Application ID: 1030259

Understanding and ameliorating the human health effects of exposure to air pollution: from knowledge to policy and public health practice.

Chief Investigators:

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Urban consolidation and sprawl, traffic congestion, mining near residential areas, climate change, heating and cooling living environments, and power generation – these modern phenomena generate headlines, policy dilemmas and challenges for science, the economy, the environment, and our health in Australia, our region and the world. Air quality and its effects on human health thread through much of the popular concern about them. National Environment Protection Measures form the basis for regulating air quality in Australia. Beyond these, high quality, multi-disciplinary research is crucial to addressing progress in handling these challenges through policy and action.

Australia has substantial intellectual and scientific resources engaged in research into these challenges – atmospheric physics and chemistry, toxicology, epidemiology, biostatistics and respiratory medicine are examples. However, these fields of research have not often been brought together. Consequently, new knowledge that comes from local integrated research has not been readily accessible for policy makers. In other countries, this integration and policy translation has occurred either by establishing a substantive research centre within the responsible regulatory agency (the US Environmental Protection Agency and state agencies) or through partnerships among government agencies and industry, such as the Health Effects Institute in the U.S, which has been operating since 1980. These bodies undertake research to fill gaps relevant to health policy concerning air pollution. No such centres exist in Australia.

This application proposes the first stage in addressing this deficiency in Australia's capacity to determine the human health impact of air pollution and to propose ways, operating through the complex, integrated systems of a modern industrial society, to manage them. We will create opportunities now and in the future for researchers, in diverse but related disciplines to create knowledge of both national and international interest. The application proposes ways of leveraging existing capacity and resources to generate new knowledge, build capacity in a cohort of scientists (including clinical scientists) who are then equipped to address air pollution and its effects on health, and with the skills to transfer existing and new knowledge into policy proposals in multiple portfolios.

Australian cities generally have lower air pollution concentrations compared to many U.S. and European cities where most air pollution and health research has been based. Our cities also regularly experience distinctive extreme air pollution events due to a range of unregulated sources including bushfires, hazard reduction burns and dust storms. We will take advantage of these unique exposure profiles in large population centres to investigate air pollution and health effects across the range of exposure-response relationships for both urban and biomass sources of air pollution. Our goal is not simply description: we wish to conduct research directed also towards solutions.

1 Generate new knowledge that leads to improved health outcomes

Themes of our research

Our research focuses on the following themes:

A. Longer-term and short-term outcomes of exposure to air pollutants in adults and in children. There are no published Australian studies on long-term effects of exposure to air pollution, despite this being an important emerging theme in the international literature (1-5).

B. The biological basis of adverse human effects of air pollutants including gene-environment interactions and environmental toxicology, an emerging area in air pollution research.

C. Effects of air pollutants on vulnerable populations including children, the elderly, pregnant women and those with pre-existing chronic diseases.

D. Methodological advances in the study of air pollutants and their human health effects including: the synergistic and confounding effects of multiple pollutants and the consequences that must be considered when determining regulation; methods for assessing

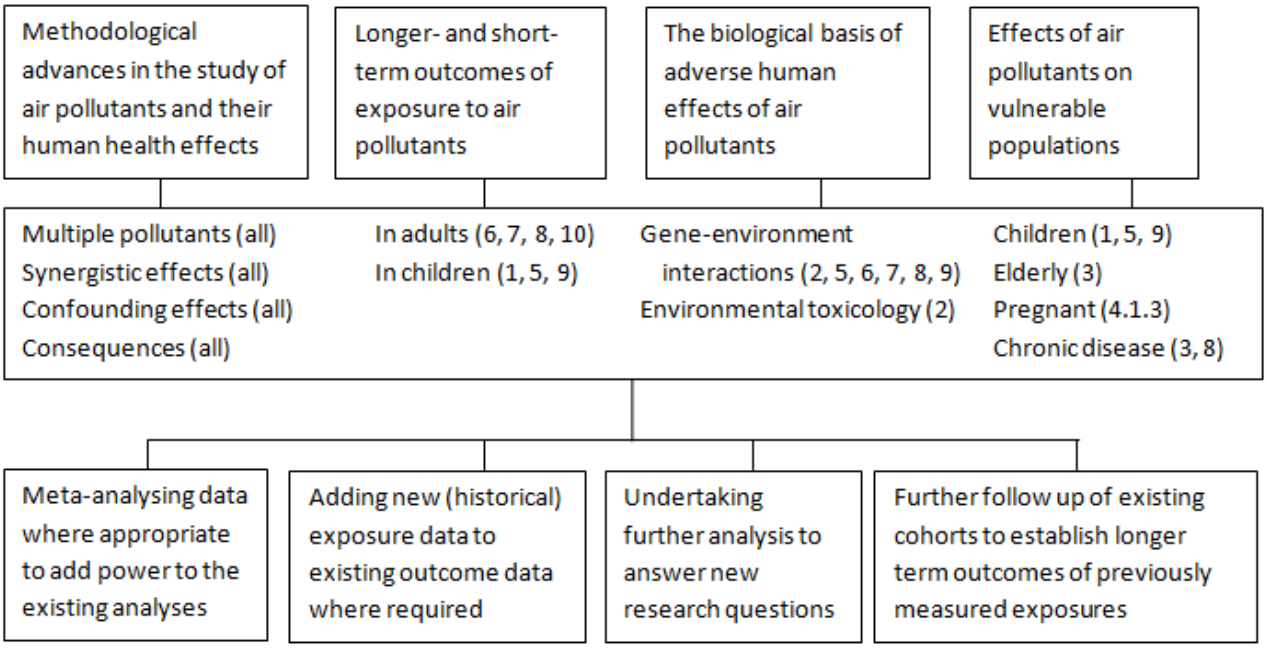
the environmental impacts of new pollutants; improved exposure assessment techniques including advances in geospatial analysis and the application of remote sensing data about air pollution to epidemiological studies; and economic analyses.

In relation to each of these fields, we will remain vigilant for opportunities to provide the results of the research in a form and manner that matches the interests of policy makers.

In this section, we outline the major research projects that will be encompassed within the CRE including:

- their aims and objectives;
- current investigators involved;
- a summary of the existing and proposed research methodology;
- the current status of the research with respect to funding, progress in data collection, analysis and findings;
- opportunities for extension within the CRE in particular by engagement of new collaborators from the CRE, by involvement of CRE-funded post-doctoral fellows and/or PhD scholars, by the use of seed funding to leverage new grant-funding, and by funding syntheses of existing evidence;
- relevance to one or more of the research themes listed above; and
- significance of the new knowledge

The figure below illustrates the relations among the current and proposed projects within the CRE. The numbers refer to projects listed within section 1, below.



1.1 Australian Children's Air Pollution Study (ACHAPS)

1.1.1 Aims and Objectives

This study arose from the scientific needs of the National Environment Protection (Ambient Air Quality) Measure (AAQ NEPM) review (6). The primary aims were:

1) To provide an evidence-base of long-term and short-term health effects of exposure to air pollutants in Australian children that will contribute to the review of AAQ NEPM;

2) To obtain quantitative effect estimates for the association between children's historical lifetime exposure to criteria air pollutants covered by AAQ NEPM and (a) the period prevalence of respiratory symptoms, and (b) lung function;

1.1.2 Current Investigators involved: CIs Williams, Marks and Jalaludin.

1.1.3 Summary of the research methodology

This study is the only national Australian study examining air pollution effects on child health. It involves a cross-sectional study to examine the effects of cumulative exposure to air pollutants on children's respiratory health and a nested panel study to assess short-term effects. Thirty air quality monitoring stations across six major Australian cities were selected in a manner that maximised the observed variability in air pollutants, specifically particulates (PM), ozone (O_3), nitrogen dioxide (NO_2), sulphur dioxide (SO_2) and carbon monoxide (CO). Around 3,000 children aged 8 to 11 years were randomly selected from 60 schools located within a 2.5km radius of the 30 air quality monitoring stations. Data on symptoms, respiratory illnesses, lung function, and airway inflammation were collected. Monitoring station sites and child residences have been geo-coded. The panel study selected a sub-group of children with a history of asthma who recorded daily measures of symptoms and lung function for a 4 week period. Multivariate multi-level (random effects) models were used for analyses.

