Expansion of the multi-city mortality and morbidity study

Environment Protection and Heritage Council

FINAL REPORT

Executive summary and summary report

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Executive summary

Introduction

A number of single city studies in Australia and New Zealand have examined the impact of air pollution on health outcomes, for example, for Brisbane, Sydney, Melbourne, Christchurch and Perth. However, such studies have been criticised for bias, and generally differ in the statistical approaches, making comparisons difficult. Further, results for cities with smaller populations tend to be very sensitive to the methodology used, and the estimates for the increases in mortality or morbidity that might arise with increases in air pollution have higher levels of uncertainty.

It has been recognised that a dependence on 'published, single-estimate, single-site analyses is an invitation to bias' as 'investigators tend to report, if not believe, the analysis that produces the strongest signal' (Goodman et al. 2005). Three separate reviews (Bell et al. 2005; Ito et al. 2005; Levy et al. 2005) of meta-analyses of studies on the associations between ozone and mortality have clearly shown this, and Bell et al. (2005) conclude:

> We recommend caution against using the results of single city studies, whether individually or pooled, for impact assessment. Multi-city approaches such as NMMAPS or APHENA offer a now-feasible alternative that is less subject to publication bias.

The multi-city approach was adopted in this study and is preferable, as it uses a uniform analytical framework for all cities. City-specific estimates are pooled to derive an overall estimate of the impact of pollutants on mortality and morbidity in the cities. Pooling the results improves the statistical power of the analysis. It also allows a better exploration of differences in the results between cities. The study builds on an earlier study of Brisbane, Melbourne, Perth and Sydney conducted by the same chief investigators (and is referred to in this report as the SPIRT study), with additional pollutant data, particularly particulate matter, and additional cities, two of them in New Zealand. This current study is an expansion of the (earlier) multi-city study, and is referred to in this report as the EPHC study.

International benchmarking was carried out in collaboration with Professor Joel Schwartz, Professor of Environmental Epidemiology at the Harvard School of Public Health in the United States. Professor Schwartz is an international expert in the fields of air pollution and epidemiology, and he has worked on statistical modelling for multi-city studies in the USA and in Europe. He was also involved with the APHENA study (air pollution and health in Europe and North America), which focused on cities in the USA, Canada and Europe.

This report details results from the Environment Protection and Heritage Council (EPHC) funded project: 'Expansion of the Multi-City Mortality and Morbidity Study'. The study examined the effects of air pollution on health in Australian and New Zealand cities for a four-year period from January 1998 to December 2001; the study derived estimates for the associations between increases in daily outdoor

concentrations of major air pollutants and increases in daily hospital admissions and daily mortality counts. The cities considered were Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth and Sydney.

The external reviewing of the work envisaged in the consultancy contract (on which this report is based) was to be the publication of papers by peer review in selected international and local journals.

The following papers have been published.

Barnett, A, Williams, G, Schwartz, J, Neller, A, Best T, Petroeschevsky, A & Simpson, R 2005, 'Air pollution and child respiratory health: a case-crossover study in Australia and New Zealand', *Am J Respir Crit Care Med* 171:1272-8.

Barnett, A, Williams, GM, Schwartz, J, Best, T, Neller, A, Petroeschevsky, A, Simpson, R 2006, The effects of air pollution on the cardiovascular health of elderly people in Australia and New Zealand, *Environmental Health Perspectives,* vol. 114, pp. 1018-23 (IF: 3.929).

It is anticipated that other papers, relating to work carried out during this study, will be submitted for publication. This report is based on papers already prepared, or being prepared, for publication.

Research design

Data sources

Daily health, air quality and weather data were collected for the years 1998–2001 in five cities in Australia (Brisbane, Canberra, Melbourne, Perth and Sydney) and two cities in New Zealand (Auckland and Christchurch). In 2001, these cities comprised 53% of the Australian population and 44% of the New Zealand population, for a total population of just under 12 million people.

Health data were collected from state government health departments in Australia and the New Zealand Health Information Service (Ministry of Health) in New Zealand. Disease groups were classified according to the International Classification of Diseases 9th and 10th Revisions, as appropriate. All cause mortality, cardiovascular mortality and respiratory mortality were the main mortality outcomes. The following categories for cardiovascular admissions were examined in this study: cardiac, ischemic heart disease, stroke, arrhythmia, cardiac failure and myocardial infarction. The respiratory disease groups considered included total respiratory disease, asthma, chronic obstructive pulmonary disease and pneumonia and acute bronchitis. Some age-stratified analyses were conducted.

The pollutants considered were $PM_{2.5}$ ($\mu g.m^{-3}$), PM_{10} ($\mu g.m^{-3}$), nitrogen dioxide (NO_2) (ppb), ozone (O_3) (ppb), and carbon monoxide (CO) (ppm). A range of pollutant averaging periods were selected based on the National Environment Protection Measure (NEPM) reporting requirements: daily 24-hour averages for $PM_{2.5}$, PM_{10} and NO_2; daily 1-hour maxima for NO_2 and O_3; daily average 8-hour maxima for CO and O_3; and a daily average 4-hour maxima for O_3. Air quality data were provided by the environmental protection agency in each jurisdiction.

The EPHC study used virtually all available data between 1998 and 2001 for daily mortality, daily hospital admissions and ambient air quality in the seven cities.

Demographic data were supplied by the Australian Bureau of Statistics (ABS) and Statistics New Zealand.

Statistical methods

The raw data used for the presented analyses are in the form of multivariate time series, that is, daily measures of air pollution exposure, and daily counts of health outcome events.

The analytical approaches include generalised additive models and case-crossover analyses (to evaluate short-term health effect estimates and their heterogeneity across cities), distributed lag models (to investigate harvesting in relation to mortality) regression models, and hierarchical models to examine effect modifiers. The estimates across cities were combined using a random effects meta-analysis method. The I-squared statistic was used to quantify heterogeneity, and is the percentage of total variation due to heterogeneity between cities. Statistical tests were used to test the significance of the I-squared results. To test whether one city had an undue influence on the meta-analysis, a leave-one-city-out sensitivity analysis was used. To identify differences between countries, separate meta-analyses were conducted for the Australian and New Zealand cities. These sensitivity analyses were performed for both the case-crossover and distributed lag models.

Results and discussion

Given time and budget constraints, and the availability of data that could be used in the analyses undertaken, this EPHC study has a number of shortcomings:

- The statistical methodology adopted was based on advice from Professor Schwartz, so no detailed review of the literature has been undertaken (although there are references to such reviews) to identify a range of approaches and compare and contrast them.

- Data sets adequate for the analysis used were only available for all seven Australian and New Zealand cities for some air pollutants — nitrogen dioxide (NO_2) and carbon monoxide (CO). Ozone and $PM_{2.5}$ data sets were used for four Australian cities (Brisbane, Melbourne, Perth, Sydney), and PM_{10} for five cities (Brisbane, Christchurch, Melbourne, Perth, Sydney).

This EPHC study concentrates on identifying the short-term effect of air pollutants on health outcomes; that is, the acute effects arising from immediate exposure to air pollution. Consequently, we only examine the health effects arising from exposure to air pollution on the same day or the previous day (used as an average of exposures on both days). Table 1 summarises the significant associations between increases in each mortality outcome and increases in each air pollutant. The criteria of statistical significance are used as an approach to filter those findings which are suggestive of effects not arising by chance. Owing to the large number of tests performed, this represents an over-inclusive approach. Discussion then focuses on those associations

which display consistent patterns in terms of effect sizes, taking into account the magnitude of confidence intervals.

Table 1: Mortality outcomes showing significant increases associated with increases in air pollutants - by age group

Pollutant	All ages	75+ years	Cities used in analyses
Nitrogen dioxide	All cause mortality Total cardiovascular Total respiratory	All cause mortality Total cardiovascular Total respiratory	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
Carbon monoxide	-*	-*	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
PM_{10}[1]	All cause mortality Total cardiovascular	All cause mortality Total cardiovascular Total respiratory	Brisbane, Melbourne, Perth, Sydney
$PM_{2.5}$ [2]	Total cardiovascular	Total cardiovascular	Brisbane, Christchurch, Melbourne, Perth, Sydney
Ozone (warm period)†	All cause mortality Total cardiovascular	Total cardiovascular	Brisbane, Melbourne, Perth, Sydney

* Carbon monoxide generally was associated with increases, but they were not statistically significant
† Ozone levels for warm period of year (November-April)
[1] As measured by concentrations of particulate matter (PM) with diameters less than 10 microns
[2] As measured by concentrations of particulate matter (PM) with diameters less than 2.5 microns

Tables 2 and 3 summarise the significant associations between increases in the concentrations of each air pollutant and increases in hospital admissions due to cardiovascular disease for adults (15 years or older) and due to respiratory disease, respectively.

Table 2: Significant increases in hospital admissions due to cardiovascular disease for adults (15 years and older) associated with increases in air pollutant concentrations

Pollutant	15-64 years	65+ years	Cities used in analyses
Nitrogen dioxide	Total cardiovascular, All cardiac, cardiac failure, arrhythmia	Total cardiovascular, All cardiac, cardiac failure, IHD*, MI*	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
Carbon monoxide	Total cardiovascular, All cardiac, cardiac failure, arrhythmia	Total cardiovascular**, All cardiac**, cardiac failure**, IHD*, MI*	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
PM_{10}[1]	-	All cardiac, cardiac failure	Brisbane, Christchurch, Melbourne, Perth, Sydney
$PM_{2.5}$[2]	-	Total cardiovascular, All cardiac, cardiac failure, IHD*, MI*	Brisbane, Melbourne, Perth, Sydney

* IHD = ischemic heart disease; MI = myocardial infarction
** Evidence for heterogeneity for these outcomes with Sydney results higher than the other cities, but pooled estimates for the remaining cities still significant and positive
[1] As measured by concentrations of particulate matter (PM) with diameters less than 10 microns
[2] As measured by concentrations of particulate matter (PM) with diameters less than 2.5 microns

Table 3: Significant increases in hospital admissions due to respiratory disease for adults (15 years and older) associated with increases in air pollutant concentrations

Pollutant	15-64 years	65+ years	Cities used in analyses
Nitrogen dioxide	Total respiratory	-	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
PM_{10}[1]	-	pneumonia & acute bronchitis	Brisbane,, Christchurch, Melbourne, Perth, Sydney
$PM_{2.5}$[2]	Total respiratory, asthma	Total respiratory, COPD*, pneumonia & acute bronchitis	Brisbane, Melbourne, Perth, Sydney

* COPD = chronic obstructive pulmonary disease
[1] As measured by concentrations of particulate matter (PM) with diameters less than 10 microns
[2] As measured by concentrations of particulate matter (PM) with diameters less than 2.5 microns

It was found that the average (pooled) estimates for increases in adult cardiovascular hospital admissions derived for each group of cities in Table 2 could be used to estimate the increase in adult cardiovascular hospital admissions for any city in that group. This was also the case for groups of cities shown in Table 3 for adult respiratory hospital admissions.

