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# **EPIDEMIOLOGY OF NON-COMMUNICABLE DISEASES**

A Collection of Published papers Presented in Application for the  
Degree of Doctor of Science at Massey University

(Volume 1)

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## **ABSTRACT**

The scientific publications contained in this thesis represent more than 20 years of work in the epidemiology of non-communicable disease. Chapter 1 includes methodological papers that are relevant to non-communicable diseases and epidemiology in general. This work falls into four main areas. Firstly, several papers discuss the analysis of epidemiologic studies. These particularly involve work that I did in the 1980s on the analysis of cohort studies, particularly involving time-related factors. At that time, there were well-established methods for analysing case-control studies, but the analysis of cohort studies was less developed, and there were few programmes or analytical approaches available for taking time-related factors into account. More recently, I have published on epidemiologic concepts of interaction and the implications for approaches to data analysis. Secondly, two papers from the 1980s discuss the epistemological basis of epidemiologic research. At that time, the leading textbook of epidemiology advocated a Popperian approach to the philosophy of science. These papers discussed the limitations of the Popperian approach, and showed that the actual practice of epidemiologists was more consistent with alternative approaches to the philosophy of science. Thirdly, several papers discuss the principles of epidemiologic study design. My contributions particularly involve the theory and practice and case-control studies, and the demonstration that these do not involve “backwards causality” or a radically different study design to that used for cohort studies. Finally, in recent years I have played a major role in an ongoing debate on the future of epidemiology, and published a series of papers on the need for epidemiology to rediscover the population perspective and to use theories and methods that take the population context into account.

Chapters 2-5 then include substantive studies of these particular public health issues, as well as more specific methodological papers arising from these studies. My early interest was in occupational and environmental health, with a particular emphasis on cancer, and this work is included in chapter 2. This work falls into three major areas. Firstly, my methodological work particularly includes the textbook of occupational epidemiology published by Oxford University Press in 1989, which I co-authored. This also produced a series of papers on the theory, practice, and teaching of occupational epidemiology. Once again, it particularly involved the analysis of cohort studies, and the design of case-control studies for the specific situation of occupational

health research. Secondly, my occupational cancer work has particularly included studies of cancer in farmers and related occupations. These studies were the first to show that meat workers have an increased risk of some types of cancer. This work has also included the first occupational cancer cohort study in New Zealand, which examined cancer risk in nuclear test veterans. Finally, I have also studied the particular issues of occupational cancer in developing countries, and the more general issues of environmental change and human health.

Chapter 3 includes papers on socio-economic determinants of health, with a particular emphasis on non-communicable disease. In the 1980s I conducted the first studies of socio-economic differences in health and life expectancy in New Zealand. Since the first publication in 1983, at a time when there was little interest in this field of research, this has grown to become a major area of research in New Zealand. My work in Maori health has involved assisting the work of the late Professor Eru Pomare and others in documenting and discussing the causes of differences in health between Maori and non-Maori in New Zealand. This included the first studies to show that the high mortality rates in Maori were not solely due to socio-economic factors, but also represented problems of access to health care for Maori.

Chapter 4 covers studies of asthma mortality, particularly the studies of the role of fenoterol in the New Zealand asthma mortality epidemic of the 1970s and 1980s. These studies were the first to identify that the beta agonist fenoterol was responsible for an epidemic of asthma deaths in New Zealand. These studies were highly controversial, and were strongly criticised, but eventually the New Zealand Ministry of Health restricted the availability of fenoterol in New Zealand and the asthma death rate immediately fell by one half. Unlike the other chapters in this thesis, the work described in this chapter was more clearly done as part of a group, rather than by myself as an individual. The group included an epidemiologist (myself), a clinical research, respiratory physician and a pharmacologist. Inevitably with such a multidisciplinary approach the authorship was variable, although I played the major role in the design and analysis of the epidemiological studies. I have included several review papers since they give an overview of research in this area, and the relative contribution of my own studies to the development of this debate.

Finally, chapter 5 includes studies on the prevalence, causes and management of asthma, as well as related methodological work. This work falls into four main areas. Firstly, I have produced a textbook of asthma epidemiology, published by Oxford University Press. This has involved a substantial amount of work in developing the theory and practice of epidemiology in the context of asthma. This is a relatively new field, since asthma is a non-fatal chronic disease that is difficult to diagnose, and asthma studies usually involve prevalence rather than incidence or mortality. This work has led to a number of review papers on asthma epidemiology methods. Secondly, I have been heavily involved in the development of the International Study of Asthma and Allergies in Childhood (ISAAC). Phase I of the study involved more than 700,000 children in 155 centres in 60 countries, and Phase III is currently in progress. Thirdly, in more recent years my research has focussed on the primary causes of asthma, and particularly on the role of non-allergic mechanisms. In addition to specific studies on environmental and occupational causes of asthma, I have published a series of reviews and commentaries that question the importance of allergic mechanisms for asthma. This series of papers is becoming increasingly influential in re-orienting asthma research towards a greater interest in non-allergic mechanisms. My current research interests focus on studies of these mechanisms.

## ACKNOWLEDGEMENTS

The scientific publications contained in this thesis represent collaborations with a large number of people over more than 20 years. I was introduced to the field of epidemiology by Professor Allan Smith and the late Professor Ken Newell, and much of my early work in occupational and environmental health (chapter 1) was conducted in collaboration with the former (who was my PhD supervisor). After completing my PhD I spent two years at the University of North Carolina at Chapel Hill, particularly working with Professor Carl Shy and Dr Harvey Checkoway. In recent years much of this work has been done with various PhD students, including Peter Bethwaite and Dave McLean, and with collaborators at the International Agency for Research on Cancer (IARC) where I spent one year on sabbatical; the latter particularly include Dr Paolo Boffetta and Dr Manolis Kogevinas. My work in socio-economic determinants of health (chapter 2) has particularly been conducted with Professor Peter Davis, and the Maori health aspects have been conducted with the late Professor Eru Pomare and more recently with Irihapeti Ramsden, Lis Ellison-Loschmann and Chris Cunningham. Much of my work in asthma mortality, morbidity, prevalence and causes has been conducted with colleagues at the Wellington Asthma Research Group at the Wellington School of Medicine (Professors Richard Beasley, Julian Crane and Carl Burgess), and the late Professor Eru Pomare has particularly contributed to my work on asthma management.

Most of this work was conducted at the Wellington School of Medicine (University of Otago), but in recent years I have been based at Massey University and I wish to thank the University and its staff for its excellent support for my ongoing research programme. I wish to thank all past and present staff of my various research groups, but particularly those currently working with me at the Massey University Centre for Public Health Research for making it such an enjoyable and stimulating place to work.

Finally, I acknowledge the many years of love and support from my family, Lynette, Anna and Lucy.

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## INTRODUCTION

The scientific publications contained in this thesis represent more than 20 years of work in the epidemiology of non-communicable disease. I started this work in 1979 as a bio-statistician at the Wellington School of Medicine. I rapidly realised that doing your own studies was much more interesting than analysing other people's, and I therefore completed a PhD in epidemiology, and have worked in the field ever since, moving to Massey in the year 2000. During this time, my work has covered a number of different aspects of the epidemiology of non-communicable diseases, as well as more fundamental issues of the theory and practice of epidemiology. This is the focus of this thesis and I have not included work in other fields (e.g. hepatitis B, clinical trials) that is not relevant to the epidemiology of non-communicable disease.