1.1.4 Current status of the research

The research was funded by an ARC linkage grant in which the major industry partner was the National Environment Protection Council (NEPC). Fieldwork and analysis relevant to the primary objectives have been completed and a draft report submitted to NEPC. The principal finding was consistent evidence of adverse respiratory effects of NO_2 exposure for both recent and life-time exposure. These adverse effects were manifest as increased risk of asthma-like symptoms, increased airway inflammation and reduced lung volumes. A manuscript is in preparation.

1.1.5 Proposed expansion of the existing project within the CRE and relevance to themes

The existing dataset will be used to address a number of important additional objectives relevant to several themes:

A. Methodological development

1. Comparison and cross-validation of methods to assess exposure to ambient air pollution: monitoring stations, emission inventory, dispersion models and land use regression models.
2. Distinguish early life, long- and short-term health effects of air pollution. Daily lifetime exposure data are available for each child and each site, allowing the identification of these exposures and thus the relative importance of exposure periods.
3. Comparisons of various statistical methods for assessing the short-term effects of air pollution on children's lung function, symptoms and medication use.

B. Long-term outcomes

Data on long-term outcomes in relation to cumulative estimated exposure to pollutants have been reported in the primary analysis. However this will be extended, using data on residential address history, to examine the cumulative impact of proximity to traffic of varying density. Home and school characteristics can also be used to produce potentially enhanced measures of exposure. This is an area of increasing international interest (4, 5, 7-10). We have experience in the application of this methodology (#10447300, #5413479), but its use in the analysis of a nationwide dataset is challenging, exciting and unique. We expect, during the course of this CRE, to develop a new proposal for further follow-up of this cohort to examine change in clinical and physiological endpoints over time and their relation to change in pollutant exposure.

C. The biological basis of adverse human effects of air pollutants

Our data on airway inflammation, lung function and atopy in a large population of children with associated data on proximity to traffic and cumulative exposure to specific pollutants is unique in Australia and rare internationally. It provides a powerful basis for exploration of pathways and

mechanisms. We propose to enhance this by developing nested case control studies to examine gene-environment interactions. Data from this study will be merged with similar data from other sources, described below.

D. Vulnerable populations: This work focuses on effects of air pollution on children's health.

1.1.6 Significance of the new knowledge

This study provides a rare opportunity to understand, more completely than ever before, the relation between exposure to air pollutants and child health. The large nationwide sample, rich and detailed data on clinical endpoints and potential for expansion using geocoded residential data in nested studies all place us in strong position to make substantial contributions to knowledge.

1.2 Lane Cove Tunnel Investigation

1.2.1 Aims and Objectives

The opening of a dual stack ventilated road tunnel in inner north-western Sydney in early 2007 provided a unique opportunity to assess the impact of road-traffic intervention on air quality exposures and health in the local community. The tunnel was designed to divert traffic off a heavily congested surface road. The main aim of the study was to establish whether changes in air quality occurring after the tunnel opened affected the health of the local community.

1.2.2 Current Investigators involved: CI Marks and Jalaludin, AIs Smith and Brunekreef and proposed PRP Cowie.

1.2.3 Summary of the research methodology

The project comprised several elements. The core element was a cohort study in which approximately 3000 subjects were surveyed during 2006, before the tunnel opened, and again in 2007 and 2008, after the tunnel opened. The survey included information on respiratory, other symptoms and illness and potential confounding factors. Subjects were recruited from four zones within the region of interest: along the bypassed road that was expected to experience a reduction in air pollution, near the approach roads that were expected to experience an increase in air pollution, surrounding one of the ventilation stacks, and a control zone that was not expected to be affected by changes in traffic or air pollution. A sub-group in each of the four zones took part in a more detailed study that included measurement of lung function and FeNO as well as a twice daily record of symptoms and peak expiratory flow rate for two months.

We also recorded data on air quality using a range of measures including four fixed site air quality monitoring stations and a network of 40 NO_2 passive samplers. The latter were used, together with traffic and land use data, to develop a land use regression model. These data and the associated model allowed us to assign ambient NO_2 exposure to any household in the study area for any two week period during the study.

1.2.4 Current status of the research

The project was funded by the CRC for Asthma & Airways with NSW Department of Health as a partner. Data collection and primary analysis have been completed. Principal findings were the absence of consistent changes in regional air quality related to the tunnel intervention despite a substantial reduction in NO_2 exposure in the vicinity of the main bypassed road. These local improvements in air quality were not associated with improvements in respiratory symptoms or lung function. Manuscripts reporting the findings in relation to air quality changes and clinical outcomes are being submitted for publication and to NSW Health. Papers describing methodological developments have been published (#10447300, #5413479).

1.2.5 Proposed expansion of the existing project within the CRE and relevance to themes

Although the primary analysis has been completed, a number of important questions remain to be answered.

A. Methodological development

The analysis of these data involves the modelling of categorical outcomes with one or two random effects. The addition of a spatial dimension to the analysis makes this even more complex and challenging. We will also compare and cross-validate methods for assessing exposure to ambient air pollution. We will work with CI Williams to explore the validity of various alternative approaches.

B. Long-term and short-term outcomes

We have currently limited the analysis to subjects assigned to the four zones described above. However, there is an opportunity, using the land use regression model, to estimate actual household exposure to NO_2 through the study period. We will use these data to assess the impact of changes in exposure to NO_2 on endpoints using a time series analysis and analysis of personal NO_2 concentrations. Further follow-up of this cohort will allow us to explore long-term health outcomes.

C. The biological basis of adverse human effects of air pollutants

We have collected genetic material using buccal cell swabs and have funding to conduct candidate gene analysis. Our target genes for this analysis will be the glutathione transferase genes (11-13) that have been implicated as mediating heterogeneity in the effects of air pollutants. We will also explore Mendelian randomisation as a method of understanding mechanisms of air pollution health effects (14). We will combine data from this cohort with that from other cohorts described below to examine gene-environment interactions.

D. Effects of specific pollutant sources on human health

We will use these data to explore the effects of pollutants on children and on people with pre-existing respiratory disease.

1.2.6 Significance of the new knowledge

Traffic-related air pollution, including NO_2 and other oxides of nitrogen, are increasingly recognised as a key source of pollutant exposure in urban environments. Intervention studies in this field are extremely rare and offer a unique opportunity to assess the impact of changes in air pollution, unconfounded by meteorological events that are usually responsible for natural changes.

1.3 Older People's Air Pollution Study (OPAS) – in association with the Social, Economic and Environmental Factors (SEEF) study

1.3.1 Aims and Objectives

The aim of OPAS is to investigate, in the Australian population aged 45 years and above, associations between current and past exposure to urban ambient air pollutants and health status, quality of life, hospitalisations, ED visits and deaths due to respiratory and cardiovascular diseases:

1.3.2 Current Investigators involved: CIs Jalaludin and Morgan.

1.3.3 Summary of the research methodology

The NSW 45 and Up Study is the largest population-based cohort study in the Southern Hemisphere and has now recruited 260,000 people aged 45 years and over from the general population. The SEEF sub-study has recruited 60,000 subjects from this cohort. Each respondent has completed a questionnaire concerning social, economic and environmental factors, in addition to the 45 and Up Study baseline questionnaire. A unique strength of this study is the linkage to routinely collected health datasets, including hospitalisation, emergency department (ED) and Medicare data.

