (0.96, 1.07) P = 0.69
Recent itchy rash for 6 months	1.00 (0.96, 1.05) P = 0.87	1.07 (0.96, 1.20) P = 0.21	1.06 (0.91, 1.23) P = 0.4730	1.07 (0.96, 1.18) P = 0.21

Table 3.37. Lifetime exposure: effects per unit pollutant: restricted O_3. Bolded entries represent effects significant at the p=0.05 level.

Measure	NO_2 (ppb): One pollutant model	NO_2 (ppb): Two pollutant model	O_3 (ppb): One pollutant model	O_3 (ppb): Two pollutant model
Recent wheeze	1.01 (0.97, 1.06) P = 0.65	1.01 (0.95, 1.08) P = 0.73	0.97 (0.89, 1.06) P = 0.52	0.98 (0.89, 1.08) P = 0.69
Recent wheeze after exercise	1.03 (0.99, 1.07) P = 0.17	1.02 (0.96, 1.09) P = 0.47	0.95 (0.88, 1.02) P = 0.17	0.97 (0.88, 1.06) P = 0.49
Current asthma	1.03 (0.98, 1.08) P = 0.28	0.98 (0.92, 1.05) P = 0.55	**0.91 (0.84, 0.99) P = 0.026**	**0.90 (0.82, 0.99) P = 0.029**
Recent visit to GP/ED/hospital	1.04 (0.97, 1.11) P = 0.24	**1.10 (1.01, 1.20) P = 0.037**	0.96 (0.87, 1.05) P = 0.38	1.02 (0.91, 1.15) P = 0.68
Recent use of beta-agonist (short-term)	1.01 (0.96, 1.06) P = 0.70	0.99 (0.93, 1.06) P = 0.78	0.98 (0.92, 1.04) P = 0.52	0.97 (0.90, 1.05) P = 0.47
Recent cough	1.03 (0.99, 1.07) P = 0.16	1.01 (0.96, 1.07) P = 0.65	1.00 (0.94, 1.07) P = 0.96	1.01 (0.94, 1.08) P = 0.77
Recent rhinitis	0.99 (0.93, 1.04) P = 0.58	1.04 (0.97, 1.10) P = 0.26	1.03 (0.95, 1.12) P = 0.46	1.06 (0.96, 1.16) P = 0.23
Recent itchy rash for 6 months	1.03 (0.97, 1.09) P = 0.41	1.04 (0.96, 1.13) P = 0.29	0.96 (0.88, 1.04) P = 0.34	0.99 (0.90, 1.09) P = 0.83

Table 3.38. Recent exposure: effects per unit pollutant: restricted O_3. Bolded entries represent effects significant at the p=0.05 level.

Measure	NO_2 (ppb): One pollutant model	NO_2 (ppb): Two pollutant model	O_3 (ppb): One pollutant model	O_3 (ppb): Two pollutant model
Recent wheeze	1.03 (0.98, 1.08) P = 0.29	1.07 (0.99, 1.17) P = 0.08	1.01 (0.94, 1.08) P = 0.74	1.05 (0.97, 1.14) P = 0.22
Recent wheeze after exercise	**1.06 (1.01, 1.11) P = 0.025**	**1.15 (1.08, 1.23) P < 0.0001**	1.03 (0.96, 1.11) P = 0.41	**1.12 (1.03, 1.22) P = 0.006**
Current asthma	1.05 (0.99, 1.10) P = 0.10	1.07 (0.98, 1.16) P = 0.14	0.99 (0.91, 1.07) P = 0.75	1.02 (0.93, 1.12) P = 0.60
Recent visit to GP/ED/hospital	1.06 (0.99, 1.14) P = 0.08	**1.18 (1.04, 1.34) P = 0.012**	0.99 (0.89, 1.10) P = 0.83	1.09 (0.96, 1.24) P = 0.19
Recent use of beta-agonist (short-term)	1.02 (0.97, 1.07) P = 0.46	1.02 (0.96, 1.10) P = 0.46	1.01 (0.94, 1.08) P = 0.83	1.02 (0.95, 1.10) P = 0.56
Recent cough	**1.05 (1.00, 1.09) P = 0.049**	1.03 (0.98, 1.09) P = 0.25	1.00 (0.92, 1.08) P = 0.95	1.01 (0.93, 1.10) P = 0.72
Recent rhinitis	0.97 (0.91, 1.03) P = 0.29	1.01 (0.94, 1.09) P = 0.74	1.05 (0.96, 1.14) P = 0.27	1.05 (0.97, 1.14) P = 0.19
Recent itchy rash for 6 months	1.03 (0.96, 1.11) P = 0.38	1.07 (0.95, 1.22) P = 0.27	1.01 (0.93, 1.10) P = 0.78	1.05 (0.92, 1.21) P = 0.46

3.8.3. Interaction models

Models were extended to incorporate interaction terms to allow for the detection of modification of pollutant effects by atopy, current asthma and gender. Evidence of an interactive effect was assumed when the interaction was significant and at least one subgroup effect was significant at the 5% level.

Atopy

Where effect modification occurred, effects were greater in non-atopic children. This occurred most noticeably for lifetime exposure of $PM_{2.5}$ and history of wheezing, asthma, and asthma medications and recent asthma, use of beta-agonists and recent itchy rash for six months (Table 3.39). Other specific effects for non-atopic children included lifetime CO exposure and current asthma, lifetime SO_2 exposure and history of wheezing, asthma and asthma medication, and recent itchy rash for 6 months, recent Bsp exposure and current asthma, recent PM_{10} exposure and current asthma and recent cough, and recent SO_2 exposure and recent itchy rash for 6 months.

Gender

Atopic status was included in the interaction models for gender.

No consistent effects appeared.

Table 3.39. Modification of $PM_{2.5}$ ($\mu g/m^3$) effects by atopic status· Bolded entries represent effects significant at the p=0.05 level

Outcome	Lifetime exposure	P	Recent exposure	P
Ever had wheezing				
Atopic	**1.04 (0.98, 1.10)**	**0.19**		
Non-Atopic	**1.12 (1.02, 1.23)**	**0.018**		
Interaction	**1.07 (1.02, 1.13)**	**0.007**		
Ever had Asthma				
Atopic	**1.02 (0.97, 1.08)**	**0.45**		
Non-Atopic	**1.14 (1.07, 1.23)**	**0.0001**		
Interaction	**1.12 (1.07, 1.17)**	**< 0.0001**		
Ever had medication for asthma/wheezing				
Atopic	**1.02 (0.95, 1.10)**	**0.55**		
Non-Atopic	**1.11 (1.02, 1.21)**	**0.021**		
Interaction	**1.09 (1.04, 1.14)**	**0.0002**		
Ever had rhinitis				
Atopic	1.05 (0.98, 1.13)	0.16		
Non-Atopic	1.10 (1.02, 1.19)	0.013		
Interaction	1.05 (0.99, 1.10)	0.08		
Recent wheeze				
Atopic	1.05 (0.97, 1.13)	0.23	1.10 (0.80, 1.52)	0.55
Non-Atopic	1.13 (0.97, 1.32)	0.11	1.15 (0.72, 1.84)	0.56
Interaction	1.08 (0.98, 1.19)	0.12	1.04 (0.85, 1.28)	0.68
Recent wheeze after exercise				
Atopic	1.04 (0.94, 1.15)	0.44	0.94 (0.65, 1.36)	0.75
Non-Atopic	1.09 (0.91, 1.31)	0.35	0.82 (0.48, 1.41)	0.47
Interaction	1.05 (0.95, 1.16)	0.37	0.87 (0.67, 1.14)	0.31
Current asthma				
Atopic	**1.10 (0.86, 1.42)**	**0.4395**	1.23 (0.83, 1.81)	0.30
Non-Atopic	**1.63 (1.13, 2.35)**	**0.0082**	1.56 (0.87, 2.79)	0.13
Interaction	**1.48 (1.24, 1.76)**	**< 0.0001**	1.27 (0.99, 1.63)	0.058
Recent visit to GP/ED/hospital				
Atopic	1.00 (0.92, 1.08)	0.92	1.04 (0.80, 1.35)	0.77
Non-Atopic	1.02 (0.91, 1.13)	0.78	1.03 (0.71, 1.50)	0.86
Interaction	1.02 (0.96, 1.09)	0.56	0.99 (0.79, 1.25)	0.96
Recent use of beta-agonist (short-term)				
Atopic	**1.02 (0.95, 1.09)**	**0.65**	1.04 (0.78, 1.39)	0.08
Non-Atopic	**1.12 (1.02, 1.23)**	**0.021**	1.07 (0.73, 1.56)	0.73
Interaction	**1.10 (1.05, 1.16)**	**0.0002**	1.03 (0.86, 1.24)	0.75
Recent cough				
Atopic	0.98 (0.89, 1.07)	0.6	0.89 (0.61, 1.31)	0.56
Non-Atopic	0.93 (0.84, 1.03)	0.16	0.91 (0.59, 1.40)	0.66
Interaction	0.95 (0.90, 1.01)	0.11	1.02 (0.84, 1.24)	0.84
Recent rhinitis				
Atopic	1.07 (0.99, 1.15)	0.09	1.11 (0.82, 1.49)	0.50
Non-Atopic	1.11 (1.02, 1.21)	0.017	1.09 (0.79, 1.51)	0.60
Interaction	1.04 (0.99, 1.09)	0.14	0.98 (0.85, 1.14)	0.83
Recent itchy rash for 6 months				
Atopic	**1.02 (0.93, 1.11)**	**0.72**	0.94 (0.71, 1.25)	0.68
Non-Atopic	**1.12 (1.03, 1.23)**	**0.008**	1.24 (0.87, 1.77)	0.23
Interaction	**1.11 (1.02, 1.20)**	**0.01**	1.32 (0.91, 1.90)	0.14

4. DISCUSSION

The cross-sectional component of ACHAPS involved a national sample of approximately 2,900 children, in six jurisdictions in Australia.

4.1. Summary of findings

The cross-sectional study showed consistent evidence of respiratory adverse effects of NO_2, associated with both recent and life-time exposure. These adverse effects were manifested as increased risk of asthma-like symptoms (in particular, wheeze), increased airway inflammation, and reduced lung volumes. There was no evidence that the effects were stronger in atopic subjects, apart from SO_2. The absence of a greater effect in atopic subjects, the finding that lung volumes, rather than airway calibre (reflected in FEV_1/FVC ratio), and persistence of the effect after bronchodilator imply that the consequence of NO_2 exposure is not typical asthma; rather, more non-specific lung effects are implicated.

Particulate matter exposures showed varied results. PM_{10} was associated with decline in FEV_1 post-bronchodilator and increase in exhaled NO, but no overall increase in current symptoms. $PM_{2.5}$ was associated with an adverse effect on FVC post-bronchodilator and on exhaled NO, with no overall effects on current symptoms, but showed increased risk of lifetime wheezing, asthma, and asthma medication, and current asthma, use of beta-agonists and itchy rash in non-atopic children. Bsp was associated with a decline in change in FEV_1 post-bronchodilator and an increased risk of recent cough. Females had an increase in FEV_1/FVC ratio pre-bronchodilator for lifetime and recent Bsp, recent $PM_{2.5}$, and recent PM_{10}, with non-significant effects in males. Despite the absence of effect on current symptoms, a reduction in lung volume at this age may have longer-term adverse consequences if it persists into later life.

O_3 showed some effects in a beneficial direction (perhaps due to the NO_2 effects and the negative association between O_3 and NO_2) but these were eliminated in the joint O_3- NO_2 model. FEV_1/FVC ratio decreased significantly with lifetime O_3 exposure in females, with no effect in males.

Exposure to SO_2 in the last year, after adjustment for O_3, showed an adverse effect on lung function measures. SO_2 effects on lung function were modified by atopic status, being more deleterious in atopic children, and non-significant in non-atopic status. Males had greater adverse effects of SO_2, for FVC post-bronchodilator and FEV_1/FVC ratio pre-bronchodilator. Reported history of wheezing, asthma and asthma medication, and recent itchy rash for 6 months increased with SO_2 in non-atopic children, with no effect in atopic children.

4.2. Comparison with other studies of chronic exposure in school children

Australia

Few other studies have been conducted in Australia on the chronic or longer-term health effects of outdoor air pollution on children's health, although a larger number have examined the acute effects. The latter will be discussed in Section C of this report.

A cross-sectional survey of the respiratory health of 3,023 children aged 8-10 years from industrial and non-industrial sites in the Hunter and Illawarra regions in New South Wales

examined the relationship between outside air quality (PM_{10}, TSP and SO_2) and respiratory symptoms (asthma, wheeze, cough, chest colds, hay fever, and eczema) (Lewis et al, 1998). A positive association was found between PM_{10} and both night cough and chest colds. An increase of 10 $\mu g/m^3$ PM_{10} was associated with an increase in chest colds (OR 1.43, 95%CI 1.12-1.82), and night time cough (OR 1.34, CI 1.19-1.53). No associations were found between SO_2 and night cough, chest colds, and wheeze. No association was found between PM_{10} and wheeze.

Measured air pollution cross-sectional studies

Raizenne et al. (1996) examined the health effects of exposure to acidic air pollution on pulmonary function among 10,251 white children aged 8-12 years living in 24 communities throughout the United States and Canada. Pulmonary function was measured by FVC, FEV_1, $FEV_{0.75}$, $FEF_{25-75\%}$, and PEFR. Measures of PM_{10}, $PM_{2.5}$, fine particle strong acidity, fine particle sulphate, gaseous acids, and O_3 were collected for one year prior to the pulmonary tests. Particle strong acidity was associated with a 3.5% decrement in FVC (CI: -4.9 to -2.0) and a 3.1% decrement in FEV_1 (CI: 1.6-4.6%). PM_{10} was also associated with a 2.4% (CI: 0.5-4.3%) decrement in FVC. Stratified analyses showed no differences in the associations with regard to geography, year of study, gender, and exercise levels. Further results showed that O_3 was associated with a decrease in pulmonary function with mean daytime O_3 having the strongest association.

Dockery et al. (1996) examined respiratory symptoms among 13,369 white children within the same study. Particle strong acidity and fine particulate sulphate were associated with significantly higher reporting of bronchitis (1.64, CI 1.12-2.42 & 1.65, CI 1.12-2.42, respectively). Gaseous acids were associated with a higher risk of asthma and asthma symptoms (OR 2.00, CI 1.14-3.53). There was no association between O_3 and any of the respiratory symptoms. No subgroups were more sensitive to particle strong acidity than the overall sample.

The cross-sectional sub-study of the SCCHS examined the prevalence of respiratory diseases within a sample of 3,676 school children (Peters et al., 1999a), and also the effects on pulmonary function in a sample of 3,293 school children (Peters et al., 1999b). The main respiratory symptoms that were examined were asthma, wheeze, cough, and bronchitis. Results showed that only the prevalence of wheeze (OR 1.26, CI 1.01-1.57) in all subjects was associated with acid vapour. Exposure to NO2 and acid vapour was associated with wheeze in boys only (OR 1.47, CI 1.04-2.09). No other associations were found between air pollutants and respiratory symptoms and the overall results showed no consistent or large excesses of morbidity in subjects who lived in the most polluted communities. The authors stated that this might indicate

> …1) little effect of even the most severe outdoor pollution; 2) an increase of uncontrolled risk factors in cleaner communities; 3) our inability to detect important effects, because of exposure misclassification, inadequate sensitivity of health measures, or bias in diagnostic practices between communities; or 4) effects of self selection of place of residence inherent in cross-sectional comparisons.

In the baseline SCCHS, PM_{10}, $PM_{2.5}$, and NO_2 were each significantly associated with lower FVC, FEV_1, and maximal midexpiratory flow (MMEF); acid vapour with lower FVC, FEV_1, PEFR, and MMEF; and O_3 with lower PEFR and MMEF. Effects were generally larger in those girls spending more time outdoors. Stepwise regression of adjusted pulmonary function values for girls in the 12 communities showed that NO_2 was most strongly associated with lower FVC

($r = -0.74$, $p < 0.01$), $PM_{2.5}$ with FEV_1 ($r = -0.72$, $p < 0.01$), O_3 with PEFR ($r = -0.75$, $p < 0.005$), and $PM_{2.5}$ with MMEF ($r = -0.80$, $p < 0.005$). There was a statistically significant association between O_3 exposure and decreased FVC and FEV_1 in girls with asthma. For boys, significant associations were seen between peak O_3 exposures and lower FVC and FEV_1, but only in those spending more time outdoors (Peters et al., 1999b).

However, among SCCHS children with asthma, positive associations were found between air pollution and bronchitis and phlegm (McConnell et al., 1999). As PM_{10} increased across communities, risk of bronchitis increased: per IQR OR 1.4/19 $\mu g/m^3$; 95% CI: 1.1-1.8). Increased prevalence of phlegm was significantly associated with increasing exposure to all ambient pollutants except O_3. The strongest association was for NO_2, based on relative risk per IQR in the 12 communities (OR 2.7 per 24 ppb; CI, 1.4-5.3).

To examine evidence relating to traffic-related pollution and asthma, a sample of children was randomly selected from participants in the SCCHS, a prospective cohort designed to investigate associations between air pollution and respiratory health in children 10-18 years of age (Gauderman et al., 2005; Peters et al., 1999a). Lifetime history of doctor-diagnosed asthma was associated with outdoor NO_2; the OR was 1.83 (95% CI: 1.04-3.22) per increase of 1 IQR (IQR=5.7 ppb) in exposure. Increased asthma was associated with closer residential distance to a freeway (1.89 per IQR; 1.19-3.02) and with model-based estimates of outdoor pollution from a freeway (2.22 per IQR; 1.36-3.63). These two indicators of freeway exposure and measured NO_2 concentrations were also associated with wheezing and use of asthma medication. Asthma was not associated with traffic volume on roadways within 150 m of homes or with model-based estimates of pollution from non-freeway roads.

A sample of 217 children was selected from participants in the SCCHS. NO_2 monitors were placed outside children's homes for two weeks in the summer and two weeks in the fall-winter season as a marker of traffic-related air pollution (Jerrett et al., 2008). Incident asthma was positively associated with traffic pollution, with a hazard ratio (HR) of 1.29 (95% CI: 1.07-1.56) across the average within-community IQR of 6.2 ppb in annual residential NO_2. Using the total IQR for all measurements of 28.9 ppb increased the HR to 3.25 (95% CI, 1.35-7.85).

A cross-sectional study of current asthma and other respiratory symptoms recruited 1,080 children living at varying distances from high-traffic roads in the San Francisco Bay Area, California, a highly urbanised region characterised by good regional air quality (Kim et al., 2008). Exposure was assessed using residential proximity to traffic and major roads. Traffic-related pollutants (NO_X) were measured for a subset of households. Children whose residences were in the highest quintile of exposure had approximately twice the adjusted odds of current asthma (that is, asthma episode in the preceding 12 months) compared with children whose residences were within the lowest quintile. The highest risks were among those living within 75 m of a freeway/highway.

The 2001 California Health Interview Survey was linked to air monitoring and traffic data to estimate associations between traffic density or outdoor air pollutant concentrations and childhood asthma morbidity (Wilhelm et al, 2008). Children with asthma living in high O_3 areas and areas with high concentrations of PM_{10} experienced symptoms more frequently, and those living close to heavy traffic reported more emergency department visits or hospitalisations.

Results from the pulmonary function tests showed significant associations between air pollution levels and lung function in females only. Negative associations were found between peak O_3 and MMEF and PEFR ($\beta = -69.5$; $p < 0.01$ & $\beta = -128.3$; $p < 0.01$ respectively). Adjusted

pulmonary function values in girls showed that NO_2 was associated with FVC ($r = -0.74$; $p < 0.01$), $PM_{2.5}$ with FEV_1 ($r = -0.72$; $p < 0.01$), O_3 with PEFR ($r = -0.75$; $p < 0.005$), and $PM_{2.5}$ with MMEFR ($r = -0.80$; $p < 0.005$). It is interesting to note that associations were found with males only with regard to prevalence of wheeze, and associations were found with females only with regard to pulmonary function.

The **S**wiss Study on **C**hildhood **A**llergy and **R**espiratory Symptoms with respect to Air **POL**lution (SCARPOL) was conducted throughout 10 communities during 1992/1993 and involved a sample of 4,470 children aged 6-15 years. Questionnaires were used to collect information about respiratory and allergic symptoms (Braun-Fahrlander et al., 1997). Ambient measures of SO_2, NO_2, O_3 and PM_{10} were collected continuously throughout the study period in each of the 10 communities. Results showed associations between PM_{10} and chronic cough (OR 3.07, CI 1.62-5.81) and nocturnal dry cough (OR 2.88, CI 1.69-4.89). Smaller associations were also observed between chronic cough and NO_2 (OR 1.58, CI 1.14-2.18), nocturnal dry cough and NO_2 (OR 1.99, CI 1.51-2.61), SO_2 (OR 1.57, CI 1.02-2.42) and PM_{10} (OR 2.88, CI 1.69-4.89). PM_{10} was also associated with bronchitis (OR 2.17, CI 1.21-3.87). No associations were found with asthma, current wheeze, sneezing attacks during pollen season, and hay fever. Furthermore, no associations were found between O_3 and symptom rates when annual mean concentrations were considered. However, when peak O_3 hours were considered, there were small positive associations with nocturnal dry cough, bronchitis, and conjunctivitis. Stratified analyses showed stronger associations in children with a reported family history of respiratory, bronchitis and conjunctivitis symptoms.

The cross-sectional Health Effects of School Environment Study, based in Norway, Sweden, Denmark, France and Italy found PM_{10} and CO_2 levels in a day of normal classroom activity were related to wheezing, dry cough at night and rhinitis in 654 children aged 10 years (Simoni et al., 2010). Disorders were more prevalent in children in poorly ventilated classrooms.

ACHAPS findings of adverse effects of NO_2 in relation to history of asthma, and other respiratory symptoms, are consistent with the SCCHS, although effects are somewhat weaker and apply to current rather than lifetime asthma only. The findings are also consistent in relation to NO_2 and PM effects and lung function, with little consistent evidence of effect modification by gender. ACHAPS found favourable effects of O_3 (contrary to the SCCHS) but these appeared related to negative confounding with NO_2 - assuming the effect is null, the O3 findings are consistent with the SCCHS and the SCARPOL.

Comparative high-low pollution/proxy studies

Many cross-sectional studies conducted throughout the world have examined associations between road traffic-related air pollution and lung function and prevalence of respiratory symptoms in children. Studies investigating road traffic-related air pollution often use residential and school proximity to major roads, and traffic counts as proxies for exposure.

A European study found mixed results when investigating associations between road traffic density and child respiratory symptoms. In 10 areas of northern and central Italy varying in size, latitude, climate, and level of urbanisation, 39, 275 children aged 6-7 years and 13-14 years were surveyed (Cicconne et al., 1998). Children's parents reported on medical diagnosis of asthma, occurrences of other respiratory symptoms, and medical history of respiratory diseases in the first two years of life (if the children had never changed residence). Parents were also asked to give a subjective evaluation of traffic density in the zone of residence. The validity of

the subjective traffic density data was further evaluated with NO_2 sampling at various locations and objective measures of traffic density. Overall, the results showed only weak and inconsistent associations between respiratory symptoms and traffic density. However, in areas of high truck traffic density, positive associations with respiratory symptoms were found. The strongest associations were found with lower respiratory tract infections early in life (OR 1.39, CI 1.19-1.62) and current respiratory problems (OR 1.29, CI 1.15-1.45). No relevant differences were found between age groups and sexes. A second phase of this study (Migliore et al., 2009) found that overall traffic density was weakly associated with asthma symptoms, but there was a stronger association with cough or phlegm production (OR 1.24; 95% CI (1.04-1.49).

Other studies have used traffic density counts and proximity to major roads and freeways as air pollution exposure variables. Van Vliet et al. (1997) examined whether motor vehicle exhaust from freeways has an effect on respiratory symptoms in children. A sample of 1,068 primary school children was recruited from six residential areas in South Holland where a large number of houses were located within 300 m of a major freeway. The study measured the distance from children's homes and schools from the freeways and also the traffic density of the freeways. Of the 1,068 children, 878 were living within 1,000 m of a freeway. In two of the six areas, measures of PM_{10}, $PM_{2.5}$, black smoke, and NO_2 were collected. Levels of black smoke and NO_2 decreased with increasing distances from the freeways. Measures of PM_{10} and NO_2 were also collected from within 12 of the 13 participating primary schools. Results showed that chronic cough, wheeze, and rhinitis were more prevalent in children living within 100 m of the freeways. The same respiratory symptoms, with the addition of asthma attacks, were also more prevalent in areas of high truck traffic density. When the analysis was restricted to children living within 300 m of the freeway, associations were found between truck traffic density and bronchitis (OR 3.52, CI 0.91-13.6, p=0.10), and also between chronic cough (OR 2.94, CI 0.98-8.89, p<0.10), rhinitis (OR 5.84, CI 1.43-20.0) and black smoke in schools. The effects were stronger in girls than boys.

The same study also analysed lung function (FEV, FEV_1 and $FEF_{25-75\%}$) of the children living near freeways (Brunekreef et al., 1997). For all the children living within 1,000 m of the freeways, results showed an association between truck traffic density and FEV_1, PEF, and $FEF_{25-75\%}$. When the analysis included only children living within 300 m of the freeways, the association was stronger. Lung function was also found to be associated with black smoke measured in schools. Similar to the respiratory symptom analysis, all the associations were stronger in girls than boys.

Residential proximity to major roads was also used as a traffic-related air pollution exposure variable in an English study (Venn et al., 2001) on wheezing in children. Spatial analysis techniques in a geographical information system were used to establish the distance from children's homes to the closest main road. A total of 6,147 primary school children and 3,709 secondary children from Nottingham, England were surveyed about respiratory symptoms. Results for the overall sample of primary school children showed that the distance to the main road was not significantly associated with the risk of wheeze. However, of the 1,541 primary school children living within 150 m of a main road, there was a trend toward an increase in risk of wheeze (OR 1.08, CI 1.00-1.16) per 30 m increase in proximity to the road. The effect was more prominent in girls than boys. Similar results were reported for the secondary school children (OR 1.16, CI 1.02-1.32). A positive association between risk of wheeze and proximity to a main road was only found for children living within 150 m of a main road. Effects were slightly stronger for secondary school girls than boys.

It should be noted that the Venn et al. (2001) study was a nested study within a much larger cross-sectional/longitudinal study (Venn et al., 2000) that investigated the prevalence, severity,

and persistence of wheeze in a sample of 22, 968 primary school children and 27,826 secondary school children. The exposure variable was traffic density in the locality of the schools the children attended. It is interesting to note that in the cross-sectional data analysis there were no significant associations found between the prevalence of wheeze in both primary and secondary school children and traffic density. In contrast, there were associations between wheeze and the proximity of children's homes to freeways. The longitudinal data analysis used follow-up data from a survey conducted in 1988. Results showed a weak linear correlation between persistence of wheeze and traffic density.

Oosterlee and colleagues (Oosterlee et al., 1996) used only traffic density counts as an air pollution exposure variable. They examined whether children and adults living along streets with high traffic density had a higher prevalence of chronic respiratory symptoms. Results showed a higher prevalence for wheeze (OR 2.10, CI 0.99-4.4) and respiratory medication use (OR 2.2, CI 1.10-4.60) among children living in the high traffic areas when compared to children living in the control areas. The effect was much greater for girls than boys. It is interesting to note that mild dyspnoea was the only self-reported respiratory symptom in adults that was significantly higher among adults living in the high traffic density area. These results support the argument that children are more susceptible than adults.

Cross-sectional studies have also found associations between traffic-related air pollution and atopic sensitisation in children. Kramer and colleagues (Kramer et al., 2000) studied 317 children who lived near major roads in Dusseldorf, Germany. Data regarding respiratory and allergy symptoms were collected via questionnaires, skin prick tests, serum tests for IgE antibodies, and a symptom diary (completed by the parents for a period of one year). Outdoor NO_2 was measured at 158 sampling points in three selected areas. Personal monitoring of NO_2 was also conducted; 191 children agreed to wear personal air samplers during two non-consecutive months of the study period. The mean values of personal NO_2 were below 50% of the outdoor NO_2 measurements and there was only a weak correlation. Results showed an association between allergic rhinitis and outdoor NO_2 (OR 1.81, CI 1.02-3.21). The observed effects were more pronounced in girls than boys. No associations were found between indoor NO_2 and allergic symptoms.

A similar study by Duhme and colleagues (Duhme et al., 1996) examined the self-reported symptoms of asthma and allergic rhinitis in 3,703 students aged 12-15 years in association with self-reported exposure to road traffic density. Results showed a positive association between symptoms of 'frequent' and 'constant' wheeze (OR 1.53, CI 1.15-2.05 and OR 2.15, CI 1.44-3.21 respectively) and allergic rhinitis (OR 1.71, CI 1.36-2.15 and OR 1.96, CI 1.40-2.76 respectively) and self-reported frequency of truck traffic density.

School children aged 8-12 years were recruited from two areas in Hong Kong with differing levels of air pollution (Yu et al., 2001). Parents of 1,660 children completed questionnaires on respiratory symptoms and 1,294 children participated in spirometric tests (FEV_1, FVC, $FEF_{25-75\%}$). Routine monitoring was done for SO_2, NO_2, and respirable suspended particulate (RSP) in the two areas. Results showed that children from the more polluted area had higher crude rates for all respiratory symptoms than children in the low polluted area, except bronchitis in boys. After adjusting for age, gender, and other covariates, the ORs for frequent cough (OR 1.74, CI 1.28-2.38), frequent sputum (OR 1.87, CI 1.28-2.78), chronic sputum (OR 1.84, CI 1.06-3.19), and asthma (OR 1.98, CI 1.24-3.18) were all statistically significant. Boys had a higher risk than girls for frequent sputum, wheezing with shortness of breath, and asthma. Results from the lung function tests showed that the adjusted means for both sexes were higher

in the lower polluted area. Significant differences between the two areas were found for all spirometric tests except for FVC in boys. The differences in lung function between the two districts were greater in girls than boys.

A study of southern Californian communities exposed to high levels of traffic emissions, including truck and ship emissions arising from port activity, found that **a**pproximately 1,600 (9%) of all childhood asthma cases in Long Beach and 690 (6%) in Riverside were attributed to traffic proximity (Perez et al., 2009). Ship emissions accounted for 1,400 (21%) bronchitis episodes and, in more modest proportions, health care visits for asthma. Considerably greater reductions in asthma morbidity could be obtained by reducing NO_2 and O_3 concentrations to levels found in clean coastal communities.