Rather than give an overview in this introduction of my contributions to the field, I have discussed my contributions in the context of each separate chapter. Thus, each chapter starts with an introduction that discusses my work in the relevant field, and my specific contributions to the papers which are included in this thesis. The total number of publications is quite large, and includes several books. For each chapter I have therefore only included the key papers (and copies of the tables of contents of the key books), and other publications are listed but the full texts are not included. Almost all of this work was done in collaboration with various colleagues (see acknowledgements) and there are many key papers for which I am not the first author. In particular, I was not the first author for papers produced by colleagues or students that I was supervising, even if I had conceived the project and written the protocol and grant application. On the other hand, I have produced a number of review papers, and presented a number of invited plenary presentations to conferences, which give an overview of my work in these fields. I have therefore included some of these as key papers, and I have listed the relevant invited presentations. I have only listed such presentations if they were invited plenary addresses, and I have not listed more routine conference presentations or seminars.

Chapter 1 includes methodological papers that are relevant to non-communicable diseases and epidemiology in general. Chapters 2-5 then include substantive studies of these particular public health issues, as well as more specific methodological papers arising from these studies.

My early interest was in occupational and environmental health, with a particular emphasis on cancer, and this work is included in chapter 2.

Chapter 3 includes papers on socio-economic determinants of health, with a particular emphasis on non-communicable disease. This includes not only work on social class and health, but also work on ethnic differences in health.

Chapters 4 and 5 cover my work on asthma epidemiology, including studies of asthma mortality (chapter 4), and asthma prevalence, causes and management (chapter 5).

## CHAPTER 1

### Epidemiologic methods

#### Introduction

In the last twenty years I have worked on a number of different aspects of the epidemiology of non-communicable diseases. However, an underlying theme has been an interest in epidemiologic methods for studying these conditions. This chapter includes general papers on epidemiologic methods that are relevant to non-communicable disease and/or epidemiology and public health in general. Methodological papers that have arisen out of studies of specific non-communicable diseases (e.g. occupational cancer) are included in other chapters. In this chapter I have featured 19 papers on epidemiologic methods (other publications in this area are listed as references, but the papers themselves are not included). In all instances I am the first author, and there are only 7 papers that involve co-authors.

This work falls into four main areas.

Firstly, several papers (1,2,5,7,9) discuss the analysis of epidemiologic studies. These particularly involve work that I did in the 1980s on the analysis of cohort studies, particularly involving time-related factors. At that time, there were well-established methods for analysing case-control studies, but the analysis of cohort studies was less developed, and there were few programmes or analytical approaches available for taking time-related factors into account. More recently, I have published on epidemiologic concepts of interaction (ref 4) and the implications for approaches to data analysis.

Secondly, two papers (6,8) from the 1980s discuss the epistemological basis of epidemiologic research. At that time, the leading textbook of epidemiology advocated a Popperian approach to the philosophy of science. In theory, many prominent epidemiologists advocated a Popperian approach, but in practice very few followed such an approach, and those that tried to did not

yield useful results. These papers discussed the limitations of the Popperian approach, and showed that the actual practice of epidemiologists was more consistent with alternative approaches to the philosophy of science. This work included an invited presentation at the Latin American Congress on Epidemiology, Bahia, Brazil in 1995.

Thirdly, several papers (3,10,11,14,16,17) discuss the principles of epidemiologic study design. My contributions particularly involve the theory and practice and case-control studies, and the demonstration that these do not involve “backwards causality” or a radically different study design to that used for cohort studies. This work has led to invited presentations at the Workshop on Multicentric Studies in Europe (Florence, Italy, 1993), the 6<sup>th</sup> International Symposium on Epidemiology and Occupational Risks (Graz, Austria, 1998), and the European Respiratory Society Research Seminar on Post Genome Respiratory Epidemiology (Paris, France, 2002).

Finally, in recent years I have played a major role in an ongoing debate on the future of epidemiology (12,13,15,18,19) and the need for epidemiology to rediscover the population perspective and to use theories and methods that take the population context into account. This has involved invited plenary addresses at the First International Panum Seminar (Copenhagen, Denmark, 1999), the Millennial Symposium Series on the Future of Public Health (Harvard School of Public Health, Boston, USA, 2000), the International Epidemiology Association European Regional Meeting (Kaunas, Lithuania, 2000), and the Australasian Epidemiology Association (Canberra, Australia, 2000).

### **Featured publications**

1. Pearce NE, Cryer PC. Analysis of the components of a linear trend in proportions. *Am J Epidemiol* 1986; 124: 127-33.
2. Pearce NE, Checkoway H. A simple computer program for generating person-time data in cohort studies involving time-related factors. *Am J Epidemiol* 1987; 125: 1085-91.
3. Pearce NE, Checkoway HA. Case-control studies using other diseases as controls: problems of excluding exposure-related diseases. *Am J Epidemiol* 1988; 127: 851-6.
4. Pearce NE. Analytical implications of epidemiological concepts of interaction. *Int J Epidemiol* 1989; 18: 976-80.

5. Pearce NE, Jackson RT. Statistical testing and estimation in medical research. *NZ Med J* 1988; 101: 569-70.
6. Pearce NE, Crawford-Brown DJ. Critical discussion in epidemiology: problems with the Popperian approach. *J Clin Epidemiol* 1989; 42: 177-84.
7. Pearce NE. Incidence density matching with a simple SAS computer program. *Int J Epidemiol* 1989; 18: 981-4.
8. Pearce NE. White swans, black ravens, and lame ducks: necessary and sufficient causes in epidemiology. *Epidemiology* 1990; 1: 47-50.
9. Pearce NE. Time-related confounders and intermediate variables. *Epidemiol* 1992; 3: 279-81.
10. Pearce NE. What does the odds ratio estimate in a case-control study? *Int J Epidemiol* 1993; 22: 1189-92.
11. Pearce N, Sanjose S, Boffetta P, Kogevinas M, Saracci R, Savitz D. Limitations of biomarkers of exposure in cancer epidemiology. *Epidemiol* 1995; 6: 190-4.
12. Pearce N. Traditional epidemiology, modern epidemiology, and public health. *AJPH* 1996; 86: 678-83.
13. Pearce N, McKinlay J. Back to the future in epidemiology and public health. *J Clin Epidemiol* 1998; 51: 643-6.
14. Pearce N. The four basic epidemiologic study types. *J Epidemiol Biostat* 1998; 3: 171-7.
15. Pearce N. Epidemiology as a population science. *Int J Epidemiol* 1999; 28: S1015-8.
16. Pearce N. Issues in the design of epidemiological studies. Proceedings of the International Symposium on epidemiology and occupational risks, April 22-24, 1998, Graz, Austria. Wien, Austria: ISSA, 1999, pp 39-45.
17. Pearce N. Interpreting the results of epidemiological studies. Proceedings of the International Symposium on epidemiology and occupational risks, April 22-24, 1998, Graz, Austria. Wien, Austria: ISSA, 1999, pp 61-7.
18. Pearce N. The ecologic fallacy strikes back. *J Epidemiol Comm Health* 2000; 54: 326-7.
19. Pearce N. The future of epidemiology: a problem-based approach using evidence-based methods. *Australasian Epidemiologist* 2001; 8.1: 3-7.