For OPAS, we will develop exposure metrics for current and cumulative past exposure to ambient air pollutants using geocoded residential addresses and air quality data from routine air monitoring stations. Individual exposures will be calculated using inversely weighted distance from the nearest three air monitoring stations (15). We will also further develop methods to use individuals' residence distance to main roads and traffic density as a marker for exposure to traffic-related air pollution (#5413479).

We will then use health outcome data derived from surveys and the linked health datasets to determine associations between exposure to ambient air pollution and health status (quality of life,

COPD, asthma, heart disease), health service utilisation (hospital admissions, ED visits). The longitudinal data collection will enable this analysis to examine within-subject associations.

1.3.4 Current status of the research

The SEEF study has only recently completed the survey of 100,000 randomly selected subjects from the 45 and Up study with a 60% response rate. The cleaned dataset will be available to SEEF investigators in June 2011.

1.3.5 Proposed expansion of the existing project within the CRE and relevance to themes

A. Methodological development

The use of linked data for research is still limited in Australia. The analyses of these data will require expertise in statistical programming for linked datasets where there will be repeated measurements for many subjects. We will work with CI Williams on this aspect.

B. Long-term outcomes

Linking the SEEF study questionnaire to routinely collected datasets, both prospectively and retrospectively, ensures a uniquely useful cohort sample enabling us to study the long- term effects of air pollution. This cohort will be analogous to the American Cancer Society cohort which has produced several landmark papers (e.g. 2, 16, 17) on the effects of long-term exposure to air pollution on deaths.

D. **Vulnerable populations:** This study will focus on air pollution effects in the elderly.

1.3.6 Significance of the new knowledge

This proposed study, capitalising on the strengths and resources already invested in the 45 and Up Study, will provide information on the effects of ambient air pollution and traffic related air pollution in older Australians in a timely and resource efficient manner. For the first time we will be able to investigate long-term effects of air pollution, which is crucial for regulatory purposes.

1.4 Biomass smoke and health

1.4.1 Aims and Objectives

Bushfire smoke is associated with an increase in hospitalisation for respiratory diseases (#761285). However, it is currently unclear if PM from biomass sources has the same effects on cardio-respiratory health as PM from urban sources.

1.4.2 Current Investigators involved: CIs Morgan, Jalaludin, and Abramson, AI Johnston and proposed PRP Dennekamp.

1.4.3 Summary of the research methodology

The ARC-funded project has developed a validated database on landscape fire events (bushfires, hazard reduction burns and others) and dust events from 1994 to 2006 for Sydney, Perth, Hobart, and Launceston. This methodology will be applied to Melbourne and other Australian cities to identify and validate extreme particulate pollution events and examine the association of these events with mortality and hospitalisation. We will also investigate the effects of wood smoke from solid fuel heaters in affected Australian towns and cities. The studies will focus on identifying potential differences in health effects due to PM derived from various sources.

1.4.4 Current status of the research

Several papers have been published or submitted including: reviews of the health effects of bushfires (18); approach to monitoring smoke from vegetation fires for public health (19); differences in the effects on mortality and hospital admissions of PM from urban sources and bushfires (#574012); validated methodology for creating an historical record of extreme bushfire events in Australian cities (20); and the effects on mortality of extreme air pollution events from bushfires and dust storms (Environ Res, under review).

1.4.5 Proposed expansion of the existing project within the CRE and relevance to themes

We will further develop the validated database of landscape fire events and dust to cover a broader range of locations. We will link this event database with other CRE epidemiological studies to investigate the health effects of landscape fire events on long term health outcomes. For example, the database will be linked to birth data (ICAPPO 4.1.3) to investigate the effect of air pollution events on adverse birth outcomes. We will also assess the utility of linking the air pollution event data on acute exposures to the cohort studies of respiratory health eg: MACS (1.8), TAHS (1.7), ACHAPS (1.1), CAPS (1.9), and SEEF (1.3). We will investigate the effects of events recorded in other routinely collected data sources such as hospital ED visits and ambulance call-out data.

A. Methodological development

The current studies of biomass smoke and health generally use city wide estimates of exposure. While some of these events produce spatially homogeneous exposures, other events have a more heterogeneous spatial distribution due to factors such as the proximity of the source and/or wind direction. We will use a range of methods to determine the spatial distribution of events and the associated population exposures, which will produce more robust estimates of health effects.

B. Long-term outcomes

Current studies of biomass smoke and health investigate the short term effect of acute exposures. By linking the validated landscape fire smoke database to CRE cohort studies, we can investigate potential long term health effects of short term extreme air pollution exposure events.

C. Effects of specific pollutant sources on human health

Most epidemiologic studies of the health effects of air pollution have been conducted in urban settings where particulate pollution is derived from a variety of sources. This complicates efforts to disentangle the health effects of particulates from various sources and size fractions, and remains a major gap in current evidence (21). Particulate matter from bushfires is an increasing source of air pollution, covering wide geographic areas and frequently affecting major population centres. Bushfire activity is likely to increase with global warming and with associated changes in vegetation burning practices (22). Deliberate fuel-reduction burns designed to avert major fire disasters (23) and wood burning for domestic heating are also increasing as sources of biomass smoke (24). Therefore understanding the possible health effects of biomass combustion smoke is becoming increasingly important.

1.4.6 Significance of the new knowledge

The studies we propose will add to the developing literature on this topic. These data will inform policy on prescribed fuel reduction burning, health warnings associated with extreme smoke and dust events, and provide input into revision of the NEPM for PM_{10} and $PM_{2.5}$.

1.5 Ultrafine Particles from Traffic Emissions and Children's Health (UPTECH)

1.5.1 Aims

Despite evidence of the toxicological effects of ultrafine (UF) particles (<0.1 μm), there have been no studies published that examine the relation between validly-measured environmental exposure to these particles and adverse health effects in children. This project seeks to determine the effect of the exposure to airborne UF particles emitted from motor vehicles on the health of school children. The main hypothesis is that, among children aged 8 to 11 years, variation in long-term exposure to UF particles is associated with variation in respiratory, cardiovascular and inflammatory outcomes and that variation is independent of the effects of other spatially varying characteristics including other air pollutants, housing conditions, indoor exposures and socio-economic factors.

1.5.2 Current Investigators involved: CIs Morawska, Williams, Marks and Jalaludin, AI Brunekreef and proposed PRP Mazaheri.

1.5.3 Summary of the research methodology

The hypothesis is being tested in a cross-sectional study focussing on spatial variation in the exposure-health outcome relationship. Thirty schools across Brisbane have been selected to maximise potential variation in exposure to traffic-derived UF particles. Exposures are measured at several sites in each school over a two week period coinciding with the clinical measurements. In each school we have selected 30 children for clinical assessment including a respiratory questionnaire and state-of-the-art measurements of airway function and inflammation. We will use multi-level models to examine the association between exposures and clinical outcomes.

1.5.4 Current status of the research

The field work for this study commenced in Sept 2010 and is expected to be completed mid-2012.

1.5.5 Proposed expansion of the existing project within the CRE and relevance to themes

A. Methodological development

Although the main focus of this research is on UF particles, concurrently acquired data on other pollutants will allow us to construct multi-pollutant models to test for synergistic and confounding effects. We are collecting data on routes of travel to and from school. Analyses of these data will entail the development of novel geospatial techniques, which will facilitate more accurate individual-level exposure assessment. In this study we are using sophisticated physiological tests in the field. Multi-breath nitrogen washout (25) has never previously been used to assess air pollution effects in a field study. Within the CRE we will further explore the utility of this and other methods of detecting the physiological consequences of air pollution exposures.

B. Long-term and short-term outcomes

This study focuses on long-term outcomes of air pollutant exposure. Further follow-up of this cohort is anticipated.