A large English cross-sectional study, based on the Health Survey of England, made findings that contrasted with those of the southern Californian study. They found that distance to main roads did not predict risk of wheeze, asthma, eczema, or hay fever or level of serum immunoglobulin E (an indicator of allergy) or forced expiratory volume in one second (FEV1, an indicator of airflow obstruction). (Pujades-Rodriguez, 2009).

A school-based cross-sectional study in France used a validated dispersion model combining data on traffic conditions, topography, meteorology and background pollution to relate 3-yrs averaged concentrations of major urban pollutants at the sites of schools to skin prick tests, exercise-induced asthma and reported asthma and allergies in 6,683 children (9-11 yrs) attending 108 randomly selected schools in six French communities (Penard-Morand et al., 2005, 2010). Asthma (exercise induced, past year and lifetime) was significantly positively associated with benzene, SO_2, PM_{10}, NO_X and CO. Eczema (lifetime and past year) was significantly positively associated with benzene, PM_{10}, NO_2, NO_X and CO, lifetime allergic rhinitis with PM_{10} and sensitisation to pollens with benzene and PM_{10}.

A Dutch study correlated air pollution exposures at the birth address (estimated using land use regression models) with reported asthma, hay fever and related symptoms during the first 8 years of life in a sample of 3,863 children (Gehring et al., 2010). $PM_{2.5}$ levels were associated with a significant increase in incidence of asthma, (OR 1.28; 95% CI, 1.10-1.49), prevalence of asthma (OR 1.26; 1.04-1.51), and prevalence of asthma symptoms (OR 1.15; 1.02-1.28). Findings were similar for NO_2 and soot. No associations were found with atopic eczema, allergic sensitisation, and bronchial hyperresponsiveness.

In Rome, 2,107 children aged 9-14 years from 40 schools in Rome in 2000-2001 were included in a cross-sectional survey (Rosenlund et al., 2009). Respiratory symptoms were assessed in 1,760 children by parental questionnaires, while allergic sensitisation was measured by skin prick tests and lung function was measured by spirometry on 1,359 children. Three indicators of traffic-related air pollution exposure were assessed: self-reported heavy traffic outside the child's home; the measured distance between the child's home and busy roads; and the residential NO_2 levels estimated by a land use regression model. There was a strong association between estimated NO_2 exposure per 10 $\mu g/m^3$ and lung function, especially expiratory flows, in linear regression models adjusted for age, gender, height and weight: -0.62% (95% CI -1.05 to -0.19) for FEV_1 as a percentage of VC, -62 ml/s (95% CI -102 to -21) for FEF25-75, and -85 ml/s (95% CI -135 to -35) for PEF. The other two exposure indicators showed similar but weaker associations. The associations appeared stronger in girls, older children, in children of high socio-economic status and in those exposed to parental smoking.

There was not a consistent association between traffic-related air pollution exposure and prevalence of respiratory symptoms or allergic sensitisation.

In order to assess repeated hospital presentations for asthma in children, and its association with traffic-related air pollution near the residence, hospital records for 2,768 Californian children aged 0–18 years were obtained for a catchment area of two hospitals in northern Orange County, California (Delfino et al., 2009). A line source dispersion model was used to estimate individual seasonal exposures to local traffic-generated pollutants (NO_x and CO) longitudinally, beginning with the first hospital encounter. Adjusted HRs for IQR increases in NO_x (4.00 ppb) and CO (0.056 ppm) were 1.10 (95% CI, 1.03-1.16) and 1.07 (1.01-1.14), respectively. The study concluded that locally generated air pollution near the home affects asthma severity in children.

A hospital-based longitudinal study of a southern California urban catchment area around two adjacent children's hospitals examined the association between nearby traffic and repeated hospital encounters among children with asthma (Chang et al., 2009). Living within 300 m of arterial roads or freeways increased risk of repeated hospital encounters in 3,297 children age 18 years or less. At highest risk were children in the top quintile of traffic density (HR = 1.21; 95% CL 0.99 to 1.49) and those who had 750 m or more of arterial road and freeway length within 300 m of their residence (HR = 1.18; 95% CL 0.99 to 1.41).

The consistent findings of adverse associations between proximity to traffic and respiratory symptoms and lung functions support ACHAPS findings in relation to NO_2, a major constituent of traffic-related pollution.

Prospective studies

A four-year follow-up cohort of 1,678 children from the SCCHS found significant deficits in lung function growth rate were associated with exposure to acid vapour, NO_2, $PM_{2.5}$, and elemental carbon (Gauderman et al., 2002). Exposure to acid vapour was also associated with reductions in the ratio of MMEF to FVC (P = 0.02), whereas exposure to O_3 was correlated with reduced growth in peak flow rate (P = 0.006). Larger deficits in lung function growth rate were observed in children who reported spending more time outdoors. In children with asthma, respiratory symptoms were associated with the yearly variability of $PM_{2.5}$ (OR 1.09 per $\mu g/m^3$, 95% CI 1.01-1.17), organic carbon (OR 1.41per $\mu g/m^3$, 95% CI 1.12-1.78), NO_2 (OR 1.07 per ppb, 95% CI 1.02-1.13), and O_3 (OR 1.06 per ppb, 95% CI 1.00-1.12) (McConnell et al, 2003).
A five-year follow-up cohort of 3,535 children from the SCCHS, with no history of asthma at recruitment, found that children living in communities with high O_3 concentrations and playing three or more sports had an increased risk of developing asthma: OR 3.3 (95% CI 1.9-5.8), compared to children in the same communities playing no sports (RR 3.3, 95% CI 1.9-5.8) (McConnell et al., 2002). Sports had no effect in areas of low O_3 concentration (0.8, 0.4-1.6). Time spent outside was associated with a higher incidence of asthma in areas of high O_3 (1.4, 1.0-2.1), but not in areas of low O_3. Exposure to pollutants other than O_3 did not alter the effect of team sports.

An eight-year follow-up of 1,759 children from the SCCHS (average age, 10 years) measured lung function annually for eight years (Gauderman et al., 2004). Over the eight-year period, deficits in the growth of FEV_1 were associated with exposure to NO_2 (P=0.005), acid vapour (P=0.004), $PM_{2.5}$ (P=0.04), and elemental carbon (P=0.007), even after adjustment for several

potential confounders and effect modifiers. Associations were also observed for other spirometric measures. Exposure to pollutants was associated with clinically and statistically significant deficits in the FEV_1 attained at the age of 18 years.

A further follow-up study of 3,677 children from the SCCHS examined lung function growth from 10–18 years and its association with traffic exposure (Gauderman et al., 2007). Children who lived within 500 m of a freeway had substantial deficits in eight-year growth of forced expiratory volume in 1 s (FEV(1), -81 ml, p=0.01 [95% CI -143 to -18]) and MMEF rate (MMEF, -127 ml/s, p=0.03 [-243 to -11), compared with children who lived at least 1,500 m from a freeway. Local exposure to freeways and regional air pollution had detrimental, and independent, effects on lung-function growth. Pronounced deficits in attained lung function at age 18 years were recorded for those living within 500 m of a freeway, with mean per cent-predicted 97.0% for FEV_1 (p=0.013, relative to >1500 m [95% CI 94.6-99.4]) and 93.4% for MMEF (p=0.006 [95% CI 89.1-97.7]).

Lin et al. (2008) followed a birth cohort born in New York State during 1995-1999 to first asthma admission or until 31 December 2000 and linked these data with ambient O_3 data (8-hr maximum). Asthma admissions were significantly associated with increased O_3 levels for all chronic exposure indicators (ORs, 1.16-1.68), with a positive dose-response relationship. Stronger associations were found among younger children and low socio-demographic groups.

ACHAPS has no measures of lung function growth, which would require a follow-up of ACHAPS sample of children. However, again, it appears that NO_2 and PM are implicated in poorer lung development.

Ecological studies

The 2001-2004 National Health Interview Survey included 34,073 children aged 3-17 years in US metropolitan areas (Akinbami et al., 2010). Reported asthma history was linked to monitored air quality (SO_2, NO_2, O_3, PM) in their county of residence over the recent 12 months. Results suggested that chronic (12 month) exposure to O_3 increased the risk of asthma in children with an OR for current asthma of 1.56 (95% CI 1.15-2.10), comparing highest and lowest quartiles of exposure, and a corresponding OR for recent asthma of 1.38 (0.99-1.91). No associations were found for SO_2 and NO_2, while results for PM were suggestive.

A similar analysis was based on approximately 70,000 children from the 1999-2005 National Health Interview Survey and ambient pollution monitoring data from the US Environmental Protection Agency (Parker et al., 2009). Increased respiratory allergy or hay fever was associated with increased summer O_3 levels: (adjusted OR 1.20 per 10 ppb, 95% CI 1.15-1.2) and increased $PM_{2.5}$ (OR 1.23 per 10 $\mu g/m^3$, 95% CI 1.10-1.38). These associations persisted after stratification by urban-rural status, inclusion of multiple pollutants, and definition of exposures by differing exposure radii. No associations between the other pollutants and the reporting respiratory allergy/hay fever were apparent.

The International Study of Asthma and Allergies in Childhood (ISAAC) Phase One showed up to 10 to 20-fold worldwide variability in the prevalence of symptoms of asthma, rhinoconjunctivitis and eczema. Ecological analyses at city level demonstrated a weak inverse relationship between city-level PM_{10} and symptoms of the three conditions, after controlling for

Gross National Product, while multi-centre meta-analyses of data from countries with multiple centres found a consistent pattern of weak positive associations.

These studies largely link O_3 to adverse health effects on children, contrary to the large individual studies.

4.2.1. Methodological issues

ACHAPS is cross-sectional and relies on historical NEPM monitoring for measures of exposure. While the study differentiated between average lifetime exposure (measured from the time the child began living in the area) and recent exposure (averaged over the last year), it remained difficult to distinguish between long-term and shorter-term effects, due to correlations of effects over time. In addition, the study relied on the availability of routine monitored air pollutants. While this was considerable for many sites, gaps in data were left as sites, in general, did not monitor all pollutants over the entire period of the study. This also limited data available to explore multiple-pollutant models.

Each child had an individual exposure metric calculated for each pollutant. However, due to the cluster design and the dependence on the NEPM monitoring stations for measures of air quality, exposure variability within sites was limited. Thus, the study relied very much on variability among sites for its power to detect associations. This variability was optimised in the original selection of sites; sites were purposefully chosen to maximise the range of pollutant levels (based on historic data prior to the start of the study) and with NEPM stations with the greatest number of criterion air pollutants measured.

A consequence of this choice of sites was that it was difficult to judge the representativeness of the sample of children, in relation to the target population of all urban primary-school aged children. The characteristics of the sample in terms of prevalence of asthma and other conditions appear to correspond to published estimates from national surveys (AIHW, 2007).

However, as the study was essentially a comparative one, examining the way in which the health of this sample of children varied with exposure to air pollutants, and based in community samples, it is argued that the presence of a factor likely to modify the observed associations is unlikely.

However, a challenge for any spatially-constructed study is that of confounding, particularly by spatial-level confounders. A major contender for confounding is socio-economic status which is spatially distributed, and which may separately relate to both exposure and health outcome. The analyses presented in this report have been adjusted at the cluster level for the SEIFA indices for relative socio-economic advantage and disadvantage, and for education, and at the individual level for parent's education. Sensitivity analyses which incorporated other spatial measures showed, in fact, very few variables (for example, household characteristics) altered estimates of effects once the standard variables (age, sex, socio-economic status - as just described) were included in models.

Health outcomes were determined in multiple ways to enhance the reliability and validity of the findings. We performed lung function tests, which have acknowledged validity and

reliability, along with administering validated questionnaires used in previous studies to ascertain parental reports of diagnoses and symptoms.

Determining the temporal sequence of exposure and outcomes in a cross-sectional study such as this one may be problematic. The examination of effects by lifetime outcomes and lifetime exposures, and, separately, by recent outcomes and recent and lifetime outcomes was an attempt to clarify this — an association of a recent health effect with recent exposure that is stronger than, but consistent with, the association of the same recent health effect with lifetime exposure, would support an argument for a causal effect.

Part C

The panel study:

acute exposure to air pollution: effects upon children's health

1. PANEL STUDY DESIGN AND MEASUREMENT

1.1. Aims and objectives

1) To obtain quantitative estimates of the prospective day-to-day association between the criteria air pollutants and (a) incidence of respiratory symptoms, and (b) lung function, in school children with a history of asthma, aged 7–11 years at baseline; and,
2) To determine whether the effects are modified by other factors, such as socioeconomic disadvantage, geographical area, sex, activity patterns and obesity.

1.2. Methods

1.2.1. Participant selection

Children for the panel study were selected from those who had participated in the cross-sectional study. Criteria for panel study eligibility included the following:

(i) answering 'yes' to Q11: 'Have you ever been told by a doctor or nurse that your child has asthma?" **AND**

(ii) answering 'yes' to:
   a. Q4: 'Has your child had wheezing or whistling in the chest in the past 12 months?' **OR**
   b. Q13: 'Does he/she still have asthma?' **OR**
   c. Q16: 'In the past 12 months, has your child had an asthma attack, episode of wheezing or episode of bronchitis for which he/she:
      i. Visited your family doctor (GP) or medical centre' **OR**
      ii. Attended a hospital's Emergency Department (casualty)?' **OR**
      iii. Was admitted to hospital?'
   d. Q22: 'In the past 12 months, has your child had any cough?' **OR**

(iii) answering 'some days', 'more than once a month', 'more than once a week' to:
   a. Q15: 'In the past 12 months, has asthma, wheezing or bronchitis limited your child's activities?' **OR**
   b. Q17: 'In the past 12 months, has your child missed school because he/she had asthma or wheezed?' **AND**

(iv) living within a 3 km radius from the corresponding monitoring station.

The distance from the corresponding monitoring station to their home addresses was calculated using Metroview Version: 2.50 (c) (Metroview Systems Pty Limited, Sydney, Australia). Parents of symptomatic children living within the specified radius were asked to consent to their child's participation in the panel study. One week prior to the school testing day, parents were contacted by telephone to seek consent to participate in the panel study. The target number of panel study participants was 11 at each site.

1.2.2. Panel study measurements

Information about lung function measurements, symptoms and time-activity patterns were collected in paper diaries and in electronic peak flow devices (Miniwright Digital, MWD,

Clement Clarke, Essex, UK). The paper diaries were designed to facilitate easy recording of data (Peak Flow and Symptom Diary and the Time-Activity Diary, see Appendices, Part A).

Peak expiratory flow measurements

Children were instructed to conduct lung function measurements every morning and evening for 30 days. Lung function was measured using an electronic peak flow meter, before any inhaled medication was used. Peak expiratory flow rate (PEF; litres/minute) and forced expiratory volume in one second (FEV_1; litres) were measured. The electronic peak flow meters were given to each child and they recorded three successive measurements in the morning and three successive measurements in the evening. The highest PEF and FEV_1 from these three successive measurements were automatically stored in the electronic peak flow device with a date and time stamp.

Symptoms and medication use measurements

Children were instructed to complete a paper symptom and medication use diary every morning and evening for 30 days. This diary collected information about:

(i) presence of the following respiratory symptoms during the night:
   a. cough and/or phlegm;
   b. wheeze and/or chest tightness; and,
   c. shortness of breath.

   This information was recorded in the morning. Each of these symptoms was recorded on a zero to four scale (0=no symptoms during the night, 1=symptoms, but did not disturb sleep, 2=symptoms that disturbed part of child's sleep, 4=symptoms that disturbed all or most of child's sleep). In the panel study analysis, symptoms were categorized as either 'No symptoms' or 'Any symptoms'.

(ii) presence of any cough and/or phlegm, wheeze and/or chest tightness, and shortness of breath during the night (categorized as 'Yes' or' No').

(iii) Whether any asthma reliever medication was used during the night (categorized as 'Yes' or 'No').

(iv) presence of the following respiratory symptoms during the day:
   a. cough and/or phlegm;
   b. wheeze and/or chest tightness;
   c. shortness of breath;
   d. runny/blocked nose;
   e. eye irritation; and,
   f. fever/sore throat.

   This information was recorded in the evening. Each of these symptoms was recorded on a zero to four scale (0=no symptoms during the day, 1=symptoms, but did not disturb child's daily activities, 2=symptoms that disturbed part of child's daily activities, 4=symptoms that disturbed all or most of child's daily activities). In the panel study analysis, symptoms were categorized as either 'No symptoms' or 'Any symptoms'.

(v) presence of any cough and/or phlegm, wheeze and/or chest tightness, shortness of breath, runny/blocked nose, eye irritation and fever/sore throat during the day (categorized as 'Yes' or' No').

(vi) use of any asthma reliever and asthma preventer medication during the day. Medication use was categorized as 'Yes' and' No' and also whether the asthma medications (relievers and preventers) were taken as part of the child's normal medication routine or because of symptoms.

(vii) use of oral corticosteroids in the previous 24 hours (categorized as 'Yes' or 'No').

Outdoor physical activity

The time of the day the child spent time outdoors at home, school or elsewhere and the amount of time they did any vigorous physical activity during these periods of time were also collected for the panel study. Vigorous physical activity was defined as any activity which made the child breathe heavily, for example, playing tennis, cycling, running and swimming. Parents and children were asked to complete this time-activity diary once in the evenings. This diary was collected on the same days the peak flow and symptom diaries were collected. In absence of any pre-existing suitable format, we designed our own time-activity diary to record this information.

The total amount of time spent outdoors engaging in any vigorous physical activity was calculated for each child. This information was used in the panel study analyses.

Air pollution measures

The air pollution measures of interest for the panel study included:

1. particulate matter less than 2.5 microns in diameter ($PM_{2.5}$) - 24-hour average ($PM_{2.5}$ 24-hr)
2. particulate matter less than 10 microns in diameter (PM_{10}) - 24-hour average (PM_{10} 24-hr)
3. nitrogen dioxide (NO_2) - 1-hour maximum (NO_2 1-hr) and 24-hour average (NO_2 24-hr)
4. ozone (O_3) - 1-hour maximum (O_3 1-hr), 4-hour rolling average (O_3 4-hr) and 8-hour rolling average (O_3 8-hr)
5. carbon monoxide (CO) – 8-hour rolling average (CO 8-hr)
6. sulphur dioxide (SO_2) – 1-hour maximum (SO_2 1-hr) and 24-hour average (SO_2 24-hr)

Particulates were measured as micrograms per meter squared (ug/m^3). NO_2, O_3 and SO_2 were measured in parts per billion (ppb) and CO was measured in parts per million (ppm).

1.2.3. Panel study adherence maintenance procedures

Initial meeting with parents and children

Research staff made face to face appointments with parents and children after school or at their home to discuss the panel study. During this face-to-face meetings, parents were informed in detail about the panel study and signed a written consent form. Research staff explained the use of the electronic peak flow meter and taught parents and children how to fill out the peak flow and symptom diary and the time-activity diary.

Follow-up procedures

Weekly contact was instituted to keep participants and their parents motivated during the study. During the panel study, diaries were completed daily by the participants' parent/guardian. Diaries were posted to the study centre weekly and research staff reviewed the diaries and telephoned the parents to thank them for filling out the diary. At this telephone call, missing data pertaining to the week as a whole was sought. However, no attempt was made to obtain data that were missing on a day-by-day basis. This process was followed until all diaries were completed and the final diaries and peak flow meters were posted back to the research team.

1.3. Statistical analyses

Descriptive analyses (frequencies, means and medians, correlation coefficients and cross-tabulations) of the panel, air pollution and diary data were initially conducted.

We used generalized linear models to analyse the panel data (identity link function for continuous outcomes using Proc Mixed and logit link function for binary outcomes using Proc Glimmix). We centered daily mean temperature at 20 degrees Centigrade and number of hours spent outdoors in vigorous physical activity at two hours. All regression models then included the centered values for mean daily temperature and number of hours spent outdoors in vigorous physical activity.

Mean daily temperature, daily number of hours spent outdoors in vigorous physical activity, and interaction terms between the air pollutant and mean daily temperature and daily number of hours spent outdoors in vigorous physical activity were included in all models. Child and school specific intercepts were included as random effects in all models with continuous outcomes. For binary outcomes, only the child specific intercepts were included as a random effect. All regression models also included a first order autoregressive term.

In the models with morning reported outcomes (children measured their lung function in the morning and recorded whether they had symptoms and any reliever use during the night) as the dependent variable, air pollutants and time varying covariates (temperature and number of hours spent outdoors engaged in vigorous physical activity) were lagged by one day.

In models with evening reported outcomes (children measured their lung function in the evening and recorded symptoms and reliever/preventer use during the day) as the dependent variable, the same day (lag zero) air pollutant concentrations and covariates were used.

In all analyses, we excluded the first three days of PEF recordings to minimize any learning effects. Only children with seven or more days of diary data were included in the regression analyses.

All analyses were conducted using SAS v9.2 statistical software (SAS Institute Inc., Cary, NC, USA). Associations between air pollutants and outcomes were deemed to be statistically significant if the p-value was less than 0.05.

Results of the regression models (beta coefficients and odds ratios and their associated ninety five percent confidence intervals) are presented for a one unit increase in the air pollutant. All

results should be interpreted at a daily mean temperature of 20 degrees Centigrade and two hours spent outdoors in vigorous physical activity.

2. RESULTS

2.1. Demographic and baseline data

Two hundred and seventy subjects met the inclusion criteria for the panel study and their data are presented in this section. These 270 children are from SA (n=36; 13.3%), QLD (n=38; 14.1%), ACT (n=11; 4.1%), VIC (n=81; 30.0%), WA (n=40; 14.8%) and NSW (n=64; 23.7%). These subjects came from 51 different schools.

Demographic and clinical characteristics of the 270 subjects are presented in Table 2.1**Error! Reference source not found.**.

Table 2.1. Demographic and clinical characteristics of the subjects meeting the inclusion criteria for the panel study

	Total Number	Number positive	%
Sex			
• Females	269	123	45.7
Symptoms			
• Ever wheezed	270	235	87.0
• Wheezed in the past 12 months	269	138	51.3
• Doctor diagnosed asthma	270	270	100
• Current asthma	266	156	58.7
• Cough in last 12 months	269	252	93.7
• Visit GP last 12 months for asthma	245	102	45.6
• Visit ED last 12 months for asthma	235	14	6.0
• Admitted to hospital last 12 months for	235	3	1.3
• Asthma limited activities in last 12 months	244	102	41.8
• Missed school due to asthma in last 12 months	247	76	30.8
Atopy status			
• Any atopy	255	137	53.7
• House dust mite atopy	255	120	47.1
Use of medicines for asthma			
• Any medications ever	268	259	96.6
• Short-acting bronchodilators last 12	265	181	68.3
• Long-acting bronchodilators (alone) last	254	5	2.0
• Inhaled corticosteroids (alone) last 12	257	54	21.0
• Combined Inhaled corticosteroids and	258	50	19.4
• Leukotriene receptor antagonist last 12	255	13	5.1
• Oral steroids last 12 months	254	31	12.2
Environmental exposures			
Smoking inside the house	269	11	4.9
Types of heating			
• Unflued gas heating	270	46	17.0
• Open fire	270	38	14.1
Gas for cooking	268	198	73.9
Pets (cats/dogs) in the home	236	195	82.6
		Mean	*SD*
Age (years)	258	10.0	1.21
Weight (kg)	260	37.0	10.56
Height (cm)	261	140.9	9.52

2.2. Diary data

The panel study was conducted in six jurisdictions - (Australian Capital Territory (ACT), Victoria (VIC), Queensland (QLD), South Australia (SA), Western Australia (WA) and New South Wales (NSW). The panel study was conducted in 2007, except for NSW, where the panel study was conducted in 2008, with start and completion dates as shown in Table 2.2.

Table 2.2. Timing of panel study in each jurisdiction

Jurisdiction	Start Date	Completion Date
ACT	3/4/2007 to 4/4/2007	27/4/2007
NSW	28/2/2008 to 9/5/2008	30/3/2008 to 8/6/2008
Qld	24/7/2007 to 2/8/2007	26/8/2007 to 21/10/2007
SA	31/10/2007 to 8/11/2007	2/12/2007 to 9/12/2007
Vic	21/5/2007 to 28/06/2007	24/6/2007 to 12/8/2007
WA	28/8/2007 to 6/9/2007	30/9/2007-2/9/2007

The final sample included 270 children and 8,691 diary days for analyses after excluding those not eligible for inclusion in the panel study (n=5 children; 116 records) and those diary days with missing or out of range dates (157 records).

The mean and median number of diary days were 32.8 and 35 respectively (range=7-49 days). Eighty percent (n=216) of the children kept a diary for between 35 and 40 days. About 94% of the children kept a diary for at least four weeks.

There were at least seven days of diary recordings (n=237 children) for morning and evening PEF and morning and evening FEV_1. Eighteen children did not have recordings for PEF and FEV_1. At least 7 days of diary entries were made by 260 children for evening symptoms and by 259 children for evening reliever medication use. At least 7 days of diary entries were made by 257 children for morning symptoms.

Table 2.3**Error! Reference source not found.** shows the available data (diary days) for each of the outcome variables. The mean number of diary days for recorded lung function was less than the mean number of diary days for recorded symptoms. For example, morning FEV_1 was recorded on 19.6 days on average whereas morning and evening symptoms were recorded on an average of about 26 days.

Table 2.4 presents descriptive statistics for selected outcome variables.

Table 2.3. Available diary days per child (N = 270) for selected outcome variables

Health outcomes	Mean	SD	Median	Range
Morning FEV_1	19.61	9.38	22	0-34
Evening FEV_1	19.61	9.37	21	0-35
Within-subject residual morning	19.81	9.48	22	0-34
Within-subject residual evening	19.87	9.52	21	0-35
Amplitude difference of FEV_1	15.05	9.05	15	0-32
Morning PEF	19.61	9.38	22	0-34
Evening PEF	19.56	9.35	21	0-35
Within-subject residual morning PEF	19.81	9.48	22	0-34
Within-subject residual evening PEF	19.87	9.52	21	0-35
Amplitude difference of PEF	15.00	9.03	15	0-33
Any day time symptom	26.21	7.89	29	2-35
Mean of day time score of cough, wheeze, shortness of breath, runny nose, eye irritation and fever	26.12	7.87	29	2-35
Mean of day time score of runny nose, eye irritation and fever (upper respiratory symptoms)	26.11	7.88	29	2-35
Day time cough	26.11	7.87	29	2-35
Day time wheeze	26.11	7.88	29	2-35
Day time shortness of breath	26.11	7.88	29	2-35
Day time runny nose	26.11	7.88	29	2-35
Day time eye irritation	26.11	7.88	29	2-35
Day time fever	26.11	7.88	29	2-35
Used reliever for symptoms during the day	26.58	8.07	30	0-36
Used preventers for symptoms during the day	26.26	8.35	30	0-35
Used any medications for symptoms during the day	26.70	8.12	30	0-36
Any chest symptoms during the	26.11	7.73	29	2-36
Night cough	26.05	7.71	29	2-36
Night wheeze	26.04	7.72	29	2-36
Night shortness of breath	26.04	7.72	29	2-36
Mean of night score of cough, wheeze and shortness of breath	26.05	7.71	29	2-36

Table 2.4. Summary statistics for selected continuous outcome variables

Health outcomes	N	Mean	SD	Median	Range
Morning PEF (litres/min)	252	260.87	57.54	255.52	120-467
Evening PEF (litres/min)	252	275.9	56.71	269.52	143-470
Within-subject residual morning PEF (litres/min)	252	0	0.09	0	-0.4 - 0.67
Within-subject residual evening PEF (litres/min)	252	-0.01	0.11	0	-0.93-0.4
Amplitude difference of PEF (litres/min)	251	-0.04	0.07	-0.03	-0.38-0.24
Morning FEV_1 (litres)	252	1.81	0.42	1.74	0.86-3.52
Evening FEV_1 (litres)	252	1.87	0.41	1.8	0.93-3.53
Within-subject residual morning FEV_1 (litres)	252	-0.01	0.08	0	-0.59-0.29
Within-subject residual evening FEV_1 (litres)	252	0	0.08	0	-0.45-0.55
Amplitude difference of FEV_1 (litres)	251	-0.02	0.08	-0.01	-0.38-0.48
Mean of day time cough, wheeze, shortness of breath, runny nose, eye irritation and fever	270	0.18	0.26	0.11	0-1.85
Mean of day time runny nose, eye irritation and fever (upper respiratory symptoms)	270	0.18	0.27	0.08	0-1.57
Mean of night cough, wheeze and shortness of breath	270	0.16	0.24	0.08	0-1.97

*Total diary days=8,848 days

Table 2.5, Table 2.6 and Table 2.7show the summary distribution of numbers of days with night symptoms, day time symptoms and medication use respectively.