## **Other publications**

20. Toniolo P, Boffetta P, Shuker D, Rothman N, Hulka B, Pearce N, (eds). Methodological issues in the use of biomarkers in cancer epidemiology. Lyon: IARC, 1997 [ISBN 92-832-2142-7].
21. Smith AH, Pearce NE. Examining mortality rates. In: Gubbins S, Rhoades DA, Vere-Jones D (eds). Statistics at work, pp 46-70. Wellington: New Zealand Statistical Association, 1982.
22. Boffetta P, Pearce N. Epidemiological studies on genetic polymorphisms: study design issues and measures of occurrence and association. In: Vineis P, Malats N, Lang M, d'Errico A, Caporaso N, Cuzick J, Boffetta P (eds). Metabolic polymorphisms and susceptibility to cancer. Lyon: IARC, 1999, pp 97-108.
23. Baker D, Pearce N. Review of epidemiological principles. In: Baker D, Calderon R, Kjellström T, Pastides H (eds). Environmental epidemiology. Geneva: WHO, 1999, pp 41-64.
24. Pearce N. Analysis and interpretation of a study. In: Baker D, Calderon R, Kjellström T, Pastides H (eds). Environmental epidemiology. Geneva: WHO, 1999, pp 181-212.
25. Brisson CS, Loomis D, Pearce NE. Is social class standardisation appropriate in occupational studies? *J Epidemiol Comm Health* 1987; 41: 290-4.
26. Savitz DA, Pearce NE. Control selection with incomplete case ascertainment. *Am J Epidemiol* 1988; 127: 1109-17.
27. Smith AH, Pearce NE, Callas PW. Cancer case-control studies with other cancers as controls. *Int J Epidemiol* 1988; 17: 298-306.
28. Crawford-Brown DJ, Pearce NE. Sufficient proof in the scientific justification of environmental actions. *Environmental Ethics* 1989; 11: 153-67.
29. Blair A, Stewart WF, Stewart PA, Sandler DP, Axelson O, Vineis P, Checkoway H, Savitz D, Pearce N, Rice C. A philosophy for dealing with hypothesized uncontrolled confounding in epidemiologic investigations. *Medicina Lavoro* 1995; 86: 106-10.

## **Invited presentations**

- June 1993:           Invited presentation on "Study design issues in multicentric studies".  
Workshop on Multicentric Studies in Europe, Florence, Italy
- April 1995:           Invited presentation on "The Philosophy of epidemiology". Latin  
American Congress on Epidemiology, Bahia, Brazil

- March 1996: Invited presentation on “Limitations of biomarkers in cancer epidemiology”. IARC Working Group on the Use of Biomarkers in Epidemiological Studies, Lyon, France
- April 1998: Invited presentations on “Issues in the design of epidemiological studies” and “Interpreting the results of epidemiological studies”. 6<sup>th</sup> International Symposium on Epidemiology and Occupational Risks, Graz, Austria
- September 1998: Invited presentation on “Molecular epidemiology in occupational and environmental health”. 13<sup>th</sup> International Symposium on Epidemiology in Occupational Health, Helsinki, Finland
- November 1998: Invited presentation on “Exposure assessment in occupational studies”. 10<sup>th</sup> Annual Colloquium of the Spatial Information Research Centre, Workshop on Exposure Assessment Methodologies, Dunedin
- January 1999: Invited presentation on “What is the future of epidemiology?” First International Panum Seminar, Danish Epidemiology Science Centre, Copenhagen
- September 1999: Invited presentation on “Chronic diseases in individuals and populations” XV International Scientific Meeting of the International Epidemiological Association, Florence, Italy
- October 1999: Invited contributions to the NIEHS Workshop on Environmental Epidemiology in the 121<sup>st</sup> Century, Raleigh, NC, USA
- February 2000: Invited presentation on “The future of epidemiology”. A celebration of Ian Prior’s life and work. Wellington School of Medicine, Wellington
- March 2000: Invited presentation on “Epidemiology and health by the people”. Symposium on “Health by the people: a celebration of the life of Ken Newell”. Liverpool School of Tropical Medicine, Liverpool, United Kingdom
- May 2000: Invited presentation on “The future of epidemiology”. Millennial Symposium Series on The Future of Public Health. Harvard School of Public Health, Boston, USA
- July 2000: Invited presentation on “Epidemiology and Health by the People”. Public Health Association Annual Conference, Palmerston North
- August 2000: Invited Presentation on “Public Health Epidemiology” at the Symposium on “The future of epidemiology” at the International Epidemiology Association European Regional Meeting, Kaunas, Lithuania

- November 2000: Invited Plenary Address on “The future of epidemiology” at the Australasian Epidemiology Association Annual Meeting, Canberra, Australia
- July 2001: Invited Plenary Address on “Public Health in the Pacific” at the Pasifika Medical Association Annual Conference, Rarotonga, Cook Islands
- August 2001: Invited presentation on “Explanations for socioeconomic differences in health in New Zealand”. Presented at the Special Symposium on Socioeconomic Differences in Health, Centre for Public Health Research, Massey University, Wellington
- December 2001: Invited presentation on “Research funding – trends and challenges”. New Zealand/Australia Health Services & Policy Research Conference, Wellington
- January 2002: Invited presentation on “The impact of recent genetic trends in the performance of epidemiology”. European Respiratory Society Research Seminar on Post Genome Respiratory Epidemiology, Paris, France

## **CHAPTER 2**

### **Occupational and environmental health**

#### **Introduction**

My work in this area has particularly focussed on occupational cancer and epidemiological methods for studying occupational and environmental health. I am first author of all but four of the 19 featured papers. This work falls into three major areas.

Firstly, my methodological work particularly includes the textbook (ref 8) of occupational epidemiology published by Oxford University Press in 1989. I was co-author of this textbook (Professor Harvey Checkoway was first author), but I contributed substantially to all aspects of the text. Overall, Professor Checkoway and myself wrote and contributed approximately equal amounts, while a third author contributed to only a few chapters. This work followed on from the methodological work described in chapter 1, but developed it in the specific context of occupational health. It produced a series of papers (3,6,7,9-12,14, 18,19,21) on the theory, practice, and teaching of occupational epidemiology. Once again, it particularly involved the analysis of cohort studies, and the design of case-control studies for the specific situation of occupational health research. This led to a number of invited presentations including the 8<sup>th</sup> International Symposium on Epidemiology in Occupational Health (Paris, France, 1991), the Finnish Institute of Occupational Health Symposium on New Epidemics in Occupational Health (Helsinki, Finland, 1994), and the 13<sup>th</sup> International Symposium on Epidemiology in Occupational Health (Helsinki, Finland, 1998).

Secondly, my occupational cancer work has particularly included studies of cancer in farmers (1,2,4) and related occupations (5,15). These studies were the first to show that meat workers have an increased risk of some types of cancer, and these studies have eventually led to the establishment of an international collaborative study by the International Agency for Research on Cancer (IARC), and agency of the World Health Organisation (WHO). This work has also

included the first occupational cancer cohort study in New Zealand, which examined cancer risk in nuclear test veterans (13,20). Other studies have examined cancer risks in pesticide producers, pulp and paper workers, and firefighters. The latter areas involve collaborative studies with IARC and other colleagues, and in most instances I am a co-author (rather than first author) but nevertheless made a substantial contribution to the study design and analysis. This work in occupational causes of cancer has led to invited plenary addresses to the US National Conference on Agricultural, Occupational and Environmental Health (Iowa, USA, 1988), and the National Cancer Institute (NCI) Workshop on non-Hodgkin's lymphomas (Washington DC, USA, 1991).

Finally, I have also studied the particular issues of occupational cancer in developing countries (16,17), and the more general issues of environmental change and human health (22,23). This work has included editing a book on occupational cancer in developing countries for IARC, and an invited contribution to the UNESCO Encyclopaedia of Life Support Systems.