C. The biological basis of adverse human effects of air pollutants

We have collected and stored DNA from whole blood samples to enable examination of gene-environment interactions (see section 1.2.5). In addition, measurement of highly sensitive C-reactive protein (hs-CRP) in the present study will allow exploration of the role of systemic inflammation as a mediator of adverse health effects of UF and other pollutant exposures.

D. **Vulnerable populations:** Children are the focus of this study.

1.6 European Community Respiratory Health Survey (ECHRS)

1.6.1 Aims:

The ECRHS was established to explore reasons for variation in the prevalence of asthma between countries. This CRE component will investigate the contribution of long term exposure to traffic derived air pollutants on incidence of respiratory symptoms and decline in lung function.

1.6.2 ***Role of CRE Investigators:*** CIs Abramson & Dharmage.

1.6.3 Summary of the research methodology

ECRHS was originally a cross-sectional study of adults aged 20 to 44 years. In 1992, we recruited 876 subjects in Melbourne, of whom 757 attended the laboratory. It has since developed into a cohort study, the members of which have now been studied three times, most recently in 2004. . A range of outcomes have been assessed including respiratory symptoms, lung function, airway hyperresponsiveness and atopy by skin prick tests (SPT).

1.6.4 Current Status:

The findings of ECRHSI (26) and ECRHSII (27) have been published. ECRHSIII has been funded by NHMRC to undertake the next follow-up commencing in 2011. A clean dataset is available from previous waves of the study.

1.6.5 Opportunities for further work and relevance to CRE

Addresses have been geocoded and this will form the basis of improving assessment of long term exposure to air pollutants. Longitudinal analysis of lung function can be undertaken using generalised estimating equations. Once the 4th follow-up has been completed, the time series can be extended, cases of COPD identified and decline in lung function analysed more precisely.

1.6.6 Significance:

ECRHS is the major international study of lung health in young (and now middle aged) adults. The findings can be compared with those from the European centres and will inform the NEPM reviews, especially for $PM_{2.5}$.

1.7 Tasmanian Longitudinal Health Study (TAHS)

1.7.1 Aims:

TAHS is a population-based multi-wave longitudinal family study of respiratory health. This CRE component will investigate the contribution of long term exposure to air pollutants on incidence of respiratory symptoms and decline in lung function.

1.7.2 Role of CRE Investigators: CIs Dharmage and Abramson*.*

1.7.3 Summary of the research methodology

TAHS commenced in 1968 by assessing respiratory health and lung function of 8,585 7-year old Tasmanian children. Parents (16,267) and siblings (21,044) were also surveyed. Probands were then followed up in 1974 (7,500), 1979 (850), 1992 (1,500) and 2003-2006 (survey of 6000 and lung function and skin prick testing of 1500). Siblings were resurveyed (15,000) and had their spirometry assessed and SPT done (1,700). All parents are currently being resurveyed. We have genotyped proband and sibling DNA. Asthmatic probands are part of the Genome Wide Association Studies (GWAS) within the Australian Asthma Genetic Consortium (AAGC). We have also assayed the serum of the probands for six cytokines.

1.7.4 Current Status:

Postal survey of all the parents and a further follow-up of the probands to assess their airway hyperresponsiveness are underway. Both are funded by NHMRC. A clean data-set is available from previous waves of the study.

1.7.5 Opportunities for further work and relevance to CRE

Addresses of the Launceston participants (~1000) have been geocoded. The CSIRO air pollution model (TAPM) has been used to assign exposure to these geocoded addresses and the cross sectional association between these exposures and respiratory symptoms have been analysed. Historical data for air pollution are available for the period from 1992 onwards. Further work looking at the cross sectional associations between TAPM exposures and lung function, as well as longitudinal analysis investigating the long-term impact on symptoms and lung function can be undertaken. The remaining addresses can be geocoded and similar analyses can be conducted. Genetic and cytokine data will allow investigation into the biological basis of the effects.

1.7.6 Significance:

TAHS is the largest, longest running respiratory cohort study in Australia and is well placed to investigate air pollution and longitudinal change of respiratory symptoms and lung function. Its major strengths are its duration, sample size and lung function measurements at age 7 years.

1.8 Melbourne Atopic Cohort Study (MACS)

1.8.1 Aims:

MACS is a population-based multi-wave longitudinal family study of childhood allergies and asthma in a high risk cohort. The objective of this component is to investigate the contribution of long term exposure to air pollutants upon incidence and remission of respiratory and allergy symptoms, change in sensitization and lung function.

1.8.2 Role of CRE Investigators: CIs Dharmage & Abramson and proposed PRP Dennekamp.

1.8.3 Summary of the research methodology

The MACS began as a randomised controlled trial assessing the impact of 3 different infant formulas. It has now become one of the leading international studies identifying the natural history, environmental and genetic risk factors for childhood asthma and allergies. MACS recruited 620 children through antenatal clinics in inner eastern Melbourne. Only families with at least one family member who had an atopic disease were invited. The babies, who were born between 1990 and 1994 are referred to as probands. The family environment, both parents and all older siblings were investigated during the antenatal period. Probands were then assessed regularly since birth i.e. every 4 weeks during the first 2 years, annually from 3 to 7 and then at the most recent follow-up at age 10 years. SPTs were conducted at 6, 12, 24 months and at ten years. Lung function was measured at the 10 year follow-up.

1.8.4 Current Status:

15-year follow-up of the MACS probands and all the family members, funded by NHMRC, is currently underway. In this follow-up we are measuring spirometry, FeNO, trans epidermal water loss and collecting expired breath condensate. DNA will be genotyped for ten candidate genes. MACS asthmatic probands are part of the Australian Asthma Genetics Consortium GWAS analysis. A clean dataset is available from previous waves of the study.

1.8.5 Opportunities for further work and relevance to CRE

Addresses of the MACS participants have been geocoded. Currently the association between traffic air pollution and eczema at two years is being investigated. Further work investigating the associations between exposure to ambient air pollutants, incidence and persistence of other allergic diseases and lung function can be undertaken.

1.8.6 Significance:

The strength of the MACS is its in-depth data on a range of phenotypes in a high risk cohort.

1.9 Childhood Asthma Prevention Study (CAPS)

1.9.1 Aims:

The original aim of this study was to test the effectiveness of house dust mite avoidance and dietary fatty acid modification, implemented for the first five years of life, as interventions to prevent the onset of asthma in children with a family history of asthma.

1.9.2 Role of CRE Investigators: CIs Marks and Leeder**.**

1.9.3 Summary of the research methodology

This started as an RCT of interventions for the prevention of asthma that was implemented for the first five years of life in a cohort with a positive family history of asthma. The cohort has now been closely followed, with measures of indoor environmental exposures and careful measures of respiratory, cardiovascular and metabolic outcomes, to age 11.5 years. Further follow-up at age 14 is about to commence. Of 616 subjects initially randomised, 450 were followed-up at age 8 years (#10447302).

1.9.4 Current Status:

The project has been continuously funded by NHMRC project grants (apart from one year) from 1997 to 2014.

1.9.5 Opportunities for further work and relevance to the CRE

The data will be used to examine the effect of life-time exposure to ambient and traffic-related air pollution on respiratory, cardiovascular and metabolic outcomes. DNA from the subjects with asthma has been contributed to the Australian Asthma Genetics Consortium GWAS analysis.

1.9.6 Significance:
This study is a highly innovative community-based randomised controlled trial of preventive interventions. The richness of the data on outcomes and potential confounders makes it very valuable for air pollution studies.

1.10 Burden of Obstructive Lung Disease (BOLD)

1.10.1 Aims:
This study sought to describe the prevalence, outcomes and management of obstructive lung disease in people aged 40 years and over in Australia.