Table 4 summarises the significant associations between increases in the concentrations of each air pollutant and increases in hospital admissions due to respiratory disease for children (aged less than 15 years).

Table 4: Significant increases in hospital admissions due to respiratory disease for children (aged less than 15 years) associated with increases in air pollutant concentrations

Pollutant	<1 year	1 -4 years	5-14 years	Cities used in analyses
Nitrogen dioxide	-	Total respiratory	Total respiratory, asthma	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
PM_{10}[1]	-	Total respiratory	Total respiratory	Brisbane, Christchurch, Melbourne, Perth, Sydney
$PM_{2.5}$[2]	Total respiratory, pneumonia & acute bronchitis	Total respiratory, pneumonia & acute bronchitis	-	Brisbane, Melbourne, Perth, Sydney
Ozone (warm) †	-	Total respiratory, asthma	-	Brisbane, Melbourne, Perth, Sydney

† Ozone levels for warm period of year (November-April)
[1] As measured by concentrations of particulate matter (PM) with diameters less than 10 microns
[2] As measured by concentrations of particulate matter (PM) with diameters less than 2.5 microns

It was found that the average (pooled) estimates for increases in respiratory hospital admissions for children derived for each group of cities in Table 4 could be used to estimate the increase in hospital admissions in children for any city in that group.

There are significant associations between increases in mortality counts and increases in concentrations of NO_2 (for all outcomes), particles and ozone, and generally all the Australian and New Zealand cities studies show similar results. The matching analyses indicate that the NO_2 and particle effects may be arising from similar air pollution events as these pollutants have similar emission sources (such as motor vehicle exhaust emissions), significantly contributing to the overall pollution load for each.

For cardiovascular hospital admissions, NO_2 and CO associations are significant for all Australian and New Zealand cities studied and the matching analyses indicate again that these impacts are linked to the same pollution episodes. There is also evidence that particle effects are linked to those of the gases as well, and all effects generally peak in winter.

For respiratory hospital admissions, NO_2 and particle associations are significant for all Australian and New Zealand cities studied and the matching analyses also indicate that these impacts are linked to the same pollution episodes. However, there is also a significant ozone effect peaking in the warm season which may be linked to warm season NO_2 effects.

Therefore, the results here are probably referring to the impacts of an air pollution 'mixture' of gases and particles, including all or part of the concentrations for CO, NO_2, $PM_{2.5}$, PM_{10} and ozone (warm season). All the components of such a mixture probably share similar emission sources (such as motor vehicle exhausts) and the most notable surrogate or 'marker' for this mixture found in this study is NO_2.

Harvesting

Early findings of associations in time between mortality and air pollution levels were interpreted by some as simply indicating the bringing forward (by a few days perhaps) of an inevitable and imminent death, due to the stress of a bad pollution day on the health of people already seriously ill. Methods for detecting this phenomenon are complex and comparatively recent and some work is presented here.

Estimates were derived in the study for the so-called 'harvesting (or mortality displacement) hypothesis', using methodologies adopted by the Harvard School of Public Health. Some overseas studies suggest that when the influence of the previous 30 to 40 days of air pollution exposure is estimated, then the increase in deaths is much higher, indicating that the short-term calculations underestimate the impact of air pollution and that 'harvesting' does not occur.

Most overseas studies have concentrated on the impact of PM_{10}. For this EPHC study, there were limited data sets for $PM_{2.5}$ and PM_{10} and the use of the overseas approach for these pollutants does not yield clear results as to whether 'harvesting' occurs. However, the use of these methodologies for the more complete data sets for NO_2 and CO shows significant increases in impact over 40 days, compared to the short-term impacts, indicating that harvesting does not affect the results derived. Thus, it would appear that while mortality advancement may occur in very frail individuals, such mortality advancement does not account for the majority of pollutant-related mortality.

Comparison with other multi-city and meta-analysis studies

The other major meta-analysis studies overseas have been for US (NMMAPS: Samet et al. 2000, 2003) and European (APHEA2: Katsouyanni et al. 2001; Dominici et al. 2002a) cities. The results in these studies show increases in mortality and hospital admissions with increases in particle concentrations, and we found no evidence to suggest that there is any difference between these results and those found in this EPHC study.

Three separate meta-analyses were carried out for ozone and mortality (Bell et al. 2005; Ito et al. 2005; Levy et al. 2005), and these results are also compared with those in this EPHC study. The results in these overseas studies show increases in mortality with increases in ozone concentrations, and we found no evidence to suggest that there is any difference between these overseas results and those found in this EPHC study.

The results for the previous multi-city study for Brisbane, Melbourne, Perth and Sydney (SPIRT study) for 1996 to 1999 were also compared with those from this EPHC study. There are generally few differences, with the case-crossover estimates here similar to the SPIRT results (positive increases for similar outcomes and pollutants), but here the associations with respiratory hospital admissions are usually more significant.

Comparison with other single city Australian and New Zealand studies

The results for each city derived here were compared with earlier studies conducted in Sydney, Melbourne, Brisbane and Perth. The results were also compared with the earlier SPIRT multi-city study. The studies where the impacts of bushfires or controlled burns were controlled for showed much smaller associations for particles than those derived here. The comparisons for cardiovascular admissions showed the most agreement among the studies, which used different statistical methodologies and were for different time periods. The results for respiratory admissions appeared to be the most sensitive to the methodologies chosen. Generally, the results for the studies showed the same positive increases (and decreases) in mortality and hospital admissions counts for the same pollutants, but the mean effect estimates and statistical uncertainties differed. Results from this EPHC study demonstrate the statistical power in pooling estimates for all the cities.

Conclusions

The results of the study indicate that increases in concentrations of the air pollutant nitrogen dioxide (NO_2) are significantly associated with increases in daily mortality and hospital admissions counts for a large range of disease categories, and in both the young and the old in populations in all the Australian and New Zealand cities studied in this EPHC study. However, there is no evidence to suggest that the health effects were arising from the impacts of NO_2 alone. Rather, the analyses indicated that the NO_2 effects could be 'markers' or 'surrogates' for the impacts found for the other pollutants studied — carbon monoxide (CO), particles and ozone (in warm season) — as these air pollutants are usually significantly correlated with each other (probably due to similar emissions sources, such as motor exhausts).

Throughout the analyses, we found NO_2 and particle associations confounded each other, as did NO_2 and CO, where CO associations became significant. Some of the warm season ozone associations also appeared to be confounded by the NO_2 associations. Therefore, the results are probably referring to the impacts of an air pollution 'mixture' of gases and particles, including all or part of the concentrations for CO, NO_2, $PM_{2.5}$, PM_{10} and ozone (warm season). All the components of such a mixture probably share similar emission sources (such as motor vehicle exhausts) and the most notable surrogate for this mixture found in this study was NO_2.

This study indicates that other Australian and New Zealand studies need to be carried out to investigate this air pollution mix more closely.

Statistical tests generally indicated that there was no evidence for heterogeneity (that is, differences) between the results for cities sharing common data sets, so the average estimates derived were applicable to all the cities considered in each analysis. The results indicate that increases in concentrations of the urban mixture of air pollutants in each Australian and New Zealand city studied here — Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, and Sydney — are significantly associated with:

- increases in mortality for total all cause, cardiovascular and respiratory disease categories (and the impact on the elderly is the strongest)

- increases in cardiovascular hospital admissions for a range of disease categories including all cardiac, ischemic heart disease (IHD), myocardial infarction (MI), and cardiac failure (and the impact on the elderly is the strongest), and increases in arrhythmia hospital admissions in the adult population in the age group 15 to 64 years old

- increases in respiratory hospital admissions for a range of disease categories, including all respiratory, asthma, COPD (chronic obstructive pulmonary disease), pneumonia and acute bronchitis (and the impact on the child age groups is the strongest, except for COPD).

Most of the analyses used in this study examined the short-term effects, that is, the acute health effects arising from exposure to pollutants on the same day or the day before. It has been suggested that the resulting mortality results may exaggerate the effects of air pollutants as people who are already very ill may simply die a few days or weeks earlier because of enhanced air pollution exposures – the 'harvesting' or mortality displacement hypothesis. The results from this EPHC study show no evidence for that effect for the mixture of air pollutants.

Summary report

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1. Introduction

This report details results from the Environment Protection and Heritage Council (EPHC) funded project: 'Expansion of the Multi-City Mortality and Morbidity Study'. The EPHC study examined the effects of air pollution on health in Australian and New Zealand cities for a four-year period from January 1998 to December 2001; the study derived estimates for the associations between increases in daily outdoor concentrations of major air pollutants and increases in daily hospital admissions and daily mortality counts. The cities considered were Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth and Sydney.

There have been a number of single city studies in Australia and New Zealand examining the impacts of air pollution on health outcomes, for example, for Brisbane, Sydney, Melbourne, Christchurch and Perth. However, such studies have been criticised for publication and reporting bias, and generally differ in statistical approach, making comparisons difficult.

The multi-city approach adopted here is preferable, as it uses a uniform analytical framework for all cities, and city-specific estimates are pooled to derive an overall estimate of the impact of pollutants on mortality and morbidity in the cities. It also allows a better exploration of differences in the results between cities.