### **Featured publications**

1. Pearce NE, Smith AH, Howard JK, Sheppard RA, Giles HJ, Teague CA. Non-Hodgkin's lymphoma and exposure to phenoxyherbicides, chlorophenols, fencing work and meat works employment: a case-control study. *Brit J Ind Med* 1986; 43: 75-83.
2. Pearce NE, Smith AH, Howard JK, Sheppard RA, Giles HJ, Teague CA. Case-control study of multiple myeloma and farming. *Br J Cancer* 1986; 54: 493-500.
3. Pearce NE, Checkoway HA, Shy CM. Time-related factors as potential confounders and effect modifiers in studies based on an occupational cohort. *Scand J Work Environ Health* 1986; 12: 97-107.
4. Pearce NE, Sheppard RA, Smith AH, Teague CA. Non-Hodgkin's lymphoma and farming: an expanded case-control study. *Int J Cancer* 1987; 39: 155-61.
5. Pearce NE, Smith AH, Reif JS. Increased risks of soft tissue sarcoma, malignant lymphoma and acute myeloid leukemia in abattoir workers. *Am J Ind Med* 1988; 14: 63-72.
6. Pearce NE, Checkoway HA, Dement JM. Exponential models for analyses of time-related factors, illustrated with asbestos textile worker mortality data. *J Occ Med* 1988; 30: 517-22.

7. Pearce N. Multistage modeling of lung cancer mortality in asbestos textile workers. *Int J Epidemiol* 1988; 17: 747-52.
8. Checkoway H, Pearce NE, Crawford-Brown DJ. *Research methods in occupational epidemiology*. New York: Oxford University Press, 1989.
9. Checkoway H, Pearce NE, Dement JM. The design and conduct of occupational epidemiology studies. I: design aspects of cohort studies. *Am J Ind Med* 1989; 15: 363-73.
10. Checkoway H, Pearce NE, Dement JM. The design and conduct of occupational epidemiology studies. II: the analysis of cohort data. *Am J Ind Med* 1989; 15: 375-94.
11. Pearce NE, Checkoway H, Dement JM. The design and conduct of occupational epidemiology studies. III: design aspects of case-control studies. *Am J Ind Med* 1989; 15: 395-402.
12. Pearce NE, Checkoway H, Dement JM. The design and conduct of occupational epidemiology studies. IV: the analysis of case-control data. *Am J Ind Med* 1989; 15: 403-16.
13. Pearce NE, Prior IAM, Methven D, Culling C, Marshall S, Auld J, de Boer G, Bethwaite P. Follow-up study of New Zealand participants in United Kingdom atmospheric nuclear weapons tests in the Pacific. *Br Med J* 1990; 300: 1161-6.
14. Pearce NE. Methodological problems of time-related variables in occupational cohort studies. *Rev Epidem et Santé Publ* 1992; 40: S43-S54.
15. Pearce NE, Bethwaite P. Increasing incidence of non-Hodgkin's lymphoma: occupational and environmental factors. *Cancer Res* 1992; 52: 5496S-5500S.
16. Pearce NE, Matos E, Vainio H, Boffetta P, Kogevinas M (eds). *Occupational cancer in developing countries*. Lyon: IARC, 1994.
17. Pearce NE, Matos M, Boffetta P, Kogevinas M, Vainio H. Occupational exposures to carcinogens in developing countries. *Annals Acad Med Singapore* 1994; 23: 684-9.
18. Pearce N. Disease clusters and high-risk occupations. *People and Work. Research Reports 1. Proceedings of the International Symposium on New Epidemics in Occupational Health*. Helsinki: Finnish Institute of Occupational Health, 1994, pp 214-20
19. Pearce N, Crane J. Epidemiologic methods. In: Harber P, Schenker M, Balmes J (eds). *Occupational and environmental respiratory disease*. St Louis, MI: Mosby, 1995, pp 13-27.

20. Pearce N, Winkelmann R, Kennedy J, Lewis S, Purdie G, Slater T, Prior I, Fraser J. Further follow-up of New Zealand participants in United Kingdom nuclear weapons tests in the Pacific. *Cancer Causes and Control* 1997; 8: 139-45.
21. Pearce N. Occupation. In: Olsen J, Saracci R, Trichopoulos D (eds). *Teaching epidemiology*. 2<sup>nd</sup> ed. Oxford: Oxford University Press, 2001, pp 117-27.
22. Pearce N, McMichael AJ. Interactions of environmental change and human health. In: *Our fragile world: challenges and opportunities for sustainable development*. Oxford: UNESCO-EOLSS, 2001, pp 795-804.
23. Pekkanen J, Pearce N. Environmental epidemiology: challenges and opportunities. *Environ Health Perspectives* 2001; 109: 1-5.

### **Other publications**

24. Pearce NE, Sheppard RA, Howard JK, Fraser J, Lilley BM. Leukemia among New Zealand agricultural workers: a Cancer Registry based study. *Am J Epidemiol* 1986; 124: 402-9.
25. Smith AH, Pearce NE. Update on soft tissue sarcoma and phenoxyherbicides in New Zealand. *Chemosphere* 1986; 15: 1795-8.
26. Smith AH, Fisher DO, Pearce NE, Teague CA. Do agricultural chemicals cause soft tissue sarcoma? Initial findings of a case-control study in New Zealand. *Community Health Studies* 1982; 6: 114-9.
27. Smith AH, Fisher DO, Pearce NE, Chapman CJ. Congenital defects and miscarriages among New Zealand 2,4,5-T sprayers. *Arch Environ Health* 1982; 37: 197-200.
28. Smith AH, Fisher DO, Giles HJ, Pearce NE. The New Zealand soft tissue sarcoma case-control study: interview findings concerning phenoxyacetic acid exposure. *Chemosphere* 1983; 12: 565-71.
29. Smith AH, Pearce NE, Fisher DO, Giles HJ, Teague CA, Howard JK. Soft tissue sarcoma and exposure to phenoxyherbicides and chlorophenols in New Zealand. *J Natl Cancer Inst* 1984; 73: 1111-7.
30. Pearce NE, Smith AH, Fisher DO. Malignant lymphoma and multiple myeloma linked with agricultural occupations in a New Zealand Cancer Registry based study. *Am J Epidemiol* 1985; 121: 225-37.
31. Pearce NE, Howard JK. Occupational mortality in New Zealand males 1974-78. *Community Health Studies* 1985; 9: 212-9.

