# The Epidemiology of Asthma and Bronchial Hyperresponsiveness in Auckland Children

*Philip Keith Pattemore*

A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Medicine

**University of Auckland**

**1991**

*Dedicated to my father, Errol Keith Pattemore, and my mother, Elizabeth Pattemore, who have always encouraged me to pursue excellence and aim for the highest*

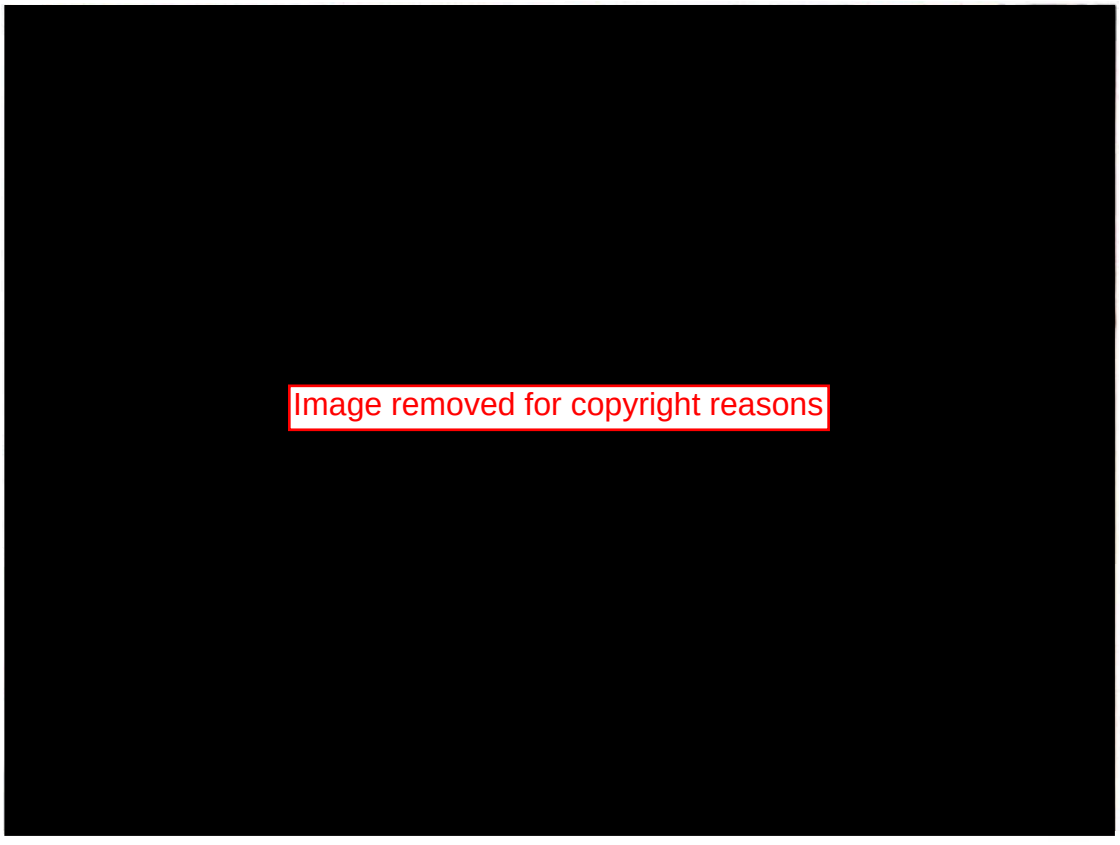
Image removed for copyright reasons

# ABSTRACT

# ABSTRACT

In New Zealand (NZ) asthma mortality rates are higher than in any other developed country studied, and hospital admission rates for asthma are among the highest. Within NZ, both mortality and hospital admission rates for asthma are higher among Polynesians than among Europeans. To investigate the possibility that these differences were due to differences in asthma prevalence, a study was initiated to measure the prevalence and severity of asthma among both Europeans and Polynesians in Auckland, using methods identical to those used in an overseas study.

From all primary schools in the Auckland Urban Area, classes were sampled by two-stage, random, stratified sampling. In the winter of 1985, the children in the sampled classes were studied employing a questionnaire and a rapid, portable method of bronchial challenge testing with histamine which had been used to study schoolchildren aged 8 to 10 years in two areas in New South Wales (NSW), Australia. Participation was 83%, the participants comprising 1084 European, 509 Maori, and 460 Pacific Island children, who were closely matched in gender and age to the NSW children. Prevalence of various items was compared including asthma symptoms, diagnosed asthma, and bronchial hyperresponsiveness (BHR), defined as a 20% fall in the one-second forced expiratory volume (FEV1), on or before the administration of a cumulative dose of 7.8 μmol histamine.