Such a multi-city approach was adopted in an earlier study on Brisbane, Melbourne, Perth and Sydney run by the same chief investigators; this study reported the associations between increases in concentrations of air pollution (nitrogen dioxide (NO_2), particle or PM (particulate matter) measures, and ozone (O_3)) and increases in mortality and morbidity counts. However, the particle measures did not include all PM measures (due to unavailability of data), namely $PM_{2.5}$ (PM less than 2.5 microns in diameter – fine particles) and PM_{10} (PM less than 10 microns in diameter), and these are included in this EPHC study for at least some of the cities. There are also three more cities, two of them from New Zealand. Therefore, this current study is referred to as an expansion of the (earlier) multi-city mortality and morbidity study.

The multi-city framework has been used in Europe and US, and we took advice from Professor Joel Schwartz from Harvard University, who has been involved in past and current overseas multi-city studies, on the methodology we should adopt here.

Given time and budget constraints, and the availability of data that could be used in the analyses undertaken, this study has a number of shortcomings:

- The statistical methodology adopted was based on advice from Professor Schwartz, so no detailed review of the literature has been undertaken (although there are references to such reviews) to identify a range of approaches and compare and contrast them.

- Data sets adequate for the analysis used here were only available for all seven Australian and New Zealand cities for two air pollutants – NO_2 and CO. Ozone and $PM_{2.5}$ data sets were used for four Australian cities (Brisbane, Melbourne, Perth, Sydney), and PM_{10} for five cities (Brisbane, Christchurch, Melbourne, Perth, Sydney).

The external reviewing of the work envisaged in the Consultancy Contract (on which this report is based) is to be the publication of papers by peer review in selected international and local journals.

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Barnett, A, Williams, G, Schwartz, J, Neller, A, Best T, Petroeschevsky, A & Simpson, R 2005, 'Air pollution and child respiratory health: a case-crossover study in Australia and New Zealand', *Am J Respir Crit Care Med* 171:1272-8.

Barnett, A, Williams, GM, Schwartz, J, Best, T, Neller, A, Petroeschevsky, A, Simpson, R 2006, The effects of air pollution on the cardiovascular health of elderly people in Australia and New Zealand, *Environmental Health Perspectives,* vol. 114, pp. 1018-23 (IF: 3.929).

The following paper is undergoing internal review before being submitted for publication:

Barnett, A, Williams, G, Schwartz, J, Neller, A, Best, T, Petroeschevsky, A & Simpson, R, '*The associations between exposure to outdoor concentrations of air pollution and mortality in Australian and New Zealand cities: results for Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth and Sydney*'.

It is anticipated that other papers, relating to work carried out during this study, will be submitted for publication. This report is based on papers already prepared, or being prepared, for publication.

1.1 Air pollutants under study

The major air pollutants that are examined here are the gases — nitrogen dioxide (NO_2), ozone (O_3) and carbon monoxide (CO) — and particles or particulate matter (PM). Most of these pollutants are the products of combustion processes (such as motor vehicle engines, industrial operations, home heating) and are emitted directly into the atmosphere (such as NO_2, CO and PM). Other (secondary) pollutants can be formed in the atmosphere by chemical interactions between pollutants emitted into the atmosphere and normal atmospheric constituents (for example, in photochemical smog production, which produces ozone and PM). A summary of the major air pollutants and their sources is shown in Table 1, and a summary of the types of health effects associated with air pollution exposure is shown in Table 2.

Table 1: Air pollutants studied here and their sources

Pollutant	Source
Nitrogen oxides (NO, NO_2)	Combination of nitrogen and oxygen during high temperature combustion
Dust, particulates, soot	Combustion and mining processes, land clearing
Ozone (O_3)	Formed in the atmosphere through photochemical reactions of nitrogen oxides and hydrocarbons emitted from motor vehicles and industry
Carbon monoxide (CO)	Combustion, particularly motor vehicles

Table 2: Health effects and populations 'at risk'

Pollutant	Health effects	Population at risk
Nitrogen dioxide	Hospital admissions for respiratory disease; decreases in lung function; cardiovascular disease	Sufferers of respiratory disease, such as children with asthma; those with cardiovascular disease
Particulates	Mortality due to cardiovascular and respiratory diseases; hospital admissions due to respiratory and cardiovascular disease; decreases in lung function	Elderly people with respiratory and cardiovascular diseases; people with respiratory diseases, such as children with asthma
Ozone	Mortality due to respiratory and cardiovascular diseases; hospital admissions due to respiratory diseases; decreases in lung function	Elderly people; people with respiratory diseases.
Carbon monoxide	Mortality and increased hospital admissions due to heart diseases	People with ischemic heart conditions

1.2 Air pollution and health studies

The two types of studies most commonly used to examine effects of pollution on health are clinical and epidemiological investigations. Clinical investigations consider the health impacts on subjects (human or animal) exposed to controlled doses of air pollution in laboratory chambers. This study is an epidemiological one, as it examines the effect of air pollution exposure on a population.

The main types of epidemiological investigations used are longitudinal/temporal studies (such as time series), cross-sectional/geographical studies, and, more recently, cohort studies which include between as well as within area comparisons.

Longitudinal/temporal studies examine the effect of a pollutant on a population over time. Cross-sectional/geographical studies examine and compare the health status of populations in different geographical locations. Cohort studies follow participants in time and prospectively measure health outcomes associated with historical exposure.

The major advantages of epidemiological investigations are that exposure is studied under natural conditions, with large numbers of individuals and for long periods of time. Probably the major limitation of this type of study is that the population as a whole is examined, with no knowledge of individual exposures to pollutants and little understanding of other confounding factors. Because an individual's health is dependent on a number of factors associated with the individual's environment and behaviour, studies that examine the effect of a pollutant on the population as a whole are inadequate in measuring any individual's true exposure. Alternatives, such as personal monitoring, are expensive and must involve willing and reliable subjects, and as a consequence sample sizes become small, reducing statistical power.

2. The current project

In 1998, the National Environment Protection Council (NEPC) made a NEPM for ambient air quality which sets national air quality standards for the six major pollutants — nitrogen dioxide (NO_2), particles (as PM_{10}), carbon monoxide (CO), ozone (O_3), sulfur dioxide (SO_2), and lead (Pb). In 2003, the NEPM was varied to incorporate standards for $PM_{2.5}$.

The NEPM (ambient air quality) standards have been set to be protective of human health. These standards are based primarily on studies conducted overseas. Whether these findings can be extrapolated to the Australian situation has been the subject of much debate. There has been relatively little work carried out in Australia: in Sydney (Morgan et al. 1998a, 1998b), Brisbane (Simpson et al. 1997; Petroeschevsky et al. 2001), Melbourne (Simpson et al. 2000; EPA Victoria 2000, 2001) and in Perth (DoE 2003). These studies indicate that current levels of ambient air pollution in these cities are making significant contributions to variations in daily mortality and hospital admissions for cardiovascular and respiratory disease, and that the effects observed overseas may occur in Australia as well.

However, a number of questions remain about these studies regarding (a) the robustness of the statistical techniques used (would a different technique give a different result), (b) whether all confounding effects were included, (c) how important are the impacts on public health (for example, is the effect on acute mortality only a 'harvesting' effect where very sick people are dying only days or weeks earlier, with no impact on annual mortality rates), and (d) how applicable are these few studies to all the major Australian cities. There was a commitment in the NEPM to undertake a full review of the NEPM, commencing in the year 2005, and including the standards for all pollutants. An important part of this review was to be the expansion of the local database relating to air quality and health issues.

Given NEPC has had to set national air quality health standards based primarily on overseas epidemiological studies, a comprehensive Australian study was warranted which would address the issues of the robustness of the statistical techniques, the control for confounding effects, the significance of the impacts, and the general applicability of these studies in Australia.

A project was designed to develop a research protocol, using international benchmarking with USA and European groups, to address these issues in estimating the associations between air pollution and daily mortality and morbidity in Melbourne, Sydney, Perth and Brisbane (the only cities where there were comprehensive data sets available for air pollution for about 3-4 years), and a submission was made in 1999 to the Strategic Partnerships with Industry — Research and Training (SPIRT) Scheme (now referred to as the Australian Research Council (ARC) Linkage Scheme). The NSW Health Department, EPA Victoria, Queensland Health and WA Department of Environmental Protection were involved in this project.

The research protocol developed for the use of health and environmental data in the statistical modelling undertaken were subjected to international benchmarking by exchanging information and data with an international group of scientists from the

APHEA project (short-term effects of air pollution on health - European approach; includes scientists from Greece, UK, France, Germany, the Netherlands, among others) and the NMMAPS study in the USA, conducted by the Health Effects Institute (HEI).

In late 1999, the SPIRT scheme funded the project, which was entitled 'The assessment of the impact of air pollution on daily mortality and morbidity in Australian cities using a protocol based on international benchmarking' (Simpson et al. 2001). The project commenced in late 2000 and was completed in early 2003 and results are set out in published papers (Simpson et al. 2005a; 2005b).

The study examined the short-term health effects of air pollution on daily mortality and daily hospital admissions in four Australian cities — Brisbane, Melbourne, Perth and Sydney — for the period 1996 to 1999, and used a similar protocol to APHEA2 studies overseas. Given the limitations on the data sets available for the analysis, the only air pollutants considered were: NO_2, particles (as measured by nephelometry) and ozone.

The conclusions from the SPIRT study can be summarised as follows:

- *Mortality* — there are significant associations between all non-accidental mortality counts and NO_2, particles and ozone, and the estimates for Australian cities were similar to the findings in other studies overseas. No significant heterogeneity was found, but the NO_2 and particle effects may refer to the same impacts.

- *Hospital admissions* — similar to overseas studies, air pollution has an impact on hospital admissions in Australian cities, but there can be significant differences between cities. Fine particles (measured by nephelometry) and NO_2 have a significant impact on cardiovascular admissions, and particles, NO_2 and ozone have a significant impact on respiratory admissions. In all analyses, the particle and NO_2 impacts appear to be related. However, the results for respiratory admissions were sensitive to the time series model used.