32. Pearce NE, Sheppard RA, Howard JK, Fraser J, Lilley BM. Time trends and occupational differences in cancer of the testis in New Zealand. *Cancer* 1987; 59: 1677-82.
33. Pearce NE, Sheppard RA, Fraser J. Case-control study of occupation and cancer of the prostate in New Zealand. *J Epidemiol Comm Health* 1987; 41: 130-2.
34. Savitz DA, Pearce NE. Occupational leukemias and lymphomas. *Semin Occ Med* 1987; 2: 283-9.
35. Checkoway HA, Pearce NE, Crawford-Brown DJ, Cragle DL. Radiation doses and cause specific mortality among workers at a nuclear materials fabrication plant. *Am J Epidemiol* 1988; 127: 255-66.
36. Reif J, Pearce NE, Kawachi I, Fraser J. Soft tissue sarcoma, non-Hodgkin's lymphoma and other cancers in New Zealand forestry workers. *Int J Cancer* 1989; 43: 49-54.
37. Pearce NE, Reif J, Fraser J. Case-control studies of cancer in New Zealand electrical workers. *Int J Epidemiol* 1989; 18: 55-9.
38. Reif JS, Pearce NE, Fraser J. Cancer risks among New Zealand meat workers. *Scand J Work Environ Health* 1989; 15: 24-9.
39. Kawachi I, Pearce NE, Jackson RT. Deaths from lung cancer and ischaemic heart disease due to passive smoking in New Zealand. *NZ Med J* 1989; 102: 337-40.
40. Savitz DA, Pearce NE, Poole C. Methodologic issues in the epidemiology of electromagnetic fields and cancer. *Epidemiologic Reviews* 1989; 11: 59-78.
41. Bonassi S, Merlo F, Pearce NE, Puntoni R. Bladder cancer and occupational exposure to polycyclic aromatic hydrocarbons. *Int J Cancer* 1989; 44: 648-51.
42. Reif JS, Pearce NE, Fraser J. Occupational risks for brain cancer: a New Zealand Cancer Registry-based study. *J Occ Med* 1989; 31: 863-7.
43. Kawachi I, Pearce NE, Fraser J. A New Zealand Cancer Registry based study of cancer in wood workers. *Cancer* 1989; 64: 2609-2613.
44. Reif J, Pearce NE, Fraser J. Cancer risks in New Zealand farmers. *Int J Epidemiol* 1989; 18: 768-74.
45. L'Abbe KA, Johnson ES, Winkelmann R, Kogevinas M, Saracci R, Bertazzi P, Bueno de Mesquita HB, Coggon D, Green LM, Kauppinen T, Littorin M, Lynge E, Mathews JD, Pearce NE, Thomas P. Use of exposure information in the International Register of persons exposed to phenoxy herbicides and contaminants. Proceedings of "Exposure monitoring in industry: an international symposium". Antwerp, Belgium, November, 1989.

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54. Bethwaite P, Pearce NE. Electromagnetic fields and cancer: an ongoing debate. *NZ Med J* 1991; 104: 225-6.
55. Kawachi I, Pearce NE. Aluminium in drinking water: is it safe? *Aust J Publ Health* 1991; 15: 84-7.
56. Saracci R, Kogevinas M, Bertazzi P, Bueno de Mesquita BH, Coggon D, Green LM, Kauppinen T, L'Abbe KA, Littorin M, Lynge E, Mathews JD, Neuberger M, Osman J, Pearce NE, Winkelmann R. Cancer mortality in an international cohort of workers exposed to chlorophenoxy herbicides and chlorophenols. *Lancet* 1991; 338: 1027-32.

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Hodgkin's lymphoma in workers exposed to phenoxy herbicides, chlorophenols and dioxins: two nested case-control studies. *Epidemiol* 1995; 6: 396-402.

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74. Bethwaite P, Cook A, Kennedy J, Pearce N. Acute leukemia in electrical workers: a New Zealand case-control study. *Cancer Causes and Control* 2001; 12: 683-9.
75. Bates M, Fawcett J, Garrett N, Arnold R, Pearce N, Woodward A. Is testicular cancer an occupational disease of fire fighters? *Am J Ind Med* 2001; 40: 263-70.
76. McLean D, Pearce N, Colin D, Boffetta P. Mortality and cancer incidence in New Zealand pulp and paper mill workers. *NZ Med J* 2002; 115: 186-90
77. Douwes J, Thorne PS, Pearce N, Heederik D. Biological agents – recognition. In: Perkins J (ed). *Modern industrial hygiene*. Vol 4. Cincinnati, OH: ACGIH, in press.
78. Carel R, Boffetta P, Kauppinen T, Teschke K, Anderson A, Jäppinen P, Pearce N, Rix BA, Bergeret A, Coggon D, Persson B, Szadkowska-Stanczyk I, Kielkowski D, Henneberger P, Kishi R, Facchini LA, Sunyer J, Colin D, Kogevinas M. Exposure to

asbestos and lung and pleural cancer mortality among pulp and paper workers. *J Occup Environ Med*, in press.

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### **Invited presentations**

- May 1988: IARC International Meeting on Cancer and Exposure to Electromagnetic Fields, Lyon
- May 1988: NCI Working Group on Pesticides and Cancer, Keystone, Colorado, USA
- September 1988: Invited presentation on "Cancer in farmers". National Conference on Agricultural, Occupational and Environmental Health, Iowa State University, USA
- February 1989: IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, Volume 48 - Flame Retardants and Textile Chemicals and Exposures in the Textile Industry, Lyon
- October 1990: IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, Volume 53 - Pesticides, Lyon
- September 1991: Invited presentation on "Methodological problems of time-related variables in occupational cohort studies". 8th International Symposium on Epidemiology in Occupational Health, Paris, France
- October 1991: Invited presentation on "Increasing incidence of non-Hodgkin's lymphoma: occupational and environmental factors". NCI Workshop on non-Hodgkin's Lymphomas. National Cancer Institute, Washington DC, USA
- December 1991: Invited presentation on "Electromagnetic fields and cancer". Symposium on Radiation and Health, Adelaide, Australia
- February 1993: IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, Volume 58 - Metals and Occupational Exposures in the Glass Industry, Lyon
- May 1994: Invited presentation on "Disease clusters and high risk occupations". FIOH Symposium on New Epidemics on Occupational Health, Helsinki, Finland

- February 1995: Invited presentation on “Electromagnetic fields and cancer”. ICOH Symposium on Radiofrequency Radiation, Auckland, New Zealand
- June 1995: NIEHS/IARC/WHO Committee on Feasibility of a Vietnam Agent Orange Studies, Vietnam
- May 1997: Invited presentation on “Dioxins and health”. Annual Scientific meeting of the Royal Australasian College of Physicians, Auckland
- September 1998: Invited presentation on “Molecular epidemiology in occupational and environmental health”. 13<sup>th</sup> International Symposium on Epidemiology in Occupational Health, Helsinki, Finland
- November 1998: Invited presentation on “Exposure assessment in occupational studies”. 10<sup>th</sup> Annual Colloquium of the Spatial Information Research Centre, Workshop on Exposure Assessment Methodologies, Dunedin
- October 1999: Invited contributions to the NIEHS Workshop on Environmental Epidemiology in the 121<sup>st</sup> Century, Raleigh, NC, USA

## **CHAPTER 3**

### **Socioeconomic determinants of health**

#### **Introduction**

This chapter includes a series of analyses I have conducted of socio-economic differences in health in New Zealand. It also includes work on related issues, particularly Maori health research which was conducted with Professor Eru Pomare.

In the 1980s I conducted the first studies (1-3,5-8,10,12) of socio-economic differences in health and life expectancy in New Zealand. This work was not particularly original in the international context (and hence did not lead to invited presentations internationally), but nevertheless played an important role establishing the importance of such factors in the New Zealand context, and exploring the methodological issues of conducting such studies in New Zealand. Since the first publication in 1983, at a time when there was little interest in this field of research, this has grown to become a major area of research in New Zealand. My main contribution internationally, apart from my general contributions to debates about the importance of studying socio-economic factors (see chapter 1), has been to make a proposal for, and to co-edit, a text on social inequalities in cancer for the International Agency for Research on Cancer (IARC) (ref 11).

My work in Maori health has involved assisting the work of the late Professor Eru Pomare and others (refs 4,9,11) in documenting and discussing the causes of differences in health between Maori and non-Maori in New Zealand. This included the first studies (3,4) to show that the high mortality rates in Maori were not solely due to socio-economic factors, but also represented a serious failing in the health services and problems of access to health care for Maori.