Table 2.5. Number of children by percentage of diary days with night symptoms

% of diary days	N	Percent	Cumulative Frequency	Cumulative Percent
Any night symptoms				
Less than 20%	148	54.81	148	54.81
20 to 39%	55	20.37	203	75.19
40-to 59%	25	9.26	228	84.44
60 to 79%	18	6.67	246	91.11
80% or more	24	8.89	270	100
Night cough				
Less than 20%	162	60	162	60
20 to 39%	50	18.52	212	78.52
40-to 59%	21	7.78	233	86.3
60 to 79%	19	7.04	252	93.33
80% or more	18	6.67	270	100
Night wheeze				
Less than 20%	229	84.81	229	84.81
20 to 39%	22	8.15	251	92.96
40-to 59%	10	3.7	261	96.67
60 to 79%	3	1.11	264	97.78
80% or more	6	2.22	270	100
Night shortness of breath				
Less than 20%	253	93.7	253	93.7
20 to 39%	8	2.96	261	96.67
40-to 59%	7	2.59	268	99.26
60 to 79%	1	0.37	269	99.63
80% or more	1	0.37	270	100

Table 2.6. Number of children by percentage of diary days with day time symptoms

% of diary days	N	Percent	Cumulative Frequency	Cumulative Percent
Any day time symptoms				
Less than 20%	96	35.56	96	35.56
20 to 39%	63	23.33	159	58.89
40-to 59%	39	14.44	198	73.33
60 to 79%	30	11.11	228	84.44
80% or more	42	15.56	270	100
Day time cough				
Less than 20%	142	52.59	142	52.59
20 to 39%	53	19.63	195	72.22
40-to 59%	32	11.85	227	84.07
60 to 79%	19	7.04	246	91.11
80% or more	24	8.89	270	100
Day time wheeze				
Less than 20%	213	78.89	213	78.89
20 to 39%	34	12.59	247	91.48
40-to 59%	10	3.7	257	95.19
60 to 79%	8	2.96	265	98.15
80% or more	5	1.85	270	100
Day time shortness of breath				
Less than 20%	239	88.52	239	88.52
20 to 39%	18	6.67	257	95.19
40-to 59%	5	1.85	262	97.04
60 to 79%	6	2.22	268	99.26
80% or more	2	0.74	270	100
Day time runny nose				
Less than 20%	160	59.26	160	59.26
20 to 39%	49	18.15	209	77.41
40-to 59%	24	8.89	233	86.3
60 to 79%	19	7.04	252	93.33
80% or more	18	6.67	270	100
Day time eye irritation				
Less than 20%	234	86.67	234	86.67
20 to 39%	22	8.15	256	94.81
40-to 59%	2	0.74	258	95.56
60 to 79%	8	2.96	266	98.52
80% or more	4	1.48	270	100
Day time fever				
Less than 20%	233	86.3	233	86.3
20 to 39%	17	6.3	250	92.59
40-to 59%	10	3.7	260	96.3
60 to 79%	5	1.85	265	98.15
80% or more	5	1.85	270	100

Table 2.7. Number of children by percentage of diary days with medication use

% of diary days	N	Percent	Cumulative Frequency	Cumulative Percent
Use of preventers during the day for symptoms				
Less than 20%	253	94.05	253	94.05
20 to 39%	8	2.97	261	97.03
40-to 59%	2	0.74	263	97.77
60 to 79%	5	1.86	268	99.63
80% or more	1	0.37	269	100
Use of any medications during the day for symptoms				
Less than 20%	230	85.5	230	85.5
20 to 39%	22	8.18	252	93.68
40-to 59%	7	2.6	259	96.28
60 to 79%	7	2.6	266	98.88
80% or more	3	1.12	269	100
Use of routine relievers during the day				
Less than 20%	252	93.68	252	93.68
20 to 39%	4	1.49	256	95.17
40-to 59%	6	2.23	262	97.4
60 to 79%	7	2.6	269	100
Use of routine preventers during the day				
Less than 20%	230	85.5	230	85.5
20 to 39%	3	1.12	233	86.62
40-to 59%	4	1.49	237	88.1
60 to 79%	10	3.72	247	91.82
80% or more	22	8.18	269	100

2.3. Air pollution data

Air pollution and data from 27 air quality monitors (AQMs) were used in the panel study. The AQMs were located in SA (n=4), QLD (n=4), ACT (n=1), VIC (n=8), WA (n=3) and NSW (n=7).

All AQMs except those from NSW provided data from 1 January 2007 to 31 December 2007. NSW AQMs provided data from January 2008 to 30 September 2008. $PM_{2.5}$ data were provided by 15 AQMs, PM_{10} data by 27 AQMs, ozone by 23 AQMs, NO_2 by 26 AQMs, CO by 17 AQMs and SO_2 by 14 AQMs.

Across all the 27 AQMs, mean PM_{10} 24-hr and $PM_{2.5}$ 24-hr concentrations were 17.6 ug/m^3 (range: 1.2-166.7 ug/m^3) and 7.2 ug/m^3 (range: 0.1-131.9 ug/m^3) respectively; the mean 1-hr, 4-hr and 8-hr ozone concentrations were 30.5 ppb (range: 0-127 ppb), 28.8 ppb (range: 0.3-115 ppb) and 26.4 ppb (range: 0.4-99 ppb) respectively; mean 1-hr and 24-hr NO_2 concentrations were 18.7 ppb (range: 0-69 ppb) and 7.9 ppb (range: 0-30.8 ppb) respectively; mean CO 8-hr was 0.45 ppm (range: 0.01-2.9 ppm); and, mean SO_2 1-hr and SO_2 24-hr concentrations were 9.8 ppb (range: 0-594 ppb) and 1.9 ppb (range: 0-59.7 ppb) respectively. Descriptive data for each of the

air quality monitoring stations and by each State/Territory and season are presented in Appendices Part C.

2.4. Associations between air pollutants and lung function, symptoms and medication use

We conducted seven sets of analyses on the panel data:

1. All air pollutants and all outcomes. For the morning recorded lung function (PEF, FEV_1) and night symptoms and night reliever medication use, analyses were conducted using air pollution concentrations at lag 1, lag 2 and lag 3. For the evening recorded lung function (PEF, FEV_1) and day time symptoms and day time reliever and preventer medication use, analyses were conducted using air pollution concentrations at lag 0, lag 1 and lag 2.
2. A sub-analysis for the effects of ozone during the warm months (November to April).
3. A sub-analysis for the effects of SO_2 after excluding children from Port Pirie.
4. A sub-analysis for the effects of SO_2 in two pollutant models with PM_{10} .
5. A sub-analysis for the effects of NO_2 in two pollutant models with ozone.
6. A sub-analysis for the effects of NO_2 in the subgroup of children who have unflued gas heating in their home.
7. A sub-analysis for the effects of PM_{10} in two pollutant models (ie. PM_{10} plus the gaseous air pollutants).

Lung function effects are presented as the beta coefficients with the associated 95% confidence intervals and the p-values. Effects of air pollution on symptoms and medication use are presented as odds ratios and association 95% confidence intervals and the p-values.

Across all the 27 AQMs, there was moderate correlation between PM_{10} and $PM_{2.5}$ (r=0.65). There were very high correlations among the three metrics for ozone (r=0.94-0.99), the two metrics for SO_2 (r=0.90) and the two metrics for NO_2 (r=0.84). Otherwise, the correlations between air pollutants were generally weak. Correlation coefficients by State/Territory are presented in Appendices Part C.

2.4.1. Associations between any air pollutants and lung function, symptoms and medication use

There were few associations between air pollutants and lung function (Table 2.8**).** These were mainly positive associations between 1-hr NO_2 and morning lung function, and 24-hr SO_2 with lung function.

Tables 2.9- 2.11 and present the findings for air pollutants and symptoms and medication use. Negative effects are seen mainly with CO, NO_2 and PM_{10} whereas positive effects are generally seen with ozone and SO_2. More adverse effects were observed with 24-hr NO_2 compared to 1-hr NO_2. Similarly, more adverse effects were seen with PM_{10} than with $PM_{2.5}$.

Table 2.8. Associations between air pollutants and lung function

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
$PM_{2.5}$ 24-hr				
lag0	-0.2076 (-1.7232 to 1.3080), p=0.79	-0.0022 (-0.0119 to 0.0076), p=0.66		
lag1	0.8534 (-0.5868 to 2.2936), p=0.25	0.0058 (-0.0036 to 0.0151), p=0.23	0.1960 (-0.8843 to 1.2762), p=0.72	0.0024 (-0.0056 to 0.0103), p=0.56
lag2	0.3709 (-1.0164 to 1.7583), p=0.60	0.0001 (-0.0091 to 0.0092), p=0.99	0.2315 (-0.8657 to 1.3286), p=0.68	0.0037 (-0.0043 to 0.0118), p=0.37
lag3			-0.8327 (-1.9529 to 0.2874), p=0.15	-0.0035 (-0.0116 to 0.0046), p=0.40
PM_{10} 24-hr				
lag0	-0.0619 (-0.3833 to 0.2595), p=0.71	0.0004 (-0.0018 to 0.0025), p=0.74		
lag1	0.1204 (-0.2078 to 0.4487), p=0.47	0.0008 (-0.0013 to 0.0030), p=0.46	0.1880 (-0.0564 to 0.4324), p=0.13	0.0011 (-0.0006 to 0.0028), p=0.21
lag2	-0.0279 (-0.3741 to 0.3183), p=0.87	-0.0001 (-0.0025 to 0.0022), p=0.91	-0.0155 (-0.2834 to 0.2523), p=0.91	0.0001 (-0.0018 to 0.0020), p=0.94
lag3			-0.0899 (-0.3755 to 0.1957), p=0.54	-0.0006 (-0.0026 to 0.0014), p=0.57
NO_2 1-hr				
lag0	0.0586 (-0.3451 to 0.4623), p=0.78	-0.0003 (-0.0030 to 0.0024), p=0.81		
lag1	0.0155 (-0.3831 to 0.4140), p=0.94	0.0011 (-0.0015 to 0.0038), p=0.41	0.2165 (-0.0772 to 0.5101), p=0.15	0.0016 (-0.0006 to 0.0037), p=0.15
lag2	0.1877 (-0.2250 to 0.6003), p=0.37	0.0009 (-0.0019 to 0.0037), p=0.52	-0.3102 (-0.6241 to 0.0038), p=0.053	**-0.0030 (-0.0052 to -0.0008), p=0.007**
lag3			**0.3541 (0.0439 to 0.6642), p=0.025**	0.0017 (-0.0005 to 0.0039), p=0.13
NO_2 24-hr				
lag0	0.2562 (-0.5916 to 1.1041), p=0.55	0.0022 (-0.0035 to 0.0078), p=0.45		
lag1	-0.2076 (-1.0393 to 0.6242), p=0.62	0.0008 (-0.0047 to 0.0064), p=0.77	0.0037 (-0.6227 to 0.6301), p=0.99	-0.0026 (-0.0070 to 0.0019), p=0.26
lag2	0.3475 (-0.4809 to 1.1759), p=0.41	0.0016 (-0.0040 to 0.0073), p=0.57	-0.0702 (-0.7089 to 0.5685), p=0.83	-0.0026 (-0.0071 to 0.0019), p=0.26
lag3			0.2670 (-0.3603 to 0.8943), p=0.40	0.0017 (-0.0028 to 0.0061), p=0.46
O_3 1-hr				
lag0	-0.1139 (-0.4480 to 0.2201), p=0.50	-0.0005 (-0.0027 to 0.0018), p=0.68		
lag1	-0.0409 (-0.3590 to 0.2772), p=0.80	-0.0009 (-0.0031 to 0.0012), p=0.39	0.1636 (-0.0668 to 0.3939), p=0.16	0.0007 (-0.0009 to 0.0023), p=0.39
lag2	0.1639 (-0.1568 to 0.4847), p=0.32	0.0009 (-0.0013 to 0.0030), p=0.42	-0.0331 (-0.2679 to 0.2018), p=0.78	-0.0005 (-0.0021 to 0.0011), p=0.57
lag3			-0.1207 (-0.3520 to	-0.0003 (-0.0018 to

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
			0.1106), p=0.31	0.0013), p=0.75
O_3 4-hr				
lag0	-0.2039 (-0.5728 to 0.1649), p=0.28	-0.0012 (-0.0037 to 0.0013), p=0.34		
lag1	-0.0249 (-0.3744 to 0.3247), p=0.89	-0.0007 (-0.0030 to 0.0016), p=0.56	0.1664 (-0.0902 to 0.4230), p=0.20	0.0007 (-0.0011 to 0.0025), p=0.43
lag2	0.2023 (-0.1484 to 0.5530), p=0.26	0.0009 (-0.0015 to 0.0032), p=0.46	0.0000 (-0.2594 to 0.2595), p=1.00	-0.0003 (-0.0020 to 0.0015), p=0.75
lag3			-0.1383 (-0.3921 to 0.1156), p=0.29	-0.0003 (-0.0020 to 0.0014), p=0.74
O_3 8-hr				
lag0	-0.2220 (-0.6396 to 0.1956), p=0.30	-0.0018 (-0.0046 to 0.0010), p=0.20		
lag1	0.0069 (-0.3950 to 0.4088), p=0.97	-0.0004 (-0.0031 to 0.0023), p=0.77	0.1783 (-0.1197 to 0.4764), p=0.24	0.0008 (-0.0013 to 0.0028), p=0.46
lag2	0.2517 (-0.1579 to 0.6613), p=0.23	0.0012 (-0.0016 to 0.0040), p=0.40	0.0006 (-0.3077 to 0.3089), p=1.00	-0.0000 (-0.0021 to 0.0021), p=0.98
lag3			-0.1043 (-0.4105 to 0.2019), p=0.50	-0.0006 (-0.0027 to 0.0015), p=0.58
CO 8-hr				
lag0	0.5490 (-13.762 to 14.8604), p=0.94	0.0228 (-0.0756 to 0.1212), p=0.65		
lag1	5.3164 (-8.8404 to 19.4732), p=0.46	0.0443 (-0.0526 to 0.1413), p=0.37	1.9066 (-8.6810 to 12.4943), p=0.72	-0.0319 (-0.1088 to 0.0450), p=0.42
lag2	0.5428 (-13.935 to 15.0201), p=0.94	-0.0027 (-0.1016 to 0.0962), p=0.96	-5.4271 (-15.771 to 4.9173), p=0.30	-0.0295 (-0.1052 to 0.0463), p=0.45
lag3			4.8370 (-4.6149 to 14.2889), p=0.32	0.0140 (-0.0552 to 0.0832), p=0.69
SO_2 1-hr				
lag0	0.2848 (-0.0329 to 0.6026), p=0.079	0.0011 (-0.0011 to 0.0033), p=0.31		
lag1	-0.0750 (-0.3208 to 0.1708), p=0.55	0.0007 (-0.0010 to 0.0025), p=0.40	0.0362 (-0.1621 to 0.2345), p=0.72	0.0002 (-0.0011 to 0.0015), p=0.76
lag2	-0.0810 (-0.3682 to 0.2062), p=0.58	-0.0014 (-0.0034 to 0.0006), p=0.18	0.1137 (-0.0906 to 0.3179), p=0.28	0.0005 (-0.0009 to 0.0018), p=0.47
lag3			-0.1482 (-0.3499 to 0.0536), p=0.15	0.0001 (-0.0013 to 0.0014), p=0.94
SO_2 24-hr				
lag0	**1.6181 (0.1404 to 3.0958), p=0.032**	0.0052 (-0.0049 to 0.0154), p=0.31		
lag1	-1.0652 (-2.5482 to 0.4179), p=0.16	0.0022 (-0.0081 to 0.0125), p=0.68	-0.6026 (-1.7145 to 0.5094), p=0.29	-0.0044 (-0.0119 to 0.0031), p=0.25
lag2	0.4314 (-1.1946 to 2.0575), p=0.60	-0.0009 (-0.0122 to 0.0104), p=0.87	**1.2686 (0.0857 to 2.4514), p=0.036**	0.0078 (0.0000 to 0.0157), p=0.050
lag3			-1.0547 (-2.2404 to 0.1310), p=0.081	-0.0048 (-0.0127 to 0.0032), p=0.24

Table 2.9. Associations between air pollutants and night symptoms and medication use

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
$PM_{2.5}$ 24-hr					
lag1	1.0285 (0.9539 to 1.1088), p=0.46	1.0401 (0.9333 to 1.1592), p=0.48	0.9944 (0.8520 to 1.1606), p=0.94	1.0180 (0.9493 to 1.0918), p=0.62	0.9286 (0.8274 to 1.0421), p=0.21
lag2	1.0767 (0.9998 to 1.1596), p=0.051	1.0222 (0.9145 to 1.1425), p=0.70	1.0503 (0.8938 to 1.2343), p=0.55	1.0553 (0.9844 to 1.1313), p=0.13	0.9342 (0.8334 to 1.0472), p=0.24
lag3	1.0718 (0.9928 to 1.1570), p=0.076	0.9851 (0.8803 to 1.1025), p=0.79	1.0302 (0.8824 to 1.2027), p=0.71	1.0418 (0.9703 to 1.1186), p=0.26	0.9544 (0.8537 to 1.0669), p=0.41
PM_{10} 24-hr					
lag1	**1.0187 (1.0047 to 1.0329), p=0.009**	1.0190 (0.9988 to 1.0396), p=0.065	1.0034 (0.9725 to 1.0354), p=0.83	1.0131 (0.9994 to 1.0269), p=0.060	1.0013 (0.9776 to 1.0255), p=0.92
lag2	**1.0180 (1.0041 to 1.0322), p=0.011**	**1.0238 (1.0036 to 1.0444), p=0.021**	1.0166 (0.9862 to 1.0479), p=0.29	**1.0163 (1.0029 to 1.0298), p=0.017**	0.9813 (0.9542 to 1.0092), p=0.19
lag3	**1.0173 (1.0024 to 1.0325), p=0.023**	1.0151 (0.9938 to 1.0368), p=0.17	1.0112 (0.9772 to 1.0464), p=0.52	1.0138 (0.9996 to 1.0282), p=0.057	0.9948 (0.9679 to 1.0225), p=0.71
NO_2 1-hr					
lag1	1.0164 (0.9984 to 1.0347), p=0.074	1.0116 (0.9868 to 1.0371), p=0.36	1.0304 (0.9961 to 1.0660), p=0.083	1.0165 (0.9996 to 1.0338), p=0.056	1.0102 (0.9828 to 1.0383), p=0.47
lag2	**1.0282 (1.0096 to 1.0473), p=0.003**	1.0180 (0.9923 to 1.0445), p=0.17	1.0104 (0.9746 to 1.0474), p=0.57	**1.0244 (1.0067 to 1.0424), p=0.007**	0.9968 (0.9689 to 1.0255), p=0.83
lag3	**1.0257 (1.0066 to 1.0451), p=0.008**	1.0201 (0.9934 to 1.0474), p=0.14	1.0110 (0.9725 to 1.0509), p=0.58	**1.0227 (1.0047 to 1.0410), p=0.013**	1.0110 (0.9824 to 1.0404), p=0.45

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
NO_2 24-hr					
lag1	**1.0504 (1.0175 to 1.0844), p=0.002**	**1.0640 (1.0186 to 1.1114), p=0.005**	**1.0771 (1.0183 to 1.1392), p=0.010**	**1.0442 (1.0126 to 1.0768), p=0.006**	1.0459 (0.9973 to 1.0969), p=0.064
lag2	**1.0599 (1.0261 to 1.0948), p=0.0004**	**1.0545 (1.0083 to 1.1028), p=0.020**	1.0545 (0.9923 to 1.1207), p=0.087	**1.0577 (1.0250 to 1.0915), p=0.0005**	1.0358 (0.9867 to 1.0873), p=0.16
lag3	**1.0757 (1.0407 to 1.1118), p=0.0000**	**1.0581 (1.0124 to 1.1057), p=0.012**	1.0283 (0.9658 to 1.0947), p=0.38	**1.0682 (1.0349 to 1.1026), p=0.0000**	1.0439 (0.9943 to 1.0959), p=0.083
O_3 1-hr					
lag1	0.9935 (0.9783 to 1.0089), p=0.40	0.9805 (0.9598 to 1.0017), p=0.071	**0.9598 (0.9277 to 0.9929), p=0.018**	0.9924 (0.9786 to 1.0064), p=0.28	0.9945 (0.9715 to 1.0181), p=0.64
lag2	0.9999 (0.9840 to 1.0161), p=0.99	**0.9753 (0.9523 to 0.9988), p=0.039**	0.9675 (0.9326 to 1.0038), p=0.078	1.0005 (0.9859 to 1.0153), p=0.95	0.9927 (0.9684 to 1.0176), p=0.56
lag3	0.9946 (0.9782 to 1.0114), p=0.53	**0.9636 (0.9404 to 0.9874), p=0.003**	**0.9613 (0.9256 to 0.9984), p=0.041**	0.9892 (0.9742 to 1.0045), p=0.17	0.9891 (0.9635 to 1.0154), p=0.41
O_3 4-hr					
lag1	0.9931 (0.9770 to 1.0095), p=0.41	**0.9751 (0.9533 to 0.9975), p=0.029**	**0.9558 (0.9223 to 0.9905), p=0.013**	0.9911 (0.9765 to 1.0060), p=0.24	0.9932 (0.9688 to 1.0183), p=0.59
lag2	0.9990 (0.9821 to 1.0162), p=0.91	**0.9703 (0.9460 to 0.9951), p=0.019**	**0.9616 (0.9248 to 0.9998), p=0.049**	0.9985 (0.9830 to 1.0143), p=0.85	0.9919 (0.9660 to 1.0185), p=0.55
lag3	0.9941 (0.9766 to 1.0119), p=0.51	**0.9604 (0.9359 to 0.9855), p=0.002**	**0.9581 (0.9204 to 0.9972), p=0.036**	0.9892 (0.9732 to 1.0054), p=0.19	0.9844 (0.9575 to 1.0120), p=0.27

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
O_3 8-hr					
lag1	0.9906 (0.9728 to 1.0087), p=0.31	**0.9619 (0.9383 to 0.9862), p=0.002**	**0.9519 (0.9162 to 0.9890), p=0.011**	0.9882 (0.9722 to 1.0043), p=0.15	0.9899 (0.9632 to 1.0174), p=0.47
lag2	0.9949 (0.9762 to 1.0140), p=0.60	**0.9562 (0.9299 to 0.9832), p=0.002**	**0.9537 (0.9139 to 0.9952), p=0.029**	0.9933 (0.9763 to 1.0107), p=0.45	0.9846 (0.9560 to 1.0141), p=0.30
lag3	0.9926 (0.9732 to 1.0125), p=0.46	**0.9530 (0.9263 to 0.9805), p=0.0009**	**0.9536 (0.9129 to 0.9960), p=0.032**	0.9883 (0.9707 to 1.0062), p=0.20	0.9750 (0.9454 to 1.0055), p=0.11
CO 8-hr					
lag1	1.6304 (0.9819 to 2.7073), p=0.059	1.8501 (0.9353 to 3.6594), p=0.077	**2.3444 (1.0130 to 5.4260), p=0.047**	1.5380 (0.9296 to 2.5445), p=0.094	1.1206 (0.5303 to 2.3680), p=0.77
lag2	**1.9233 (1.1552 to 3.2020), p=0.012**	1.8100 (0.9163 to 3.5751), p=0.088	1.9437 (0.8032 to 4.7034), p=0.14	**1.9502 (1.1704 to 3.2498), p=0.010**	0.7411 (0.3443 to 1.5955), p=0.44
lag3	1.0988 (0.6760 to 1.7862), p=0.70	1.0803 (0.5623 to 2.0754), p=0.82	1.5933 (0.6735 to 3.7691), p=0.29	1.0118 (0.6273 to 1.6320), p=0.96	1.0453 (0.5199 to 2.1016), p=0.90
SO_2 1-hr					
lag1	1.0048 (0.9915 to 1.0184), p=0.48	1.0027 (0.9795 to 1.0264), p=0.82	0.9401 (0.8725 to 1.0129), p=0.10	1.0055 (0.9928 to 1.0184), p=0.40	**1.0255 (1.0033 to 1.0482), p=0.024**
lag2	0.9939 (0.9797 to 1.0084), p=0.41	0.9995 (0.9743 to 1.0252), p=0.97	**0.9192 (0.8480 to 0.9964), p=0.041**	0.9974 (0.9839 to 1.0111), p=0.71	1.0195 (0.9977 to 1.0417), p=0.080
lag3	1.0046 (0.9904 to 1.0190), p=0.52	0.9966 (0.9697 to 1.0241), p=0.80	0.9199 (0.8452 to 1.0013), p=0.054	1.0042 (0.9904 to 1.0181), p=0.56	0.9509 (0.8986 to 1.0062), p=0.081

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
SO_2 24-hr					
lag1	0.9787 (0.9053 to 1.0582), p=0.59	0.9786 (0.8575 to 1.1168), p=0.75	0.8482 (0.6143 to 1.1711), p=0.32	0.9843 (0.9142 to 1.0597), p=0.67	1.1044 (0.9660 to 1.2627), p=0.15
lag2	0.9506 (0.8750 to 1.0327), p=0.23	1.0062 (0.8813 to 1.1488), p=0.93	0.8827 (0.6656 to 1.1706), p=0.39	0.9785 (0.9054 to 1.0575), p=0.58	1.0571 (0.9146 to 1.2217), p=0.45
lag3	0.9948 (0.9184 to 1.0776), p=0.90	0.9068 (0.7682 to 1.0704), p=0.25	**0.6063 (0.4053 to 0.9069), p=0.015**	0.9850 (0.9110 to 1.0652), p=0.71	0.8244 (0.6575 to 1.0336), p=0.094

Table 2.10. Associations between air pollutants and day time symptoms

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
$PM_{2.5}$ 24-hr							
lag0	1.0409 (0.9753 to 1.1109), p=0.23	1.0096 (0.9198 to 1.1082), p=0.84	0.9747 (0.8678 to 1.0948), p=0.67	**1.0873 (1.0143 to 1.1656), p=0.018**	0.9982 (0.8895 to 1.1201), p=0.98	0.9002 (0.8026 to 1.0096), p=0.072	1.0285 (0.9707 to 1.0897), p=0.34
lag1	1.0188 (0.9516 to 1.0908), p=0.59	0.9512 (0.8642 to 1.0470), p=0.31	0.9956 (0.8768 to 1.1304), p=0.95	1.0375 (0.9657 to 1.1147), p=0.31	1.0968 (0.9787 to 1.2293), p=0.11	0.9341 (0.8336 to 1.0466), p=0.24	1.0053 (0.9467 to 1.0676), p=0.86
lag2	1.0460 (0.9759 to 1.1210), p=0.20	0.9668 (0.8778 to 1.0649), p=0.49	1.0152 (0.8952 to 1.1512), p=0.81	1.0210 (0.9490 to 1.0985), p=0.58	1.0759 (0.9562 to 1.2106), p=0.22	0.9723 (0.8707 to 1.0858), p=0.62	1.0229 (0.9624 to 1.0873), p=0.47
PM_{10} 24-hr							
lag0	1.0058 (0.9922 to 1.0197), p=0.40	**1.0211 (1.0034 to 1.0392), p=0.019**	1.0070 (0.9850 to 1.0294), p=0.54	1.0040 (0.9888 to 1.0194), p=0.61	0.9847 (0.9603 to 1.0097), p=0.23	1.0054 (0.9851 to 1.0261), p=0.60	0.9990 (0.9869 to 1.0112), p=0.87
lag1	1.0092 (0.9943 to 1.0243), p=0.23	1.0082 (0.9885 to 1.0284), p=0.42	1.0222 (0.9987 to 1.0463), p=0.064	0.9992 (0.9823 to 1.0165), p=0.93	0.9980 (0.9726 to 1.0241), p=0.88	0.9982 (0.9759 to 1.0211), p=0.88	1.0048 (0.9919 to 1.0179), p=0.47
lag2	**1.0177 (1.0028 to 1.0327), p=0.019**	1.0137 (0.9936 to 1.0341), p=0.18	1.0118 (0.9874 to 1.0367), p=0.35	0.9984 (0.9817 to 1.0154), p=0.85	1.0034 (0.9778 to 1.0296), p=0.80	1.0086 (0.9873 to 1.0304), p=0.43	1.0070 (0.9944 to 1.0198), p=0.28
NO_2 1-hr							
lag0	1.0150 (0.9984 to 1.0318), p=0.077	**1.0356 (1.0130 to 1.0586), p=0.002**	1.0212 (0.9949 to 1.0483), p=0.11	1.0008 (0.9840 to 1.0179), p=0.93	0.9863 (0.9605 to 1.0129), p=0.31	0.9998 (0.9762 to 1.0239), p=0.98	1.0052 (0.9910 to 1.0197), p=0.47
lag1	1.0144 (0.9976 to 1.0316), p=0.094	**1.0230 (1.0007 to 1.0458), p=0.043**	1.0208 (0.9927 to 1.0497), p=0.15	1.0040 (0.9866 to 1.0216), p=0.66	0.9895 (0.9636 to 1.0161), p=0.44	0.9862 (0.9626 to 1.0105), p=0.26	1.0045 (0.9899 to 1.0192), p=0.55

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
lag2	**1.0186 (1.0013 to 1.0362), p=0.035**	1.0040 (0.9816 to 1.0269), p=0.73	1.0101 (0.9828 to 1.0382), p=0.47	0.9893 (0.9719 to 1.0069), p=0.23	0.9985 (0.9715 to 1.0262), p=0.91	0.9921 (0.9679 to 1.0169), p=0.53	0.9995 (0.9847 to 1.0145), p=0.94
NO_2 24-hr							
lag0	**1.0535 (1.0219 to 1.0861), p=0.0008**	**1.1107 (1.0681 to 1.1550), p=0.0000**	**1.0594 (1.0134 to 1.1075), p=0.011**	1.0153 (0.9835 to 1.0481), p=0.35	0.9825 (0.9325 to 1.0352), p=0.51	1.0112 (0.9689 to 1.0552), p=0.61	**1.0387 (1.0109 to 1.0673), p=0.006**
lag1	**1.0387 (1.0071 to 1.0713), p=0.016**	**1.0730 (1.0320 to 1.1155), p=0.0004**	**1.0557 (1.0075 to 1.1063), p=0.023**	1.0141 (0.9815 to 1.0477), p=0.40	0.9792 (0.9302 to 1.0308), p=0.42	0.9799 (0.9385 to 1.0232), p=0.36	1.0212 (0.9933 to 1.0499), p=0.14
lag2	**1.0494 (1.0170 to 1.0829), p=0.003**	1.0402 (1.0002 to 1.0818), p=0.049	1.0426 (0.9950 to 1.0925), p=0.080	0.9966 (0.9641 to 1.0303), p=0.84	0.9971 (0.9456 to 1.0513), p=0.91	0.9878 (0.9454 to 1.0320), p=0.58	1.0202 (0.9921 to 1.0491), p=0.16
O_3 1-hr							
lag0	0.9899 (0.9762 to 1.0039), p=0.16	0.9980 (0.9789 to 1.0175), p=0.84	1.0118 (0.9889 to 1.0352), p=0.31	1.0023 (0.9881 to 1.0166), p=0.76	0.9985 (0.9750 to 1.0225), p=0.90	0.9910 (0.9712 to 1.0111), p=0.38	0.9948 (0.9833 to 1.0065), p=0.38
lag1	0.9923 (0.9778 to 1.0070), p=0.30	0.9855 (0.9661 to 1.0053), p=0.15	1.0096 (0.9842 to 1.0357), p=0.46	0.9981 (0.9833 to 1.0132), p=0.81	0.9988 (0.9755 to 1.0227), p=0.92	0.9922 (0.9718 to 1.0130), p=0.46	0.9945 (0.9824 to 1.0067), p=0.37
lag2	0.9942 (0.9791 to 1.0096), p=0.46	0.9830 (0.9622 to 1.0042), p=0.12	0.9978 (0.9720 to 1.0243), p=0.87	0.9954 (0.9800 to 1.0110), p=0.56	1.0025 (0.9760 to 1.0297), p=0.86	0.9922 (0.9709 to 1.0141), p=0.48	0.9907 (0.9782 to 1.0034), p=0.15
O_3 4-hr							
lag0	0.9891 (0.9745 to 1.0039), p=0.15	0.9959 (0.9758 to 1.0165), p=0.70	1.0126 (0.9886 to 1.0372), p=0.30	1.0022 (0.9872 to 1.0174), p=0.78	1.0034 (0.9788 to 1.0287), p=0.79	0.9923 (0.9715 to 1.0137), p=0.48	0.9940 (0.9818 to 1.0064), p=0.34
lag1	0.9910 (0.9756 to 1.0066), p=0.26	0.9804 (0.9601 to 1.0012), p=0.065	1.0103 (0.9838 to 1.0374), p=0.45	0.9974 (0.9817 to 1.0133), p=0.75	1.0010 (0.9764 to 1.0262), p=0.94	0.9930 (0.9715 to 1.0150), p=0.53	0.9939 (0.9811 to 1.0069), p=0.36
lag2	0.9910 (0.9749 to	0.9826 (0.9607 to	0.9987 (0.9714 to	0.9951 (0.9788 to	1.0042 (0.9763 to	0.9934 (0.9708 to	0.9884 (0.9751 to