2.1 Rationale for the current project

A meeting was convened on 24-25 July 2002 in Melbourne by the EPHC to discuss the health effects of air pollution and to make recommendations to the EPHC on which future research projects should be supported to inform the review of the Ambient Air Quality NEPM. Preliminary results for the SPIRT study were presented and the recent results of the overseas studies (APHEA, NMMAPS) presented by Professor Ross Anderson, School of Medicine, University of London. The meeting highlighted a number of issues:

- It was clear from overseas studies that the results differed in different regions of the USA and in different regions of Europe. The preliminary SPIRT results in Australia also showed different results for different localities for some outcomes.

- Overseas, there was an ongoing re-analysis of studies as new data and new statistical techniques became available. It was clear this was necessary in the Australian studies. In particular, the use of new statistical techniques, such as a meta-analysis or a pooled analysis, would allow both a study on why different cities yield different results, as well as an estimate of a mean effect for Australian cities.

- All the overseas studies emphasised the importance of the health impacts of fine particles ($PM_{2.5}$). The SPIRT study spanned 1996-1999 and extensive $PM_{2.5}$ data sets were not available for that period, but are now for later periods so another study to investigate the impact of $PM_{2.5}$ was considered, and the number of Australian cities contributing expanded if possible.

- New Zealand cities could also be included in any new meta-analysis of cities.

2.2 Aims

In this project, a research protocol was developed to examine the association between outdoor air pollution concentrations and daily mortality and morbidity in Australian cities (cities with available data were included, these were Brisbane, Canberra, Melbourne, Perth, Sydney) and New Zealand cities (Auckland and Christchurch).

2.3 Research design

The EPHC study used all available data sets from 1998 to 2001 for daily mortality, daily hospital admissions and air pollution data for all available pollutants. All pollutants were included as they are often correlated with each other and studying one in isolation may lead to misleading results. The results are to be used in the review of the NEPM, as well as to identify any regional differences in impacts.

Pooling the individual city results produces an overall estimate of the effect of each pollutant for all the cities, as well as obtaining an assessment of whether these effects differed from city to city. This approach also attempted to identify factors that may lead to different effects in different cities, for example, different climates and different lifestyles.

It was important that there were complete data sets for each pollutant in each city; for example in the SPIRT study, ozone, nitrogen dioxide and particles (as nephelometer measurements) were common to the four cities studied. In particular, $PM_{2.5}$ was of interest for the current study and there are complete data sets from 1998-2001 in a number of Australian cities.

International benchmarking was to be carried out in collaboration with Professor Joel Schwartz, Professor of Environmental Epidemiology in the Harvard School of Public Health in the United States. Professor Schwartz is an international expert in the fields of air pollution and epidemiology, and he has worked on statistical modelling for multi-city studies in the NMMAPS study in the USA and the APHEA studies in Europe. Since then, a new study using cities in the USA, Canada and Europe has

been conducted — APHENA (Air Pollution and Health in Europe and North America), with Professor Schwartz also an investigator in that study.

2.4 Rationale for multi-city studies – publication bias

It has been recognised that 'depending on published, single-estimate, single-site analyses is an invitation to bias' as 'investigators tend to report, if not believe, the analysis that produces the strongest signal' (Goodman et al. 2005). Three recent separate reviews (Bell et al. 2005; Ito et al. 2005; Levy et al. 2005) of meta-analyses of studies on the associations between ozone and mortality have clearly shown this. Bell et al. (2005) conclude:

> We recommend caution against using the results of single city studies, whether individually or pooled, for impact assessment. Multi-city approaches, such as NMMAPS or APHENA, offer a now-feasible alternative that is less subject to publication bias.

The approach adopted here is to reduce bias by using a multi-city approach similar to that used in NMMAPS, APHEA, and APHENA. This approach has the following advantages:

- The averaging time for the air pollution exposure is set a priori to avoid the bias of looking for the lags or averages that give the highest value (here, the period chosen is the 2-day average of the pollution on the same day and the day previous to the health outcome, following the APHEA approach).

- The same statistical modelling is carried out for each city; this avoids the error in pooling results from studies using different methodologies.

2.5 Statistical methods used

The current study is an epidemiological study, and raw data used are in the form of daily measures of air pollution exposure (for example, daily 1-hour maximum, 24-hour averages), and daily counts of health outcome events (such as counts of the number of hospital admissions and daily death counts). The aim of such studies is to identify associations between air pollution concentrations and daily hospital admissions or daily death counts. However, there are a number of other factors, described below, that may lead to changes in the health outcomes.

- Seasonal variation in both health outcomes and air pollution due to meteorological effects:
    - The rate of illness or death may peak in the same season as air pollutants simply because each is being influenced separately by season. This phenomenon is known as *confounding*. For example, temperature is associated with both air pollutant concentrations and rates of illness, so an association between health outcomes and air pollution when pollution rises may not be due to pollution, but due to the change in temperature. Such confounding effects need to be controlled in any analysis.

- Interference of other time-dependent confounding effects:
    - It is important to consider the effects of other factors such as day of the week. This may influence pollutant emissions, as well as being related to health outcomes (decreased hospital admissions on Sundays, increased admissions on Mondays). Conversely, it follows that any factor which does not change over the time period under study (e.g. smoking habits) is not confounding.

Other statistical methodological issues to consider are:

- Lagged effects:
    - Should we examine the air pollutant concentration on the same day, the day before, or averaged over the week prior to the day on which we measure the health outcome counts? Goodman et al. (2005) notes that epidemiologists are trained to report the largest or the statistically strongest estimates and pooled estimates of singles-city results recently for ozone and mortality have shown the 'publication bias' in choosing from a large range of lagged effects. One strong recommendation from such analyses (for example, Bell et al. 2005) is to adopt the multi-city approach adopted here with an a priori lag or lags adopted and the same statistical models used for each city analysis.

- 'Harvesting' or mortality displacement:
    - Early findings of associations in time between mortality and air pollution levels were interpreted by some as simply indicating the bringing forward (by a few days perhaps) of an inevitable and imminent death, due to the stress of a bad pollution day on the health of people already seriously ill. Methods for detecting this phenomenon are complex and comparatively recent and some work is presented here.

- Combined effects of air pollutants:
    - It is also important to try to separate the effects of individual pollutants. For example, nitrogen dioxide, carbon monoxide and particles can arise from the same sources (such as motor vehicle exhausts) and therefore may show very similar daily patterns if these sources predominate. Therefore, it may be difficult to separate out the impacts of each pollutant on health outcomes.

- Differing effects of air pollutants in different cities: effect modification by city factors:
    - In combining the results of multi-city studies, it is sometimes observed that the effects of air pollutants vary across cities. This 'effect modification' may be due to a range of different city-specific factors: differences in the sources and distributions of air pollutants, quality of the air pollution monitoring, prevailing meteorological conditions, or demographic characteristics. There are statistical techniques for identifying non-chance variability, leading then to an examination of the differences between cities that might account for this.

- Differing effects of air pollutants in different season: effect modification by season:
    - It may be hypothesised that pollutants could have differing effects with differing prevailing meteorological conditions, even within the same city. Of particular interest, given the importance of temperature, is the differentiation of effects in warm and cool periods.

These complexities have led researchers to develop sophisticated statistical approaches to try to discern the specific health effects attributable to air pollution and the form of the relationship. By far the most important analytical issue is to ensure that confounding is controlled, so that the inference of a causal relationship between air pollution and health outcome may be justified. An appropriate model achieves this by predicting the number of health events that are associated with a particular change in the level of a pollutant, when other influential variables (such as temperature) do not change. Professor Schwartz advised on the appropriate statistical methods to be used in the multi-city Australian and New Zealand study so that it could be benchmarked against studies such as APHENA. He subsequently advised that more recent and different techniques to those used in the SPIRT study be used in this project.

2.5.1 Different statistical models

To estimate the effect of air pollution on health outcomes, this study examined the use of two time series methods: general additive models (GAMs) and the case-crossover method.

GAMs fit general mathematical functions to the time series data of mortality or morbidity counts to filter out the confounding effects of other variables (such as season, temperature, day of week) in order to investigate the separate effect of air pollution. The case-crossover design compares the level of the risk factor at the time of the illness (or at the time when the risk factor exerts its effect) with the level in a nearby period when people did not have the illness

Both methods assume the daily counts of outcomes have a Poisson distribution. Both methods control for season, temperature, days of the week and flu epidemics. The difference is in the way they control for these covariates:

- GAMs use filters that control for the known slow seasonal change in outcomes. The case-crossover method controls for season by matching; that is, by comparing cases and controls that are within a given time period (here, 28 days was chosen) of each other, these outcomes are assumed to be in the same season.

- GAMs control for flu epidemics using a binary covariate (one covariate for each winter). The case-crossover method can control for flu epidemics by matching but the short space of time between cases and controls means that the flu epidemic conditions can be assumed to be similar.

- GAMs control for the often non-linear effect of temperature using a smoothed mathematical function (spline). The case-crossover method eliminates much of this non-linearity by only comparing temperatures in the same time (28-day) period, so the remaining effect of temperature can be modelled by linear term.

There are other important issues to note:

- GAMs are more complex to create because they require each smooth term (e.g. season, temperature) to be estimated for each model. Case-crossover models are much easier to create because the smoothness is determined by the size of the control window (in this study — fixed at 28 days).

- GAMs and case-crossover methods are based on the same statistical inference and give identical results under specific model specifications (i.e. a simple model with only linear covariates). Differences can arise because of the way the models control for covariates, particularly the non-linear (such as temperature) and seasonal covariates. The estimated effects of pollution from both methods should have a similar mean and variance.

There have been a number of the recent problems in using GAMS (Samet et al. 2003), mainly due to the confounding variables (such as season, weather) being strongly correlated and the numerical computer programs having potential errors in calculating the estimated effects. GAMs were used in the NMMAPS, APHEA and SPIRT studies, but these problems have required the re-analysis of much of the work (for example, Dominici et al. 2002a; 2002b; Katsouyanni et al. 2003). The SPIRT study needed to use three different modelling approaches to check the accuracy of the final results (Simpson et al. 2005a; 2005b). Given these problems, and the advantages of the case-crossover method, the case-crossover method was recommended for use here by Professor Joel Schwartz (Schwartz 2004) and mainly used here (some comparative work was carried out using GAMs).