## **Featured publications**

1. Pearce NE, Davis PB, Smith AH, Foster FH. Mortality and social class in New Zealand. I: Overall male mortality. NZ Med J 1983; 96: 281-5.
2. Pearce NE, Davis PB, Smith AH, Foster FH. Mortality and social class in New Zealand. II: Male mortality by major disease groupings. NZ Med J 1983; 96: 711-6.
3. Pearce NE, Davis PB, Smith AH, Foster FH. Mortality and social class in New Zealand. III: Male mortality by ethnic group. NZ Med J 1984; 97: 31-5.
4. Smith AH, Pearce NE. Determinants of differences in mortality between New Zealand Maoris and non-Maoris aged 15-64. NZ Med J 1984; 97: 101-8.
5. Pearce NE, Davis PB, Smith AH, Foster FH. Social class, ethnic group and male mortality in New Zealand 1974-78. J Epidemiol Comm Health 1985; 39: 9-14.
6. Pearce NE, Howard JK. Occupation, social class and male cancer mortality in New Zealand, 1974-78. Int J Epidemiol 1986; 15: 456-62.
7. Pearce NE, Marshall S, Borman B. Undiminished social class differences in New Zealand men. NZ Med J 1991; 104: 153-6.
8. Pearce NE, Pomare E, Marshall S, Borman B. Mortality and social class in Maori and non-Maori New Zealand men: changes between 1975-1977 and 1985-1987. NZ Med J 1993; 106: 193-6.
9. Pomare E, Keefe-Ormsby V, Ormsby C, Pearce N, Reid P, Robson B, Watene-Haydon N. Hauora: Maori Standards of Health III. A study of the years 1970-1991. Wellington: Te Ropu Rangahau Hauora a Eru Pomare, 1995 [ISSN 0303-7894].
10. Pearce N, Bethwaite P. Social class and male cancer mortality in New Zealand, 1984-1987. NZ Med J 1997; 110: 200-2.
11. Kogevinas M, Pearce N, Susser M, Boffetta P (eds). Social inequalities and cancer. Lyon: IARC, 1997 [ISBN 92-832-2138-9].
12. Pearce N, Davis P, Sporle A. Persistent social class mortality differences in New Zealand men aged 15-64: an analysis of mortality during 1995-1997. Aust NZ J Publ Health 2002; 26: 17-22.

## Other publications

13. Smith AH, Pearce NE, Joseph JG. Major colorectal cancer aetiological hypotheses do not explain mortality trends among Maori and non-Maori New Zealanders. *Int J Epidemiol* 1985; 14: 79-85.
14. Smith AH, Pool DI, Pearce NE, Lyon JL, Lilley BM, Davis PB, Prior IAM. Mortality among New Zealand Maori and non-Maori Mormons. *Int J Epidemiol* 1985; 14: 265-71.
15. Pearce NE, Newell KW, Carter H. Incidence of hepatocellular carcinoma in New Zealand, 1974-78: ethnic, sex and geographical differences. *NZ Med J* 1985; 98: 1033-6.
16. Bethwaite PB, Baker M, Pearce NE, Kawachi I. Unemployment and the public health. *NZ Med J* 1990; 103: 48-9.
17. Kawachi I, Marshall S, Pearce NE. Social class inequalities in the decline of coronary heart disease among New Zealand men, 1975-77 to 1985-87. *Int J Epidemiol* 1991; 20: 393-8.
18. Marshall SW, Kawachi I, Pearce NE, Borman B. Social class differences in mortality from diseases amenable to medical intervention in New Zealand. *Int J Epidemiol* 1993; 22: 255-61.
19. Pearce N. Economic policy and health in The Year of the Family. *NZ Med J* 1994; 107: 379-81.
20. Pearce N, Bethwaite P. Social class and male cancer mortality in New Zealand, 1984-1987. *NZ Med J* 1997; 110: 200-2.
21. Davis P, Graham P, Pearce N. Health expectancy in New Zealand, 1981-1991: social variations and trends in a period of rapid social and economic change. *J Epidemiol Comm Health* 1999; 53: 919-27.
22. Davis P, McLeod K, Ransom M, Ongley P, Pearce N, Howden-Chapman P. The New Zealand Socioeconomic Index: developing and validating an occupationally-derived
23. Blakely T, Woodward A, Pearce N, Salmond C, Kiro C, Davis P. Socio-economic factors and mortality among 25-64 year olds followed from 1991 to 1994: The New Zealand Census Mortality Study. *NZ Med J* 2002; 115: 93-7.
24. Blakely T, Pearce N. Socioeconomic position is more than just NZDep. *NZ Med J* 2002; 115: 109-11.
25. Sporle A, Pearce N, Davis P. Social class differences in Maori and non-Maori aged 15-64 during the last two decades. *NZ Med J* 2002; 115: 127-31.

## CHAPTER 4

### Asthma mortality

#### Introduction

This chapter covers studies of asthma mortality, particularly the studies of the role of fenoterol in the New Zealand asthma mortality epidemic of the 1970s and 1980s. These studies were the first to identify that the beta agonist fenoterol was responsible for an epidemic of asthma deaths in New Zealand (refs 1-3). These studies were highly controversial, and were strongly criticised, but eventually the New Zealand Ministry of Health restricted the availability of fenoterol in New Zealand and the asthma death rate immediately fell by one half. The medication was also restricted in Australia and Japan (ref 8). The medication was not restricted in other countries, but the dose was halved by the company, under pressure from regulatory authorities.

Unlike the other chapters in this thesis, the work described in this chapter was more clearly done as part of a group, rather than by myself as an individual. The group included an epidemiologist (myself), a clinical research, respiratory physician and a pharmacologist. Inevitably with such a multidisciplinary approach the authorship was variable, although I played the major role in the design and analysis of the epidemiological studies. Thus, I was first author of one (ref 2), and second author of the other two papers (1,3) which first reported the association, and in practice I was supervisor of the design, analysis and writing of all three papers. I was also first author of the paper which reported the fall in mortality following the restriction of the availability of the medication (ref 6).

I have included several review papers (4,5,7,9,10) since they give an overview of research in this area, and the relative contribution of my own studies to the development of this debate. In particular, I was first author of four of the five papers, including a comprehensive review for Epidemiologic Reviews. This work also to an invited presentation at the US Food and Drug Administration (FDA) hearings on beta agonists and asthma deaths (Washington, DC, 1991), as

well as at the 2<sup>nd</sup> National Asthma Mortality Workshop (Adelaide, Australia, 1990) and the 5<sup>th</sup> West Pacific Allergy Symposium and 7<sup>th</sup> Korea-Japan Joint Allergy Symposium (Seoul, Korea, 1997).

### **Featured publications**

1. Crane J, Pearce NE, Flatt A, Burgess C, Jackson R, Kwong T, Ball M, Beasley R. Prescribed fenoterol and death from asthma in New Zealand, 1981-1983: a case-control study. *Lancet* 1989; i: 917-22.
2. Pearce NE, Grainger J, Atkinson M, Crane J, Burgess C, Culling C, Windom H, Beasley R. Case-control study of prescribed fenoterol and death from asthma in New Zealand, 1977-1981. *Thorax* 1990; 45: 170-5.
3. Grainger J, Woodman K, Pearce NE, Crane J, Burgess C, Keane A, Beasley R. Prescribed fenoterol and death from asthma in New Zealand, 1981-1987: a further case-control study. *Thorax* 1991; 46: 105-11.
4. Pearce NE, Crane J, Burgess C, Jackson R, Beasley R. Beta agonists and asthma mortality: déjà vu. *Clin Exper Allergy* 1991; 21: 401-10.
5. Beasley R, Pearce NE (eds). *The role of beta receptor agonist therapy in asthma mortality*. New York: CRC Press, 1993. [ISBN 0-8493-6761-1]
6. Pearce N, Beasley R, Crane J, Burgess C, Jackson R. End of the New Zealand asthma mortality epidemic. *Lancet* 1995; 345: 41-4.
7. Pearce NE, Beasley R, Crane J, Burgess C. Epidemiology of asthma mortality. In: Busse W, Holgate S. *Asthma and rhinitis*. Oxford: Blackwell Scientific, 1995, pp 58-69.
8. Pearce N, Crane J, Beasley R. Isoprenaline, fenoterol and asthma deaths in Japan. *Japanese J Allergy Clin Immunol* 1997; 11: 307-16.
9. Pearce NE, Beasley R, Crane J, Burgess C. Pharmacoepidemiology of asthma deaths. In: Hartzema AG, Porta MS, Tilson HH (eds). *Pharmacoepidemiology: an introduction*. 3rd ed. Cincinnati, OH: Harvey Whitney, 1998, pp 473-94.
10. Pearce N, Hensley MJ. Epidemiologic studies of beta agonists and asthma deaths. *Epidemiologic Reviews* 1998; 20: 173-86.