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
	1.0074), p=0.28	1.0049), p=0.13	1.0267), p=0.93	1.0117), p=0.56	1.0330), p=0.77	1.0166), p=0.57	1.0020), p=0.094
O_3 8-hr							
lag0	0.9869 (0.9711 to 1.0029), p=0.11	0.9944 (0.9729 to 1.0164), p=0.61	1.0138 (0.9880 to 1.0403), p=0.30	1.0064 (0.9902 to 1.0230), p=0.44	1.0071 (0.9799 to 1.0350), p=0.61	0.9923 (0.9698 to 1.0153), p=0.51	0.9953 (0.9821 to 1.0086), p=0.49
lag1	0.9850 (0.9684 to 1.0020), p=0.083	**0.9737 (0.9518 to 0.9961), p=0.022**	1.0065 (0.9781 to 1.0357), p=0.66	0.9971 (0.9802 to 1.0144), p=0.74	1.0023 (0.9749 to 1.0305), p=0.87	0.9928 (0.9697 to 1.0165), p=0.55	0.9919 (0.9781 to 1.0059), p=0.25
lag2	0.9825 (0.9648 to 1.0006), p=0.057	**0.9755 (0.9518 to 0.9998), p=0.048**	0.9929 (0.9628 to 1.0240), p=0.65	0.9942 (0.9762 to 1.0126), p=0.54	1.0078 (0.9771 to 1.0394), p=0.62	0.9900 (0.9654 to 1.0151), p=0.43	**0.9839 (0.9693 to 0.9989), p=0.035**
CO 8-hr							
lag0	1.5407 (0.9323 to 2.5461), p=0.092	**2.7767 (1.5451 to 4.9897), p=0.0006**	1.3386 (0.6802 to 2.6343), p=0.40	1.2845 (0.7714 to 2.1388), p=0.34	0.4708 (0.1950 to 1.1365), p=0.094	0.8095 (0.3938 to 1.6642), p=0.57	**1.5834 (1.0025 to 2.5008), p=0.049**
lag1	1.2686 (0.7630 to 2.1092), p=0.36	1.6562 (0.9086 to 3.0192), p=0.100	1.1589 (0.5752 to 2.3351), p=0.68	1.1641 (0.6912 to 1.9608), p=0.57	0.6731 (0.2932 to 1.5450), p=0.35	0.7040 (0.3427 to 1.4459), p=0.34	1.2596 (0.7916 to 2.0044), p=0.33
lag2	1.5223 (0.9179 to 2.5245), p=0.10	1.4512 (0.7972 to 2.6416), p=0.22	1.1550 (0.5763 to 2.3149), p=0.68	1.2208 (0.7202 to 2.0693), p=0.46	0.9836 (0.4286 to 2.2574), p=0.97	0.8661 (0.4185 to 1.7924), p=0.70	1.1934 (0.7480 to 1.9040), p=0.46
SO_2 1-hr							
lag0	0.9993 (0.9875 to 1.0113), p=0.91	0.9736 (0.9327 to 1.0162), p=0.22	0.9806 (0.9377 to 1.0256), p=0.39	1.0092 (0.9961 to 1.0225), p=0.17	0.9634 (0.9140 to 1.0156), p=0.17	1.0007 (0.9767 to 1.0252), p=0.96	1.0034 (0.9938 to 1.0130), p=0.49
lag1	0.9974 (0.9856 to 1.0093), p=0.66	0.9900 (0.9584 to 1.0225), p=0.54	0.9922 (0.9491 to 1.0373), p=0.73	1.0051 (0.9925 to 1.0178), p=0.43	0.9995 (0.9669 to 1.0332), p=0.98	1.0017 (0.9838 to 1.0199), p=0.86	0.9975 (0.9873 to 1.0079), p=0.63

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
lag2	0.9939 (0.9810 to 1.0069), p=0.35	**0.9577 (0.9194 to 0.9976), p=0.038**	0.9866 (0.9482 to 1.0266), p=0.51	1.0068 (0.9928 to 1.0210), p=0.34	**0.9208 (0.8535 to 0.9933), p=0.033**	0.9765 (0.9462 to 1.0078), p=0.14	0.9925 (0.9809 to 1.0042), p=0.21
SO_2 24-hr							
lag0	1.0047 (0.9405 to 1.0733), p=0.89	0.8608 (0.7185 to 1.0313), p=0.10	0.9327 (0.7679 to 1.1330), p=0.48	1.0551 (0.9808 to 1.1351), p=0.15	0.9959 (0.8530 to 1.1627), p=0.96	0.9275 (0.8004 to 1.0749), p=0.32	1.0250 (0.9693 to 1.0838), p=0.39
lag1	0.9634 (0.8934 to 1.0389), p=0.33	0.8705 (0.7374 to 1.0275), p=0.10	0.9225 (0.7358 to 1.1567), p=0.48	1.0413 (0.9654 to 1.1232), p=0.29	0.9675 (0.8120 to 1.1529), p=0.71	0.9665 (0.8599 to 1.0862), p=0.57	0.9860 (0.9256 to 1.0503), p=0.66
lag2	0.9907 (0.9191 to 1.0678), p=0.81	**0.7680 (0.6165 to 0.9568), p=0.019**	0.9026 (0.7501 to 1.0860), p=0.28	1.0825 (0.9979 to 1.1743), p=0.056	0.8742 (0.6405 to 1.1932), p=0.40	**0.8463 (0.7231 to 0.9905), p=0.038**	0.9889 (0.9251 to 1.0572), p=0.74

Table 2.11. Associations between air pollutants and day time medication use

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
$PM_{2.5}$ 24-hr			
lag0	0.9464 (0.8549 to 1.0478), p=0.29	0.9475 (0.8186 to 1.0967), p=0.47	0.9734 (0.8870 to 1.0682), p=0.57
lag1	0.9671 (0.8738 to 1.0703), p=0.52	1.0494 (0.9014 to 1.2216), p=0.53	1.0170 (0.9263 to 1.1166), p=0.72
lag2	0.9250 (0.8329 to 1.0273), p=0.15	0.9841 (0.8408 to 1.1518), p=0.84	0.9771 (0.8879 to 1.0752), p=0.63
PM_{10} 24-hr			
lag0	1.0031 (0.9832 to 1.0235), p=0.76	1.0060 (0.9797 to 1.0331), p=0.66	0.9963 (0.9771 to 1.0160), p=0.71
lag1	1.0124 (0.9909 to 1.0345), p=0.26	1.0206 (0.9913 to 1.0508), p=0.17	1.0103 (0.9899 to 1.0311), p=0.33
lag2	1.0110 (0.9887 to 1.0338), p=0.34	**1.0335 (1.0012 to 1.0669), p=0.042**	1.0132 (0.9922 to 1.0347), p=0.22
NO_2 1-hr			
lag0	1.0117 (0.9879 to 1.0361), p=0.34	1.0088 (0.9739 to 1.0450), p=0.63	1.0097 (0.9878 to 1.0321), p=0.39
lag1	1.0065 (0.9829 to 1.0306), p=0.59	1.0173 (0.9816 to 1.0543), p=0.35	1.0096 (0.9878 to 1.0320), p=0.39
lag2	1.0034 (0.9796 to 1.0278), p=0.78	0.9905 (0.9542 to 1.0282), p=0.62	1.0051 (0.9832 to 1.0274), p=0.65
NO_2 24-hr			
lag0	**1.0537 (1.0110 to 1.0983), p=0.013**	1.0339 (0.9714 to 1.1005), p=0.29	**1.0480 (1.0080 to 1.0897), p=0.018**
lag1	**1.0480 (1.0058 to 1.0920), p=0.025**	1.0430 (0.9797 to 1.1104), p=0.19	**1.0473 (1.0079 to 1.0883), p=0.018**
lag2	**1.0478 (1.0049 to 1.0925), p=0.029**	1.0410 (0.9763 to 1.1100), p=0.22	**1.0570 (1.0166 to 1.0990), p=0.005**
O_3 1-hr			
lag0	0.9887 (0.9682 to 1.0096), p=0.29	1.0157 (0.9871 to 1.0452), p=0.29	0.9925 (0.9732 to 1.0123), p=0.46
lag1	0.9959 (0.9752 to 1.0171), p=0.70	1.0217 (0.9912 to 1.0531), p=0.16	0.9999 (0.9802 to 1.0200), p=0.99
lag2	0.9854 (0.9638 to 1.0074), p=0.19	0.9848 (0.9530 to 1.0177), p=0.36	0.9840 (0.9631 to 1.0053), p=0.14

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
O_3 4-hr			
lag0	0.9884 (0.9669 to 1.0104), p=0.30	1.0180 (0.9879 to 1.0490), p=0.24	0.9929 (0.9725 to 1.0137), p=0.50
lag1	0.9916 (0.9698 to 1.0139), p=0.46	1.0163 (0.9847 to 1.0489), p=0.31	0.9961 (0.9753 to 1.0174), p=0.72
lag2	0.9814 (0.9586 to 1.0047), p=0.12	0.9846 (0.9515 to 1.0188), p=0.37	0.9801 (0.9581 to 1.0027), p=0.084
O_3 8-hr			
lag0	0.9858 (0.9628 to 1.0095), p=0.24	1.0145 (0.9824 to 1.0477), p=0.38	0.9900 (0.9681 to 1.0123), p=0.38
lag1	0.9838 (0.9601 to 1.0080), p=0.19	1.0048 (0.9709 to 1.0399), p=0.79	0.9887 (0.9663 to 1.0117), p=0.33
lag2	0.9751 (0.9501 to 1.0008), p=0.058	0.9820 (0.9460 to 1.0194), p=0.34	**0.9748 (0.9507 to 0.9996), p=0.046**
CO 8-hr			
lag0	1.2503 (0.6416 to 2.4365), p=0.51	1.2708 (0.4472 to 3.6110), p=0.65	1.3906 (0.7427 to 2.6037), p=0.30
lag1	1.1383 (0.5806 to 2.2318), p=0.71	1.5484 (0.5742 to 4.1751), p=0.39	1.4509 (0.7824 to 2.6907), p=0.24
lag2	1.4964 (0.7654 to 2.9257), p=0.24	1.2664 (0.4780 to 3.3549), p=0.63	1.8111 (0.9774 to 3.3557), p=0.059
SO_2 1-hr			
lag0	0.9820 (0.9503 to 1.0147), p=0.28	0.9921 (0.9530 to 1.0328), p=0.70	1.8111 (0.9774 to 3.3557), p=0.059
lag1	0.9951 (0.9655 to 1.0255), p=0.75	1.0178 (0.9888 to 1.0475), p=0.23	1.0074 (0.9847 to 1.0306), p=0.53
lag2	0.9978 (0.9669 to 1.0297), p=0.89	0.9441 (0.8827 to 1.0097), p=0.093	0.9933 (0.9613 to 1.0265), p=0.69
SO_2 24-hr			
lag0	0.9259 (0.7974 to 1.0751), p=0.31	0.9962 (0.8375 to 1.1849), p=0.97	0.9470 (0.8321 to 1.0779), p=0.41
lag1	0.9469 (0.8104 to 1.1063), p=0.49	1.0256 (0.8695 to 1.2097), p=0.76	0.9740 (0.8558 to 1.1085), p=0.69
lag2	0.9250 (0.7760 to 1.1025), p=0.38	0.9632 (0.7259 to 1.2781), p=0.79	0.9059 (0.7555 to 1.0862), p=0.29

2.4.2. Associations between ozone and lung function, symptoms and medication use in the warm season

There were no adverse associations between ozone and lung function, symptoms and medication use in this sub-analysis (Table 2.12, Table 2.13, Table 2.14, Table 2.15). There were a few positive associations (beneficial effects) with night wheeze, that is, children experienced less wheeze symptoms during the night when ozone levels were high the previous day (Table 2.13).

Table 2.12. Associations between warm season ozone and lung function

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
O_3 1-hr				
lag0	-0.0889 (-0.3522 to 0.1743), p=0.51	-0.0003 (-0.0022 to 0.0016), p=0.75		
lag1	-0.0390 (-0.2803 to 0.2023), p=0.75	-0.0006 (-0.0024 to 0.0012), p=0.52	-0.0073 (-0.2975 to 0.2829), p=0.96	0.0000 (-0.0018 to 0.0019), p=0.96
lag2	0.1515 (-0.0980 to 0.4011), p=0.23	0.0005 (-0.0013 to 0.0024), p=0.55	0.0033 (-0.2891 to 0.2957), p=0.98	-0.0004 (-0.0023 to 0.0014), p=0.64
lag3			-0.0792 (-0.3745 to 0.2161), p=0.60	0.0001 (-0.0017 to 0.0019), p=0.88
O_3 4-hr				
lag0	-0.1657 (-0.4680 to 0.1366), p=0.28	-0.0009 (-0.0031 to 0.0012), p=0.40		
lag1	-0.0091 (-0.2811 to 0.2628), p=0.95	-0.0001 (-0.0022 to 0.0020), p=0.93	0.0170 (-0.3116 to 0.3456), p=0.92	0.0001 (-0.0020 to 0.0021), p=0.94
lag2	0.1953 (-0.0849 to 0.4755), p=0.17	0.0003 (-0.0017 to 0.0023), p=0.78	-0.0026 (-0.3302 to 0.3251), p=0.99	-0.0005 (-0.0025 to 0.0016), p=0.64
lag3			-0.0512 (-0.3788 to 0.2763), p=0.76	0.0003 (-0.0017 to 0.0023), p=0.75
O_3 8-hr				
lag0	-0.1718 (-0.5828 to 0.2392), p=0.41	-0.0014 (-0.0041 to 0.0013), p=0.31		
lag1	0.0495 (-0.3137 to 0.4128), p=0.79	0.0005 (-0.0020 to 0.0031), p=0.69	0.0559 (-0.3518 to 0.4635), p=0.79	0.0005 (-0.0021 to 0.0030), p=0.71
lag2	0.2832 (-0.0611 to 0.6275), p=0.11	0.0005 (-0.0021 to 0.0032), p=0.69	-0.0586 (-0.4664 to 0.3491), p=0.78	-0.0006 (-0.0032 to 0.0019), p=0.63
lag3			0.0419 (-0.3708 to 0.4546), p=0.84	0.0003 (-0.0022 to 0.0028), p=0.83

Table 2.13. Associations between warm season ozone and night symptoms and medication use

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
O_3 1-hr					
lag1	0.9984 (0.9779 to 1.0195), p=0.88	0.9745 (0.9443 to 1.0057), p=0.11	0.9517 (0.9023 to 1.0039), p=0.069	0.9961 (0.9774 to 1.0151), p=0.69	0.9997 (0.9673 to 1.0331), p=0.98
lag2	1.0088 (0.9871 to 1.0309), p=0.43	0.9874 (0.9528 to 1.0233), p=0.49	0.9623 (0.9069 to 1.0211), p=0.20	1.0142 (0.9942 to 1.0346), p=0.17	1.0004 (0.9668 to 1.0352), p=0.98
lag3	1.0086 (0.9864 to 1.0313), p=0.45	**0.9520 (0.9182 to 0.9870), p=0.008**	0.9597 (0.9019 to 1.0212), p=0.19	0.9995 (0.9793 to 1.0201), p=0.96	1.0055 (0.9666 to 1.0460), p=0.79
O_3 4-hr					
lag1	0.9980 (0.9756 to 1.0208), p=0.86	0.9691 (0.9364 to 1.0029), p=0.073	0.9471 (0.8941 to 1.0031), p=0.064	0.9943 (0.9741 to 1.0150), p=0.59	0.9988 (0.9634 to 1.0355), p=0.95
lag2	1.0098 (0.9861 to 1.0340), p=0.42	0.9837 (0.9464 to 1.0226), p=0.41	0.9594 (0.9001 to 1.0227), p=0.20	1.0134 (0.9917 to 1.0356), p=0.23	1.0024 (0.9652 to 1.0410), p=0.90
lag3	1.0107 (0.9866 to 1.0355), p=0.39	**0.9466 (0.9097 to 0.9849), p=0.007**	0.9546 (0.8926 to 1.0209), p=0.17	1.0013 (0.9793 to 1.0238), p=0.91	1.0086 (0.9654 to 1.0537), p=0.70
O_3 8-hr					
lag1	0.9968 (0.9701 to 1.0242), p=0.82	**0.9573 (0.9192 to 0.9971), p=0.036**	0.9512 (0.8906 to 1.0159), p=0.14	0.9932 (0.9693 to 1.0176), p=0.58	0.9975 (0.9559 to 1.0410), p=0.91
lag2	1.0068 (0.9787 to 1.0357), p=0.64	0.9768 (0.9342 to 1.0214), p=0.30	0.9711 (0.9028 to 1.0446), p=0.43	1.0111 (0.9857 to 1.0371), p=0.39	0.9972 (0.9532 to 1.0432), p=0.90
lag3	1.0154 (0.9867 to 1.0449), p=0.30	**0.9369 (0.8942 to 0.9817), p=0.006**	0.9568 (0.8852 to 1.0342), p=0.27	1.0051 (0.9793 to 1.0317), p=0.70	1.0093 (0.9589 to 1.0623), p=0.72

Table 2.14. Associations between warm season ozone and day time symptoms

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
O_3 1-hr							
lag0	0.9863 (0.9676 to 1.0054), p=0.16	0.9993 (0.9717 to 1.0276), p=0.96	1.0250 (0.9912 to 1.0601), p=0.15	1.0111 (0.9905 to 1.0321), p=0.29	0.9846 (0.9509 to 1.0194), p=0.38	1.0030 (0.9736 to 1.0334), p=0.84	0.9982 (0.9824 to 1.0142), p=0.82
lag1	0.9974 (0.9771 to 1.0180), p=0.80	0.9864 (0.9586 to 1.0150), p=0.35	0.9918 (0.9552 to 1.0298), p=0.67	1.0022 (0.9809 to 1.0239), p=0.84	0.9957 (0.9622 to 1.0305), p=0.81	1.0186 (0.9883 to 1.0497), p=0.23	1.0020 (0.9854 to 1.0188), p=0.82
lag2	1.0002 (0.9788 to 1.0221), p=0.98	0.9831 (0.9522 to 1.0150), p=0.29	0.9827 (0.9459 to 1.0209), p=0.37	1.0140 (0.9917 to 1.0368), p=0.22	1.0223 (0.9808 to 1.0655), p=0.30	1.0141 (0.9808 to 1.0486), p=0.41	1.0002 (0.9830 to 1.0176), p=0.99
O_3 4-hr							
lag0	0.9845 (0.9641 to 1.0054), p=0.14	0.9968 (0.9674 to 1.0272), p=0.84	1.0269 (0.9903 to 1.0649), p=0.15	1.0125 (0.9902 to 1.0353), p=0.28	0.9897 (0.9534 to 1.0273), p=0.58	1.0071 (0.9750 to 1.0403), p=0.67	0.9977 (0.9805 to 1.0152), p=0.80
lag1	0.9956 (0.9736 to 1.0181), p=0.70	0.9841 (0.9544 to 1.0147), p=0.30	0.9889 (0.9494 to 1.0301), p=0.59	1.0027 (0.9797 to 1.0261), p=0.82	0.9987 (0.9622 to 1.0365), p=0.94	1.0224 (0.9896 to 1.0562), p=0.18	1.0008 (0.9829 to 1.0191), p=0.93
lag2	0.9973 (0.9740 to 1.0211), p=0.82	0.9839 (0.9508 to 1.0182), p=0.35	0.9824 (0.9421 to 1.0244), p=0.40	1.0173 (0.9930 to 1.0422), p=0.16	1.0244 (0.9794 to 1.0715), p=0.29	1.0195 (0.9832 to 1.0571), p=0.30	0.9988 (0.9801 to 1.0179), p=0.90
O_3 8-hr							
lag0	0.9826 (0.9585 to 1.0074), p=0.17	0.9988 (0.9648 to 1.0341), p=0.95	1.0372 (0.9933 to 1.0830), p=0.098	1.0226 (0.9958 to 1.0500), p=0.099	0.9899 (0.9479 to 1.0337), p=0.65	1.0202 (0.9817 to 1.0603), p=0.31	1.0017 (0.9814 to 1.0224), p=0.87
lag1	0.9909 (0.9652 to 1.0173), p=0.50	0.9820 (0.9480 to 1.0173), p=0.31	0.9858 (0.9398 to 1.0341), p=0.56	1.0059 (0.9790 to 1.0336), p=0.67	0.9966 (0.9543 to 1.0408), p=0.88	1.0352 (0.9964 to 1.0755), p=0.076	1.0018 (0.9807 to 1.0234), p=0.87
lag2	0.9898 (0.9626 to 1.0178), p=0.47	0.9821 (0.9440 to 1.0218), p=0.37	0.9775 (0.9293 to 1.0282), p=0.38	1.0270 (0.9979 to 1.0568), p=0.069	1.0301 (0.9789 to 1.0840), p=0.25	1.0279 (0.9859 to 1.0717), p=0.20	0.9988 (0.9767 to 1.0214), p=0.92

Table 2.15. Associations between warm season ozone and day time medication use

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
O_3 1-hr			
lag0	0.9968 (0.9672 to 1.0273), p=0.83	1.0196 (0.9781 to 1.0628), p=0.36	1.0020 (0.9735 to 1.0313), p=0.89
lag1	1.0018 (0.9716 to 1.0329), p=0.91	1.0171 (0.9736 to 1.0625), p=0.45	1.0132 (0.9836 to 1.0437), p=0.38
lag2	0.9844 (0.9522 to 1.0176), p=0.35	0.9863 (0.9390 to 1.0361), p=0.58	0.9846 (0.9529 to 1.0172), p=0.35
O_3 4-hr			
lag0	0.9969 (0.9649 to 1.0301), p=0.85	1.0222 (0.9772 to 1.0693), p=0.34	1.0031 (0.9723 to 1.0349), p=0.84
lag1	0.9986 (0.9662 to 1.0322), p=0.94	1.0164 (0.9697 to 1.0654), p=0.50	1.0126 (0.9807 to 1.0455), p=0.44
lag2	0.9818 (0.9468 to 1.0182), p=0.32	0.9905 (0.9387 to 1.0452), p=0.73	0.9831 (0.9485 to 1.0189), p=0.35
O_3 8-hr			
lag0	1.0036 (0.9663 to 1.0423), p=0.85	1.0248 (0.9732 to 1.0792), p=0.35	1.0066 (0.9707 to 1.0438), p=0.72
lag1	0.9933 (0.9559 to 1.0321), p=0.73	1.0077 (0.9560 to 1.0622), p=0.77	1.0099 (0.9735 to 1.0478), p=0.60
lag2	0.9725 (0.9315 to 1.0154), p=0.21	0.9933 (0.9335 to 1.0571), p=0.83	0.9791 (0.9386 to 1.0214), p=0.33

2.4.3. Associations between SO_2 and lung function, symptoms and medication use after excluding children from Port Pirie

A significant negative association is now seen between 1-hr SO_2 and morning PEF (Table 2.16). There was no association for night time symptoms (Table 2.17). The beneficial effects on day time symptoms are no longer apparent when children from Port Pirie were excluded from the analyses (Table 2.18). In fact, there are now adverse effects especially with cough and runny nose. Children also tended to use more day time preventer medication for symptoms on days with higher 1-hr SO_2 levels (Table 2.19).

Table 2.16. Associations between SO_2 and lung function after excluding children from Port Pirie

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
SO_2 1-hr				
lag0	0.1918 (-0.5797 to 0.9633), p=0.63	-0.0010 (-0.0063 to 0.0043), p=0.72		
lag1	-0.1427 (-0.8951 to 0.6096), p=0.71	0.0014 (-0.0039 to 0.0066), p=0.61	0.2526 (-0.2815 to 0.7868), p=0.35	0.0015 (-0.0020 to 0.0051), p=0.40
lag2	0.0179 (-0.7337 to 0.7695), p=0.96	-0.0007 (-0.0059 to 0.0046), p=0.81	0.1762 (-0.3372 to 0.6896), p=0.50	0.0014 (-0.0020 to 0.0047), p=0.43
lag3			**-0.6132 (-1.1394 to -0.0871), p=0.022**	-0.0034 (-0.0069 to 0.0001), p=0.057
SO_2 24-hr				
lag0	0.3566 (-2.9728 to 3.6860), p=0.83	-0.0110 (-0.0339 to 0.0119), p=0.35		
lag1	-0.8262 (-4.0907 to 2.4383), p=0.62	0.0088 (-0.0140 to 0.0316), p=0.45	0.3566 (-1.9700 to 2.6832), p=0.76	-0.0022 (-0.0177 to 0.0134), p=0.78
lag2	-0.1299 (-3.5071 to 3.2473), p=0.94	-0.0031 (-0.0266 to 0.0204), p=0.80	0.7237 (-1.6062 to 3.0536), p=0.54	0.0067 (-0.0086 to 0.0221), p=0.39
lag3			-2.3497 (-4.7141 to 0.0146), p=0.051	-0.0139 (-0.0297 to 0.0018), p=0.083

Table 2.17. Associations between SO_2 and night symptoms and medication use after excluding children from Port Pirie

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
SO_2 1-hr					
lag1	1.0124 (0.9764 to 1.0498), p=0.50	1.0082 (0.9575 to 1.0615), p=0.76	0.9844 (0.9039 to 1.0720), p=0.72	1.0118 (0.9774 to 1.0473), p=0.51	1.0161 (0.9617 to 1.0735), p=0.57
lag2	1.0049 (0.9677 to 1.0435), p=0.80	1.0219 (0.9697 to 1.0769), p=0.42	1.0093 (0.9299 to 1.0955), p=0.82	1.0236 (0.9881 to 1.0603), p=0.20	1.0237 (0.9705 to 1.0798), p=0.39
lag3	1.0068 (0.9682 to 1.0470), p=0.73	0.9771 (0.9179 to 1.0400), p=0.47	0.9577 (0.8710 to 1.0530), p=0.37	1.0019 (0.9648 to 1.0405), p=0.92	0.9901 (0.9274 to 1.0570), p=0.76
SO_2 24-hr					
lag1	0.9884 (0.8380 to 1.1657), p=0.89	1.0129 (0.7995 to 1.2833), p=0.92	0.9029 (0.6232 to 1.3081), p=0.59	0.9933 (0.8484 to 1.1629), p=0.93	1.0070 (0.7790 to 1.3018), p=0.96
lag2	0.9977 (0.8422 to 1.1819), p=0.98	1.1035 (0.8710 to 1.3981), p=0.41	0.9723 (0.6733 to 1.4040), p=0.88	1.0977 (0.9359 to 1.2874), p=0.25	1.1241 (0.8728 to 1.4476), p=0.36
lag3	0.9648 (0.8115 to 1.1471), p=0.69	0.8261 (0.6334 to 1.0774), p=0.16	0.8321 (0.5652 to 1.2248), p=0.35	0.9370 (0.7928 to 1.1075), p=0.45	0.9228 (0.6884 to 1.2372), p=0.59

Table 2.18. Associations between SO_2 and day time symptoms after excluding children from Port Pirie

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
SO_2 1-hr							
lag0	**1.0405 (1.0053 to 1.0769), p=0.024**	0.9830 (0.9338 to 1.0347), p=0.51	0.9991 (0.9412 to 1.0606), p=0.98	1.0323 (0.9976 to 1.0683), p=0.068	1.0182 (0.9571 to 1.0831), p=0.57	0.9693 (0.9198 to 1.0215), p=0.24	1.0289 (0.9992 to 1.0596), p=0.056
lag1	1.0155 (0.9786 to 1.0538), p=0.42	1.0175 (0.9667 to 1.0710), p=0.51	1.0075 (0.9416 to 1.0780), p=0.83	**1.0428 (1.0047 to 1.0823), p=0.027**	1.0504 (0.9845 to 1.1206), p=0.14	0.9889 (0.9396 to 1.0408), p=0.67	**1.0437 (1.0105 to 1.0780), p=0.010**
lag2	1.0191 (0.9809 to 1.0588), p=0.33	0.9577 (0.9018 to 1.0170), p=0.16	1.0187 (0.9581 to 1.0832), p=0.55	1.0311 (0.9949 to 1.0685), p=0.093	0.9865 (0.9096 to 1.0698), p=0.74	0.9717 (0.9194 to 1.0270), p=0.31	1.0030 (0.9720 to 1.0350), p=0.85
SO_2 24-hr							
lag0	**1.1816 (1.0145 to 1.3764), p=0.032**	0.9593 (0.7620 to 1.2077), p=0.72	1.0304 (0.7973 to 1.3317), p=0.82	**1.1779 (1.0117 to 1.3714), p=0.035**	1.2340 (0.9427 to 1.6153), p=0.13	0.8708 (0.6914 to 1.0967), p=0.24	1.1261 (0.9890 to 1.2821), p=0.073
lag1	1.0290 (0.8720 to 1.2142), p=0.74	1.0108 (0.7985 to 1.2797), p=0.93	1.0140 (0.7497 to 1.3714), p=0.93	**1.2176 (1.0312 to 1.4377), p=0.020**	1.1907 (0.8882 to 1.5962), p=0.24	0.9202 (0.7279 to 1.1634), p=0.49	**1.1629 (1.0085 to 1.3408), p=0.038**
lag2	1.0072 (0.8499 to 1.1936), p=0.93	0.7745 (0.5939 to 1.0100), p=0.059	1.0773 (0.8155 to 1.4233), p=0.60	1.1474 (0.9785 to 1.3455), p=0.090	0.9007 (0.6366 to 1.2745), p=0.55	0.8416 (0.6589 to 1.0749), p=0.17	0.9714 (0.8444 to 1.1174), p=0.68

Table 2.19. Associations between SO_2 and day time medication use after excluding children from Port Pirie

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
SO_2 1-hr			
lag0	1.0154 (0.9661 to 1.0673), p=0.55	1.0256 (0.9538 to 1.1029), p=0.49	1.0133 (0.9655 to 1.0636), p=0.59
lag1	1.0312 (0.9813 to 1.0837), p=0.22	**1.0792 (1.0057 to 1.1581), p=0.034**	1.0366 (0.9877 to 1.0879), p=0.14
lag2	1.0283 (0.9766 to 1.0827), p=0.29	1.0382 (0.9607 to 1.1220), p=0.34	1.0203 (0.9696 to 1.0735), p=0.44
SO_2 24-hr			
lag0	1.0602 (0.8468 to 1.3274), p=0.61	1.0686 (0.7697 to 1.4836), p=0.69	1.0622 (0.8531 to 1.3225), p=0.59
lag1	1.0977 (0.8741 to 1.3786), p=0.42	1.2795 (0.9223 to 1.7751), p=0.14	1.1418 (0.9143 to 1.4259), p=0.24
lag2	1.0278 (0.8115 to 1.3017), p=0.82	0.9953 (0.7033 to 1.4084), p=0.98	0.9925 (0.7860 to 1.2532), p=0.95

2.4.4. Associations between SO_2 and lung function, symptoms and medication use in two pollutant models with PM_{10}

In these two pollutant models with PM_{10}, the SO_2 effects were similar to the effect estimates from single pollutant models (Table 2.20, Table 2.21, Table 2.22, Table 2.23). Three estimates that were significant in the single pollutant models were no longer significant in the two pollutant models (lag 2 SO_2 24-hr and morning PEF and FEV_1; lag 2 SO2 1-hr and night shortness of breath).