2.6 Description of data used

Daily health, air quality and weather data were collected for the years 1998-2001 in five cities in Australia (Brisbane, Canberra, Melbourne, Perth and Sydney) and two cities in New Zealand (Auckland, Christchurch). Some air quality data were available for Adelaide, but was assessed as of insufficient quantity and quality and Adelaide was excluded from the study. These cities covered 53% of the Australian population and 44% of the New Zealand population, for a total population of approximately 12 million people, as shown in Table 3 (the median income and population data came from the ABS and Statistics New Zealand). (Volume 3: Appendix 1 contains a full set of summary statistics for health, air pollutant and weather data in each city).

Health data

Health data were collected from state government health departments in Australia and the New Zealand Health Information Service (Ministry of Health) in New Zealand. The definition of the study regions for the collection of health data for

Brisbane, Canberra, Melbourne and Perth came from the ABS statistical division (SD), but for Sydney, the SD was modified in the data supplied by NSW Health to exclude areas that are not considered to be represented by the air quality monitoring network (Morgan 1998a; 1998b). For the New Zealand cities, the study regions were defined using the Statistics New Zealand divisions for the Auckland and Christchurch regions. Summary statistics on mortality and hospital admission for each city are given in Table 3.

Hospital admissions data

Both respiratory and cardiovascular admissions were considered. Emergency attendances, scheduled admissions, transfers from other hospitals and admissions arranged through a general practitioner were excluded to minimise the delay and level of uncertainty associated with the period between onset of symptoms and day of admission to hospital. Disease groups were classified according to the international classification of diseases (ICD). (See *Volume 2: Project results and conclusions*, Table 1.2 for the ICD codes)

The following categories for cardiovascular admissions were examined in this study:

- total cardiovascular disease
- cardiac (all)
- IHD
- stroke
- arrhythmia
- cardiac failure
- MI.

The respiratory disease groups considered included:

- total respiratory disease
- asthma
- chronic obstructive pulmonary disease (COPD)
- pneumonia and acute bronchitis.

Disease categories have been chosen from the list of categories used in overseas studies.

Reaction to air pollution is very dependent upon age; therefore, the analyses were stratified by age group, depending on the disease category. The age groups used were:

- less than one year of age (< 1 yr)
- 1–4 years
- 5–14 years
- 15–64 years
- 65 years and greater.

For example, asthma admissions in the less than one-year age group were not considered in the analysis due to difficulties in accurate diagnosis of the condition in this age group.

Mortality data

The total mortality data sets here exclude accidental and other external causes of death (for the ICD codes, see Table 1.2 in *Volume 2: Project results and conclusions*). The disease categories were:

- total (all-cause) mortality
- total cardiovascular mortality
- total respiratory mortality.

All analyses were stratified by the age groups:

- total (all ages)
- 75 years and greater.

Table 3: Summary statistics for demographic data, hospital admission and mortality rates per million population (years 1998-2001)

	Auckland	Brisbane	Canberra	Christchurch	Melbourne	Perth	Sydney
Demographic data							
Total population	1,158,891	1,627,535	311,518	316,224	3,366,542	1,339,993	3,997,321
Median weekly individual income	$400-$499	$300-$399	$500-$599	$300-$399	$400-$499	$300-$399	$400-$499
Percentage of population <15 yrs	22.9%	21.0%	21.2%	19.3%	19.8%	20.7%	20.2%
Percentage of population >65 yrs	10.0%	11.0%	8.3%	13.7%	12.1%	11.3%	11.9%
Daily mortality: mean (range)							
Total all cause*	17.1 (5,46)	15.4 (6,34)	10.7 (0,77)	21.3 (0,63)	16.5 (5,27)	15.1 (4,31)	14.2 (8,23)
Respiratory	1.6 (0,8)	1.3 (0,7)	0.8 (0,13)	1.9 (0,13)	1.4 (0,4)	1.2 (0,5)	1.3 (0,5)
Cardiovascular	7.2 (1,20)	6.8 (1,23)	4.3 (0,32)	9.7 (0,44)	6.6 (3,12)	6 (1,16)	6.2 (2,12)
Daily admissions: mean (range)							
Respiratory	32.4 (5,90)	23.8 (7,62)	27.8 (0,87)	36.1 (0,114)	20.7 (8,39)	24.6 (7,60)	23.3 (10,47)
Asthma	6.0 (0,20)	6.1 (0,23)	4.3 (0,26)	6.6 (0,38)	4.7 (0,15)	5.6 (0,16)	5.9 (1,20)
COPD**	5.4 (0,20)	4.5 (0,14)	3.5 (0,19)	7.5 (0,38)	4.2 (0,10)	4.9 (0,15)	4.4 (1,11)
Pneumonia & bron.	12.7 (0,50)	6.8 (1,24)	7.1 (0,39)	10.2 (0,47)	6.6 (1,16)	6.6 (0,25)	6.7 (1,20)
Cardiovascular	32.3 (5,58)	28 (13,46)	37.9 (0,109)	36.4 (0,79)	24.2 (13,37)	26.8 (10,44)	23.3 (14,36)
Cardiac	23.3 (2,47)	21.6 (9,37)	24.8 (0,64)	25.3 (0,63)	17.1 (9,29)	19.7 (6,35)	17.1 (9,26)
IHD**	11.8 (0,31)	12.1 (4,23)	10.8 (0,42)	14.7 (0,41)	8.9 (4,15)	10.1 (2,19)	8 (4,14)
Stroke	5.5 (0,14)	4.1 (0,10)	3.6 (0,22)	7.4 (0,32)	4.4 (1,10)	4.4 (0,12)	4.1 (1,9)
Arrhythmia	5.0 (0,14)	3.5 (0,10)	4.5 (0,19)	4.0 (0,22)	2.9 (0,8)	3.3 (0,9)	3.2 (1,7)
Cardiac failure	3.8 (0,12)	3.7 (0,12)	2.8 (0,16)	4.0 (0,22)	3.7 (1,9)	4.2 (0,13)	3.4 (1,10)
Myocardial infarct.	4.1 (0,14)	3.8 (0,10)	2.5 (0,19)	6.5 (0,28)	3.1 (1,7)	3.7 (0,11)	2.8 (1,6)

*Total all cause mortality excluding accidental other external causes of death

**COPD=chronic obstructive pulmonary disease; IHD=ischemic heart disease

Air pollutant and weather data

The unit of measurement for gaseous pollutants is usually parts per million by volume (ppm) or parts per billion (ppb). Another unit of measurement is based on the weight of pollutant per volume of air in micrograms per cubic metre ($\mu g.m^{-3}$). The pollutants considered were $PM_{2.5}$ in $\mu g.m^{-3}$, PM_{10} in $\mu g.m^{-3}$, nitrogen dioxide and ozone in ppb, and carbon monoxide in ppm.

Air pollution data was provided by the environmental protection agency in each city. The selection of sites was determined by each state in consultation with the relevant environment authorities; individual sites were included based on the representativeness of each site of the daily outdoor air quality in that city. The air pollutant data used in the study was calculated by averaging data from a network of sites across each city.

The number of monitors used for the network average of each individual pollutant varied between and within cities. Also, some air pollutants were unavailable in some cities. Daily air quality data were required for the analysis, and in some cases these were not available. Where hi-volume samplers were used, particle readings were given only once every six days; therefore, this data could not be used in the analysis. Data from hi-volume samplers included PM_{10} and $PM_{2.5}$ in Auckland and PM_{10} in Canberra. The more sites used in a network average, the better the representativeness of the data to the general exposure of the population in that city. See Table 1.8 in *Volume 2: Project results and conclusions* for the number of monitors in each city, and Table 1.9 in the same volume for summary statistics for air pollutant data.

Where less than 25% data were missing over the relative averaging period linear interpolation was used. Where missing data exceeded this amount, the value was recorded as missing. Data were combined using arithmetic averages.

Daily temperature, dew point temperature, relative humidity, barometric pressure and rainfall were collected from the Australian Bureau of Meteorology and from the New Zealand National Climate Database. See Volume 2: Section 1.4, Table 1.9, for summary statistics for weather data in each city.

3. Results and discussion

3.1 Pooled results for all the cities: the pooled estimates

Only NO_2 and CO were monitored on a daily basis in all cities for long enough periods to allow the time series methods to be used effectively, so it was only for these air pollutants that results could be pooled for all cities and an overall mean estimate could be calculated.

However, results could be derived for smaller groupings of the cities for particles (as measured by $PM_{2.5}$ - Brisbane, Melbourne, Perth, and Sydney; as measured by PM_{10} - Brisbane, Melbourne, Perth, Sydney and Christchurch) and ozone (Brisbane, Melbourne, Perth, Sydney).

We also tested whether the results for all cities showed any statistically significant differences; that is, whether all cities were all showing increases, decreases or no change in health outcomes associated with increases in air pollution, and whether these changes were similar in magnitude in each city, given the statistical uncertainty in the analyses.

If the results were not similar (that is, heterogeneous), we needed to examine why that might be the case, as in such instances the pooled estimate would over-estimate or under-estimate the associations found.

3.1.1 Nitrogen dioxide

NO_2 is one of the air pollutants monitored on a daily basis in all the cities considered in this study, but the number of air pollution monitors measuring ambient outdoor air pollutant concentrations is different in each city. In Auckland there are 2 monitors, Brisbane 7 monitors, Canberra 1 monitor, Christchurch 1 monitor, Melbourne 8 monitors, Perth 5 monitors and Sydney 13 monitors.

Association with death counts

In pooling the estimates for all the cities we found that, for all age mortality, increases in concentrations of NO_2 (maximum 1-hour) were significantly associated with increases in death counts due to all causes, due to all cardiovascular disease and due to all respiratory disease. The results were also significant and stronger for the age group 75 years or more. When NO_2 was averaged over the 24-hour period for the day, the estimates were not significant.