## Other publications

11. Pearce NE, Crane J, Burgess C, Grainger J, Beasley R. Fenoterol and asthma mortality in New Zealand. *NZ Med J* 1990; 103: 73-5.
12. Windom HH, Burgess CD, Crane J, Pearce NE, Kwong T, Beasley R. The self-administration of inhaled beta agonist drugs during severe asthma. *NZ Med J* 1990; 103: 205-7.
13. Beasley R, Smith K, Pearce NE, Crane J, Burgess C, Culling C. Trends in asthma mortality in New Zealand, 1908-1986. *Med J Aust* 1990; 152: 570-3.
14. Beasley R, Burgess C, Pearce NE, Crane J. Drug therapy and asthma death - a New Zealand experience. In: Ruffin RE (ed). *Asthma mortality: Proceedings of the second national asthma mortality workshop*, pp 6-9. Sydney: Excerpta Medica, 1990.
15. Pearce NE, Crane J, Burgess C, Beasley R. Study designs for examining death from asthma: the case-control approach. In: Ruffin RE (ed). *Asthma mortality: Proceedings of the second national asthma mortality workshop*, pp 23-6. Sydney: Excerpta Medica, 1990.
16. Beasley R, Crane J, Burgess C, Holloway L, Pearce NE. Asthma mortality and morbidity: relationship to beta agonist therapy. In: Morley J (ed). *Preventive therapy in asthma*. New York: Academic Press, 1991, pp 55-72.
17. Beasley R, Pearce NE, Crane J, Windom H, Burgess C. Asthma mortality and inhaled beta agonist therapy. *Aust NZ J Med* 1991; 21: 753-63.
18. Woodman K, Pearce NE, Beasley R, Burgess C, Crane J. Albuterol and deaths from asthma in New Zealand from 1969 to 1976: a case-control study. *Clin Pharmacol Therapeutics* 1992; 51: 566-71.
19. Crane J, Pearce NE, Burgess C, Woodman K, Robson B, Beasley R. Markers of risk of asthma death or readmission in the 12 months following a hospital admission for asthma. *Int J Epidemiol* 1992; 21: 737-44.
20. Burgess C, Beasley R, Pearce NE, Crane J. The role of fenoterol in the second epidemic of asthma deaths in New Zealand. *Allergo J* 1992; 1: 4-11.
21. Pearce NE. Adverse reactions: the fenoterol saga. In: Davis PB (ed). *For health or profit: the pharmaceutical industry in New Zealand*. Auckland: Oxford University Press, 1992, pp 75-97.
22. Beasley R, Pearce NE, Burgess C, Crane J. Different patterns of asthma mortality and their association with beta-agonist therapy. In: Mann RD, Costello JF (eds). *Beta agonists in the treatment of asthma*. London: Parthenon, 1992, pp 109-116.

23. Pearce NE, Crane J. Epidemiological methods for studying the role of beta receptor agonist therapy in asthma mortality. In: Beasley R, Pearce NE (eds). *The role of beta agonist therapy in asthma mortality*. New York: CRC Press, 1993, pp 67-83.
24. Beasley R, Pearce NE. The use of near-fatal asthma for investigating asthma deaths. *Thorax* 1993; 48: 1093-4.
25. Crane J, Burgess C, Pearce NE, Beasley R. The beta agonist controversy - a perspective. *Eur Resp J* 1993; 3: 475-82.
26. Burgess, C, Pearce NE, Thiruchelvam R, Wilkinson R, Linaker C, Woodman K, Crane J, Beasley R. Prescribed drug therapy and near-fatal asthma attacks. *Eur Resp J* 1994; 7: 498-503.
27. Beasley R, Pearce NE, Burgess C, Woodman K, Crane J. Confounding by severity does not explain the association between fenoterol and asthma death. *Clin Exper Allergy* 1994; 24: 660-8.
28. Burgess C, Crane J, Pearce N, Beasley R. Current issues relating to inhaled beta<sub>2</sub> agonist therapy in asthma. In: Commelin DJA, Midha KK, Nagai T (eds). *Topics in Pharmaceutical Sciences*. Stuttgart: Scientific Publishers, 1994; pp 63-75.
29. Beasley R, Burgess C, Crane J, Pearce N. The New Zealand asthma mortality epidemic. *Clinical Science Regional Focus Series* 1995; 88: 14-7.
30. Beasley R, Pearce N, Crane J, Burgess C. The withdrawal of fenoterol and the end of the New Zealand asthma mortality epidemic. *Int Arch Allergy Immunol* 1995; 107: 325-7.
31. Beasley R, Burgess C, Crane J, Pearce N. A review of the studies of the asthma mortality epidemic in New Zealand. *Allergy Proceedings* 1995; 16: 27-32.
32. Crane J, Pearce N, Burgess C, Beasley R. Asthma and the  $\beta$ -agonist debate. *Thorax* 1995; 50: S5-S10.
33. Pearce N. Adverse reactions, social responses: a tale of two asthma mortality epidemics. In: Davis PB (ed). *Contested ground: public purpose and private interest in the regulation of prescription drugs*. New York: Oxford University Press, 1996, pp 57-75.
34. Burgess C, Beasley R, Crane J, Pearce N. Adverse effects of beta<sub>2</sub>-agonists. In: Pauwels R, O'Bryne PM (eds). *Beta<sub>2</sub>-agonists in asthma treatment*. New York: Marcel Dekker, 1997, pp 257-82.
35. Crane J, Beasley R, Pearce N, Burgess C. Asthma deaths. In: Barnes P, Grunstein M, Leff A, Woolcock A (eds) *Asthma*. Vol 1. Philadelphia: Lippincott-Raven, 1997, pp 49-62.