The prevalence rates of respiratory symptoms, BHR, severe BHR and BHR combined with symptoms were similar among the 1084 Auckland European children and 769 inland NSW children, but lower among 718 coastal NSW children than the other two sites. In Auckland, the prevalence of respiratory symptoms was higher in Maoris than among Europeans or Pacific Islanders, whereas prevalence of diagnosed asthma was similar in all three groups. Europeans had the highest rate of BHR and severe BHR followed by Maoris then Pacific Islanders. Maori and Pacific Island children reporting symptoms were less likely to receive prophylactic medication than European children.

The study design also enabled assessment of the epidemiological correlates of BHR, which had been little studied in random populations before 1985. Among the Auckland children, bronchial responsiveness was found to be unimodally distributed, with no clear separation between children with a diagnosis or symptoms of asthma and those without. The presence or absence of BHR did not accurately identify children with a diagnosis or symptoms of asthma. A 14-variable multiple logistic regression model was developed which explained 27% of the variability in BHR rates. The main variables independently increasing BHR risk were: low baseline FEV1, a history of wheeze, diagnosed asthma, atopic conditions, or bronchodilator treatment, and European (as opposed to Polynesian) ethnicity. Climatic conditions at the time of the test were less strongly associated.

In summary, neither the international nor the inter-ethnic differences in asthma mortality and asthma admission rates were adequately explained by differences in the prevalence of asthma symptoms, diagnosed asthma or BHR; however, differences in asthma severity and in the management of asthma may be contributory. In this large population-based study of children, BHR was associated independently with a number of different variables but did not precisely identify children reporting asthma symptoms or a diagnosis of asthma. Thus a single bronchial challenge test is not an ideal tool on its own for diagnosing asthma or measuring asthma prevalence.

# PREFACE & ACKNOWLEDGMENTS

# PREFACE AND ACKNOWLEDGEMENTS

The study which forms the basis for this thesis was instigated in 1984 by Drs. Innes Asher, and Edwin Mitchell, Department of Paediatrics, University of Auckland, Drs. Harry Rea and Adrian Harrison, Department of Respiratory Medicine, Greeen Lane Hospital, Auckland, and Mr. Alistair Stewart, statistician, Department of Community Health, University of Auckland. The study was funded by the Medical Research Council of New Zealand and the Asthma Foundation of New Zealand. I was appointed as MRC Research Fellow to the project in 1985 and have been continuously involved since then in analysing and writing up the data. I was supported with a part-salary in 1987 and 1988 to continue the analysis of the study by the Mackie Estates Trust of the Auckland Asthma Society and the Auckland Medical Research Foundation.

Three of the chapters of this thesis are based on the following published papers:

Chapter IV
**Asher MI, Pattemore PK, Harrison AC, Mitchell EA, Rea HH, Stewart AW, Woolcock AJ (1988).** International comparison of the prevalence of bronchial hyperresponsiveness and asthma symptoms.
*Am Rev Respir Dis* **138**:524-9.

Chapter V
**Pattemore PK, Asher MI, Harrison AC, Mitchell EA, Rea HH, Stewart AW (1989).** Ethnic differences in prevalence of asthma symptoms and bronchial hyperresponsiveness in New Zealand children.
*Thorax* **44**:168-76.

Chapter VII
**Pattemore PK, Asher MI, Harrison AC, Mitchell EA, Rea HH, Stewart AW (1990).** The interrelationship among bronchial hyperresponsiveness, the diagnosis of asthma, and asthma symptoms.
*Am Rev Respir Dis* **142**:549-54.

I am grateful to each of the co-authors for their assistance in writing the papers, and to Mr. Alistair Stewart for advice regarding the statistical analyses. Professor. Anne Woolcock of Sydney has kindly permitted me to use her figures for comparison in chapter four of the thesis. The field work for the study would not have been possible without the endeavours of Mrs Joanna Innes-Walker, research nurse, who ably organised the school visits and performed necessary liaison work, Mrs.Jan Mulder, senior technician, who was responsible for the bronchial challenge testing and equipment and wrote comprehensive technical notes, and Mrs. Lindy Gregory, Mrs. Frances.Jackson, and Mrs. Kathy Stirling, technicians who with Jan Mulder, performed over 2,200 bronchial challenge tests in two and a half months. All five assisted in the collection and coding of the data sheets. I would also like to thank various people outside the study team who provided advice and comments. Dr. Clive Osmond, statistician, MRC Environmental Epidemiology Unit, Southampton kindly provided statistical advice on the analyses in Chapter VIII and Drs. Lynn Josephs and Keith Godfrey, both research fellows in the Faculty of Medicine, University of Southampton, made valuable comments about Chapters I, VII and VIII.