1.10.2 Role of CRE Investigators: CIs Marks and Abramson***.***

1.10.3 Methodology:
The Australian study followed an international protocol (28). Randomly selected samples of approximately 600 people aged over 40 were recruited in six Australian centres: Sydney, central western NSW, Melbourne, Hobart, Busselton and the Kimberley. A standardised respiratory questionnaire was administered, lung function was measured before and after bronchodilator, atopic status was measured by SPT and airway inflammation was measured as FeNO.

1.10.4 Current Status:
Data collection has been completed. Data from the Sydney site have been published (GBM #5413391). Data from the national study will be presented at a conference in April and published soon afterwards.

1.10.5 Opportunities for further work and relevance to the CRE
We will geocode all addresses for subjects from the Sydney and Melbourne centres and use these data to estimate exposure to traffic related air pollution. With these data we will examine the association between pollutant exposure and obstructive lung disease in older Australians living in Sydney and Melbourne. Further follow-up of this cohort is planned and this will allow us to examine the effect of pollutant exposure on incident cases of obstructive lung disease.

1.10.6 Significance
This is the first nation-wide study to objectively measure the prevalence of COPD at a population level. It represents an important resource for air pollution research.

1.11 Land-Use Regression Models of Air Pollution Exposure for Brisbane, Sydney and Melbourne
We have described several population-based cohorts in three east coast capitals that have existing objective and questionnaire-based data on clinical outcomes and also have the potential to add further data with planned additional follow-up: ACHAPS (1.1), LCT (1.2), SEEF (1.3), UPTECH (1.5), ECRHS (1.6), MACS (1.8), TAHS (1.7), CAPS (1.9) and BOLD (1.10). Several have existing measures of air pollution exposure. However, only one study (LCT) has implemented land use regression that allows valid estimates of exposure to traffic-related air pollution.

Land use regression has increasingly been recognised as the most feasible and valid method of estimating spatial variation in exposure to traffic-related air pollution and of assigning individual household level exposure for epidemiological purposes (29). The method entails measuring pollutant (commonly NO_2) concentrations at a sample of sites (approximately 40) within the selected region. For each site a range of land use characteristics are ascertained including: traffic density; distance from roads; land use; topography etc. A regression model is then fitted to predict NO_2 concentrations based on land use data. This model can then be applied to all other locations within the selected region to estimate pollutant (NO_2) concentrations. Our use of this method in the Lane Cove Tunnel study represents an important advance in this field by incorporating temporal as well as spatial variation into the estimation equation (#10447300).

AI Brunekreef is PI on the European Study of Cohorts for Air Pollution Effects (ESCAPE), which is designed to investigate the long-term health effects of exposure to air pollution in Europe. This study plans to combine outcome data from 21 existing cohort studies in Europe with air pollution data acquired using a rigorous standardised exposure assessment protocol, based on land use regression to estimate NO_2 and PM exposure. CI Abramson and proposed PRP Dennekamp are currently seeking NHMRC funding to apply the ESCAPE protocol in Melbourne.

We propose the CRE will seed fund a project to establish LUR models for NO_2 and PM_{10} for Brisbane, Sydney and Melbourne. By application of these models to the geocoded residential and school addresses for subjects within the cohorts described above, we will be able to undertake ESCAPE-style analyses. Where appropriate we will combine our data with the European datasets. Where our outcomes are unique, we will publish separately.

1.12 Summary and Significance of the new knowledge that will be gained

In this section we have highlighted the range of existing studies that exist within the CRE. These existing studies arise from projects that have, or will soon have, answered their primary research question. However, the available data provide a **hugely valuable resource for the generation of additional new knowledge through the CRE**. We will leverage off this resource by:

- meta-analysing data where this is appropriate to provide maximal power and precision;
- adding new (historical) exposure data to existing outcome data where required,
- more accurately predicting exposure to spatially heterogeneous sources of air pollution such as traffic which can be a major contributor to overall urban exposure;
- undertaking further analysis to answer new research questions, and
- further follow up of existing cohorts to establish longer term outcomes of previously measured exposures.

Further, we will explore opportunities for entirely new projects in collaboration with our colleagues and collaborators in regional countries.

2 Ensure effective transfer of research outcomes into health policy and/or practice

2.1 Targets for transfer of research outcomes into policy

2.1.1 Impact on National Environment Protection Measures (NEPM)

Air quality NEPMs create the framework within which action is taken to improve air quality in Australia and the effectiveness of that action is evaluated. A critical element in this is the setting of standards for the common ambient air pollutants. Our research is directly relevant to that criterion-setting process. For example, ACHAPS (1.1) was commissioned by the responsible agency to provide data on the dose- response relation between air pollutants and children's respiratory health. However, other studies such as the Older Peoples Study (1.3) and the "ESCAPE"-type analysis based on the cohort studies in three cities (1.11) will yield outcomes, including dose-response relations, that are directly relevant to the criterion-setting process.

2.1.2 Impact on urban planning and transport planning

In the context of urban consolidation the co-location of transport corridors, particularly roads, and homes represents an increasing challenge for urban planners. Increasing personal exposure to traffic-related air pollution is one of the important consequences of this co-location. The findings of our studies that focus on the effects of traffic-related air pollution, including the Lane Cove Tunnel study (1.2), UPTECH (1.5) and the "ESCAPE"-style analyses of cohorts (1.11) are directly relevant to that policy dilemma.

2.1.3 Impact on infrastructure development

Airports, road tunnels, motorways, mines, power stations and factories all pose a threat to the local environment and, potentially, to human health. Our CIs have all had substantial experience in evaluating the health risks associated with these developments. The Lane Cove Tunnel study (1.2) arose from the need to assess the impact of infrastructure developments. There are both specific and general policy lessons to be learnt from such studies.

2.1.4 Impact on World Health Organisation guidelines

Our proposal will contribute to the provision of tools for management of air quality based on scientific knowledge, by leading and contributing to the development of WHO guideline documents. These guidelines serve as reference points for the national and international professional community. In particular, CI Morawska has worked closely with the WHO for over thirteen years, as a member of working groups for: (i) Hazard Prevention and Control in the Work Environment: Airborne Dust, 1998; (ii) WHO Health Guidelines for Episodic Vegetation Fire Events, 1999; (iii) Guidelines for Concentration and Exposure-Response Measurements of Fine and Ultra Fine Particulate Matter for use in Epidemiological Studies, 2002; (iv) WHO Air Quality Guidelines Global Update, 2005; (v) Indoor Air Quality Guidelines: Dampness, Mould and Ventilation, 2009; (vi) Biological Agents in Indoor Environments: Assessment of Health Risks, 2009; and (vii) WHO Guidelines for Indoor Air Quality: Selected Pollutants, 2010.

2.2 Advisory board

To ensure that effective knowledge transfer and translation does take place it is important to have effective communication channels with end-users. This is relevant to the framing of research questions, but also to the interpretation of research findings and their implications for policy. To this end we will establish an Advisory Board incorporating representatives from jurisdictions' environmental health branches (who are represented nationally on EnHealth) and environment departments, who are represented on the Air Quality working group (AQWG) of the EPHC. The chair of AQWG (Simon Smith) and several of the members of the committee have indicated their support for this CRE and willingness to serve on the board. This Advisory Board will be convened biennially and will also include experts in scientific communication.

2.3 Public seminars on air quality and respiratory health

The general public are key stakeholders in the subject area of this CRE. Many citizens have a keen interest in air pollution and its effects on health. We plan to host an annual series of public seminars in Brisbane, Sydney and Melbourne. These seminars will include presentations from CIs in the areas of their research expertise. This will be an opportunity for interested citizens to learn about the research our investigators are undertaking and also to hear their interpretation of the most recent data from international studies. We will time these seminars to coincide with visits by our international collaborators and AIs so that they will be able to contribute to them.