One estimate that was non-significant in the single pollutant model was significant in the two pollutant model (lag 1 SO_2 24-hr and day wheeze); however, the OR were similar (OR single pollutant model=0.8705, 95%CI: 0.7374-1.0275; OR two pollutant model=0.8131, 95%CI: 0.6681-0.9896) (Table 2.22).

Table 2.20. Associations between SO_2 and lung function in two pollutant models with PM_{10}

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
SO_2 1-hr				
lag0	0.2929 (-0.0282 to 0.6140), p=0.074	0.0012 (-0.0010 to 0.0034), p=0.28		
lag1	-0.0408 (-0.3117 to 0.2301), p=0.77	0.0006 (-0.0013 to 0.0024), p=0.53	0.0257 (-0.1738 to 0.2252), p=0.80	0.0002 (-0.0012 to 0.0015), p=0.83
lag2	-0.0282 (-0.2986 to 0.2423), p=0.84	-0.0013 (-0.0031 to 0.0006), p=0.19	-0.0263 (-0.2469 to 0.1942), p=0.81	-0.0011 (-0.0026 to 0.0004), p=0.14
lag3			-0.1879 (-0.3893 to 0.0134), p=0.067	-0.0011 (-0.0024 to 0.0003), p=0.12
SO_2 24-hr				
lag0	**1.6946 (0.1918 to 3.1973), p=0.027**	0.0057 (-0.0046 to 0.0161), p=0.28		
lag1	-0.7056 (-2.2275 to 0.8163), p=0.36	0.0050 (-0.0054 to 0.0154), p=0.34	-0.7361 (-1.8649 to 0.3926), p=0.20	-0.0051 (-0.0127 to 0.0025), p=0.18
lag2	0.1860 (-1.2380 to 1.6100), p=0.80	-0.0023 (-0.0121 to 0.0075), p=0.64	0.5679 (-0.5765 to 1.7123), p=0.33	0.0022 (-0.0056 to 0.0100), p=0.57
lag3			-0.8858 (-2.0003 to 0.2287), p=0.12	-0.0051 (-0.0126 to 0.0024), p=0.18

Table 2.21. Associations between SO_2 and night symptoms and medication use in two pollutant models with PM_{10}

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
SO_2 1-hr					
lag1	1.0031 (0.9890 to 1.0174), p=0.67	1.0038 (0.9807 to 1.0274), p=0.75	0.9839 (0.9109 to 1.0627), p=0.68	1.0043 (0.9911 to 1.0176), p=0.53	**1.0247 (1.0021 to 1.0478), p=0.032**
lag2	0.9894 (0.9728 to 1.0061), p=0.21	1.0109 (0.9854 to 1.0371), p=0.41	0.9956 (0.9508 to 1.0426), p=0.85	0.9980 (0.9831 to 1.0130), p=0.79	1.0237 (1.0027 to 1.0453), p=0.027
lag3	1.0035 (0.9913 to 1.0159), p=0.57	1.0061 (0.9836 to 1.0290), p=0.60	0.9624 (0.8912 to 1.0393), p=0.33	1.0043 (0.9924 to 1.0163), p=0.48	0.9947 (0.9681 to 1.0220), p=0.70
SO_2 24-hr					
lag1	0.9575 (0.8802 to 1.0415), p=0.31	0.9869 (0.8635 to 1.1278), p=0.85	0.8515 (0.6110 to 1.1866), p=0.34	0.9694 (0.8967 to 1.0480), p=0.43	1.0990 (0.9583 to 1.2604), p=0.18
lag2	0.9232 (0.8468 to 1.0065), p=0.070	1.0045 (0.8726 to 1.1564), p=0.95	0.8943 (0.6734 to 1.1877), p=0.44	0.9606 (0.8880 to 1.0391), p=0.32	1.0742 (0.9452 to 1.2208), p=0.27
lag3	1.0093 (0.9435 to 1.0797), p=0.79	0.9434 (0.8040 to 1.1070), p=0.48	**0.6138 (0.4186 to 0.9000), p=0.012**	1.0071 (0.9430 to 1.0756), p=0.83	0.9099 (0.7890 to 1.0494), p=0.19

Table 2.22. Associations between SO_2 and day time symptoms in two pollutant models with PM_{10}

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
SO_2 1-hr							
lag0	0.9979 (0.9856 to 1.0104), p=0.74	0.9674 (0.9236 to 1.0132), p=0.16	0.9847 (0.9426 to 1.0288), p=0.49	1.0071 (0.9933 to 1.0210), p=0.32	0.9847 (0.9446 to 1.0266), p=0.47	0.9997 (0.9749 to 1.0251), p=0.98	1.0026 (0.9929 to 1.0125), p=0.60
lag1	1.0019 (0.9894 to 1.0146), p=0.76	0.9798 (0.9406 to 1.0207), p=0.33	0.9960 (0.9583 to 1.0352), p=0.84	1.0117 (0.9998 to 1.0238), p=0.054	1.0054 (0.9750 to 1.0367), p=0.73	1.0046 (0.9863 to 1.0233), p=0.62	1.0064 (0.9965 to 1.0164), p=0.20
lag2	0.9974 (0.9846 to 1.0104), p=0.70	**0.9531 (0.9085 to 0.9999), p=0.049**	0.9808 (0.9404 to 1.0229), p=0.37	1.0061 (0.9926 to 1.0198), p=0.37	0.9768 (0.9254 to 1.0311), p=0.40	0.9859 (0.9618 to 1.0107), p=0.26	0.9984 (0.9875 to 1.0093), p=0.77
SO_2 24-hr							
lag0	0.9905 (0.9247 to 1.0610), p=0.79	0.8314 (0.6833 to 1.0116), p=0.065	0.9515 (0.7846 to 1.1538), p=0.61	1.0352 (0.9587 to 1.1177), p=0.38	0.9724 (0.8243 to 1.1471), p=0.74	0.9166 (0.7852 to 1.0700), p=0.27	1.0145 (0.9581 to 1.0743), p=0.62
lag1	0.9580 (0.8904 to 1.0308), p=0.25	**0.8131 (0.6681 to 0.9896), p=0.039**	0.9332 (0.7625 to 1.1421), p=0.50	1.0434 (0.9686 to 1.1240), p=0.26	0.9731 (0.8213 to 1.1530), p=0.75	1.0067 (0.8991 to 1.1272), p=0.91	0.9900 (0.9319 to 1.0517), p=0.74
lag2	0.9984 (0.9358 to 1.0652), p=0.96	**0.7317 (0.5829 to 0.9186), p=0.007**	0.9127 (0.7592 to 1.0973), p=0.33	1.0463 (0.9730 to 1.1251), p=0.22	0.9396 (0.7610 to 1.1601), p=0.56	0.8811 (0.7705 to 1.0076), p=0.064	0.9951 (0.9400 to 1.0534), p=0.87

Table 2.23. Associations between SO_2 and day time medication use in two pollutant models with PM_{10}

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
SO_2 1-hr			
lag0	0.9791 (0.9362 to 1.0241), p=0.36	0.9936 (0.9608 to 1.0276), p=0.71	0.9854 (0.9577 to 1.0140), p=0.31
lag1	1.0074 (0.9813 to 1.0343), p=0.58	1.0095 (0.9805 to 1.0395), p=0.52	1.0139 (0.9941 to 1.0341), p=0.17
lag2	0.9912 (0.9621 to 1.0213), p=0.56	0.9950 (0.9643 to 1.0267), p=0.75	0.9994 (0.9748 to 1.0246), p=0.96
SO_2 24-hr			
lag0	0.9141 (0.7824 to 1.0679), p=0.26	0.9901 (0.8301 to 1.1810), p=0.91	0.9432 (0.8260 to 1.0770), p=0.39
lag1	0.9859 (0.8576 to 1.1333), p=0.84	1.0009 (0.8529 to 1.1744), p=0.99	1.0038 (0.8932 to 1.1280), p=0.95
lag2	0.8813 (0.7428 to 1.0455), p=0.15	0.9213 (0.7732 to 1.0978), p=0.36	0.9301 (0.8198 to 1.0552), p=0.26

2.4.5. Associations between NO_2 and lung function, symptoms and medication use in two pollutant models with ozone

There were far fewer significant associations for NO_2 when ozone was included in the models. Many of the effects of NO_2 on symptoms and medication that were observed in single pollutant models were no longer apparent when ozone was included in two pollutant models.

In two pollutant models compared to single pollutant models, the effects on the lung function were increased whereas the effects on symptoms slightly decreased. Further, in the two pollutant models compared to single pollutant models, there were no longer any significant effects on day time medication use.

Associations between NO_2 and lung function, symptoms and medication use when ozone was included in the models are presented in Table 2.24, Table 2.25, Table 2.26, Table 2.27 for 1-hr ozone, Table 2.28, Table 2.29, Table 2.30, Table 2.31 for 4-hr ozone and Table 2.32, Table 2.33, Table 2.34, Table 2.35 for 8-hr ozone.

2.4.5.1. Associations between NO_2 and lung function, symptoms and medication use in two pollutant models with 1-hour ozone

Table 2.24. Associations between NO_2 and lung function in two pollutant models with 1-hour ozone

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
NO_2 1-hr				
lag0	0.0614 (-0.3823 to 0.5051), p=0.79	-0.0002 (-0.0032 to 0.0027), p=0.89		
lag1	0.1370 (-0.3030 to 0.5769), p=0.54	0.0013 (-0.0016 to 0.0042), p=0.38	0.2729 (-0.0492 to 0.5951), p=0.097	0.0022 (-0.0000 to 0.0045), p=0.050
lag2	0.0327 (-0.4360 to 0.5013), p=0.89	-0.0002 (-0.0033 to 0.0030), p=0.92	**-0.4042 (-0.7318 to -0.0767), p=0.016**	**-0.0025 (-0.0047 to -0.0002), p=0.031**
lag3			0.3025 (-0.0521 to 0.6571), p=0.094	0.0007 (-0.0017 to 0.0032), p=0.56
NO_2 24-hr				
lag0	0.3493 (-0.6369 to 1.3355), p=0.49	0.0007 (-0.0058 to 0.0073), p=0.83		
lag1	0.2638 (-0.7250 to 1.2526), p=0.60	0.0035 (-0.0031 to 0.0101), p=0.30	0.0434 (-0.6808 to 0.7677), p=0.91	-0.0016 (-0.0066 to 0.0034), p=0.53
lag2	0.2870 (-0.6955 to 1.2694), p=0.57	0.0006 (-0.0060 to 0.0073), p=0.85	-0.3414 (-1.0614 to 0.3786), p=0.35	-0.0027 (-0.0077 to 0.0022), p=0.28
lag3			-0.1246 (-0.8626 to	-0.0031 (-0.0082 to

			0.6134), p=0.74	0.0020), p=0.24

Table 2.25. Associations between NO_2 and night symptoms and medication use in two pollutant models with 1-hour ozone

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
NO_2 1-hr					
lag1	1.0020 (0.9801 to 1.0244), p=0.86	1.0107 (0.9798 to 1.0426), p=0.50	0.9928 (0.9440 to 1.0441), p=0.78	1.0049 (0.9849 to 1.0254), p=0.63	0.9988 (0.9637 to 1.0350), p=0.95
lag2	1.0141 (0.9926 to 1.0361), p=0.20	1.0120 (0.9815 to 1.0435), p=0.45	0.9642 (0.9166 to 1.0142), p=0.16	1.0112 (0.9915 to 1.0312), p=0.27	0.9920 (0.9580 to 1.0272), p=0.65
lag3	1.0121 (0.9905 to 1.0342), p=0.28	1.0104 (0.9785 to 1.0434), p=0.53	0.9772 (0.9278 to 1.0292), p=0.38	1.0115 (0.9915 to 1.0320), p=0.26	1.0061 (0.9715 to 1.0419), p=0.73
NO_2 24-hr					
lag1	1.0146 (0.9705 to 1.0608), p=0.52	1.0634 (0.9990 to 1.1319), p=0.054	1.0011 (0.9112 to 1.0999), p=0.98	1.0100 (0.9690 to 1.0526), p=0.64	1.0137 (0.9459 to 1.0864), p=0.70
lag2	1.0326 (0.9882 to 1.0790), p=0.15	1.0369 (0.9746 to 1.1032), p=0.25	0.9828 (0.8944 to 1.0798), p=0.72	1.0254 (0.9846 to 1.0678), p=0.23	1.0084 (0.9417 to 1.0798), p=0.81
lag3	**1.0447 (1.0015 to 1.0898), p=0.042**	1.0409 (0.9805 to 1.1051), p=0.19	0.9494 (0.8657 to 1.0412), p=0.27	1.0301 (0.9906 to 1.0712), p=0.14	1.0203 (0.9541 to 1.0911), p=0.56

Table 2.26. Associations between NO_2 and day time symptoms in two pollutant models with 1-hour ozone

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
NO_2 1-hr							
lag0	1.0046 (0.9851 to 1.0246), p=0.64	1.0155 (0.9872 to 1.0445), p=0.29	1.0161 (0.9817 to 1.0517), p=0.36	0.9896 (0.9699 to 1.0096), p=0.31	0.9833 (0.9526 to 1.0149), p=0.30	0.9888 (0.9595 to 1.0189), p=0.46	0.9942 (0.9778 to 1.0108), p=0.49
lag1	1.0037 (0.9853 to 1.0225), p=0.69	1.0070 (0.9799 to 1.0347), p=0.62	1.0138 (0.9804 to 1.0483), p=0.42	0.9950 (0.9763 to 1.0141), p=0.61	0.9804 (0.9516 to 1.0102), p=0.19	0.9798 (0.9523 to 1.0081), p=0.16	0.9920 (0.9765 to 1.0078), p=0.32
lag2	1.0048 (0.9859 to 1.0241), p=0.62	0.9917 (0.9647 to 1.0194), p=0.55	0.9835 (0.9514 to 1.0167), p=0.33	0.9822 (0.9635 to 1.0013), p=0.068	0.9832 (0.9540 to 1.0133), p=0.27	0.9769 (0.9488 to 1.0059), p=0.12	0.9921 (0.9762 to 1.0082), p=0.34
NO_2 24-hr							
lag0	1.0216 (0.9811 to 1.0638), p=0.30	**1.0722 (1.0130 to 1.1348), p=0.016**	1.0434 (0.9762 to 1.1152), p=0.21	0.9929 (0.9518 to 1.0358), p=0.74	0.9731 (0.9076 to 1.0432), p=0.44	0.9719 (0.9137 to 1.0338), p=0.37	1.0033 (0.9688 to 1.0391), p=0.85
lag1	1.0128 (0.9737 to 1.0535), p=0.53	1.0360 (0.9807 to 1.0944), p=0.21	1.0245 (0.9608 to 1.0925), p=0.46	0.9913 (0.9516 to 1.0326), p=0.67	0.9467 (0.8835 to 1.0144), p=0.12	0.9545 (0.8987 to 1.0137), p=0.13	0.9908 (0.9579 to 1.0249), p=0.59
lag2	1.0191 (0.9807 to 1.0589), p=0.34	0.9961 (0.9448 to 1.0501), p=0.88	1.0200 (0.9585 to 1.0856), p=0.53	0.9764 (0.9385 to 1.0158), p=0.24	0.9597 (0.8982 to 1.0254), p=0.22	0.9661 (0.9114 to 1.0241), p=0.25	0.9916 (0.9594 to 1.0248), p=0.62

Table 2.27. Associations between NO_2 and day time medication use in two pollutant models with 1-hour ozone

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
NO_2 1-hr			
lag0	1.0057 (0.9761 to 1.0363), p=0.71	0.9720 (0.9286 to 1.0174), p=0.22	1.0000 (0.9722 to 1.0286), p=1.00
lag1	1.0071 (0.9787 to 1.0363), p=0.63	0.9877 (0.9463 to 1.0310), p=0.57	1.0052 (0.9782 to 1.0329), p=0.71
lag2	0.9924 (0.9643 to 1.0213), p=0.60	0.9732 (0.9310 to 1.0174), p=0.23	0.9944 (0.9677 to 1.0218), p=0.69
NO_2 24-hr			
lag0	1.0448 (0.9842 to 1.1090), p=0.15	0.9640 (0.8805 to 1.0554), p=0.43	1.0356 (0.9778 to 1.0968), p=0.23
lag1	1.0330 (0.9752 to 1.0943), p=0.27	1.0174 (0.9335 to 1.1090), p=0.69	1.0315 (0.9761 to 1.0901), p=0.27
lag2	1.0282 (0.9725 to 1.0871), p=0.33	1.0067 (0.9238 to 1.0972), p=0.88	1.0350 (0.9812 to 1.0918), p=0.21

2.4.5.2 Associations between NO_2 and lung function, symptoms and medication use in two pollutant models with 4-hour ozone

Table 2.28. Associations between NO_2 and lung function in two pollutant models with 4-hour ozone

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
NO_2 1-hr				
lag0	0.0639 (-0.3788 to 0.5066), p=0.78	-0.0002 (-0.0031 to 0.0028), p=0.90		
lag1	0.1481 (-0.2911 to 0.5873), p=0.51	0.0014 (-0.0016 to 0.0043), p=0.36	0.2795 (-0.0421 to 0.6011), p=0.088	**0.0023 (0.0000 to 0.0045), p=0.048**
lag2	0.0275 (-0.4410 to 0.4959), p=0.91	-0.0002 (-0.0034 to 0.0030), p=0.90	**-0.3963 (-0.7236 to -0.0690), p=0.018**	**-0.0025 (-0.0047 to -0.0002), p=0.032**
lag3			0.2962 (-0.0585 to 0.6509), p=0.10	0.0007 (-0.0018 to 0.0032), p=0.57
NO_2 24-hr				
lag0	0.3326 (-0.6544 to 1.3197), p=0.51	0.0006 (-0.0059 to 0.0072), p=0.85		
lag1	0.2695 (-0.7189 to 1.2579), p=0.59	0.0035 (-0.0030 to 0.0101), p=0.29	0.0538 (-0.6714 to 0.7791), p=0.88	-0.0015 (-0.0066 to 0.0035), p=0.55
lag2	0.2753 (-0.7067 to 1.2573), p=0.58	0.0005 (-0.0061 to 0.0072), p=0.87	-0.3356 (-1.0556 to 0.3844), p=0.36	-0.0027 (-0.0077 to 0.0023), p=0.28
lag3			-0.1388 (-0.8768 to 0.5992), p=0.71	-0.0031 (-0.0082 to 0.0020), p=0.23

Table 2.29. Associations between NO_2 and night symptoms and medication use in two pollutant models with 4-hour ozone

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
NO_2 1-hr					
lag1	1.0014 (0.9796 to 1.0237), p=0.90	1.0110 (0.9803 to 1.0427), p=0.49	0.9914 (0.9429 to 1.0423), p=0.73	1.0046 (0.9847 to 1.0250), p=0.65	0.9985 (0.9637 to 1.0345), p=0.93
lag2	1.0138 (0.9924 to 1.0357), p=0.21	1.0127 (0.9821 to 1.0442), p=0.42	0.9647 (0.9170 to 1.0148), p=0.16	1.0111 (0.9915 to 1.0311), p=0.27	0.9920 (0.9581 to 1.0272), p=0.65
lag3	1.0121 (0.9905 to 1.0342), p=0.28	1.0108 (0.9789 to 1.0439), p=0.51	0.9778 (0.9283 to 1.0300), p=0.40	1.0116 (0.9916 to 1.0320), p=0.26	1.0062 (0.9716 to 1.0420), p=0.73
NO_2 24-hr					
lag1	1.0134 (0.9693 to 1.0596), p=0.56	1.0605 (0.9964 to 1.1288), p=0.065	0.9950 (0.9054 to 1.0935), p=0.92	1.0086 (0.9678 to 1.0512), p=0.68	1.0122 (0.9446 to 1.0846), p=0.73
lag2	1.0321 (0.9878 to 1.0785), p=0.16	1.0361 (0.9737 to 1.1025), p=0.26	0.9814 (0.8930 to 1.0785), p=0.70	1.0250 (0.9842 to 1.0674), p=0.23	1.0079 (0.9413 to 1.0793), p=0.82
lag3	**1.0447 (1.0015 to 1.0898), p=0.042**	1.0400 (0.9796 to 1.1042), p=0.20	0.9483 (0.8647 to 1.0401), p=0.26	1.0300 (0.9904 to 1.0710), p=0.14	1.0203 (0.9541 to 1.0910), p=0.56

Table 2.30. Associations between NO_2 and day time symptoms in two pollutant models with 4-hour ozone

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
NO_2 1-hr							
lag0	1.0044 (0.9849 to 1.0242), p=0.66	1.0158 (0.9877 to 1.0447), p=0.27	1.0166 (0.9824 to 1.0520), p=0.34	0.9898 (0.9702 to 1.0098), p=0.32	0.9821 (0.9516 to 1.0136), p=0.26	0.9877 (0.9586 to 1.0177), p=0.42	0.9941 (0.9778 to 1.0106), p=0.48
lag1	1.0037 (0.9853 to 1.0225), p=0.69	1.0075 (0.9804 to 1.0352), p=0.59	1.0142 (0.9809 to 1.0486), p=0.41	0.9952 (0.9765 to 1.0142), p=0.62	0.9796 (0.9508 to 1.0093), p=0.18	0.9791 (0.9517 to 1.0074), p=0.15	0.9921 (0.9766 to 1.0078), p=0.32
lag2	1.0049 (0.9860 to 1.0242), p=0.61	0.9919 (0.9649 to 1.0197), p=0.56	0.9836 (0.9515 to 1.0168), p=0.33	0.9822 (0.9635 to 1.0013), p=0.068	0.9833 (0.9541 to 1.0134), p=0.27	0.9771 (0.9490 to 1.0061), p=0.12	0.9922 (0.9763 to 1.0083), p=0.34
NO_2 24-hr							
lag0	1.0202 (0.9797 to 1.0623), p=0.33	**1.0720 (1.0129 to 1.1345), p=0.016**	1.0439 (0.9767 to 1.1157), p=0.21	0.9926 (0.9515 to 1.0355), p=0.73	0.9720 (0.9067 to 1.0421), p=0.42	0.9705 (0.9122 to 1.0324), p=0.34	1.0026 (0.9681 to 1.0383), p=0.89
lag1	1.0125 (0.9734 to 1.0531), p=0.54	1.0362 (0.9809 to 1.0945), p=0.20	1.0249 (0.9611 to 1.0929), p=0.45	0.9913 (0.9517 to 1.0326), p=0.67	0.9461 (0.8830 to 1.0138), p=0.12	0.9541 (0.8984 to 1.0133), p=0.13	0.9908 (0.9578 to 1.0249), p=0.59
lag2	1.0191 (0.9807 to 1.0590), p=0.33	0.9959 (0.9446 to 1.0500), p=0.88	1.0201 (0.9584 to 1.0856), p=0.53	0.9762 (0.9383 to 1.0156), p=0.23	0.9603 (0.8988 to 1.0260), p=0.23	0.9666 (0.9119 to 1.0245), p=0.25	0.9916 (0.9594 to 1.0248), p=0.62

Table 2.31. Associations between NO_2 and day time medication use in two pollutant models with 4-hour ozone

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
NO_2 1-hr			
lag0	1.0051 (0.9757 to 1.0354), p=0.74	0.9724 (0.9292 to 1.0175), p=0.23	0.9996 (0.9720 to 1.0280), p=0.98
lag1	1.0069 (0.9785 to 1.0360), p=0.64	0.9875 (0.9461 to 1.0307), p=0.57	1.0050 (0.9781 to 1.0327), p=0.72
lag2	0.9924 (0.9643 to 1.0213), p=0.60	0.9727 (0.9304 to 1.0169), p=0.22	0.9944 (0.9677 to 1.0218), p=0.68
NO_2 24-hr			
lag0	1.0432 (0.9829 to 1.1073), p=0.16	0.9664 (0.8829 to 1.0578), p=0.46	1.0347 (0.9770 to 1.0958), p=0.24
lag1	1.0327 (0.9749 to 1.0939), p=0.27	1.0182 (0.9342 to 1.1098), p=0.68	1.0313 (0.9759 to 1.0898), p=0.27
lag2	1.0282 (0.9726 to 1.0871), p=0.33	1.0067 (0.9237 to 1.0972), p=0.88	1.0351 (0.9812 to 1.0918), p=0.21

2.4.5.3. Associations between NO_2 and lung function, symptoms and medication use in two pollutant models with 8-hour ozone

Table 2.32. Associations between NO_2 and lung function in two pollutant models with 8-hour ozone

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
NO_2 1-hr				
lag0	0.0534 (-0.3885 to 0.4952), p=0.81	-0.0002 (-0.0032 to 0.0027), p=0.87		
lag1	0.1247 (-0.3144 to 0.5638), p=0.58	0.0012 (-0.0017 to 0.0041), p=0.43	0.2831 (-0.0380 to 0.6042), p=0.084	**0.0023 (0.0001 to 0.0045), p=0.045**
lag2	-0.0133 (-0.4876 to 0.4610), p=0.96	-0.0003 (-0.0034 to 0.0029), p=0.87	**-0.3986 (-0.7269 to -0.0702), p=0.017**	**-0.0024 (-0.0047 to -0.0002), p=0.033**
lag3			0.3112 (-0.0439 to 0.6663), p=0.086	0.0007 (-0.0018 to 0.0031), p=0.59
NO_2 24-hr				
lag0	0.1645 (-0.8381 to 1.1671), p=0.75	0.0001 (-0.0065 to 0.0067), p=0.98		
lag1	0.1651 (-0.8363 to 1.1666), p=0.75	0.0034 (-0.0032 to 0.0100), p=0.31	0.1216 (-0.6110 to 0.8543), p=0.74	-0.0013 (-0.0064 to 0.0037), p=0.61
lag2	0.1322 (-0.8630 to 1.1273), p=0.79	0.0001 (-0.0066 to 0.0068), p=0.97	-0.3357 (-1.0620 to 0.3905), p=0.36	-0.0026 (-0.0076 to 0.0024), p=0.31
lag3			-0.1235 (-0.8672 to 0.6201), p=0.74	-0.0031 (-0.0082 to 0.0020), p=0.23

Table 2.33. Associations between NO_2 and night symptoms and medication use in two pollutant models with 8-hour ozone

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
NO_2 1-hr					
lag1	1.0011 (0.9794 to 1.0232), p=0.92	1.0115 (0.9808 to 1.0431), p=0.47	0.9882 (0.9401 to 1.0388), p=0.64	1.0043 (0.9845 to 1.0246), p=0.67	0.9990 (0.9644 to 1.0348), p=0.96
lag2	1.0141 (0.9927 to 1.0359), p=0.20	1.0140 (0.9834 to 1.0455), p=0.38	0.9642 (0.9166 to 1.0142), p=0.16	1.0115 (0.9920 to 1.0315), p=0.25	0.9932 (0.9591 to 1.0284), p=0.70
lag3	1.0131 (0.9916 to 1.0352), p=0.23	1.0131 (0.9810 to 1.0461), p=0.43	0.9727 (0.9245 to 1.0234), p=0.29	1.0114 (0.9915 to 1.0317), p=0.26	1.0070 (0.9724 to 1.0428), p=0.70
NO_2 24-hr					
lag1	1.0134 (0.9692 to 1.0596), p=0.56	1.0519 (0.9881 to 1.1197), p=0.11	0.9772 (0.8888 to 1.0743), p=0.63	1.0054 (0.9647 to 1.0479), p=0.80	1.0106 (0.9430 to 1.0830), p=0.77
lag2	1.0327 (0.9884 to 1.0791), p=0.15	1.0312 (0.9692 to 1.0973), p=0.33	0.9723 (0.8853 to 1.0678), p=0.56	1.0235 (0.9829 to 1.0657), p=0.26	1.0078 (0.9411 to 1.0792), p=0.82
lag3	**1.0455 (1.0022 to 1.0905), p=0.039**	1.0378 (0.9774 to 1.1019), p=0.22	0.9434 (0.8609 to 1.0338), p=0.21	1.0289 (0.9895 to 1.0698), p=0.15	1.0208 (0.9545 to 1.0917), p=0.55

Table 2.34. Associations between NO_2 and day time symptoms in two pollutant models with 8-hour ozone

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
NO_2 1-hr							
lag0	1.0035 (0.9842 to 1.0233), p=0.72	1.0161 (0.9882 to 1.0449), p=0.26	1.0167 (0.9827 to 1.0519), p=0.34	0.9891 (0.9696 to 1.0089), p=0.28	0.9817 (0.9514 to 1.0131), p=0.25	0.9869 (0.9579 to 1.0167), p=0.39	0.9934 (0.9772 to 1.0098), p=0.43
lag1	1.0034 (0.9851 to 1.0221), p=0.72	1.0086 (0.9816 to 1.0363), p=0.54	1.0147 (0.9814 to 1.0491), p=0.39	0.9950 (0.9763 to 1.0139), p=0.60	0.9793 (0.9505 to 1.0090), p=0.17	0.9791 (0.9516 to 1.0073), p=0.14	0.9920 (0.9766 to 1.0077), p=0.32
lag2	1.0048 (0.9861 to 1.0240), p=0.62	0.9930 (0.9659 to 1.0208), p=0.62	0.9845 (0.9524 to 1.0178), p=0.36	0.9835 (0.9648 to 1.0026), p=0.090	0.9834 (0.9542 to 1.0135), p=0.28	0.9781 (0.9500 to 1.0071), p=0.14	0.9928 (0.9770 to 1.0088), p=0.38
NO_2 24-hr							
lag0	1.0177 (0.9774 to 1.0597), p=0.39	**1.0729 (1.0137 to 1.1354), p=0.015**	1.0411 (0.9742 to 1.1125), p=0.23	0.9943 (0.9532 to 1.0373), p=0.79	0.9729 (0.9075 to 1.0430), p=0.44	0.9680 (0.9098 to 1.0300), p=0.30	1.0019 (0.9675 to 1.0376), p=0.91
lag1	1.0113 (0.9723 to 1.0518), p=0.58	1.0375 (0.9822 to 1.0959), p=0.19	1.0225 (0.9590 to 1.0903), p=0.50	0.9920 (0.9524 to 1.0332), p=0.70	0.9465 (0.8833 to 1.0143), p=0.12	0.9526 (0.8970 to 1.0116), p=0.11	0.9905 (0.9577 to 1.0244), p=0.58
lag2	1.0189 (0.9806 to 1.0586), p=0.34	0.9965 (0.9451 to 1.0506), p=0.90	1.0191 (0.9576 to 1.0845), p=0.55	0.9773 (0.9395 to 1.0167), p=0.26	0.9607 (0.8992 to 1.0265), p=0.24	0.9669 (0.9123 to 1.0247), p=0.26	0.9921 (0.9600 to 1.0252), p=0.64

Table 2.35. Associations between NO_2 and day time medication use in two pollutant models with 8-hour ozone

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
NO_2 1-hr			
lag0	1.0049 (0.9757 to 1.0350), p=0.74	0.9737 (0.9308 to 1.0186), p=0.25	0.9998 (0.9723 to 1.0280), p=0.99
lag1	1.0064 (0.9782 to 1.0354), p=0.66	0.9871 (0.9463 to 1.0296), p=0.54	1.0049 (0.9781 to 1.0324), p=0.72
lag2	0.9909 (0.9631 to 1.0196), p=0.53	0.9701 (0.9289 to 1.0131), p=0.17	0.9934 (0.9669 to 1.0206), p=0.63
NO_2 24-hr			
lag0	1.0406 (0.9805 to 1.1043), p=0.19	0.9687 (0.8858 to 1.0595), p=0.49	1.0335 (0.9760 to 1.0943), p=0.26
lag1	1.0319 (0.9744 to 1.0929), p=0.28	1.0209 (0.9373 to 1.1119), p=0.63	1.0314 (0.9762 to 1.0898), p=0.27
lag2	1.0276 (0.9721 to 1.0863), p=0.34	1.0073 (0.9250 to 1.0968), p=0.87	1.0350 (0.9813 to 1.0916), p=0.21

2.4.6. Associations between NO_2 and lung function, symptoms and medication use in children with unflued gas heating in the home

There were stronger adverse effects of NO_2 on children with unflued gas heating in the home compared to all children in the study. These stronger effects were seen for morning PEF, symptoms and medication use (Table 2.36, Table 2.37, Table 2.38, Table 2.39).