These effect estimates were similar in each city for mortality due to all cardiovascular and all respiratory disease. For deaths due to all causes we found that all cities gave similar results except Brisbane, which yielded higher increases than the other cities. The pooled estimates without Brisbane showed a non-significant association between increases in mortality and increases in NO_2 concentrations.

Separate analyses were carried out for the warm (November - April) and cool (May - October) periods to identify if there are different effects in each period (due to different emission patterns or photochemical smog events). The effects tended to be smaller and not significant during the warm period.

In the seasonal analysis no significant differences were found between the cities.

Associations with hospital admissions

In pooling the estimates for all the cities we found that increases in concentrations of NO_2 were significantly associated with increases in hospital admissions for a range of cardiovascular and respiratory disease and age categories (see Tables 5-7).

3.1.2 Carbon monoxide

Carbon monoxide (CO) is also one of the air pollutants monitored on a daily basis in all the cities under study here, but the number of air pollution monitors measuring ambient outdoor air pollutant concentrations is different in each city. In Auckland there are 3 monitors, Brisbane 1 monitor, Canberra 1 monitor, Christchurch 2 monitors, Melbourne 3 monitors, Perth 3 monitors and Sydney 4 monitors.

Association with death counts

In pooling the estimates for all the cities we found that increases in concentrations of CO (8-hour daily maximum) were associated with increases in death counts due to all causes, cardiovascular disease and respiratory disease, but these pooled estimates were not statistically significant. In the seasonal analysis there were no significant differences found between the cool and warm periods.

Associations with hospital admissions

There were no statistically significant associations found between increases in concentrations of CO and increases in hospital admissions due to respiratory disease in any disease category or age category considered.

In pooling the estimates for all the cities we found that increases in concentrations of CO (daily 8-hour maximum) were significantly associated with increases in hospital admissions for cardiovascular conditions. The effect estimates for most cardiovascular conditions and in most age categories were larger and more often significant during the cool period than the warm period.

3.1.3 Particles

Here, only 24-hour average data for $PM_{2.5}$ and PM_{10} were used. For $PM_{2.5}$ the estimates for the Australian cities (Brisbane, Melbourne, Perth, Sydney) were pooled, and for PM_{10} the estimates for the cities (Brisbane, Melbourne, Perth, Sydney, and Christchurch) were pooled.

Association with death counts

We found that increases in particle concentrations as measured by $PM_{2.5}$ were associated with increases in death counts due to all causes, cardiovascular disease and respiratory disease, and most of these increases were statistically significant. The results were also similar for all cities.

We found that increases in particle concentrations as measured by PM_{10} were associated with increases in death counts due to all causes, cardiovascular disease and respiratory disease.

However, the results were only statistically significant for cardiovascular disease where the results were also similar for all of these cities. For the other disease categories, there appeared to be differences between the cities (Brisbane higher than the others, Perth lower and sometimes negative – a decrease).

The results for warm and cool periods for the associations of particle concentrations with cardiovascular, respiratory and total mortality indicate there are much stronger associations in winter than in warm season.

Associations with hospital admissions

We found that increases in particle concentrations as measured by $PM_{2.5}$ were significantly associated with increases in hospital admissions for both cardiovascular and respiratory diseases.

We found that associations of increases in $PM_{2.5}$ concentrations with increases in hospital admissions for cardiac disease were influenced by the city rainfall or humidity – the lower the rainfall and humidity, the higher the association. This may be occurring due to rainfall 'washing out' particles in the atmosphere.

For cardiac failure hospital admissions, a similar effect was found in the influence of barometric pressure: the greater increases occurred in the cities with the higher average barometric pressure, a climate condition usually associated with lower average rainfall and humidity. For cardiac failure hospital admissions, there also appeared to be greater increases in cities with a higher proportion of people over 65 years of age.

We found that increases in PM_{10} concentrations were significantly associated with increases in hospital admissions for several cardiovascular and respiratory disease and age categories (see Table 5, 6 and 7).

In examining the different results for cool and warm periods, we found less seasonal variations than with gaseous pollutants.

3.1.4 Ozone

Results were derived for maximum 1-hour, 4-hour and 8-hour ozone concentrations (during the daytime). The estimates were pooled for the Australian cities – Brisbane, Melbourne, Perth, and Sydney. Generally, the results were similar for all averaging times.

Association with death counts

We found that increases in ozone concentrations were in general associated with increases in death counts due to all causes, cardiovascular disease and respiratory diseases, but the increases were not always statistically significant.

An examination of the results for the warmer six months of the year showed significant results for all cause and cardiovascular death counts, and there was no evidence showing the results for the cities were different.

Associations with hospital admissions

We found that increases in ozone concentrations in the warmer six months of the year (when there are warm season smog episodes) were significantly associated with increases in hospital admissions for all cause respiratory diseases, particularly asthma in children.

3.1.5 Summary of results and confounding

Tables 4–7 summarise the significant associations with each health outcome and air pollutant. The matching analyses indicate that the NO_2 and particle effects may be arising from similar air pollution events.

For cardiovascular hospital admissions, NO_2 and CO associations are significant for all Australian and New Zealand cities studied and the matching analyses indicate again that these impacts are linked to the same pollution episodes. There is also evidence that particle effects are linked to those of the gases as well, and all effects generally peak in winter.

For respiratory hospital admissions, NO_2 and particle associations are significant for all Australian and New Zealand cities studied and the matching analyses also indicate that these impacts are linked to the same pollution episodes. However, there is also a significant ozone effect peaking in warm season which may be linked to warm season NO_2 effects.

Table 4 summarises the significant associations between increases in each mortality health outcome and increases in concentrations (lag 0-1) for each air pollutant.

Table 4: Mortality outcomes showing significant increases associated with increases in air pollutants - by age group

Pollutant	All ages	75+ years	Cities
NO_2 (Maximum 1-h average)	All cause mortality Total cardiovascular Total respiratory	All cause mortality Total cardiovascular Total respiratory	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
Carbon monoxide (Maximum 8-h average)	- *	- *	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
PM_{10} (24-h average)	Total cardiovascular	Total cardiovascular	Brisbane, Christchurch, Melbourne, Perth, Sydney
$PM_{2.5}$ (24-h average)	All cause mortality Total cardiovascular	All cause mortality Total cardiovascular Total respiratory	Brisbane, Melbourne, Perth, Sydney
Ozone[1] (Warm)[2]	All cause mortality Total cardiovascular	Total cardiovascular	Brisbane, Melbourne, Perth, Sydney

* Carbon monoxide generally was associated with increases, but they were not statistically significant

[1] Same for maximum 1-h, 4-h, 8-h averages

[2] Ozone levels for warm period of year (November-April)

We found that the average (pooled) estimates for increases in mortality derived for each group of cities in Table 4 can be used to estimate the increase in mortality for any city in that group.

Tables 5 and 6 summarise the significant associations between increases in the concentrations of each air pollutant and increases in hospital admissions due to cardiovascular disease for adults (15 years or older) and due to respiratory disease, (15 years or older), respectively.

Table 7 summarises the significant associations between increases in the concentrations of each air pollutant and increases in hospital admissions due to respiratory disease for children (aged less than 15 years).

Table 5: Significant increases in hospital admissions due to cardiovascular disease for adults (15 years and older) associated with increases in air pollutant concentrations

Pollutant	15-64 years	65+ years	Cities
Nitrogen dioxide (max 1-h)	Total cardiovascular, arrhythmia	Total cardiovascular, all cardiac, cardiac failure, IHD*, MI*	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
Nitrogen dioxide (av. 24-h)	Total cardiovascular, all cardiac, cardiac failure, arrhythmia	Total cardiovascular[1], all cardiac[1], cardiac failure[1], IHD*, MI*	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
Carbon monoxide (max 8-h)	Total cardiovascular, all cardiac, cardiac failure, arrhythmia	Total cardiovascular[2], all cardiac[2], cardiac failure[2], IHD*, MI*	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
PM_{10} (av. 24-h)	-	All cardiac, cardiac failure	Brisbane, Christchurch, Melbourne, Perth, Sydney
$PM_{2.5}$ (av. 24-h)	-	Total cardiovascular, all cardiac, cardiac failure, IHD*, MI*	Brisbane, Melbourne, Perth, Sydney

* MI = myocardial infarction; IHD = ischemic heart disease

[1] Evidence for heterogeneity for these outcomes with Christchurch results different and showing no effect

[2] Evidence for heterogeneity for these outcomes with Sydney results higher than the other cities, but pooled estimates for the remaining cities still significant and positive

Apart from some results for carbon monoxide and 24-hour average nitrogen dioxide, we found there is no evidence for heterogeneity between the results for cities in each group of cities shown in Table 5, so the pooled estimates for each group of cities can be used for any city in that city group. The pooled estimates for some (24-hour) nitrogen dioxide results overestimate the associations with increases in cardiovascular disease in the elderly (especially for cardiac failure) in Christchurch.

Table 6: Significant increases in hospital admissions due to respiratory disease for adults (15 years and older) associated with increases in air pollutant concentrations

Pollutant	15-64 years	65+ years	Cities
Nitrogen dioxide (max 1-h)	Total respiratory	-	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
Nitrogen dioxide (av. 24-h)	Total respiratory	-	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
PM_{10} (av. 24-h)	Total respiratory	pneumonia & acute bronchitis	Brisbane, Christchurch, Melbourne, Perth, Sydney
$PM_{2.5}$ (av. 24-h)	Total respiratory, asthma	Total respiratory, COPD*, pneumonia & acute bronchitis	Brisbane, Melbourne, Perth, Sydney

* COPD = chronic obstructive pulmonary disease

We found there is no evidence for heterogeneity between the results for cities in each group of cities in Table 6, so the pooled estimates for adult respiratory hospital admissions for each group of cities can be used for any city in that city group.