2.4 Website

We will use our website to host plain English descriptions of the latest findings from our research projects, notices of upcoming events and links to other informative national and international Web sites. We will also publish biennial e-bulletins to provide information about newly published systematic reviews on air pollution and health.

2.5 Training workshops

2.5.1 Risk assessment

A major stimulus for interest in the health effects of air pollution is the evaluation of risk arising from new or existing developments, especially in transport, mining or industrial infrastructure. Proponents and opponents, as well as staff from regulatory agencies, need skills to better interpret findings from epidemiological studies in undertaking or evaluating risk assessment.

2.5.2 Implications of recent research on air pollution

Regulators, engineers, planners, consultants to industry and many other professionals regularly have to consider the impact of air pollution on human health in their work. Few have access to state-of-the-art information on the subject.

All of the investigators in this CRE have substantial experience in these areas. We will utilise this experience to transfer that knowledge to interested parties in a series of workshops. We propose to conduct at least two such workshops in each of Brisbane, Sydney and Melbourne during the course of the CRE. Where possible we will attach the workshops to conferences of professional societies and involve our international visitors in them. We expect that these will be self-funding.

2.6 Research synthesis

An important aspect of our vision for this CRE is the synthesis of available evidence on key topics relevant to policy and to the direction of future research. The topics for evidence synthesis will be determined by the investigators during the progress of the CRE in the light of emerging new data and policy needs and in consultation with other researchers, clinical and public health practitioners, people working in the relevant policy areas and advocacy groups. Interaction with our advisory board will help to inform this process. Each synthesis will be performed under the supervision of one or more of the CIs or AIs. We will ensure that all of the post-doctoral fellows are actively engaged in this aspect of the CREs work.

2.7 Our team's prior involvement in transferring evidence

2.7.1 Our relationships with relevant professional organisations

The Chief Investigators are all active in their various professional societies and could be regarded as key opinion leaders locally, nationally and, indeed, internationally. This is important in giving research findings clinical and public health credibility. As can be seen from the profiles, CIs have professional networks and standing in their clinical, public health and research areas.

2.7.2 Implementation and translation of research finding into evidence-based practice

With their close interest and expertise in evidence-based medicine, our CIs are particularly able to promote the inclusion of our findings into evidence-based guideline development. For example, CI Abramson chaired and CI Dharmage was a member of the National Asthma Council committee that developed a position paper and information brochures on air pollution and asthma for GPs and the community. CI Morgan has served on several National Environment Protection Council (NEPC) and EnHealth Committees including: Health experts group to review health effects information for the review of the Ambient Air Quality NEPM (2006-2008); Editorial committee of the EnHealth Council guide to indoor air quality in the home for buyers, builders, and renovators; and the Risk Assessment Task Force, a NEPC committee evaluating risk assessment methodologies for the development of Australian ambient air pollution standards. CI Marks is the chair and CI Jones is a member of the NSW Chief Health Officer's Expert Advisory Committee on Air Pollution.

3 Develop the health and medical research workforce

Our vision for the workforce that will lead future research on air pollution and its effect on health in Australia is one that comprises individuals with deep expertise in one or two aspects of science relevant to this task but also with a broad understanding of other relevant disciplines and how they relate to their own area of expertise. For example, we will be developing biostatisticians who will be leaders in the application of cutting edge statistical methods to air pollution research and who will also have knowledge of the epidemiological methods relevant to the field as well as important aspects of air pollution measurement and modelling. We will also engage air chemists and physicists to develop their craft and expertise and enable their engagement with epidemiologists, biostatisticians and geographers. Our epidemiologists will have the opportunity to learn about air pollution measurement and to participate in research on the distribution of ultrafine particle deposition in human airways with CI Morawska.

The air pollution researchers that will emerge from this CRE will understand the policy and scientific context of their research. They will have experience in communicating with the scientific, policy and lay community about their research and that of others. They will have skills appropriate for collaboration with others. They will have demonstrated their capacity for generating original ideas for research, developing research protocols, funding and implementing their projects, and carrying them through to publication and to translation into policy.

The program of research we have outlined in section 1 is diverse, extensive and at the cutting edge of air pollution science. It represents a uniquely valuable setting in which to develop the careers of future leaders in this field of research who fulfil the vision outline above.

3.1 Post-doctoral Fellows Program

We will fund 3.0 FTE post-doctoral fellows each year for the life of the CRE. We have identified three excellent candidates for the post-doctoral fellowship positions. Christine Cowie is an epidemiologist with a background in environmental health policy who has been working on the Lane Cove Tunnel (1.2) study and will complete her PhD studies during 2011. Dr Martine Dennekamp obtained her PhD from the University of Aberdeen for a study of the health effects of particulate air pollution on patients with chronic lung disease. She was a chief investigator on an NHMRC funded study of the cardiac effects of bushfire smoke. She has published on urban air pollution and out of hospital cardiac arrests (#129080). She is leading the air pollution component of the MACS study (1.10). Mandana Mazaheri is a scientist with a multidisciplinary background in physics, nuclear engineering and environmental science, who is an expert in the Instrumental Neutron Activation Analysis (INAA) method for measuring $PM_{2.5}$ and PM_{10}. She completed her PhD in the field of aerosol physics in 2009 and she is currently working on the UPTECH study (1.5). However, all these positions will be advertised and filled by competitive recruitment. The named candidates will participate in this process. The selection criteria will include academic merit, skills relevant to the mission of the CRE and potential for a future role consistent with vision outlined above. In addition we will use the selection process to ensure that there is both a geographic and discipline-based spread of appointees. Fellows will be appointed for a maximum tenure of three years with the expectation that they will "roll-over" into other funding schemes within that period of time.

Each post-doctoral fellow will have one of the CIs as a principal mentor to guide his or her development. The mentor and fellow will cooperatively set targets for research productivity and grant success, commensurate with the career stage and the norms for the specific discipline. As part of this process mentors will encourage Fellows to achieve independent NHMRC or ARC grants success.

For each Fellow, we will establish a program of interaction with CRE CIs in their own discipline and in other disciplines relevant to air pollution research (i.e. air quality measurement, statistics, epidemiology, toxicology, and policy). We expect that this will include visits to work with interstate CIs for periods of up to six weeks. These will be funded by the CRE.

Research administration is an important part of research and we will ensure that the Fellows gain skills in this area. Each year, one Fellow will be assigned to work one day per week over-seeing the administrative aspects of the CRE as its Executive Officer (see 4.1.1). We also expect Fellows to gain experience in engaging with general public and stakeholders. Participation in the Advisory Board (section 2.2) and in other research translation activities will form part of their program.

3.2 PhD program

We will provide two forms of financial support for PhD scholars. We will provide a limited number of full PhD stipends on conditions equivalent to those of the NHMRC Post-graduate scholarships. These will be funded for up to three years for each scholar. In addition, we will provide top-up funding for candidates who have been successful in gaining NHMRC Post-graduate scholarships or Australian Post-graduate Awards (APAs). These will be valued at $10,000 per year for three years

and will contribute towards research costs and the cost of presenting work at national or international conferences.

All funding for PhD scholars will be advertised and awarded competitively. In addition to the conventional criteria the applicants will be expected to demonstrate the relevance of their work to the mission of the CRE. Each funded scholar will be required to have a CRE CI or AI as a supervisor or associate supervisor.