Table 2.36. Associations between NO_2 and lung function in children with unflued gas heating in the home

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
NO_2 1-hr				
lag0	-0.6089 (-1.7861 to 0.5683), p=0.31	-0.0041 (-0.0122 to 0.0040), p=0.32		
lag1	-0.6411 (-1.8515 to 0.5693), p=0.30	0.0001 (-0.0081 to 0.0082), p=0.98	0.0833 (-0.6371 to 0.8038), p=0.82	0.0016 (-0.0037 to 0.0069), p=0.55
lag2	0.0350 (-1.2237 to 1.2937), p=0.96	0.0017 (-0.0067 to 0.0101), p=0.70	**-1.0481 (-1.8306 to -0.2655), p=0.009**	-0.0046 (-0.0105 to 0.0013), p=0.12
lag3			-0.4617 (-1.2757 to 0.3524), p=0.27	-0.0017 (-0.0079 to 0.0045), p=0.59
NO_2 24-hr				
lag0	-0.3496 (-2.5388 to 1.8397), p=0.75	-0.0033 (-0.0179 to 0.0114), p=0.66		
lag1	-1.9496 (-4.2067 to 0.3074), p=0.090	-0.0073 (-0.0223 to 0.0076), p=0.34	0.3852 (-1.0634 to 1.8337), p=0.60	0.0035 (-0.0071 to 0.0141), p=0.52
lag2	0.0713 (-2.3798 to 2.5224), p=0.95	-0.0020 (-0.0180 to 0.0140), p=0.81	-1.1664 (-2.6869 to 0.3542), p=0.13	-0.0091 (-0.0204 to 0.0022), p=0.12
lag3			-0.5003 (-2.0914 to 1.0908), p=0.54	-0.0013 (-0.0132 to 0.0107), p=0.83

Table 2.37. Associations between NO_2 and night symptoms and medication use in children with unflued gas heating in the home

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
NO_2 1-hr					
lag1	1.0056 (0.9538 to 1.0601), p=0.84	1.0724 (0.9939 to 1.1571), p=0.072	1.1189 (0.9586 to 1.3060), p=0.15	1.0071 (0.9587 to 1.0579), p=0.78	**1.1016 (1.0204 to 1.1893), p=0.013**
lag2	**1.0555 (1.0014 to 1.1126), p=0.044**	1.0081 (0.9341 to 1.0879), p=0.84	1.0911 (0.9341 to 1.2744), p=0.27	1.0248 (0.9768 to 1.0752), p=0.32	1.0378 (0.9616 to 1.1200), p=0.34
lag3	**1.0752 (1.0190 to 1.1345), p=0.008**	1.0269 (0.9539 to 1.1055), p=0.48	1.0080 (0.8321 to 1.2212), p=0.93	**1.0516 (1.0011 to 1.1047), p=0.045**	1.0366 (0.9550 to 1.1253), p=0.39
NO_2 24-hr					
lag1	1.0402 (0.9579 to 1.1296), p=0.35	**1.1939 (1.0525 to 1.3545), p=0.006**	1.1178 (0.8883 to 1.4066), p=0.34	1.0434 (0.9649 to 1.1282), p=0.29	**1.2156 (1.0699 to 1.3811), p=0.003**
lag2	1.0787 (0.9949 to 1.1695), p=0.066	1.0907 (0.9636 to 1.2345), p=0.17	1.1103 (0.8574 to 1.4379), p=0.43	1.0467 (0.9695 to 1.1300), p=0.24	1.1289 (0.9976 to 1.2775), p=0.055
lag3	**1.1339 (1.0443 to 1.2313), p=0.003**	1.0977 (0.9657 to 1.2478), p=0.15	1.0123 (0.7499 to 1.3666), p=0.94	**1.1113 (1.0274 to 1.2022), p=0.009**	1.1144 (0.9699 to 1.2804), p=0.13

Table 2.38. Associations between NO_2 and day time symptoms in children with unflued gas heating in the home

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
NO_2 1-hr							
lag0	1.0126 (0.9641 to 1.0635), p=0.62	1.0385 (0.9783 to 1.1024), p=0.21	**1.1094 (1.0218 to 1.2045), p=0.013**	1.0269 (0.9710 to 1.0860), p=0.35	0.9254 (0.8155 to 1.0501), p=0.23	1.0380 (0.9621 to 1.1200), p=0.34	0.9961 (0.9537 to 1.0404), p=0.86
lag1	1.0080 (0.9586 to 1.0599), p=0.76	1.0610 (0.9994 to 1.1263), p=0.052	**1.0978 (1.0109 to 1.1922), p=0.027**	1.0335 (0.9782 to 1.0920), p=0.24	0.9555 (0.8535 to 1.0697), p=0.43	1.0224 (0.9506 to 1.0996), p=0.55	1.0015 (0.9584 to 1.0465), p=0.95
lag2	1.0276 (0.9774 to 1.0803), p=0.29	0.9910 (0.9328 to 1.0529), p=0.77	1.0536 (0.9719 to 1.1422), p=0.20	1.0341 (0.9788 to 1.0925), p=0.23	0.9206 (0.7962 to 1.0645), p=0.26	1.0019 (0.9286 to 1.0810), p=0.96	0.9938 (0.9498 to 1.0397), p=0.79
NO_2 24-hr							
lag0	1.0523 (0.9711 to 1.1404), p=0.21	**1.1134 (1.0073 to 1.2307), p=0.036**	**1.1653 (1.0323 to 1.3154), p=0.013**	1.0730 (0.9796 to 1.1752), p=0.13	0.9887 (0.7533 to 1.2977), p=0.93	1.0447 (0.9214 to 1.1845), p=0.49	1.0294 (0.9568 to 1.1076), p=0.44
lag1	1.0106 (0.9324 to 1.0955), p=0.80	**1.1350 (1.0244 to 1.2576), p=0.016**	**1.1763 (1.0370 to 1.3343), p=0.012**	1.0641 (0.9745 to 1.1620), p=0.17	1.0091 (0.8222 to 1.2384), p=0.93	1.0394 (0.9225 to 1.1711), p=0.53	1.0035 (0.9321 to 1.0802), p=0.93
lag2	1.0518 (0.9692 to 1.1414), p=0.23	1.0626 (0.9621 to 1.1737), p=0.23	1.1815 (1.0346 to 1.3493), p=0.014	1.0909 (0.9972 to 1.1934), p=0.057	0.9192 (0.7386 to 1.1439), p=0.45	0.9795 (0.8661 to 1.1076), p=0.74	1.0099 (0.9373 to 1.0881), p=0.80

Table 2.39. Associations between NO_2 and day time medication use in children with unflued gas heating in the home

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
NO_2 1-hr			
lag0	1.0099 (0.9375 to 1.0879), p=0.80	1.0257 (0.8944 to 1.1762), p=0.72	0.9920 (0.9241 to 1.0649), p=0.82
lag1	1.0276 (0.9528 to 1.1083), p=0.48	**1.1265 (1.0029 to 1.2654), p=0.045**	1.0216 (0.9537 to 1.0943), p=0.54
lag2	0.9795 (0.9069 to 1.0579), p=0.60	1.0509 (0.9356 to 1.1804), p=0.40	0.9832 (0.9167 to 1.0545), p=0.63
NO_2 24-hr			
lag0	1.0532 (0.9381 to 1.1825), p=0.38	1.0138 (0.8062 to 1.2748), p=0.91	1.0140 (0.9082 to 1.1321), p=0.80
lag1	1.0735 (0.9547 to 1.2072), p=0.24	1.2068 (0.9964 to 1.4617), p=0.055	1.0822 (0.9707 to 1.2066), p=0.15
lag2	1.0510 (0.9344 to 1.1822), p=0.41	1.0965 (0.9113 to 1.3195), p=0.33	1.0670 (0.9572 to 1.1895), p=0.24

2.4.7. Associations between PM_{10} and lung function, symptoms and medication use in two pollutant models

In this section, results are presented for the associations between PM_{10} and lung function, symptoms and medication use from two pollutant models: 1-hr NO_2 (Table 2.40, Table 2.41, Table 2.42, Table 2.43), 24-hr NO_2 (Table 2.44, Table 2.45, Table 2.46, Table 2.47), 1-hr ozone (Table 2.48, Table 2.49, Table 2.50, Table 2.51), 4-hr ozone (Table 2.52, Table 2.53, Table 2.54, Table 2.55), 8-hr ozone (Table 2.56, Table 2.57, Table 2.58, Table 2.59), 8-hr CO (Table 2.60, Table 2.61, Table 2.62, Table 2.63), 1-hr SO_2 (Table 2.64, Table 2.65, Table 2.66, Table 2.67) and 24-hr SO_2 (Table 2.68, Table 2.69, Table 2.70, Table 2.71).

In two pollutant models, changes in the effects were seen with evening lung function. The adverse effects were greatly increased when 1-hr ozone (Table 2.48) and SO_2 (Table 2.64) for 1-hr SO_2 and Table 2.68 for 24-hr SO_2) were added to the model.

Associations between PM_{10} and both night and day time symptoms generally persisted when NO_2, CO and SO_2 were added to the models (Table 2.41,Table 2.42 for 1-hr NO_2, Table 2.45, Table 2.46 for 24-hr NO_2, Table 2.61, Table 2.62 for 8-hr CO, Table 2.65, Table 2.66 for 1-hr SO_2 and Table 2.69, Table 2.70 for 24-hr SO_2). The odds ratios were generally greater in the two pollutant models compared to the single pollutant models.

There were no significant associations when ozone was added to the models (Table 2.49, Table 2.50, Table 2.53, Table 2.54, Table 2.57, Table 2.58 for 1-hr ozone, 4-hr ozone and 8-hr ozone respectively).

Significant increased use of day time medication use was only observed in two pollutant models with CO (Table 2.63). However, the odds ratios in all models were consistently greater in the two pollutant models compared with single pollutant models especially for lag 1 PM_{10} and lag 2 PM_{10}.

2.4.7.1 Associations between PM_{10} and lung function, symptoms and medication use in two pollutant models with 1-hour NO_2

Table 2.40. Associations between PM_{10} and lung function in two pollutant models with 1-hour NO_2

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
PM_{10} 24-hr				
lag0	-0.0322 (-0.4865 to 0.4221), p=0.89	0.0010 (-0.0020 to 0.0040), p=0.50		
lag1	-0.0569 (-0.5126 to 0.3987), p=0.81	-0.0001 (-0.0031 to 0.0030), p=0.97	0.2559 (-0.0742 to 0.5860), p=0.13	0.0019 (-0.0005 to 0.0043), p=0.11
lag2	-0.0603 (-0.5152 to 0.3945), p=0.79	-0.0001 (-0.0031 to 0.0029), p=0.96	-0.1348 (-0.4815 to 0.2120), p=0.45	-0.0007 (-0.0032 to 0.0018), p=0.58
lag3			-0.0427 (-0.3972 to 0.3117), p=0.81	-0.0012 (-0.0038 to 0.0013), p=0.33

Table 2.41. Associations between PM_{10} and night symptoms and medication use in two pollutant models with 1-hour NO_2

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
PM_{10} 24-hr					
lag1	1.0164 (0.9962 to 1.0370), p=0.11	1.0267 (1.0000 to 1.0543), p=0.050	0.9948 (0.9587 to 1.0324), p=0.78	1.0127 (0.9939 to 1.0318), p=0.19	0.9987 (0.9682 to 1.0301), p=0.93
lag2	**1.0220 (1.0017 to 1.0428), p=0.033**	1.0260 (0.9991 to 1.0536), p=0.058	1.0271 (0.9925 to 1.0629), p=0.13	1.0171 (0.9981 to 1.0364), p=0.078	0.9876 (0.9583 to 1.0179), p=0.42
lag3	1.0096 (0.9897 to 1.0299), p=0.35	1.0223 (0.9963 to 1.0491), p=0.093	1.0003 (0.9648 to 1.0372), p=0.99	1.0111 (0.9927 to 1.0299), p=0.24	0.9975 (0.9685 to 1.0274), p=0.87

Table 2.42. Associations between PM_{10} and day time symptoms in two pollutant models with 1-hour NO_2

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
PM_{10} 24-hr							
lag0	1.0097 (0.9914 to 1.0284), p=0.30	**1.0288 (1.0049 to 1.0534), p=0.018**	1.0089 (0.9802 to 1.0383), p=0.55	1.0073 (0.9881 to 1.0269), p=0.46	0.9930 (0.9635 to 1.0233), p=0.65	1.0065 (0.9807 to 1.0329), p=0.63	1.0042 (0.9883 to 1.0204), p=0.61
lag1	1.0157 (0.9970 to 1.0347), p=0.10	1.0091 (0.9856 to 1.0331), p=0.45	1.0193 (0.9911 to 1.0482), p=0.18	0.9969 (0.9777 to 1.0165), p=0.76	1.0153 (0.9862 to 1.0453), p=0.31	1.0062 (0.9804 to 1.0326), p=0.64	1.0110 (0.9949 to 1.0273), p=0.18
lag2	**1.0227 (1.0042 to 1.0416), p=0.016**	1.0115 (0.9881 to 1.0355), p=0.34	1.0231 (0.9950 to 1.0520), p=0.11	0.9897 (0.9704 to 1.0093), p=0.30	1.0121 (0.9835 to 1.0417), p=0.41	1.0083 (0.9829 to 1.0344), p=0.52	1.0071 (0.9914 to 1.0231), p=0.38

Table 2.43. Associations between PM_{10} and day time medication use in two pollutant models with 1-hour NO_2

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
PM_{10} 24-hr			
lag0	1.0067 (0.9807 to 1.0334), p=0.61	1.0138 (0.9781 to 1.0508), p=0.45	0.9971 (0.9726 to 1.0222), p=0.82
lag1	1.0218 (0.9963 to 1.0479), p=0.095	1.0302 (0.9947 to 1.0670), p=0.096	1.0167 (0.9925 to 1.0415), p=0.18
lag2	1.0233 (0.9974 to 1.0498), p=0.078	1.0239 (0.9882 to 1.0609), p=0.19	1.0218 (0.9973 to 1.0468), p=0.081

2.4.7.2 Associations between PM_{10} and lung function, symptoms and medication use in two pollutant models with 24-hour NO_2

Table 2.44. Associations between PM_{10} and lung function in two pollutant models with 24-hour NO_2

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
PM_{10} 24-hr				
lag0	-0.1596 (-0.6289 to 0.3096), p=0.50	0.0001 (-0.0030 to 0.0032), p=0.96		
lag1	-0.1021 (-0.5604 to 0.3561), p=0.66	-0.0003 (-0.0033 to 0.0028), p=0.87	0.3079 (-0.0302 to 0.6460), p=0.074	**0.0027 (0.0003 to 0.0051), p=0.030**
lag2	-0.1057 (-0.5638 to 0.3524), p=0.65	-0.0005 (-0.0035 to 0.0025), p=0.74	-0.1284 (-0.4756 to 0.2188), p=0.47	-0.0007 (-0.0031 to 0.0018), p=0.60
lag3			-0.0208 (-0.3761 to 0.3345), p=0.91	-0.0010 (-0.0035 to 0.0015), p=0.44

Table 2.45. Associations between PM_{10} and night symptoms and medication use in two pollutant models with 24-hour NO_2

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
PM_{10} 24-hr					
lag1	1.0160 (0.9953 to 1.0371), p=0.13	1.0181 (0.9910 to 1.0460), p=0.19	0.9774 (0.9412 to 1.0150), p=0.24	1.0104 (0.9912 to 1.0299), p=0.29	0.9870 (0.9558 to 1.0192), p=0.42
lag2	**1.0218 (1.0013 to 1.0426), p=0.037**	1.0211 (0.9942 to 1.0487), p=0.13	1.0160 (0.9819 to 1.0513), p=0.36	1.0149 (0.9959 to 1.0342), p=0.12	0.9824 (0.9527 to 1.0130), p=0.26
lag3	1.0094 (0.9895 to 1.0297), p=0.36	1.0188 (0.9929 to 1.0454), p=0.16	0.9920 (0.9571 to 1.0282), p=0.66	1.0096 (0.9912 to 1.0282), p=0.31	0.9936 (0.9646 to 1.0235), p=0.67

Table 2.46. Associations between PM_{10} and day time symptoms in two pollutant models with 24-hour NO_2

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
PM_{10} 24-hr							
lag0	1.0086 (0.9901 to 1.0274), p=0.37	1.0243 (0.9999 to 1.0492), p=0.051	1.0049 (0.9759 to 1.0347), p=0.75	1.0068 (0.9873 to 1.0266), p=0.50	1.0007 (0.9703 to 1.0321), p=0.96	1.0095 (0.9832 to 1.0366), p=0.48	1.0021 (0.9860 to 1.0184), p=0.80
lag1	1.0148 (0.9961 to 1.0337), p=0.12	1.0056 (0.9820 to 1.0297), p=0.65	1.0158 (0.9876 to 1.0448), p=0.27	0.9960 (0.9768 to 1.0155), p=0.68	1.0191 (0.9900 to 1.0491), p=0.20	1.0073 (0.9815 to 1.0337), p=0.58	1.0090 (0.9931 to 1.0253), p=0.27
lag2	**1.0218 (1.0034 to 1.0405), p=0.020**	1.0086 (0.9853 to 1.0325), p=0.47	1.0205 (0.9926 to 1.0492), p=0.15	0.9886 (0.9695 to 1.0081), p=0.25	1.0148 (0.9861 to 1.0444), p=0.31	1.0092 (0.9840 to 1.0351), p=0.48	1.0053 (0.9897 to 1.0212), p=0.51

Table 2.47. Associations between PM_{10} and day time medication use in two pollutant models with 24-hour NO_2

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
PM_{10} 24-hr			
lag0	0.9988 (0.9724 to 1.0259), p=0.93	1.0113 (0.9754 to 1.0485), p=0.54	0.9902 (0.9653 to 1.0157), p=0.45
lag1	1.0183 (0.9927 to 1.0444), p=0.16	1.0282 (0.9933 to 1.0645), p=0.11	1.0133 (0.9891 to 1.0381), p=0.28
lag2	1.0202 (0.9945 to 1.0465), p=0.12	1.0222 (0.9870 to 1.0586), p=0.22	1.0183 (0.9941 to 1.0431), p=0.14

2.4.7.3 Associations between PM_{10} and lung function, symptoms and medication use in two pollutant models with 1-hour ozone

Table 2.48. Associations between PM_{10} and lung function in two pollutant models with 1-hour ozone

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
PM_{10} 24-hr				
lag0	-0.0801 (-0.4549 to 0.2947), p=0.68	-0.0001 (-0.0026 to 0.0024), p=0.95		
lag1	-0.0212 (-0.4704 to 0.4280), p=0.93	-0.0003 (-0.0033 to 0.0027), p=0.84	0.1000 (-0.1915 to 0.3915), p=0.50	0.0000 (-0.0020 to 0.0020), p=0.98
lag2	0.0553 (-0.3831 to 0.4938), p=0.80	0.0000 (-0.0029 to 0.0029), p=0.99	**-0.3674 (-0.7291 to -0.0057), p=0.046**	-0.0017 (-0.0042 to 0.0008), p=0.18
lag3			0.1716 (-0.1923 to 0.5354), p=0.36	0.0013 (-0.0012 to 0.0038), p=0.32

Table 2.49. Associations between PM_{10} and night symptoms and medication use in two pollutant models with 1-hour ozone

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
PM_{10} 24-hr					
lag1	1.0012 (0.9814 to 1.0214), p=0.91	1.0184 (0.9942 to 1.0432), p=0.14	0.9905 (0.9507 to 1.0321), p=0.65	1.0000 (0.9819 to 1.0185), p=1.00	0.9958 (0.9638 to 1.0289), p=0.80
lag2	1.0116 (0.9892 to 1.0345), p=0.31	1.0290 (0.9995 to 1.0594), p=0.054	1.0195 (0.9798 to 1.0609), p=0.34	1.0071 (0.9867 to 1.0280), p=0.50	0.9869 (0.9516 to 1.0235), p=0.48
lag3	1.0002 (0.9779 to 1.0230), p=0.99	1.0271 (0.9991 to 1.0559), p=0.058	0.9831 (0.9396 to 1.0286), p=0.46	1.0014 (0.9815 to 1.0217), p=0.89	1.0026 (0.9685 to 1.0379), p=0.88

Table 2.50. Associations between PM_{10} and day time symptoms in two pollutant models with 1-hour ozone

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
PM_{10} 24-hr							
lag0	1.0061 (0.9891 to 1.0233), p=0.48	1.0135 (0.9920 to 1.0355), p=0.22	0.9962 (0.9672 to 1.0260), p=0.80	0.9986 (0.9798 to 1.0178), p=0.88	0.9817 (0.9533 to 1.0109), p=0.22	0.9857 (0.9603 to 1.0119), p=0.28	0.9947 (0.9799 to 1.0097), p=0.49
lag1	1.0044 (0.9845 to 1.0247), p=0.67	0.9947 (0.9679 to 1.0222), p=0.70	1.0008 (0.9680 to 1.0346), p=0.96	0.9930 (0.9724 to 1.0141), p=0.51	0.9977 (0.9667 to 1.0296), p=0.88	0.9961 (0.9677 to 1.0253), p=0.79	0.9947 (0.9778 to 1.0118), p=0.54
lag2	1.0154 (0.9957 to 1.0355), p=0.13	0.9927 (0.9660 to 1.0201), p=0.60	1.0075 (0.9747 to 1.0414), p=0.66	0.9867 (0.9662 to 1.0077), p=0.21	1.0010 (0.9710 to 1.0319), p=0.95	1.0091 (0.9823 to 1.0365), p=0.51	0.9957 (0.9792 to 1.0124), p=0.61

Table 2.51. Associations between PM_{10} and day time medication use in two pollutant models with 1-hour ozone

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
PM_{10} 24-hr			
lag0	0.9980 (0.9749 to 1.0217), p=0.87	1.0004 (0.9688 to 1.0330), p=0.98	0.9926 (0.9697 to 1.0161), p=0.53
lag1	1.0172 (0.9885 to 1.0469), p=0.24	1.0257 (0.9858 to 1.0672), p=0.21	1.0100 (0.9823 to 1.0386), p=0.48
lag2	1.0093 (0.9806 to 1.0389), p=0.53	1.0273 (0.9870 to 1.0691), p=0.19	1.0059 (0.9782 to 1.0343), p=0.68

2.4.7.4 Associations between PM_{10} and lung function, symptoms and medication use in two pollutant models with 4-hour ozone

Table 2.52. Associations between PM_{10} and lung function in two pollutant models with 4-hour ozone

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
PM_{10} 24-hr				
lag0	-0.0810 (-0.4555 to 0.2934), p=0.67	-0.0001 (-0.0026 to 0.0024), p=0.95		
lag1	-0.0198 (-0.4684 to 0.4288), p=0.93	-0.0003 (-0.0033 to 0.0027), p=0.85	0.1070 (-0.1840 to 0.3981), p=0.47	0.0000 (-0.0020 to 0.0021), p=0.96
lag2	0.0539 (-0.3844 to 0.4922), p=0.81	0.0000 (-0.0029 to 0.0029), p=1.00	-0.3599 (-0.7212 to 0.0015), p=0.051	-0.0017 (-0.0042 to 0.0008), p=0.19
lag3			0.1683 (-0.1956 to 0.5321), p=0.36	0.0013 (-0.0012 to 0.0038), p=0.32

Table 2.53. Associations between PM_{10} and night symptoms and medication use in two pollutant models with 4-hour ozone

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
PM_{10} 24-hr					
lag1	1.0011 (0.9812 to 1.0213), p=0.92	1.0177 (0.9937 to 1.0423), p=0.15	0.9894 (0.9498 to 1.0306), p=0.61	1.0000 (0.9819 to 1.0184), p=1.00	0.9957 (0.9639 to 1.0286), p=0.80
lag2	1.0115 (0.9891 to 1.0344), p=0.32	1.0288 (0.9994 to 1.0592), p=0.055	1.0190 (0.9792 to 1.0604), p=0.36	1.0070 (0.9866 to 1.0279), p=0.50	0.9870 (0.9517 to 1.0235), p=0.48
lag3	1.0002 (0.9779 to 1.0230), p=0.99	1.0267 (0.9987 to 1.0554), p=0.062	0.9823 (0.9387 to 1.0279), p=0.44	1.0013 (0.9814 to 1.0217), p=0.90	1.0026 (0.9685 to 1.0379), p=0.88

Table 2.54. Associations between PM_{10} and day time symptoms in two pollutant models with 4-hour ozone

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
PM_{10} 24-hr							
lag0	1.0058 (0.9889 to 1.0229), p=0.51	1.0137 (0.9922 to 1.0357), p=0.21	0.9968 (0.9681 to 1.0264), p=0.83	0.9989 (0.9802 to 1.0180), p=0.91	0.9816 (0.9530 to 1.0111), p=0.22	0.9856 (0.9601 to 1.0118), p=0.28	0.9947 (0.9799 to 1.0097), p=0.49
lag1	1.0042 (0.9843 to 1.0245), p=0.68	0.9950 (0.9684 to 1.0225), p=0.72	1.0013 (0.9687 to 1.0351), p=0.94	0.9934 (0.9728 to 1.0144), p=0.53	0.9975 (0.9666 to 1.0295), p=0.88	0.9959 (0.9675 to 1.0252), p=0.78	0.9947 (0.9780 to 1.0118), p=0.54
lag2	1.0153 (0.9956 to 1.0354), p=0.13	0.9927 (0.9660 to 1.0201), p=0.60	1.0075 (0.9747 to 1.0414), p=0.66	0.9867 (0.9661 to 1.0077), p=0.21	1.0016 (0.9715 to 1.0325), p=0.92	1.0092 (0.9824 to 1.0366), p=0.51	0.9957 (0.9792 to 1.0124), p=0.61

Table 2.55. Associations between PM_{10} and day time medication use in two pollutant models with 4-hour ozone