Table 7: Significant increases in hospital admissions due to respiratory disease for children (aged less than 15 years) associated with increases in air pollutant concentrations

Pollutant	<1 year	1 -4 years	5-14 years	Cities
Nitrogen dioxide (max 1-h)	-	Total respiratory	Total respiratory, asthma	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
Nitrogen dioxide (av. 24-h)	-	Total respiratory	Total respiratory[2], asthma[2]	Auckland, Brisbane, Canberra, Christchurch, Melbourne, Perth, Sydney
PM_{10} (av. 24-h)	-	Total respiratory	Total respiratory	Brisbane, Christchurch, Melbourne, Perth, Sydney
$PM_{2.5}$ (av. 24-h)	Total respiratory, pneumonia & acute bronchitis	Total respiratory, pneumonia & acute bronchitis	-	Brisbane, Melbourne, Perth, Sydney
Ozone (warm)[1]	-	Total respiratory, asthma	-	Brisbane, Melbourne, Perth, Sydney

[1] Ozone levels for warm period of year (November-April)
[2] Evidence for heterogeneity for these outcomes with Auckland results higher than the other cities, but pooled estimates for the remaining cities still significant and positive

Apart from some results for 24-hour average nitrogen dioxide, we found there is no evidence for heterogeneity between the results for cities in each group of cities shown in Table 7, so the pooled estimates for each group of cities can be used for any city in that city group.

3.1.6 Discussion

One of the most difficult problems in interpreting results such as those in the previous sections is that the increases identified cannot be proven here to be causal (Pope 2000). That is, the studies reveal that there are increases in some air pollutant concentrations that are statistically significantly associated with increases in death counts or hospital admissions, but they cannot prove that air pollutants cause the increases in deaths and admissions, unlike toxicological studies.

A further consideration is that the increases in death counts or hospital admissions associated with increases in concentrations of NO_2, CO and particles may be referring to the same effect, as these pollutants arise from similar sources (such as motor vehicle exhausts; see Table 1).

Pollutant results from similar sources

Analyses of the monitored data for CO and NO_2 showed a close relationship between these pollutants all year round in all the cities, probably due to similar emission sources such as motor vehicle exhausts, so the associations between these two pollutant gases and deaths or hospitalisations would be expected to be similar. When we matched these pollutants together in subsequent analyses, we found the results indicated the associations for CO and NO_2 were probably referring to similar air pollutant events and emission sources.

There are also similar sources for particles and the gases, CO and NO_2, such as motor vehicle exhausts (especially for fine particles, $PM_{2.5}$). It is notable that the results for hospital admissions due to cardiovascular admissions are also similar for particles, NO_2 and CO, although only NO_2 and particles show similar results for respiratory hospital admissions (especially in the younger age groups).

The associations between increases in respiratory hospital admissions for specific conditions such as childhood asthma, COPD in the elderly, and pneumonia and acute bronchitis in general is significant only for particles (usually $PM_{2.5}$). When matched analyses were carried out including particles and NO_2 together, and particles and CO together, the results showed it was not possible to identify whether one pollutant or the other was the primary cause of the associations found.

During photochemical smog events, the concentrations of ozone, particles (especially $PM_{2.5}$) and NO_2 increase (at different places and different times). As elevated ozone levels usually occur during the warm periods, there is usually only significant correlation then between the air pollutants. The exception is Brisbane with its wet summers and high sunshine winters when ozone levels can be elevated during the 'cool' period. Perth and Melbourne, with their hot dry summers and cold, wetter winters, show the cool and warm period differences most strongly.

The results for ozone do indicate significant results usually occurred only in the warm season and mainly for respiratory disease outcomes. Some (not all) of the results for the associations between respiratory hospital admissions (for children) and concentrations of particles and NO_2 do show only significant warm season estimates indicating that there may be an influence of the associations for ozone exposure on the NO_2 and particle results. When matched analyses were carried out including NO_2 together with ozone, the results showed it was not possible to identify whether one pollutant or the other was the primary cause of the associations found. There appeared to be less confounding, however, between particles and ozone, and no confounding between CO and ozone.

Therefore, the results for the associations between increases in the different air pollutant concentrations and the increases in deaths or hospital admission counts cannot be assumed to be additive. For example, the results for short-term exposure to pollutants for the estimated increases in the number of hospital admissions due to all cardiovascular disease in the elderly age group per inter-quartile range (IQR) increase in air pollutant concentration is 1.3% for $PM_{2.5}$, 3.0% for (24-hour average) NO_2 and 2.2% for (8-hour max) CO. The total impact is not obtained by adding these estimates for air pollution, as they are referring potentially to the same increase in cardiovascular admissions.

Emission source studies

A study funded by the Department of Environment and Heritage National Heritage Trust (L Denison 2005, pers.comm.) has indicated that the sources of particle emissions in Australian cities are different to overseas. The study examined the chemical composition of airborne particles in Adelaide, Brisbane, Melbourne and Sydney and identified potential sources of these particles. The results for the particles in the Melbourne, Brisbane and Sydney samples are, in general, comparable to those observed in the previous Australian studies. The results show that the contribution of the fine particle fraction ($PM_{2.5}$) to the total PM_{10} fraction is lower in Australian cities to those overseas, it being approximately 40% in Australia compared to 60-80% found in US cities. The results indicate that there is variability between cities, with the main components being crustal matter and sea-salt from natural sources, secondary nitrates and sulfates, and soot from human sources, and an organic component from both.

The results also show that within each city there is significant seasonal variability in the composition of particles in both the fine and coarse fractions. Also, the results indicate that the composition of $PM_{2.5}$ varies from city to city. The composition of $PM_{.2.5}$ in Sydney and Brisbane is very similar and has a much higher contribution of soot (an indicator of combustion processes) than Melbourne. The contribution from estimated organic components is higher in Melbourne than in the other cities as is the contribution from secondary particles during the warm season, showing that photochemical processes have a strong influence on particle production in warm season in Melbourne.

Air pollution exposure and interpretation of results

Only data sets for air pollutants that are monitored on a daily basis at outdoor fixed-point sites in the cities under study are used here in the analyses. In each city all the data from all the air pollution monitors is collated and an average air pollution concentration is derived which is assumed to be representative of the average outdoor exposure of the population under study to the air pollutant.

However, the number of air pollution monitors measuring ambient outdoor air pollutant concentrations is different in each city. The project team have used the data supplied by the government agencies in each city and have assumed the data supplied is representative, based on the assumption the monitoring networks established for NEPM monitoring have been developed to give an estimate of the average exposure of the general population. These readings are used here as surrogates for actual exposure by the population, but clearly they are not equivalent, as people spend most of their time in an indoor or enclosed (motor vehicle) environment. This is especially the case in winter with houses sealed for heating, and even in warm season if there is air conditioning. For reactive gases such as ozone, where there are no indoor sources, the indoor levels decrease quickly.

There are also indoor sources of air pollutants such as NO_2 (gas heaters, stoves), CO (home heating, smoking) and particles (home heating, stoves, smoking), so it is highly unlikely that the outdoor ambient air pollution concentrations are true measures for actual exposure, especially during winter. However, they may serve as good surrogates. For example, here we are examining the associations between day-

to-day change of deaths or hospitalisations and air pollution, and sources such as smoking, home heating, and gas cooking probably do not vary much from day to day, while the sources of outdoor pollution, such as motor vehicle exhausts, do. Therefore, the variability of the actual air pollution exposure on a day-to-day basis may be reflected in the day-to-day variability of the ambient air pollution levels, and it is this variability we are examining when we consider the associations between increases or decreases in deaths or hospitalisations and increases or decreases in air pollution levels. In using ambient air pollution data we are assuming that the relative increase or decrease in actual air pollution exposure on a day-to-day basis is effectively given by the relative increase or decrease in ambient air pollution concentrations.

3.1.7 'Harvesting'

The study included deriving estimates for the so-called 'harvesting hypothesis', using methodologies adopted by the Harvard School of Public Health to test this hypothesis. Overseas studies suggest that when the influence of the previous 30 to 40 days of air pollution exposure is estimated then the increase in deaths is much higher indicating the short-term calculations underestimate the impact of air pollution and that 'harvesting' does not occur. Most overseas studies have concentrated on the impact of PM_{10}. Here, there are limited data sets for $PM_{2.5}$ and PM_{10} and the use of the overseas approach for these pollutants in this study does not yield clear results as to whether 'harvesting' occurs. However, the use of these methodologies for the more complete data sets for NO_2 and CO shows significant increases in impact over 40 days, compared to the short-term impacts.

We have noted that particle composition in Australia is quite different to overseas studies with much lower contributions from human combustion sources such as motor vehicle exhausts and home fires, and from secondary production. The particle composition results for Australia indicate particle concentrations may not be a clear marker for these human sources given all the other sources contributing to the fine particle measurement. Therefore pollutant concentrations for CO and NO_2 may be better 'markers' for the impact of these sources.

3.1.8 Comparison with other multi-city and meta-analysis studies

The other major meta-analysis studies overseas have been for the US (NMMAPS: Samet et al. 2000, 2003; Dominici et al. 2006) and European (APHEA2: Katsouyanni et al. 2001; Dominici et al. 2002a) cities. The results in these studies show increases in mortality and hospital admissions with increases in particle concentrations, and we found no evidence to suggest that there is any difference between these results and those found in this study.

Three separate meta-analyses were carried out for ozone and mortality (Bell et al. 2005; Ito et al. 2005; Levy et al. 2005), and these results are also compared with those here. The results in these studies show increases in mortality with increases in ozone concentrations, and we found no evidence to suggest that there is any difference between these results and those found in this study.

The results for the previous multi-city study for Brisbane, Melbourne, Perth and Sydney (SPIRT study) for 1996 to 1999 were also compared with those from this study. For these four cities, the SPIRT study found significant associations between increases in mortality and hospital admissions (cardiovascular and respiratory) and increases in NO_2 and particles (as measured by nephelometry); for ozone, the significant associations were more limited (significant associations with elderly respiratory mortality and elderly respiratory admissions (asthma+COPD), no significant associations with cardiovascular or respiratory admissions).