3.3 Structured program of training

We will establish a structured program of training for CRE post-doctoral fellows and PhD scholars. This will include:

- ***Developing foundation skills*** of the PhD scholars by having them complete epidemiology and biostatistics units within MPH courses and a course on relevant statistical packages.
- ***Developing advance skills through*** *ad hoc* short courses on specialised and cutting edge aspects of epidemiological and biostatistical methods. We will engage visiting experts to run these as appropriate. Where possible, we will link these to meetings of professional societies and invite external, fee-paying participants to attend. We expect this aspect of the training program will be self-funding.
- ***Specialised training in*** engagement with the media and in risk communication.
- ***Sharing and developing knowledge and skills*** through monthly webinars with videoconferencing linking all CRE fellows and scholars in the CRE. Each of our fellows and scholars will take turns in hosting these events, which will include journal reviews and research presentations.
- ***Making sure our fellows are at the cutting edge and have opportunities to develop international links*** through a program of visits by international leaders in our fields of research. These visits will include our international AIs but will not be limited to them.

3.4 CIs track record in PhD and Post-doctoral supervision

The CIs have substantial experience in supervision of PhD students and post-doctoral fellows. CI Marks has supervised or co-supervised seven completed PhDs and has six current PhD students as well as two post-doctoral fellows. CI Jalaludin has co-supervised two PhD students to completion, is currently supervising one PhD student and one DrPH student, and co-supervising one PhD students (one with CI Marks) and one DrPH student. CI Abramson has supervised 14 PhD candidates to completion and together with CI Dharmage co-supervised 4 PhD candidates, of whom 2 have completed. One of them won a University award for his doctoral thesis. CI Dharmage has also supervised seven post-doctoral fellows, nine PhD students (six as the primary supervisor), and is currently supervising six PhD students (two as primary supervisor). CI Leeder has supervised 21 PhD students to completion. CI Morgan has supervised or co-supervised two completed PhDs and is currently supervising an NHMRC Research Fellow and two PhD students. CI Williams has been supervised nine completed supervised PhDs (four of whom won Dean's commendations) in the last five years and currently co-supervises 13 PhD students. She currently supervises (as main supervisor) two post-docs and has supervised a total of seven over the last 10 years. CI Morawska has supervised 13 completed PhDs as primary supervisor and 6 as co-supervisor. She has 10 current PhD students as primary supervisor and three as co-supervisor. She has five current and four past post-doctoral fellows. CI Jones has supervised one completed PhD and is co-supervisor for three current PhD students.

4 Facilitate collaboration

4.1 Working collaborations and intellectual exchange

Air pollution research in Australia is conducted in a piecemeal fashion by small groups working in isolation. Australia's research output and sophistication in this field lags behind the US and Europe. This CRE, encompassing a critical mass of Australian researchers engaged in air pollution research, will allow us to integrate our research efforts, increase the sophistication of our research methods (e.g. by use land use regression models and utilising existing cohorts) and also develop strategic thinking around the air pollution research directions for Australia.

Currently, the CRE investigators have collaborated on air pollution studies above and beyond the constraints imposed by limited resources. We will put the following structures and policies in place so that continuing the working collaborations and intellectual exchange within and beyond the CRE will be sustainable and independent of CIs.

4.1.1 Governance arrangements

The CRE has a bold vision, a substantial number of goals to achieve and strategies to implement, and a large cast of players with which to work. Effective governance will be crucial to a successful outcome. The CRE activities will be guided by a management committee comprising all investigators. This will be chaired by one of the CIs and will meet twice a year. It will be responsible for overall strategic directions, financial oversight, establishing and monitoring a work plan, and overseeing the activities of three main sub-committees: research; research training; and research translation & communication. These sub-committees, which will each comprise three to five CIs or AIs, will meet more often than the main committee. Each will develop a work plan for implementation of the CRE's strategy and will monitor the implementation of that work plan.

The **Research sub-committee** will be responsible for promoting research productivity and collaboration within the CRE. This will include the task of allocating seed funding grants. The **Research training sub-committee** will be responsible for awarding post-doctoral fellowships and PhD stipends and top-ups. It will also oversee the allocation of mentors and the implementation of the structured program of training. The **Research translation & communication sub-committee** will oversee these activities of the CRE, including establishment of the Advisory Board, website, workshops and seminars.

We will assign one of the post-doctoral fellows to act as **Executive Officer for the CRE** one day per week. This person will have responsibility for the week-to-week implementation of the work plan, for convening the main committee and the sub-committees, for managing communication among the members of the CRE and for overseeing the accounts. In this last task, he or she will work with the accounts staff at the Woolcock (the host institution).

4.1.2 Seed research funding

The CRE will allocate seed funding, up to the value of $20,000, for CRE researchers (including post-doctoral fellows and scholars) to support activities leading to successful external grant applications. These may be used to fund the collection of pilot data, purchase small items of equipment, preparation of systematic reviews or hosting a meeting of collaborators. Proposals deemed most likely to lead to a successful grant application will be funded and will also be allocated a CI mentor. Preference will be given to proposals that engage several collaborators from the CRE. The CRE will seed fund up to 5 projects per year. The Research sub-committee will oversee the allocation of seed funding and will develop formal selection criteria.

4.1.3 Other mechanisms for effective working collaborations and intellectual exchange

Our structured programs in training (see 3.3), extensive activities in translation (see 2) and our shared supervision and mentoring arrangements will all contribute to effective working collaborations and intellectual exchange. Some specific projects that will leverage off the collaborative arrangements of the CRE are highlighted here.

Online database

The CRE investigators will be engaged in projects holding a large amount of data on health and air pollution from various epidemiological studies. We propose to consolidate these data into a spatially- and temporally-resolved, confidential data base of Australian air pollution and health data. This online data base will facilitate efficient access to these data for CRE researchers and where appropriate future air pollution and health research. The data base will be based on a model being implemented by CI Morgan, AI Johnston and colleagues for the biomass smoke and health project (1.4) which utilises a Geographic Information System Server hosted by the National Computer Infrastructure Facility and provides online access to clean validated data for accredited users. AI Chandra will provide geospatial expertise to the CRE and collaborate in this aspect of the research.

International Collaboration on Air Pollution & Pregnancy Outcomes (ICAPPO)

There is increasing evidence that prenatal exposure to ambient particulate matter has detrimental effects on birth weight (30-32). Birth weight is an important predictor of perinatal and infant mortality (33), childhood morbidity and disability (34), and the presence of chronic diseases later in life such as cardiovascular disease and diabetes (35, 36). However, studies to date have not reported consistent results and have been difficult to synthesize. The critical next research step involves analyses of existing datasets using standardized methodological approaches for pooled data and meta-analysis to disentangle true differences in associations from methodological differences among studies, with a particular emphasis on exposure metrics, identifying sensitive periods of exposure and confounding and effect-measure modifiers (32, 37, 38).

The overall aim of ICAPPO is collaboration is to explore the effect of air pollution exposure during pregnancy on pregnancy and birth outcomes. The collaboration includes 20 research groups from 12 countries and CIs Jalaludin and Morgan are the Australian CIs (#00909462, #00909513). An important aspect of the ICAPPO strategy is to standardise exposure metrics and analytical techniques. The Australian CIs will work with the CRE investigators on this task.

Regional studies

Several of the investigators have collaborative relationships or ongoing projects in our region including Vietnam, Indonesia, Malaysia, and China. CI Jalaludin was involved in investigating the effects of the SE Asian forest fires and deaths in Malaysia(39). CI Abramson is collaborating on asthma research with the Monash campus in Kuala Lumpur. CI Marks has an ongoing active collaboration on lung health research with colleagues at the National Lung Hospital in Hanoi, Vietnam and University of Medicine and Pharmacy, in Ho Chi Minh City, Vietnam. Air pollution is an emerging area of research interest in our region and, during the course of the CRE, we will use these existing linkages and new linkages to develop new projects investigating health effects of air pollution in these countries.

4.2 The relationship with other groups in the particular field of research

There are only a small number of research groups conducting air pollution epidemiological research in Australia and they are scattered across the country. The investigators in this CRE proposal represent the majority of the research groups conducting air pollution research in NSW, Victoria, Queensland and Tasmania. They also have links with an air pollution research group in WA.