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
PM_{10} 24-hr			
lag0	0.9977 (0.9746 to 1.0213), p=0.85	1.0015 (0.9698 to 1.0342), p=0.93	0.9924 (0.9694 to 1.0158), p=0.52
lag1	1.0170 (0.9882 to 1.0466), p=0.25	1.0266 (0.9866 to 1.0681), p=0.20	1.0099 (0.9822 to 1.0384), p=0.49
lag2	1.0093 (0.9805 to 1.0389), p=0.53	1.0276 (0.9873 to 1.0695), p=0.18	1.0058 (0.9782 to 1.0342), p=0.68

2.4.7.5 Associations between PM_{10} and lung function, symptoms and medication use in two pollutant models with 8-hour ozone

Table 2.56. Associations between PM_{10} and lung function in two pollutant models with 8-hour ozone

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
PM_{10} 24-hr				
lag0	-0.1386 (-0.5181 to 0.2408), p=0.47	-0.0003 (-0.0028 to 0.0022), p=0.80		
lag1	-0.0544 (-0.5075 to 0.3987), p=0.81	-0.0003 (-0.0033 to 0.0026), p=0.82	0.1263 (-0.1661 to 0.4187), p=0.40	0.0001 (-0.0019 to 0.0021), p=0.89
lag2	0.0271 (-0.4167 to 0.4709), p=0.90	-0.0001 (-0.0030 to 0.0029), p=0.97	-0.3413 (-0.7038 to 0.0213), p=0.065	-0.0016 (-0.0041 to 0.0009), p=0.21
lag3			0.1722 (-0.1935 to 0.5380), p=0.36	0.0013 (-0.0012 to 0.0038), p=0.32

Table 2.57. Associations between PM_{10} and night symptoms and medication use in two pollutant models with 8-hour ozone

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
PM_{10} 24-hr					
lag1	1.0027 (0.9832 to 1.0226), p=0.79	1.0151 (0.9915 to 1.0393), p=0.21	0.9812 (0.9417 to 1.0223), p=0.36	1.0001 (0.9823 to 1.0182), p=0.99	0.9961 (0.9646 to 1.0286), p=0.81
lag2	1.0131 (0.9909 to 1.0359), p=0.25	1.0274 (0.9981 to 1.0576), p=0.067	1.0126 (0.9731 to 1.0537), p=0.54	1.0071 (0.9868 to 1.0278), p=0.49	0.9877 (0.9524 to 1.0242), p=0.50
lag3	1.0016 (0.9794 to 1.0243), p=0.89	1.0254 (0.9975 to 1.0541), p=0.074	0.9782 (0.9347 to 1.0238), p=0.34	1.0016 (0.9818 to 1.0218), p=0.88	1.0027 (0.9685 to 1.0381), p=0.88

Table 2.58. Associations between PM_{10} and day time symptoms in two pollutant models with 8-hour ozone

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
PM_{10} 24-hr							
lag0	1.0053 (0.9885 to 1.0224), p=0.54	1.0150 (0.9936 to 1.0369), p=0.17	0.9965 (0.9680 to 1.0259), p=0.81	1.0012 (0.9826 to 1.0201), p=0.90	0.9824 (0.9536 to 1.0120), p=0.24	0.9860 (0.9606 to 1.0121), p=0.29	0.9956 (0.9809 to 1.0104), p=0.56
lag1	1.0042 (0.9844 to 1.0243), p=0.68	0.9971 (0.9706 to 1.0245), p=0.84	1.0001 (0.9677 to 1.0337), p=0.99	0.9951 (0.9747 to 1.0160), p=0.64	0.9980 (0.9670 to 1.0299), p=0.90	0.9958 (0.9676 to 1.0248), p=0.78	0.9954 (0.9788 to 1.0123), p=0.59
lag2	1.0153 (0.9957 to 1.0354), p=0.13	0.9941 (0.9674 to 1.0216), p=0.67	1.0066 (0.9739 to 1.0403), p=0.70	0.9883 (0.9678 to 1.0092), p=0.27	1.0021 (0.9720 to 1.0331), p=0.89	1.0093 (0.9827 to 1.0367), p=0.50	0.9964 (0.9800 to 1.0131), p=0.67

Table 2.59. Associations between PM_{10} and day time medication use in two pollutant models with 8-hour ozone

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
PM_{10} 24-hr			
lag0	0.9958 (0.9727 to 1.0193), p=0.72	0.9997 (0.9681 to 1.0323), p=0.99	0.9912 (0.9684 to 1.0144), p=0.45
lag1	1.0155 (0.9870 to 1.0449), p=0.29	1.0236 (0.9846 to 1.0642), p=0.24	1.0092 (0.9818 to 1.0375), p=0.51
lag2	1.0079 (0.9793 to 1.0374), p=0.59	1.0241 (0.9847 to 1.0650), p=0.23	1.0050 (0.9775 to 1.0333), p=0.72

2.4.7.6 Associations between PM_{10} and lung function, symptoms and medication use in two pollutant models with 8-hour CO

Table 2.60. Associations between PM_{10} and lung function in two pollutant models with 8-hour CO

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
PM_{10} 24-hr				
lag0	-0.1877 (-0.6581 to 0.2826), p=0.43	-0.0001 (-0.0033 to 0.0032), p=0.97		
lag1	-0.1537 (-0.7169 to 0.4094), p=0.59	-0.0014 (-0.0052 to 0.0025), p=0.49	0.3708 (-0.0045 to 0.7460), p=0.053	**0.0028 (0.0001 to 0.0056), p=0.042**
lag2	-0.0218 (-0.5751 to 0.5314), p=0.94	-0.0002 (-0.0040 to 0.0035), p=0.90	-0.0382 (-0.4827 to 0.4063), p=0.87	-0.0005 (-0.0037 to 0.0028), p=0.78
lag3			0.0252 (-0.4326 to 0.4829), p=0.91	-0.0011 (-0.0044 to 0.0022), p=0.50

Table 2.61. Associations between PM_{10} and night symptoms and medication use in two pollutant models with 8-hour CO

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
PM_{10} 24-hr					
lag1	1.0163 (0.9960 to 1.0370), p=0.12	**1.0408 (1.0140 to 1.0682), p=0.003**	1.0207 (0.9854 to 1.0572), p=0.25	1.0152 (0.9953 to 1.0355), p=0.14	0.9991 (0.9640 to 1.0355), p=0.96
lag2	1.0194 (0.9972 to 1.0420), p=0.087	**1.0453 (1.0143 to 1.0774), p=0.004**	**1.0417 (1.0031 to 1.0819), p=0.034**	1.0206 (0.9990 to 1.0426), p=0.062	0.9941 (0.9580 to 1.0316), p=0.75
lag3	1.0114 (0.9896 to 1.0336), p=0.31	**1.0361 (1.0062 to 1.0670), p=0.018**	1.0319 (0.9927 to 1.0726), p=0.11	1.0178 (0.9969 to 1.0391), p=0.095	0.9921 (0.9561 to 1.0294), p=0.67

Table 2.62. Associations between PM_{10} and day time symptoms in two pollutant models with 8-hour CO

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
PM_{10} 24-hr							
lag0	0.9991 (0.9799 to 1.0187), p=0.93	**1.0242 (1.0016 to 1.0473), p=0.036**	1.0178 (0.9922 to 1.0441), p=0.17	1.0032 (0.9830 to 1.0239), p=0.76	0.9912 (0.9629 to 1.0204), p=0.55	1.0233 (0.9991 to 1.0480), p=0.060	0.9988 (0.9818 to 1.0160), p=0.89
lag1	**1.0229 (1.0006 to 1.0456), p=0.044**	1.0230 (0.9952 to 1.0515), p=0.11	1.0269 (0.9954 to 1.0594), p=0.094	0.9945 (0.9723 to 1.0172), p=0.63	1.0114 (0.9798 to 1.0440), p=0.49	1.0225 (0.9947 to 1.0511), p=0.11	1.0175 (0.9983 to 1.0371), p=0.073
lag2	1.0179 (0.9962 to 1.0402), p=0.11	1.0269 (1.0002 to 1.0543), p=0.049	1.0269 (0.9958 to 1.0588), p=0.090	0.9917 (0.9697 to 1.0142), p=0.47	0.9963 (0.9645 to 1.0292), p=0.82	1.0149 (0.9875 to 1.0431), p=0.29	1.0085 (0.9900 to 1.0272), p=0.37

Table 2.63. Associations between PM_{10} and day time medication use in two pollutant models with 8-hour CO

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
PM_{10} 24-hr			
lag0	1.0158 (0.9906 to 1.0418), p=0.22	1.0271 (0.9928 to 1.0627), p=0.12	1.0082 (0.9843 to 1.0327), p=0.51
lag1	**1.0349 (1.0043 to 1.0664), p=0.025**	1.0621 (1.0176 to 1.1086), p=0.006	**1.0292 (1.0005 to 1.0587), p=0.046**
lag2	**1.0508 (1.0203 to 1.0823), p=0.001**	1.0567 (1.0133 to 1.1020), p=0.010	**1.0499 (1.0211 to 1.0795), p=0.0006**

2.4.7.7 Associations between PM_{10} and lung function, symptoms and medication use in two pollutant models with 1-hour SO_2

Table 2.64. Associations between PM_{10} and lung function in two pollutant models with 1-hour SO_2

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
PM_{10} 24-hr				
lag0	-0.0118 (-0.5283 to 0.5048), p=0.96	-0.0003 (-0.0038 to 0.0033), p=0.88		
lag1	0.2130 (-0.4689 to 0.8949), p=0.54	0.0016 (-0.0031 to 0.0063), p=0.51	0.1153 (-0.2669 to 0.4974), p=0.55	0.0007 (-0.0019 to 0.0032), p=0.62
lag2	-0.2673 (-0.9349 to 0.4002), p=0.43	0.0001 (-0.0045 to 0.0047), p=0.95	**-0.7972 (-1.3148 to -0.2796), p=0.003**	**-0.0041 (-0.0076 to -0.0006), p=0.023**
lag3			0.1646 (-0.3440 to 0.6732), p=0.53	0.0028 (-0.0006 to 0.0062), p=0.11

Table 2.65. Associations between PM_{10} and night symptoms and medication use in two pollutant models with 1-hour SO_2

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
PM_{10} 24-hr					
lag1	**1.0246 (1.0016 to 1.0482), p=0.036**	0.9793 (0.9398 to 1.0204), p=0.32	0.9805 (0.9241 to 1.0402), p=0.51	1.0173 (0.9954 to 1.0396), p=0.12	0.9924 (0.9506 to 1.0361), p=0.73
lag2	1.0269 (0.9993 to 1.0552), p=0.056	1.0229 (0.9827 to 1.0648), p=0.27	1.0317 (0.9756 to 1.0912), p=0.27	1.0256 (0.9992 to 1.0528), p=0.058	0.9594 (0.9135 to 1.0077), p=0.098
lag3	1.0199 (0.9928 to 1.0478), p=0.15	0.9811 (0.9380 to 1.0261), p=0.40	1.0019 (0.9381 to 1.0701), p=0.95	1.0060 (0.9797 to 1.0329), p=0.66	0.9946 (0.9496 to 1.0416), p=0.82

Table 2.66. Associations between PM_{10} and day time symptoms in two pollutant models with 1-hour SO_2

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
PM_{10} 24-hr							
lag0	1.0156 (0.9919 to 1.0398), p=0.20	1.0153 (0.9820 to 1.0498), p=0.37	0.9926 (0.9506 to 1.0364), p=0.74	**1.0244 (1.0007 to 1.0487), p=0.044**	1.0262 (0.9800 to 1.0745), p=0.27	0.9971 (0.9599 to 1.0357), p=0.88	1.0124 (0.9922 to 1.0329), p=0.23
lag1	1.0176 (0.9899 to 1.0462), p=0.21	0.9953 (0.9581 to 1.0338), p=0.81	1.0028 (0.9563 to 1.0515), p=0.91	**1.0395 (1.0106 to 1.0692), p=0.007**	1.0481 (0.9972 to 1.1015), p=0.064	1.0082 (0.9680 to 1.0501), p=0.69	**1.0257 (1.0018 to 1.0502), p=0.035**
lag2	1.0134 (0.9854 to 1.0422), p=0.35	0.9999 (0.9585 to 1.0432), p=1.00	1.0183 (0.9668 to 1.0725), p=0.49	1.0223 (0.9953 to 1.0500), p=0.11	1.0600 (1.0020 to 1.1214), p=0.042	1.0238 (0.9820 to 1.0674), p=0.27	1.0137 (0.9912 to 1.0367), p=0.23

Table 2.67. Associations between PM_{10} and day time medication use in two pollutant models with 1-hour SO_2

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
PM_{10} 24-hr			
lag0	1.0193 (0.9821 to 1.0578), p=0.31	1.0111 (0.9588 to 1.0662), p=0.68	1.0031 (0.9673 to 1.0403), p=0.87
lag1	1.0281 (0.9868 to 1.0712), p=0.18	1.0318 (0.9764 to 1.0903), p=0.27	1.0108 (0.9711 to 1.0522), p=0.60
lag2	1.0124 (0.9682 to 1.0586), p=0.59	1.0447 (0.9896 to 1.1029), p=0.11	1.0043 (0.9629 to 1.0475), p=0.84

2.4.7.8 Associations between PM_{10} and lung function, symptoms and medication use in two pollutant models with 24-hour SO_2

Table 2.68. Associations between PM_{10} and lung function in two pollutant models with 24-hour SO_2

Lag	Evening PEF	Evening FEV_1	Morning PEF	Morning FEV_1
PM_{10} 24-hr				
lag0	-0.0552 (-0.5757 to 0.4652), p=0.84	-0.0004 (-0.0040 to 0.0031), p=0.81		
lag1	0.2011 (-0.4789 to 0.8810), p=0.56	0.0015 (-0.0032 to 0.0062), p=0.53	0.1253 (-0.2592 to 0.5098), p=0.52	0.0007 (-0.0019 to 0.0033), p=0.59
lag2	-0.2763 (-0.9362 to 0.3837), p=0.41	0.0001 (-0.0044 to 0.0047), p=0.96	**-0.8187 (-1.3325 to -0.3048), p=0.002**	**-0.0043 (-0.0078 to -0.0008), p=0.015**
lag3			0.1926 (-0.3152 to 0.7004), p=0.46	0.0030 (-0.0004 to 0.0064), p=0.083

Table 2.69. Associations between PM_{10} and night symptoms and medication use in two pollutant models with 24-hour SO_2

Lag	Night cough	Night wheeze	Night shortness of breath	Any night symptoms	Any night reliever medications use
PM_{10} 24-hr					
lag1	**1.0267 (1.0033 to 1.0507), p=0.025**	0.9800 (0.9400 to 1.0217), p=0.34	0.9841 (0.9270 to 1.0448), p=0.60	1.0188 (0.9965 to 1.0416), p=0.098	0.9911 (0.9491 to 1.0349), p=0.68
lag2	**1.0277 (1.0003 to 1.0559), p=0.047**	1.0228 (0.9827 to 1.0645), p=0.27	1.0326 (0.9762 to 1.0922), p=0.26	1.0263 (1.0000 to 1.0533), p=0.050	0.9579 (0.9124 to 1.0058), p=0.084
lag3	1.0197 (0.9926 to 1.0476), p=0.16	0.9812 (0.9378 to 1.0266), p=0.41	1.0022 (0.9382 to 1.0706), p=0.95	1.0055 (0.9793 to 1.0325), p=0.68	0.9925 (0.9478 to 1.0392), p=0.75

Table 2.70. Associations between PM_{10} and day time symptoms in two pollutant models with 24-hour SO_2

Lag	Day cough	Day wheeze	Day shortness of breath	Day runny nose	Day eye irritation	Day fever	Any day symptoms
PM_{10} 24-hr							
lag0	1.0158 (0.9919 to 1.0404), p=0.20	1.0183 (0.9843 to 1.0535), p=0.29	0.9907 (0.9484 to 1.0348), p=0.67	1.0223 (0.9985 to 1.0468), p=0.067	1.0252 (0.9789 to 1.0738), p=0.29	1.0006 (0.9628 to 1.0398), p=0.98	1.0117 (0.9913 to 1.0325), p=0.26
lag1	1.0180 (0.9903 to 1.0465), p=0.21	0.9962 (0.9588 to 1.0350), p=0.84	1.0025 (0.9557 to 1.0516), p=0.92	**1.0369 (1.0082 to 1.0664), p=0.012**	1.0481 (0.9970 to 1.1017), p=0.065	1.0097 (0.9693 to 1.0517), p=0.64	**1.0253 (1.0015 to 1.0496), p=0.037**
lag2	1.0122 (0.9845 to 1.0406), p=0.39	1.0009 (0.9595 to 1.0441), p=0.97	1.0164 (0.9672 to 1.0681), p=0.52	1.0199 (0.9927 to 1.0479), p=0.15	1.0547 (1.0004 to 1.1120), p=0.048	1.0261 (0.9833 to 1.0708), p=0.24	1.0119 (0.9893 to 1.0349), p=0.30

Table 2.71. Associations between PM_{10} and day time medication use in two pollutant models with 24-hour SO_2

Lag	Day time reliever use for symptoms	Day time preventer use for symptoms	Any day time medication use for symptoms
PM_{10} 24-hr			
lag0	1.0206 (0.9829 to 1.0598), p=0.29	1.0112 (0.9595 to 1.0657), p=0.68	1.0046 (0.9682 to 1.0424), p=0.81
lag1	1.0287 (0.9872 to 1.0720), p=0.18	1.0305 (0.9754 to 1.0887), p=0.28	1.0111 (0.9713 to 1.0526), p=0.59
lag2	1.0122 (0.9684 to 1.0579), p=0.59	1.0476 (0.9907 to 1.1077), p=0.10	1.0052 (0.9634 to 1.0487), p=0.81

3. DISCUSSION

ACHAPS is the largest panel study on ambient air pollution and children's respiratory health conducted anywhere in Australia. Two hundred and seventy primary school aged children from six cities (Sydney, Melbourne, Brisbane, Adelaide, Perth and Canberra) participated in this panel study.

We investigated the effects of six air pollutants – PM_{10} (24-hr average), $PM_{2.5}$ (24-hr average), ozone (1-hr maximum, 4-hr average, 8-hr average), NO_2 (1-hr maximum, 24-hr average), SO_2 (1-hr maximum, 2 4-hr average) and CO (8-hr average) – on children's respiratory health. Health outcomes considered included lung function, respiratory and non-respiratory symptoms, and medication use for asthma.

3.1. Single pollutant models

Single pollutant models produced only few significant adverse effects of air pollutants on children's respiratory health. Many associations showed a beneficial effect of air pollutants on respiratory health. The most consistent adverse effect was that increased NO_2 exposure was associated with an increased risk of cough and wheeze, during the day and night, and increased use of bronchodilators for symptom relief. These findings are consistent with worsening asthma or asthma-like illness. The absence of a measurable impact on lung function may be due to the relief of bronchoconstriction due to the use of bronchodilators

Morning and evening lung function

There was only one significant adverse effect on lung function (lag 2 NO_2 1-hr and morning FEV_1).

Night symptoms and use of asthma medications for symptoms

Night symptoms were associated with CO, NO_2 and PM_{10} with higher pollutant levels associated with greater risk of night symptoms, especially night cough. Relationships between NO_2 and night symptoms and effects were greater for NO_2 24-hr than for NO_2 1-hr were more consistent. There were protective effects for ozone and night wheeze and night shortness of breath and this was consistent across all the three metrics for ozone. There was only one significant association between air pollution and the use of reliever medication at night (association between SO_2 1-hr and use of reliever medication at night).

Day symptoms and use of asthma medications for symptoms

Day time symptoms were more likely to be associated with NO_2 (cough, wheeze and shortness of breath) and less likely to be associated with ozone (wheeze). Again, as was seen with night symptoms, there were more consistent relationships between NO_2 and day time symptoms and effects were greater for NO_2 24-hr than for NO_2 1-hr. Children were also more likely to use more reliever medications for asthma on days with higher NO_2 concentrations. There was one association between air pollution (lag 2 PM_{10} 24-hr) and preventer use for symptoms and a single association where higher ozone levels (lag 2 O_3 8-hr) were associated with decreased use of preventers for symptoms.

3.2. Two pollutant models

NO_2 and ozone

In two pollutant models compared to single pollutant models, the effects of NO_2 on the lung function were increased whereas the effects on symptoms slightly decreased. Further, in the two pollutant models compared to single pollutant models, effects on day time medication use were no longer significant.

PM_{10} and gases

We also investigated the effects of PM_{10} in two pollutant models with each of the gases (O_3, NO_2, SO_2 and CO). Significant negative effects on morning lung function were seen particularly when SO_2 was included in the models. Associations between PM_{10} and both night and day time symptoms (cough and wheeze) generally persisted when NO_2 and CO were added to the models. PM_{10} was also associated with runny nose when SO_2 was included in the models. Significant increased use of day time reliever medications was only observed in two pollutant models with CO. The odds ratios in all models were consistently greater in the two pollutant models compared with single pollutant models especially for
lag 1 PM_{10} and lag 2 PM_{10}.

SO_2 and PM_{10}

In these two pollutant models with PM_{10}, the SO_2 effects were similar to the effect estimates from single pollutant models. Mainly protective effects were observed.

3.3. Restricted models

Warm season ozone models

A warm season analysis was conducted for ozone as ozone levels are higher in the warmer months. The results were similar to those obtained when the analyses were conducted regardless of the season. There were no adverse associations between warm season ozone and lung function, symptoms and medication use in this sub-analysis. There were a few positive associations (beneficial effects) with night wheeze, that is, children experienced less wheeze symptoms during the night when ozone levels were high the previous day.

SO_2 analysis excluding Port Pirie

We also conducted a sub-analysis for the effects of SO_2 after excluding children from Port Pirie as Port Pirie has high ambient levels of SO_2. A significant negative association is now seen between SO_2 1-hr and morning PEF. The beneficial effects on day time symptoms are no longer apparent when children from Port Pirie were excluded from the analyses. In fact, there are now adverse effects especially with cough and runny nose. Children also tended to use more preventer medication for symptoms on days with higher SO_2 1-hr levels.

3.4. Comparisons with other studies

3.4.1. Particulate matter

In a recent systematic review of particulate matter and panel studies (daily data for at least eight weeks) in children, Ward and Ayres (2004) reviewed 22 studies on the effects of particulate matter on PEF, cough and lower respiratory symptoms. In the 14 studies of PM_{10} and PEF, all studies, but one, showed adverse effects. For a 1 ug/m^3 increase in PM_{10}, there was a 0.012 litre/min (95%CI: 0.008-0.017 litre/min) decrease in PEF. All five studies of $PM_{2.5}$ and PEF showed adverse effects on PEF. A 1 ug/m^3 increase in $PM_{2.5,}$ was associated with 0.063 litre/min (95%CI: 0.034-0.094 litre/min) decrease in PEF. In the case of PM_{10}, the pooled effect estimates for cough and lower respiratory symptoms were 1.000 (95%CI: 0.999-1.001) and 1.001 (95%CI: 1.000-1.001) for a 1 ug/m^3 increase respectively. For $PM_{2.5}$, the pooled effect estimates for cough and lower respiratory symptoms were 1.005 (95%CI: 1.003-1.007) and 1.004 (95%CI: 1.002-1.006) for a 1 ug/m^3 increase respectively. However, the significant heterogeneity detected between the panel studies results raises questions about the transferability of the estimated pooled results. There was also evidence of publication bias especially for PM_{10} and PEF, again raising concerns about the validity of the pooled results.

In a re-analysis of five panel studies, Hoek et al (Hoek, Dockery et al. 1998) found that the prevalence of decrements in PEF>10% significantly increased by 2.7% for every 10 ug/m^3 increase in PM_{10} and the population mean PEF significantly decreased by about 0.07 litres.

In an eight city analysis, Schildcrout et al (Schildcrout, Sheppard et al. 2006) investigated associations between ambient air pollutants and asthma exacerbations (symptoms and medication use). There were no associations between PM_{10} and either asthma symptoms or the use of asthma medications.

Mortimer et al (Mortimer, Neas et al. 2002) studied 846 children with asthma recruited from eight US urban centres focusing on the effects of ozone on lung function and symptoms. However, in subsidiary analysis, they demonstrated associations between cumulative lag 1-2 PM_{10} and incidence of any morning asthma symptoms of cough, chest tightness or wheeze (OR=1.26, 95%CI: 1.00-1.59) in single pollutant models for a 10 ug/m^3 change in PM_{10}. In two pollutant models (with ozone) and in four pollutant models (with ozone, SO_2 and NO_2), although the effects were of similar magnitude, they were no longer significant. There were no significant effects on morning or evening PEF (except at lag 8) or evening symptoms. As the PM_{10} analyses were restricted to only three of the centres with PM_{10} data, the lack of an effect could be due to smaller sample sizes.

A panel study of 133 children in Seattle, Washington found increases in $PM_{2.5}$ and PM_{10} to be significantly associated with an increased risk of more severe asthma attacks and medication use in children with asthma (Slaughter et al, 2003).

Lewis et al (Lewis, Robins et al. 2005) studied 86 children with asthma with daily diaries. There were no associations between PM_{10} and $PM_{2.5}$ and FEV_1 for the children who were not taking maintenance corticosteroids. In those children taking maintenance corticosteroids for their asthma, there was a significant decrease in FEV_1 with PM_{10} (beta=-2.21, 95%CI: -3.97 to -0.46; lag

2 PM_{10}) but not with $PM_{2.5}$. Adverse effects of both PM_{10} and $PM_{2.5}$ seen at lag 3-5 if children reported symptoms of upper respiratory infection on the day of lung function measurements.

Moshammer et al (Moshammer, Hutter et al. 2006) followed up 163 children with fortnightly lung function measurements. In single pollutant models, $PM_{2.5}$ was associated with decrements in PEF (-0.41%) and FEV_1 (-0.23%) for a 10 ug/m^3 increase in $PM_{2.5}$. In a two pollutant model with NO_2, effects were smaller (positive for FEV_1) and were no longer significant.

In a panel study, 861 children with persistent asthma from seven US urban communities kept two week asthma diaries every six month for two years (O'Connor, Neas et al. 2008). In single pollutant models, there were significant associations between lag 0-4 $PM_{2.5}$ (13.2 ug/m3 increase) and FEV_1 (-1.47%, 95%CI: -2.0 to -0.94%), PEF (-1.10%, 95%CI: -1.65 to -0.56%) and missed school days (OR=1.33, 95%CI: 1.06-1.66) but not with days with asthma symptoms (cough, wheeze) and nights with asthma. In three pollutant models with O_3 and NO_2, only the PEF effects remained significant.

In a study from Mexico, Escamilla-Nunez et al (Escamilla-Nunez, Barraza-Villarreal et al. 2008) recruited 147 asthmatic children and 50 healthy children in a panel study of symptoms (wheeze and cough) and asthma medication use (preventers and relievers). In single pollutant models, there was no association between $PM_{2.5}$ and cough, wheeze or medication use. In three pollutant models (with O_3 and NO_2), $PM_{2.5}$ was associated with wheeze only at lag 0. In children without asthma, there were no associations between $PM_{2.5}$ and cough, wheeze or medication use.

In a Canadian study of children with doctor diagnosed asthma , Dales et al (Dales, Chen et al. 2009) found a significant association between $PM_{2.5}$ and evening FEV_1 in both single pollutant models (0.54% decrease in FEV_1, 95%CI: 0.06-1.02% decrease, 6.0 ug/m^3 increase in $PM_{2.5}$). The association persisted in two pollutant models with ozone, NO_2 and SO_2. There were no effects of ozone, NO_2 and SO_2 on morning FEV_1. There were also no effects of $PM_{2.5}$, ozone, NO_2 and SO_2 on evening FEV_1, PEF and symptoms (cough, wheeze, difficulty breathing and chest tightness).

In Sydney, in a panel study of 125 symptomatic children conducted in 1994, there was a significant association between PM_{10} and doctor visits for asthma in both single pollution and three pollution (with ozone and NO_2) models but not between PM_{10} and evening symptoms (cough and wheeze) and evening medication use for asthma (Jalaludin, O'Toole et al. 2004a). In the same study, there was no association between PM_{10} and PEF in population regression models (Jalaludin, Chey et al. 2000).

In the Sydney panel study, the effects of bushfire PM on lung function (Jalaludin, Smith et al. 2000) and on symptoms and medication use (Jalaludin, O'Toole et al. 2004b) were also investigated. There were no associations between daily PM_{10} and PEF except in a subgroup of children without bronchial hyper-reactivity where there was a negative association between PM_{10} and PEF. In single pollutant models, the non-bushfire fraction of PM_{10} was associated with wet cough (lag 0, lag 2, lag 0-4), dry cough (lag 0, lag 0-4) and wheeze (lag 0-2, lag 0-4). There were no associations with asthma medication use.

In another study investigating the effects of biomass PM, Johnston et al (Johnston, Webby et al. 2006) conducted a panel study of children and adults in Darwin over a period of seven months to determine the effects of deliberate landscape burnings on children's symptoms, medication

use, missed school or work, and whether they saw a health care professional for asthma. In children, both $PM_{2.5}$ and PM_{10} were significantly associated with becoming symptomatic (5 ug/m^3 increase in $PM_{2.5}$: OR=1.148, 95%CI: 1.042-1.264; 10 ug/m^3 increase in PM_{10}: OR=1.247, 95%CI: 1.058-1.468). There were no associations between PM and asthma attacks, medication use, missed school and seeing a health care professional for asthma.

In a panel study of high school students from Christchurch, New Zealand, where PM_{10} is mainly from wood burning, small effects were seen in only children with asthma (Epton, Dawson et al. 2008). In this group of children, outdoor PM_{10} had small effects on evening PEF and cough.

The ACHAPS study did not find any adverse effects of PM on lung function in single pollution models and a few associations with PM_{10} and symptoms (mainly cough and wheeze with ORs between 1.017 to 1.02 for a 1 ug/m^3 increase in PM_{10}). These effect estimates are much smaller than the pooled estimates from the meta-analysis conducted by Ward and Ayres (Ward and Ayres 2004).