36. Beasley R, Pearce N, Crane J. International trends in asthma mortality. In: 1997 The rising trends in asthma. Ciba Foundation Symposium 206. Chichester: Wiley, 1997, pp 140-56.
37. Pearce N, Beasley R, Crane J. Mortality of bronchial asthma. In: Hong C-H (ed). Proceedings of the 5th West Pacific Allergy Symposium & 7th Korea-Japan Joint Allergy Symposium, June 11-14, 1997, Seoul, Korea. Bologna, Italy: Monduzzi Editore, 1997, pp 29-36.
38. Williams C, Crossland L, Finnerty J, Crane J, Holgate S, Pearce N, Beasley R. A case-control study of salmeterol and near-fatal attacks of asthma. *Thorax* 1998; 53: 7-13.
39. Crane J, Pearce N, Beasley R, Burgess C. Asthma mortality - the New Zealand experience. *Clin Asthma Rev* 1998; 2: 15-20.
40. Beasley CRW, Pearce N, Crane J. Worldwide trends in asthma mortality during the twentieth century. In: Sheffer AL, Busse WW, Eggleston PA, Platts-Mills TAE, Sears MR, Weiss KB (eds). *Fatal asthma*. New York: Marcel Dekker, 1998, pp 13-29.
41. Beasley R, Pearce N, Crane J, Burgess C.  $\beta_2$ -agonists in severe asthma: clinical indications and precautions. In: Holgate ST, Boushey HA, Fabbri LM (eds). *Difficult asthma*. London: Martin Dunitz, 1999, pp 341-70.
42. Beasley CR, Crane J, Pearce NE. International trends in asthma mortality. In: Neffen HE, Baena-Cagnani CE, Fabbri L, Holgate S, O'Byrne P (eds). *Asthma, a link between environment, immunology and the airways*. Seattle: Hogrefe & Huber, 1999, pp 7-13.
43. Pearce N, Beasley R, Crane J. Prevention of death from asthma. *Int Review Asthma* 1999; 1: 70-79.
44. Beasley R, Pearce N, Crane J, Burgess C.  $\beta$ -agonists: what is the evidence that their use increases the risk of asthma morbidity and mortality? *J Allergy Clin Immunol* 1999; 104: S18-30.
45. Beasley R, Pearce N, Crane J. The epidemiology of asthma mortality. In: O'Connor B, Giembycz M (eds). *Clinical pharmacology of asthma*. Switzerland: Birkhauser, in press.

### **Invited presentations**

- April 1990:           Invited presentation on "Study designs for examining death from asthma". The Second National Asthma Mortality Workshop, Adelaide
- December 1991:       Invited presentation on "Fenoterol and asthma deaths". FDA hearings on beta agonists and asthma deaths, Washington, DC

June 1997:

Invited presentation on "Mortality from bronchial asthma". 5th West Pacific Allergy Symposium & 7th Korea-Japan Joint Allergy Symposium, Seoul, Korea

## **CHAPTER 5**

### **Asthma prevalence, causes and management**

#### **Introduction**

This final chapter includes studies on the prevalence, causes and management of asthma, as well as related methodological work. This work falls into four main areas.

Firstly, I have produced a textbook of asthma epidemiology, published by Oxford University Press (ref 4). This has involved a substantial amount of work in developing the theory and practice of epidemiology in the context of asthma. This is a relatively new field, since asthma is a non-fatal chronic disease that is difficult to diagnose, and asthma studies usually involve prevalence rather than incidence or mortality. Thus, the methodological issues are quite different from those involved in other non-communicable diseases such as cancer. This work has led to a number of review papers on asthma epidemiology methods (2,6,711) as well as an invited presentation at the World Asthma Meeting (Barcelona, Spain, 1998).

Secondly, I have been heavily involved in the development of the International Study of Asthma and Allergies in Childhood (ISAAC). I wrote the original protocol, did the pilot study, and have been a member of the ISAAC Steering Committee since it was established in 1990, as well as being a member of the ISAAC Executive, ISAAC Publications Coordinator, and Regional Coordinator for Oceania. The Steering Group involves 20 members and is chaired by Dr Innes Asher (University of Auckland). Phase I of the study involved more than 700,000 children in 155 centres in 60 countries. Inevitably, the number of first author publications has been small, but I have nevertheless played a major role in the design, conduct and publication of this study including two first author publications (1,9), and membership of the Writing Committee for the publication of the initial findings in the Lancet (ref 3). This work has also led to invited presentations at the European Respiratory Society (Stockholm, Sweden, 1996), the World

Asthma Meeting (Barcelona, Spain, 1998), and the Pasifika Medical Association Meeting (Rarotonga, 2001).

Thirdly, in more recent years my research has focussed on the primary causes of asthma, and particularly on the role of non-allergic mechanisms in asthma. In addition to specific studies on environmental and occupational causes of asthma (e.g. ref 12), I have published a series of reviews and commentaries that question the importance of allergic mechanisms for asthma (5,8,10,13-15). In most instances I have been first author of these publications, but for some more recent publications the first author has been Dr Jeroen Douwes, a postdoctoral research fellow who has been developing this field of research under my supervision. This series of papers is becoming increasingly influential in re-orienting asthma research towards a greater interest in non-allergic mechanisms.

### **Featured publications**

1. Pearce NE, Weiland S, Keil U, Langridge P, Anderson HR, Strachan D, Bauman A, Young L, Gluyas P, Ruffin D, Crane J, Beasley R. Self-reported prevalence of asthma symptoms in children in Australia, England, Germany and New Zealand: an international comparison using the ISAAC protocol. *Eur Resp J* 1993; 6: 1455-61.
2. Pearce N, Kimbell-Dunn M, Beasley R. Studying the prevalence and causes of asthma: strategies and methodological issues. *J Epidemiol Biostat* 1997; 2: 147-59.
3. ISAAC Steering Committee (Writing Committee: Beasley R, Keil U, Von Mutius E, Pearce N). Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis and atopic eczema: ISAAC. *Lancet* 1998; 351: 1225-32.
4. Pearce N, Beasley R, Burgess C, Crane J. *Asthma epidemiology: principles and methods*. New York: Oxford University Press, 1998.
5. Pearce N, Pekkanen J, Beasley R. How much asthma is really attributable to atopy? *Thorax* 1999; 54: 268-72.
6. Pekkanen J, Pearce N. Defining asthma in epidemiological studies. *Eur Respir J* 1999; 14: 951-7.
7. Pearce N, Beasley R. Measuring morbidity in adult asthmatics. *Int J Tuberculosis Lung Dis* 1999; 3: 185-91.

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### **Other publications**

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30. Moyes CD, Waldon J, Dharmalingam R, Crane J, Pearce NE. Respiratory symptoms and environmental factors in schoolchildren in the Bay of Plenty. *NZ Med J* 1995; 108: 358-61.
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88. Ellison-Loschmann L, Cheng S, Pearce N. Time trends and seasonal patterns of asthma deaths and hospitalisations among Maori and non-Maori. *NZ Med J* 2002; 115: 6-9.
89. Moala A, Pearce N. Asthma in Pacific people in New Zealand and the South Pacific. *Pacific Health Dialogue*, in press.

### **Invited presentations**

- September 1996:      Invited presentation on "The International Study of Asthma and Allergies in Childhood (ISAAC): study design". ISAAC Symposium, European Respiratory Society Meeting, Stockholm

- November 1997: Invited presentation on “Risk factors for asthma: an international perspective”. Third International Symposium on Mites and Domestic Design, Wellington
- December 1998: Invited presentation on “The International Study of Asthma and Allergies in Childhood”. Epidemiology Working Group, World Asthma Meeting, Barcelona, Spain
- December 1998: Invited presentation on “Epidemiologic methods in high-income countries”. Postgraduate Interactive Session on “Methodological approaches in epidemiology”. World Asthma Meeting, Barcelona, Spain
- December 1998: Invited presentation on “Strengths and limitations of ecologic studies”. Interactive Session on “ISAAC: what will we learn from phases II and III?”. World Asthma Meeting, Barcelona, Spain
- June 1999: Invited presentation on “Why is asthma prevalence increasing?” Paediatric Respiratory Group meeting, Sydney
- October 2000: Invited presentation on “ISAAC in the Pacific” at the Congrès sur l’asthme et les Maladies Respiratoires, Noumea, New Caledonia
- July 2001: Invited Plenary Address on “Asthma in the Pacific” at the Pasifika Medical Association Annual Conference, Rarotonga, Cook Islands