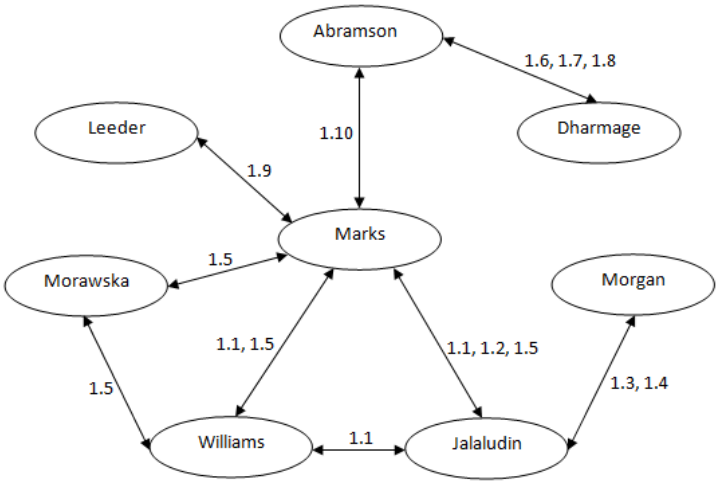
The CRE investigators have links with many government and non-government agencies related to air pollution. For example, CIs Marks, Jalaludin and Morgan and proposed PRP Cowie have strong links with the NSW Health and NSW Department of Environment (DECCW); CIs Jalaludin and Morgan and proposed PRP Cowie conducted an air pollution workshop for staff of DECCW; CIs Jalaludin and Morgan have provided consultancies to DECCW and EPA Victoria. CIs Abramson and Dharmage have also collaborated with CSIRO Marine & Atmospheric Research on NHMRC funded projects (#236934, 334098) resulting in joint publications (#33360, 761286)

CRE investigators are also been involved with international collaborators providing CRE researchers with international opportunities. Some of these are outlined in above (section 4.1.3). CI Leeder has long-standing associations with Professors Doug Dockery (Harvard University, Boston), and AI Ross Anderson (St Georges Hospital, London), both eminent air pollution epidemiologists. Our international AIs (Brunekreef and Anderson) will be instrumental in facilitating international collaborations and AI Brunekreef has hosted CI Marks on a sabbatical visit in 2008.

4.3 Integration and cohesiveness of the team

This team of Chief Investigators has been deliberately selected, not only to build on existing collaborative linkages, but also to develop a multi-disciplinary team with the necessary skills and expertise to lead air pollution research in Australia. Since the focus of this research effort is on human health effects of air pollution and its relevance to policy, there is strong core of environmental epidemiologists (CIs Marks, Jalaludin, Abramson, Morgan and Dharmage). As a group we have decided that expertise in toxicology, advanced statistics, health policy and air physics and chemistry are crucial to building the team we need to tackle the challenges of air pollution research in Australia. We are fortunate to be joined by Australia's leading experts in these fields (CIs Jones, Williams, Leeder, and Morawska), all of whom have existing collaborative linkages with one or more of the epidemiologists. In this section we highlight the strength of those collaborative linkages.

There are a number of existing collaborations among the CRE CIs that are relevant to air pollution and its health effects. The collaborations that form the basis of the CRE research projects are highlighted in the figure below (numbers refer to projects listed in section 1).



Some of collaborations among the investigators have extended over nearly two decades. CI Marks first published with CI Leeder in 1994 (40) and most recently in 2010 (#10447302), with CI Abramson first in 1995 (41) and last in 2007 (#5413430), with CI Jalaludin first in 2000 (42) and last in 2010 (#10447294), and with CI Morgan in 2002 (43). CI Jalaludin and Morgan first published together in 2005 (44) and most recently in 2010 (#5977354). CI Leeder and Jalaludin's main period of collaboration was in the 1990s (45-47). CI Dharmage and Abramson began publishing together in 1999 (48) and their most recent joint publication was in 2010 (#00203028).

The publication record highlights the substantial record of collaboration among the investigators. There have been 89 publications with 2 or more CIs as joint authors. Furthermore there have been 43 grants awarded that involve two or more of this CRE's CIs, including 12 NHMRC and 3 ARC grants. Seven of these grants involved three or more CRE CIs.

Further measures to enhance integration and cohesiveness of the CRE team will revolve around establishing criteria for authorship and intellectual property (this role will be overseen by the **CRE Research sub-committee)**, ensuring that investigators have meaningful leadership roles within the CRE, ensuring that there are group successes rather than individual successes, setting common goals and targets for measuring the success of the CRE and avenues for investigators and trainees to achieve personal goals within the CRE.

The high level multi-disciplinary nature of this team and its record of productive collaboration foreshadows cohesion and integration during the life of the CRE and beyond.

5 Record of Research and Translation Achievement

This CRE aims for excellence in research, research translation and training. Our track records indicate that we have the capacity and experience to achieve this aim. The research achievements of the CIs have been widely recognised. CI Marks was awarded the Research Medal of the Thoracic Society of Australia and New Zealand (TSANZ) in 2010 and the NHMRC Achievement Award for the higher ranked Practitioner Fellowship application in 2010. CI Abramson will be awarded the TSANZ Research Medal for 2011. CI Williams is the recipient of the Kenneth Warren Prize from the Cochrane Collaboration and the Wyeth Research medal from the Australian Medical Association.

Many of the CIs are making major contributions to their discipline. For example, CI Abramson has senior role in the Australian Lung Foundation guidelines for the management of COPD (COPDX) and has also written position papers for the National Asthma Council. CI Morawska has been Associate Editor of Science of the Total Environment (2007), on the Editorial Board of Atmospheric Environment, Indoor Air, J Aerosol Science, Environmental Science and Technology (continuing) and President of the International Society of Indoor Air Quality and Climate (2000-2003). CI Leeder received the Sidney Sax Prize from the Public Health Association of Australia. CI Morawksa has received several awards including Certificate of Achievement for Outstanding Research Success from the Faculty of Science, QUT. CI Dharmage has received awards for Excellence in early career research and Higher Degree Research Supervision from the University of Melbourne. She is also on the editorial board of Clinical & Experimental Allergy.

One recent example of the engagement of the investigators in environmental health policy was the Health and Unflued Gas Heaters study (#10447294), which involved CIs Marks and Jalaludin and AI Smith as investigators and CI Leeder as chair of the advisory committee for the NSW Dept of Education. On the day of publication of our findings the NSW Minister of Education announced that the government would replace all unflued gas heaters in NSW schools. Other examples include the ACHAPS (1.1), which was commissioned by the National Environment Protection Council and will directly influence the setting of the new air quality NEPM for Australia. Several of our CIs (Morawska, Williams, Morgan, Jalaludin, Abramson and Marks) have conducted commissioned research or reviews on behalf of the National Environment Protection Council.

Our CIs are actively engaged with the Australian community. For example, several are sought after for media comment on public health and health services policy (CI Leeder), asthma, tuberculosis and air pollution (CI Marks), asthma and COPD (CI Abramson) and air pollution (CI Morawska). Many serve on international as well as government advisory boards and committees. CI Jones has been engaged in the University of Western Sydney Headstart program – bringing indigenous kids into School Of Medicine to consider health careers/ improve health literacy.

The investigators in this CRE are each productive, innovative and successful academics with complementary skills and expertise related to research on air pollution and its effects on health. There are existing, long-standing collaborations among several of the investigator team and more recent collaborations between others. The proposal outlined here represents our approach to adding maximum value to those existing strengths by (a) sharing existing data and seeding new projects to advance research objectives, (b) extending our existing linkages with policy stakeholders and the wider community to maximise the translation of evidence into policy and practice and (c) developing a new multi-skilled research workforce that is capable of tackling the major environmental health challenges of the future.

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