3.4.2. Ozone

Most panel studies (where children have been undertaking their normal activities) have demonstrated decrements in PEF ranging from 0.2% to 2.2% for a 50 ppb increase in ambient ozone concentration
(Krzyzanowski, Quackenboss et al. 1992; Neas, Dockery et al. 1995; Romieu, Meneses et al. 1996; Romieu, Meneses et al. 1997; Gold, Damokosh et al. 1999; Neas, Dockery et al. 1999). However, Hoek et al (Hoek, Brunekreef et al. 1993) found a 4% decrease in PEF, one study found no change in PEF (Vedal, Schenker et al. 1987) and another study demonstrated a non-significant 2.4% increase in PEF (Gielen, van der Zee et al. 1997) for a 50 ppb increase in ambient ozone concentration.

The effects of ozone are greater in those studies undertaken in summer camps in the US. In some of these studies, a 50 ppb increase in ambient ozone concentration was associated with about a 5% decrease in PEF (Raizenne, Burnett et al. 1989; Studnicka, Frischer et al. 1995; Thurston, Lippmann et al. 1997; Galizia and Kinney 1999).

Mortimer et al (Mortimer, Neas et al. 2002) studied 846 children with asthma recruited from eight US urban centres focusing on the effects of ozone on lung function and symptoms. A 15 ppb increase in 5-day average 8-hr ozone was associated with a 0.59% (95%CI: 0.13-1.05%) decrease in morning PEF. There were no effects of individual daily lags (lag 1 to lag 6) and cumulative lag 1-4 ozone on morning PEF. A four day moving average ozone was significantly associated with any morning symptoms (cough, chest tightness, wheeze) (OR=1.16, 95%CI: 1.02-1.30). There were no significant associations with evening PEF or evening symptoms.

In a study of 21 children with mild asthma, Delfino et al (Delfino, Gong et al. 2003), did not find significant associations between ozone (1-hr maximum) and morning PEF, evening PEF and 'bothersome or more severe' asthma symptoms.

Lewis et al (Lewis, Robins et al. 2005) studied 86 children with asthma with daily diaries. There were no associations between O_3 and FEV_1 for the children who were not taking maintenance corticosteroids. However, in those children taking maintenance corticosteroids for their asthma, there was a significant decrease in FEV_1 (beta=-3.95, 95%CI: -6.78 to -1.12; lag 2 O_3 8-hr). Adverse effects of ozone were also more likely if children reported symptoms of upper respiratory infection on the day of lung function measurements.

In an eight city panel study analysis from the US (Schildcrout, Sheppard et al. 2006), there were no significant associations between warm season ozone and asthma symptoms and medication use.

In a panel study, 861 children with persistent asthma from seven US urban communities kept two week asthma diaries every six month for two years (O'Connor, Neas et al. 2008). In single pollutant models, there were no significant associations between lag 0-4 ozone and FEV_1, PEF, days with asthma symptoms (cough, wheeze), nights with asthma and missed school days. In three pollutant models with $PM_{2.5}$ and NO_2, ozone (lag 0-4 26.7 ppb) was now associated with decrements in PEF (-1.48%, 95%CI: -2.50 to -0.45%).

In a study from Mexico, Escamilla-Nunez et al (Escamilla-Nunez, Barraza-Villarreal et al. 2008) recruited 147 asthmatic children and 50 healthy children in a panel study of symptoms (wheeze and cough) and asthma medication use (preventers and relievers). In single pollutant models, all metrics of ozone (lag 0, lag 1, lag 2, lag 0-2, lag 0-3, lag 0-4) were significantly associated with cough, wheeze and reliever medication use. In three pollutant models (with $PM_{2.5}$ and NO_2), ozone effects were mainly seen with cough and wheeze. In children without asthma, there were no associations between ozone and cough, wheeze or medication use.

In Sydney, in a panel study of 125 symptomatic children conducted in 1994, there was a significant association between ozone and evening PEF in population regression models but not in GEE models. The association remained significant in two pollution models (ozone with PM_{10} or with NO_2) and in three pollution models (ozone with PM_{10} and NO_2) (Jalaludin, Chey et al. 2000). In the same panel study, Jalaludin et al (Jalaludin, O'Toole et al. 2004) were not able to demonstrate relationships between ambient ozone and asthma symptoms, medication use and doctor visits for asthma.

The ACHAPS study was not able to demonstrate any adverse effects of ambient ozone on children's lung function, symptoms or medication use. In fact we see the opposite effect where ambient ozone appears to have a protective effect on symptoms of cough and wheeze. In a sub-analysis restricted to the warm season (when ozone concentration would be higher), the results were similar to those obtained when the analyses were conducted regardless of the season.

3.4.3. Nitrogen dioxide

In a study from the United Kingdom, children with a history of asthma exposed to higher levels of NO_2 (> 28 ug/m^3) were more likely to experience an episode of asthma within seven days of an upper respiratory infection (OR=1.9, 95%CI: 1.1-3.4) compared to children exposed to lower levels of NO_2 (≤8 ug/m^3) (Linaker, Coggon et al. 2000).

Mortimer et al (Mortimer, Neas et al. 2002) studied 846 children with asthma recruited from eight US urban centres focusing on the effects of ozone on lung function and symptoms. However, in further analysis, they demonstrated associations between average lag 1 to lag 6 NO_2 and any morning asthma symptoms of cough, chest tightness or wheeze (OR=1.48, 95%CI: 1.02-2.16) in single pollutant models for a 20 ppb change in NO_2. Effects were no longer significant in two pollutant models (with ozone), three pollutant models (with ozone and SO_2) and four pollutant models (ozone, SO_2 and PM_{10}). There were no significant associations with morning or evening PEF or evening symptoms.

In a study of 21 children with mild asthma, Delfino et al (Delfino, Gong et al. 2003), found significant associations between 1-hr and 8-hr NO_2 and 'bothersome or more severe' asthma symptoms but there were no associations between 1-hr NO_2 and morning PEF and evening PEF.

Schildcrout et al (Schildcrout, Sheppard et al. 2006), in a panel study of 990 children in eight cities in the US, found associations between NO_2 and any asthma symptoms (lag 2 NO_2: OR=1.09, 95%CI: 1.03-1.15; lag 0-2 NO_2: OR=1.04, 95%CI: 1.01-1.07; 20 ppb change in NO_2) and with the use of rescue inhalers (lag 2 NO_2: RR=1.05, 95%CI: 1.01-1.09; lag 0-2 NO_2: RR=1.03, 95%CI: 1.01-1.05; 20 ppb change in NO_2).

Moshammer et al (Moshammer, Hutter et al. 2006) followed up 163 children with fortnightly lung function measurements. In single pollutant models, NO_2 was associated with decrements in FEV_1 of about 1% for a 10 ug/m^3 increase in NO_2. In a two pollutant model with $PM_{2.5}$, the effect on FEV_1 was similar.

In a panel study, 861 children with persistent asthma from seven US urban communities kept two week asthma diaries every six month for two years (O'Connor, Neas et al. 2008). In single pollutant models, there were significant associations between lag 0-4 NO_2 (20.4 ppb) and FEV_1 (-1.36, 95%CI: -1.92 to -0.80), PEF (-1.66, 95%CI: -2.24 to -1.08), night asthma (37%, 95%CI: 8-73%) and missed school days (OR=1.67, 95%CI: 1.18-2.36). There were no associations with days with asthma symptoms (cough and wheeze). In three pollutant models with $PM_{2.5}$ and ozone, the adverse NO_2 effects on FEV_1 and PEF remained significant; however, associations with night asthma and missed school days were now non-significant and associations with days of cough and wheeze became significant.

In a study from Mexico, Escamilla-Nunez et al (Escamilla-Nunez, Barraza-Villarreal et al. 2008) recruited 147 asthmatic children and 50 healthy children in a panel study of symptoms (wheeze and cough) and asthma medication use (preventers and relievers). In single pollutant models, all metrics of NO_2 (lag 0, lag 1, lag 2, lag 0-2, lag 0-3, lag 0-4) were significantly associated with cough, wheeze and reliever medication use. In three pollutant models (with $PM_{2.5}$ and O_3), NO_2 effects were mainly seen with cough and reliever medication use. In children without asthma, an association was observed only between lag 0-1 NO_2 and cough.

A Sydney panel study of 125 symptomatic children conducted in 1994, showed no association between NO_2 and evening PEF in single pollutant models and in two pollutant models with ozone (Jalaludin, Chey et al. 2000). In the same panel study, Jalaludin et al (Jalaludin, O'Toole et al. 2004) were able to demonstrate relationships between ambient NO_2 and prevalence of evening wet cough but not with other evening symptoms (wheeze and dry cough), medication use (inhaled relievers and preventers) and doctor visits for asthma.

In the ACHAPS study, the most consistent results were seen with NO_2. Consistent relationships between NO_2 and night symptoms (cough, wheeze and shortness of breath) and effects were greater for NO_2 24-hr than for NO_2 1-hr. There were also more consistent relationships between NO_2 and day time symptoms and effects were greater for NO_2 24-hr than for NO_2 1-hr. Children were also more likely to use more reliever medications for asthma on days with higher NO_2 concentrations.

3.4.4. Sulphur dioxide

Mortimer et al (Mortimer, Neas et al. 2002) studied 846 children with asthma recruited from eight US urban centres focusing on the effects of ozone on lung function and symptoms. However, in further analysis, they demonstrated associations between average lag 1 and lag 2 SO_2 and any morning asthma symptoms of cough, chest tightness or wheeze (OR=1.19, 95%CI: 1.06-1.35) in single pollutant models for a 20 ppb change in SO_2. Significant effects remained in two pollutant models (with ozone) and three pollutant models (with ozone and NO_2) but not in four pollutant models (with ozone, NO_2 and PM_{10}). There were no significant associations with morning or evening PEF or evening symptoms.

In a study of 21 children with mild asthma, Delfino et al (Delfino, Gong et al. 2003), found significant associations between 1-hr and 8-hr SO_2 and 'bothersome or more severe' asthma symptoms and with 1-hr SO_2 and evening PEF. There were no associations between 1-hr SO_2 and morning PEF.

In an eight city panel study analysis of 990 children from the US (Schildcrout, Sheppard et al. 2006), there were no significant associations between SO_2 and asthma symptoms and medication use.

In a panel study, 861 children with persistent asthma from seven US urban communities kept two week asthma diaries every six month for two years (O'Connor, Neas et al. 2008). In single pollutant models, there were significant associations between lag 0-4 SO_2 (12.4 ppb) and FEV_1 (-1.60, 95%CI: -2.54 to -0.67) and PEF (-2.14, 95%CI: -3.08 to -1.19) but not with days with asthma symptoms (cough, wheeze), nights with asthma and missed school days. Multi-pollutant analyses were not conducted for SO_2.

Dales et al (Dales, Chen et al. 2009) in a panel study of 182 children did not find associations between SO_2 and FEV_1 and PEF, but however found an association between SO_2 and chest tightness (OR=1.30, 95%CI: 1.06-1.58; highest quartile SO_2 [≥8.8 ppb] versus lowest quartile SO_2 [<2.3 ppb]).

In the ACHAPS study, in single pollutant models, mainly beneficial effects were seen except for lag 1 SO_2 1-hr and nighttime reliever medication use. In a restricted analysis for the effects of SO_2 after excluding children from Port Pirie, a significant negative association was seen between SO_2 1-hr and morning PEF. The beneficial effects on day time symptoms were now no longer apparent. In fact, there were now adverse effects especially with cough and runny nose. Children also tended to use more preventer medication for symptoms on days with higher SO_2 1-hr levels.

3.4.5. Carbon monoxide

In a study of 21 children with mild asthma, Delfino et al (Delfino, Gong et al. 2003), found no significant associations between 1-hr and 8-hr CO and 'bothersome or more severe' asthma symptoms and between 1-hr CO and morning PEF or evening PEF.

In an eight city panel study analysis from the US, 990 children were studied (Schildcrout, Sheppard et al. 2006) for the effects of air pollution on asthma symptoms and medication use. In single pollutant models, CO was associated with asthma symptoms (OR=1.08, 95%CI: 1.01-1.14 for 1 ppm CO) and rescue asthma inhalers (OR=1.07, 95%CI: 1.01-1.13 for 1 ppm CO).

In a panel study, 861 children with persistent asthma from seven US urban communities kept two week asthma diaries every six month for two years (O'Connor, Neas et al. 2008). In single pollutant models, there were significant associations between lag 0-4 CO (872 ppb) and increased days with asthma symptoms (cough and wheeze) (26%, 95%CI: 3-55%) and nights with asthma (35%, 95%CI: 7-71%), but not with FEV_1, PEF and missed school days. Multi-pollutant analyses were not conducted for CO.

There are no published Australian panel studies that have investigated the effects of ambient CO on childrens' respiratory health. However, in a birth cohort followed-up over five years (follow-up at age 6 weeks, 6 months, 1 year, 2 years, 3 years, 4 years and 5 years), Rodriguez et al (Rodriguez, Tonkin et al. 2007) investigated the effects of ambient air pollutants (lag 0, lag 5 and lag 0-5 for CO, NO_2, O_3, $PM_{2.5}$ and BSP) on symptoms of respiratory illness such as runny/blocked nose, cough, wheeze and fever. There were significant associations between lag 5 and lag 0-4 CO 8-hr and runny/blocked nose and wheeze with the estimates slightly larger for lag 5 (runny blocked nose: OR=1.380, 95%CI: 1.028-1.853; wheeze: OR=1.136, 95%CI: 1.016-1.260) compared to lag 0-4.

The ACHAPS study did not find associations between CO and lung function. There were three negative associations with symptoms (night cough, night shortness of breath and day wheeze). As only 17 of the 27 AQMs monitored for CO, we had a smaller sample size for the CO analyses which may made it more difficult to detect small effects.

3.5. Methodological issues

3.5.1. Measurement of lung function

In this study, lung function (PEF and FEV_1) was measured using a Mini-Wright Digital electronic peak flow meter. The electronic peak flow meters were given to each child and they recorded three successive measurements in the morning and three successive measurements in the evening. The highest PEF and FEV_1 from these three successive measurements were automatically stored in the electronic peak flow device with a date and time stamp. The use of an electronic peak flow meter where measurements are automatically stored for the researcher to download at a later time avoids the problem of under or over reporting.

Peak flow meters are widely used in longitudinal studies because they are portable and relatively inexpensive, allowing frequent measures of lung function at low cost. Furthermore, the PEFs obtained from the mini Wright peak flow meter are comparable with those derived from spirometry (Lebowitz 1982; Sanz, Martorell et al. 1990; Thurston, Lippmann et al. 1997; Lippmann and Spektor 1998). It has also been demonstrated that individual peak flow meters are highly reproducible (r=0.999) (Morrill, Dickey et al. 1981).

In a paper relevant to this current study, Lippmann et al. (Lippmann and Spektor 1998) reported that, in 91 children aged eight to 15 years, there was about a 9% underestimation of PEF measured by mini Wright peak flow meters compared to PEFs derived from spirometry. However, when both spirometry PEF and mini Wright PEF were regressed on average ozone concentration in the previous hour, the coefficients were similar (-6.78±0.73 mL/sec/ppb ozone and -6.63±0.76 mL/sec/ppb ozone respectively). The authors suggested that the mini Wright peak flow meter is a convenient and effective tool for characterising changes in PEF associated with exposure to ambient ozone.

There has also been a view that PEF is a measure of the function of the large airways (Vedal, Schenker et al. 1987) and PEF may not be able to detect changes in the small airways associated with asthma. In a cross-sectional study to determine chronic effects of air pollution on lung function in children and adults, larger reductions in PEF than in either FVC or FEV_1 were found (Schwartz 1989), suggesting that PEF might be a more sensitive indicator of the effects of air pollution on airways.

In summary, it has been demonstrated that the PEF, as measured by a mini Wright peak flow meter, is both accurate and reproducible and can be used in epidemiological studies to measure lung function. The mini Wright peak flow meter is a convenient and effective tool for characterising changes in PEF associated with exposure to ambient air pollution.

3.5.2. Fixed site air pollution monitoring

In this study, air quality data from fixed site ambient air quality monitoring stations were used to characterise individual exposure to ambient air pollutants. There have been concerns that the use of such fixed site ambient ozone monitoring stations may not adequately characterise the actual personal exposure to ambient air pollutants especially as people spend a large proportion of their time indoors where the air pollution concentrations can be much lower than ambient concentrations.

However, any misclassification of exposure would bias the results towards the null (Neas, Dockery et al. 1995; Romieu, Meneses et al. 1996). Similarly, any misreporting of lung function and symptoms in asthma diaries by children would be non-differential as parents and children would generally not know the days that were high ambient air pollution days at the time of recording and hence any subsequent bias would be towards the null (Romieu, Meneses et al. 1996).

Therefore, any measurement bias in exposure that might have operated in this study would have biased the results towards the null, and any significant association would indicate a real effect.

3.5.3. Accuracy of diary keeping

A longitudinal study where the subjects are required to measure their lung function with a peak flow meter and complete an asthma dairy twice a day for a 5-6 week period represents a significant burden on the subjects and their families. It is likely that, despite instructions to not complete diaries retrospectively, there would be children in the study who during the study period would have incorrectly reported their symptoms and medication use in the diary.

However, this incorrect reporting is most likely to be non-differential and hence any associated bias would be towards the null. However, in multivariate models, where there may also be non-differential errors in the assessment of the exposure, the effect could be less predictable (Naeher, Holford et al. 1999).

Missing data are also a recognised problem in studies that rely on self-reporting of symptoms. Neas et al. (Neas, Dockery et al. 1995) have suggested that if missing data (lung function, symptoms and medication use) are not correlated with ambient pollution levels, then it implies that the missing data occurred at random and hence would not lead to bias. It is unlikely that children and parents would be aware of high air pollution days and therefore any misreported data or missing data would most likely bias the results towards the null and minimise the potential for type 1 error.

3.5.4. Learning effect

Many investigators have excluded the first few days of observations and sometimes up to two weeks of observations to exclude a learning effect in the use of the peak flow meter. It has been assumed that the recorded lung function for a period of time up to a week could be inaccurate because the children are still learning the proper use of the peak flow meters. Although there appears to be some theoretical justification for this, some investigators have not detected a learning effect (Neas, Dockery et al. 1995; Studnicka, Frischer et al. 1995; Scarlett, Abbott et al. 1996; Naeher, Holford et al. 1999). However, in this study, the first three days of diary data were discarded so as to account for any possible learning effect.

3.5.5. Hours spent outdoors doing vigorous physical activity

Exposure to ambient ozone not only depends on the concentration of the ambient air pollutants but also on the number of hours spent outdoors and on the activity level whilst outdoors. Therefore, it would seem desirable to control for the effects of both the number of hours spent outdoors and activity levels.

Krzyzanowski et al. (Krzyzanowski, Quackenboss et al. 1992) have suggested that only measuring the number of hours spent outdoors, without also measuring the specific hours the subjects were indoors/outdoors, was not a good measure of total ambient exposure. Linn et al. (Linn, Shamoo et al. 1996) did attempt to measure time spent outdoors and activity levels (completing a questionnaire before each time spirometry was performed) in their longitudinal study of school children. However, about 25% of the questionnaires demonstrated inconsistencies in reported activity levels for successive days, so these data were not used to calculate the overall ambient ozone exposures, and only the number of hours spent outdoors was used as a measure of ambient ozone exposure.

Dales et al (Dales, Chen et al. 2009) in a panel study of 182 primary school children investigating the effects of air pollutants on FEV_1, found that associations were no different between those children who spent at least two hours daily outdoors and those who spent less than two hours daily outdoors.

In the study, participating children were asked to report, on each day, the number of hours spent outdoors doing vigorous physical activity and we used this as a covariate in the regression models.

3.5.6. Effects of temperature

There are issues about the shape of the relationship between temperature and lung function, that is, whether the relationship is linear or non-linear. Neas et al. (Neas, Dockery et al. 1995) have suggested that when there is a narrow temperature range (11^{o}C to 29^{o}C in their study), the temperature effect was likely to be linear. In this current study there were no compelling reasons to model mean daily temperature as anything other than a continuous variable. During this study, the median mean daily temperature was also in a narrow range (15^{o}C to 23^{o}C) and a linear relationship would be expected between temperature and lung function.

3.5.7. Single-pollutant versus multi-pollutant models

As well as single pollutant models, multi-pollutant models were also constructed. The Air Pollution on Health: European Approach (APHEA) project was a multinational program to determine the associations between air pollution and short term health effects (number of daily deaths and number of daily hospital admissions) (Katsouyanni, Zmirou et al. 1995). One of its aims was also to develop and standardise the methodology for the detection of short term effects in the analysis of epidemiological time-series data. As many air pollutants are often moderately to strongly correlated with each other, the APHEA protocol therefore recommends caution when modelling the effects of air pollution in multi-pollutant models (Katsouyanni, Schwartz et al. 1996; Schwartz, Spix et al. 1996), as in such models, collinearity can lead to unstable regression coefficients.

Across all the 27 AQMs, there was moderate correlation between PM_{10} and $PM_{2.5}$ (r=0.65). There were very high correlations among the three metrics for ozone (r=0.94-0.99), the two metrics for SO_2 (r=0.90) and the two metrics for NO_2 (r=0.84). Otherwise, the correlations between air pollutants were generally weak. The lack of strong correlations among the air pollutants enabled two pollutant models to be constructed to identify the independent effects of air pollutants.

3.5.8. Collinearity among the independent variables

Collinearity among the independent or explanatory variables is an important issue in air pollution research. There are often moderate to strong correlations among the air pollution and meteorological variables, especially between ambient ozone concentration and temperature. In the United States, there is also often a moderate to strong correlation between ambient ozone and ambient PM_{10} concentrations. When strong collinearity exists between two variables it is not possible to determine the independent effects of each of those two variables.

This is one of the main reasons why the APHEA protocol recommends caution when modelling the effects of air pollution in multi-pollutant models (Katsouyanni, Schwartz et al. 1996; Schwartz, Spix et al. 1996) as multi-pollutant models, where collinearity exist, can lead to unstable regression coefficients.

In this study, we centred the temperature variable so as to avoid collinearity between the air pollutants and daily mean temperature.

3.5.9. Multiple comparisons

Although many tests of association were conducted in this study, corrections for multiple comparisons (for example, Bonferroni's correction) were not employed. It has been strongly argued by Rothman (Rothman and Greenland 1998) that no adjustments for multiple comparisons need be made even if a large number of comparisons are reported at the one time, provided all results are reported (both negative and positive results, that is, both non-significant and significant results). Therefore, corrections for multiple comparisons were not employed. Subsequently, all results need to be reviewed critically, and any significant result should be considered suggestive only, unless or until supported by other published studies.

Part D

Conclusions

Despite the fact that there are some inconsistencies in the international literature on the effects of air pollution on children's respiratory health, the weight of the evidence does appear to suggest that the adverse effects of air pollution are real.

Inconsistencies in study findings may be attributed to:

- intrinsic differences between cities or regions in terms of climates, pollutant mixes, or particulate chemistry, all of which may modify or confound observed associations, or make separation of individual effects variously difficult

- differences between populations at risk in terms of inherent susceptibility, outdoor and indoor exposures, and time activity

- study designs: experimental studies in relation to air pollution and children cannot be performed, so evidence relies on a variety of study designs from ecological designs (considered the weakest in terms of scientific evidence of causality) to prospective designs (considered the strongest); however, all studies will be subject to confounding to some degree

- differing metrics for air pollutants, ranging from individualised monitors to routine fixed monitors to proxy measures such as distance to heavy traffic roads

- differing health outcomes and methods of ascertainment

- differing statistical analyses, despite development of protocols such as APHEA.

In considering these factors, one needs to separate issues of bias (attributed to uncontrolled confounding; for example, from those of imprecision (attributed to random error in measuring exposure, for example). The latter are less of a concern since they would act to attenuate associations and result in conservative findings. Bias is a far more contentious issue since findings could be invalid; that is, either over- or under-stated.

Somewhat paradoxically, though, consistent findings in different settings, with different confounding factors, argues for evidence of a real effect – if a given finding is due to confounding or use of a specific methodological approach, why should it be replicated in another environment with different confounders or methodology?

Perhaps the single most influential study of air pollution and child health is the SCCHS, which most recently has shown consistent adverse effects of measured air pollutants on lung function growth on prospectively gathered data. Other outcomes include supportive evidence from cross-sectional analyses including traffic density studies, demonstrated health improvement when children move from a higher to a lower pollution area, and implication of air pollution in onset of asthma, as opposed to exacerbation.

Many panel studies have demonstrated adverse effects of air pollutants on lung function, respiratory symptoms and medication use for asthma and, in most cases, these effects are small. For example, panel studies conducted in summer camps in the US where children are physically active outdoors show, on average, about a 5% decrease in PEF for a 50 ppb increase

in ambient O_3 concentration. Panel studies where children are engaging in their normal daily activities show smaller decrements in lung function.

Although the decreases found in lung function are relatively small and may be clinically unimportant, Hoek et al. (Hoek, Dockery et al., 1998) demonstrated some interesting outcomes in relation to exposure to ambient PM_{10}. A 10 $\mu g/m^3$ increase in PM_{10} was associated with only a 0.07% decrease in population PEF but with a 3% increase in the prevalence of PEF more than 20% below the median which would be clinically significant. The authors suggest that there was a shift in the whole PEF distribution to the left. Therefore, in population terms, even a small decrease in average lung function might have important effects at the extreme ends of the distribution (Rose and Day, 1990), and an unexpected large population impact.

Asthma is the most common chronic disease in childhood in Australia. The International Study on Asthma and Allergies in Childhood Steering Committee (ISAAC, 1998) reported that, in Australia, the prevalence of asthma in children aged 13–14 years was about 30%. More recent data suggest that 16-26% of children will ever have a diagnosis of asthma and that 18-23% of children have current asthma (AIHW Australian Centre for Asthma Monitoring, 2008). Therefore, this is a large group of children susceptible to the respiratory effects of ambient air pollution.

It is thought that air pollutants may affect the airways of children with asthma by acting as secondary or trigger factors in children with airway hyperresponsiveness, by functioning as primary factors to initiate and increase airway inflammation, thereby leading to airway hyperresponsiveness, by having a direct toxic effect on the airways leading to asthma-like symptoms in normal individuals, or by affecting the immune system resulting in sensitisation or increased allergic responses in the airways (Barnes 1994).

Children and infants may be particularly at increased risk from ambient air pollution for a number of reasons including the following:

- In the first few months after birth, an infant's metabolic pathways are still developing and due to this biochemical immaturity, an infant cannot detoxify and excrete toxins as well as adults (Tamburlini, Ehrenstein et al., 2002).
- Infants and children inhale and retain larger amounts of air pollution per unit of body weight than adults.
- The narrow bronchioles of young children are more likely to be constricted in response to environmental irritants than the bronchioles of adults.
- Children's normal growth may be affected when exposed to pollutants at critical periods (Mathieu-Nolf, 2002).
- Children spend more time outdoors than adults and, hence, are more exposed to ambient air pollutants (Bates, 1995; Mathieu-Nolf, 2002).

Exposure to ambient air pollution can also have long term impacts. There is increasing evidence that maternal exposure to ambient air pollutants is associated with adverse pregnancy outcomes, in particular, risk of low birth weight, foetal growth restriction, and pre-term delivery (Glinianaia, Rankin et al., 2004; Mannes, Jalaludin et al., 2005; Sram, Binkova et al., 2005; Jalaludin, Mannes et al., 2007; Ritz and Wilhelm, 2008), and recent qualitative reviews have concluded these effects are likely to be causal (WHO, 2005). This more recent evidence is of concern as birth weight is an important predictor of perinatal and infant mortality (McCormick, 1985), childhood morbidity and disability (Pharoah, Cooke et al., 1990) and chronic diseases later in life, such as cardiovascular disease and diabetes (Robinson, 2001;

Barker, 2004). Thus, contribution of air pollution, as a risk factor, to the burden of disease has important public health implications.

Children exposed to long-term air pollution can also be adversely affected. The cohort studies to date have mainly focused on the effects of air pollution on lung growth in children and have found associations between ambient air pollutants and reduced lung growth (Frischer, Studnicka et al., 1999; Gauderman et al., 2000, 2002, 2004; Horak, Studnicka et al., 2002). Children recruited in these studies have generally been from grade one at school and onwards (6-7 years plus). One study (Gehring, Cyrys et al., 2002) has also investigated the effects of air pollution on lung growth or the development of asthma in younger children. There are also some studies that have used a birth cohort to investigate the effects of air pollution on the incidence of asthma and allergies (Brauer, Hoek et al., 2002; Brauer, Hoek et al., 2007; Rodriguez, Tonkin et al., 2007). There is now growing evidence that there are chronic effects of air pollution on children's respiratory health.

Therefore, a continuing question remains about the chronic effects of ambient air pollutant exposure on lung function in children. As children's lungs are still growing and maturing, long-term exposure to ambient air pollutants may result in pathophysiological changes that may continue into adult life. The effects of long-term exposure (over years) to air pollutants on pulmonary function and lung growth have been increasingly studied. However, there is an urgent need for further studies on the chronic adverse health effects of ambient air pollutants on not only lung function and lung growth, but also on other health outcomes such as cardiovascular disease and diabetes.

Although air pollution levels are relatively low in most regions of Australia, they may not be low enough to prevent adverse health effects, findings that have implications for the future revisions of the Australian air quality guidelines. Major reductions in the combustion emissions (PM, CO, NO_2 and precursors of ambient O_3; that is, oxides of nitrogen and reactive organic chemicals) will be required to counter the expected increase in air pollution as a result of the demands of a growing population. While current control measures are mainly targeted at motor vehicles, these measures need to be supplemented by urban design and transport demand strategies to lower and maintain those lower levels of ambient air pollutants.

An important question is whether exposure to air pollution control should revolve around setting air quality limits; for example, NEPMs in Australia or National Ambient Air Quality Standards in the US, or whether an option would be to take the exposure-reduction approach (Laxen and Moorcroft 2005). In Australia, the current approach is to set NEPMs and require jurisdictions to meet the NEPMs. There are no requirements for jurisdictions to take measures to reduce exposure where concentrations are already below the NEPM. Such a regulatory measure is reasonable for air pollutants that have an established threshold for adverse health effects. However, many air pollutants do not have a threshold (for example, PM and O_3) (World Health Organisation, 2006, 2008) and levels even below the NEPM have been demonstrated to have adverse health effects. The exposure-reduction approach, which aims to shift the exposure of the whole population, seems a reasonable way to reduce the whole community's exposure to ambient air pollution.

Part E

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