The SPIRT analyses controlled for bushfires and control burns and over-corrected for flu epidemics (compared to the EPHC study) and used a GAMs approach similar to APHEA2. The EPHC study found significant associations between increases in mortality (see Table 4) and hospital admissions (cardiovascular and respiratory – Tables 5-7) and increases in concentrations of NO_2 and particles; increases in CO were associated with increases in cardiovascular admissions (Table 5), and ozone (warm period) with respiratory admissions (Table 7). We found no evidence to suggest that there is any difference between the results from the SPIRT and EPHC studies where comparisons could be made.

3.2 Comparison with other studies for single Australian and New Zealand cities

The results for each city derived here were compared with earlier single city studies where there were such studies. Generally, the results for the studies show the same positive increases (and decreases) in mortality and hospital admissions counts for the same pollutants, but the mean effect estimates and statistical uncertainties differ. The current results demonstrate the statistical power in pooling estimates for all the cities.

3.2.1 Brisbane

The analysis carried out by Simpson et al. (1997) for Brisbane for the period 1987–1994 found positive (and significant) increases in mortality with ozone and particles. Table 4 shows there are significant associations between increases in all cause and total cardiovascular mortality and increases in concentrations of nitrogen dioxide, particles and ozone (in the warm period), and between increases in respiratory mortality and increases in NO_2 and particles.

There were no significant cardiovascular admissions results in the previous study (Petroeschevsky et al. 2001) for Brisbane for the period 1987-1994. However, in this study, NO_2 was found to be significantly associated with an increase in cardiovascular hospital admissions (in particular stroke, cardiac disease, cardiac failure and arrhythmia), and both O_3 and CO were found to be significantly associated with an increase in cardiac failure. Table 5 shows the EPHC study found significant associations between increases in cardiovascular hospital admissions and increases in concentrations of NO_2, particles and CO.

Petroeschevsky et al. (2001) found significant associations between ozone concentrations and hospital admissions for respiratory disease for adults, and for asthma (children and adults). There was also a significant association between increases in concentrations for particles (as measured by nephelometry) and increases in respiratory admissions (adults). Tables 6 and 7 show the EPHC study found significant associations between increases in adult and children respiratory hospital admissions and increases in concentrations of NO_2 and particles, and between increases in respiratory hospital admissions for children and increases in ozone (in the warm period).

3.2.2 Christchurch

The results here were compared with those for a previous study for Christchurch (Hales et al. 2000), which found a significant increase in total mortality and respiratory mortality associated with an increase in PM_{10}. The EPHC study found increases which were not statistically significant, but there is a significant association for cardiovascular mortality (see Table 4). The pooled results in Table 4 for mortality also indicate that increases in concentrations for NO_2 and CO are significantly associated with increases in mortality for all cause, cardiovascular and respiratory disease.

The study by McGowan et al. (2002) showed significant associations between cardiac admissions and PM_{10} for the 65+years age group for the period 1988-1998. The study used GAM methodology but not the same as that adopted in the APHEA and NMMAPS studies. The pooled results in Table 5 for cardiovascular hospital admissions indicate that increases in concentrations for PM_{10}, NO_2 and CO are significantly associated with increases in admissions for a range of cardiovascular disease categories, including all cardiac. The McGowan et al. study (2002) also found significant associations between PM_{10} and hospital admissions for respiratory admissions (age groups 0-14 years, 15-64 years, 65+ years), and for asthma, chronic lung diseases, pneumonia/influenza, and acute respiratory infections. The pooled results in Tables 6 and 7 for respiratory hospital admissions indicate that increases in concentrations for PM_{10} and NO_2 are significantly associated with increases in admissions for a range of respiratory disease categories (including all respiratory, asthma, pneumonia and acute bronchitis) for both children and adult age groups.

3.2.3 Melbourne

The Melbourne study on mortality (EPA Victoria 2001; Simpson et al. 2000) used the GAM approach for five years of data, 1991-1996, and the results here indicate the case-crossover results for the 1998-2001 period have derived similar estimates. The pooled results in Table 4 for mortality indicate that increases in concentrations for ozone, $PM_{2.5}$, NO_2 and CO are significantly associated with increases in mortality.

The GAM approach used in the Melbourne study on hospital admissions (EPA Victoria 2001) for the period 1994-1997 is similar to that used here and the results here are similar, as they were for the SPIRT study for cardiovascular hospital admissions. The pooled results in Tables 6 and 7 for respiratory hospital admissions indicate that increases in ozone, $PM_{2.5}$ and NO_2 are significantly associated with

increases in admissions for a range of respiratory disease categories (including all respiratory, asthma, COPD, pneumonia and acute bronchitis) for both children and adult age groups. The pooled results in Table 5 for cardiovascular hospital admissions indicate that increases in concentrations for CO, $PM_{2.5}$ and NO_2 are significantly associated with increases in admissions for a range of cardiovascular disease categories.

3.2.4 Perth

In the previous Perth study (DoE 2003), O_3 was found to be significantly associated with an increase in cardiovascular deaths for all ages for the period, 1992-1997. The pooled results in Table 4 for mortality indicate that increase in concentrations for ozone, $PM_{2.5}$, NO_2 and CO are significantly associated with increases in mortality for all cause, cardiovascular and respiratory disease.

The previous Perth study (DoE 2003) also used a case-crossover approach and found increases in NO_2 were significantly associated with an increase in cardiovascular hospital admissions for NO_2. The pooled results in Table 5 for cardiovascular hospital admissions indicate that increases in concentrations for CO, $PM_{2.5}$ and NO_2 are significantly associated with increases in admissions for a range of cardiovascular disease categories.

The previous Perth study (DoE 2003) found significant associations between increases in concentrations for ozone, NO_2, particles ($PM_{2.5}$, nephelometry) with increases in respiratory hospital admissions for a range of disease categories (all cause, asthma, COPD, pneumonia). The pooled results in Tables 6 and 7 for respiratory hospital admissions indicate that increases in ozone, $PM_{2.5}$ and NO_2 are significantly associated with increases in admissions for a range of respiratory disease categories (including all respiratory, asthma, COPD, pneumonia and acute bronchitis) for both children and adult age groups.

3.2.5 Sydney

The Sydney study by Morgan et al. (1998a) for 1989-1993 used earlier filtering techniques than the trigonometric methods and found significant associations between particles (as measured by nephelometry), ozone, and NO_2 with all cause mortality, and between particles and cardiovascular mortality. The pooled results in Table 4 for mortality indicate that increase in concentrations for ozone, $PM_{2.5}$, NO_2 and CO are significantly associated with increases in mortality for all cause, cardiovascular and respiratory disease.

The Morgan et al. study (1998b) for the period 1990-1994 found significant associations between counts for admissions due to heart disease and particles (as measured by nephelometry) and NO_2, and the study concluded that NO_2 has a stronger association than particles. The pooled results in Table 5 for cardiovascular hospital admissions indicate that increases in concentrations for CO, $PM_{2.5}$ and NO_2 are significantly associated with increases in admissions for a range of cardiovascular disease categories.

Morgan et al. (1998b) found significant associations between NO_2 and asthma admissions (1-4 years). The pooled results in Tables 6 and 7 for respiratory hospital admissions indicate that increases in ozone, $PM_{2.5}$ and NO_2 are significantly associated with increases in admissions for a range of respiratory disease categories (including all respiratory, asthma, COPD, pneumonia and acute bronchitis) for both children and adult age groups.

The association between air pollution and emergency department visits for cardiovascular disease in the elderly in Sydney has been described (Jalaludin et al. 2005). Again, this study confirms the association between fine particles, nitrogen dioxide, and carbon monoxide and adverse cardiovascular outcomes in the Sydney region.

4. Conclusions

The results of the study indicate that increases in concentrations of the air pollutant nitrogen dioxide (NO_2), are significantly associated with increases in daily mortality and hospital admissions counts for a large range of disease categories, in both the young and the old, and in populations in all the Australian and New Zealand cities studied here. However, there is no evidence to suggest that the health effects are arising from the impacts of NO_2 alone. Rather, the analyses here indicate that the NO_2 effects could be 'markers' or 'surrogates' for the impacts due to other pollutants as air pollutants are usually significantly correlated with each other (probably due to similar emissions sources, such as motor exhausts).

Throughout the analyses, we found particle associations often confounded by NO_2 when both showed significant associations, and NO_2 and CO also confounded each other. Some of the warm season ozone associations also appeared to be confounded by the NO_2 associations when both were significant. Therefore, the results here are probably referring to the impacts of an air pollution 'mixture' of gases and particles, including all or part of the concentrations for CO, NO_2, $PM_{2.5}$, PM_{10} and ozone (warm season). All the components of such a mixture probably share similar emission sources (such as motor vehicle exhausts) and the consistent surrogate for this mixture applicable to all cities investigated here is NO_2.

Therefore, in all the Australian and New Zealand cities studied here, the results indicate that increases in concentrations of this mixture of air pollutants in urban airsheds are significantly associated with:

- increases in mortality for total all cause, cardiovascular and respiratory disease categories (and the impact on the elderly is the strongest)

- increases in cardiovascular hospital admissions for a range of disease categories including all cardiac, IHD, MI and cardiac failure (and the impact on the elderly is the strongest)

- increases in respiratory hospital admissions for a range of disease categories including all respiratory, asthma, COPD, pneumonia and acute bronchitis (and the impact on the child age groups is the strongest, except for COPD).

Statistical tests indicated there was usually no evidence for heterogeneity between the results in different cities, so each pooled estimate for a collection of cities used in each analysis could be used as the estimate for the associations in each city included in that collection.

Most of the analyses here examined the short-term effects, that is, the acute health effects arising from exposure to pollutants on the same day or the day before. It has been suggested that the resulting mortality estimates may exaggerate the effects of air pollutants as people who are already very ill may die a few days or weeks earlier because of increased air pollution exposures – the 'harvesting' or mortality displacement hypothesis. The results here show no evidence for that effect if we use NO_2 as the surrogate for the effects.

The EPHC study indicates that other Australian and New Zealand studies need to be carried out to investigate this air pollution mix more closely. Questions to be asked include the following:

What is the relationship between the air pollutant concentrations monitored at fixed outdoor sites (such as the NEPM network) and the actual exposure to air pollution?

What are the constituents of particles that contribute to the health associations found here?

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