I wish to express particular thanks to Mr. John Collins, Senior Lecturer in Surgery, University of Auckland, who first encouraged me to write up the work as a thesis and to Dr. Innes Asher, Senior Lecturer in Paediatrics, who, as my supervisor, has provided unstinting support for my work as a researcher, besides giving helpful advice on each of the chapters. Finally, I wish to pay tribute to my wife Wendy, who has made many sacrificies to enable me to write the thesis, has read and commented on the presentation, and who has given constant support, and encouragement.

# CONTENTS

# *Outline of Chapter Headings*

*Chapter I.* Introduction ..... 1
*Chapter II.* Methods ..... 40
*Chapter III.* Characteristics of sampled children ..... 80

***Results: Section A***
***Asthma Prevalence in Auckland Children*** ..... 115

*Chapter IV.* Comparison of asthma prevalence among European children in Auckland and Australia ..... 116
*Chapter V.* Comparison of asthma prevalence among European, Maori, and Pacific Island children in Auckland ..... 143
*Chapter VI.* Diagnosis and treatment of children with asthma symptoms in Auckland ..... 177

***Results: Section B***
***Epidemiological Correlates of***
***Bronchial Hyperresponsiveness***
***in a Random Field Study*** ..... 199

*Chapter VII.* The inter-relationship among bronchial hyperresponsiveness, the diagnosis of asthma, and asthma symptoms ..... 200
*Chapter VIII.* Associations of bronchial hyperresponsiveness with personal and environmental variables ..... 242

EPILOGUE ..... 326

# *Table of Contents*

**ABSTRACT** ..... iv

**PREFACE AND ACKNOWLEDGEMENTS** ..... vii

**CONTENTS** ..... x
*Outline of Chapter Headings* ..... xi
*Table of Contents* ..... xii
*List of Tables* ..... xix
*List of Illustrations* ..... xxi
*List of Abbreviations* ..... xxiii

*Chapter I*
**INTRODUCTION** ..... 1
*Outline* ..... 3

**I.1 The Epidemiology of asthma** ..... 5

***I.1.1 Early references*** ..... 5

***I.1.2 Asthma since 1960: international trends*** ..... 7
I.1.2.1 Asthma mortality and hospital admission rates ..... 7
I.1.2.2 Asthma prevalence ..... 8

***I.1.3 Asthma in New Zealand*** ..... 11
I.1.3.1 Asthma mortality ..... 11
I.1.3.2 Hospital admissions for asthma ..... 13
I.1.3.3 Sales of asthma medications ..... 14

***I.1.4 Previous comparisons of asthma prevalence*** ..... 15
I.1.4.1 Trends within New Zealand ..... 15
I.1.4.2 International comparisons ..... 16
I.1.4.3 Inter-ethnic comparisons ..... 17

***I.1.5 The need for a study of asthma prevalence in New Zealand*** ..... 20

**I.2 Methods of asthma prevalence studies** ..... 21

***I.2.1 The definition of asthma*** ..... 21
I.2.1.1 Definitions based on symptoms ..... 22
I.2.1.2 Definitions based on function ..... 22
I.2.1.3 Definitions based on pathological changes ..... 24
I.2.1.4 Definitions based on aetiology ..... 25
I.2.1.5 Describing without defining ..... 26

***I.2.2 Populations studied*** ..... 26

*I.2.3 Symptom assessment* ..... 27

*I.2.4 Bronchial challenge testing* ..... 28
I.2.4.1 Background ..... 28
I.2.4.2 Methods of performing bronchial challenge tests ..... 30
I.2.4.3 Comparison of three standardised methods of bronchial challenge ..... 33
I.2.4.4 Bronchial hyperresponsiveness: definition, mechanisms & significance ..... 35

**I.3 A study of asthma prevalence in Auckland children: Aims and choice of method** ..... 38

*Chapter II*
**METHODS** ..... 40
*Outline* ..... 42

**II.1 Study Design** ..... 44

*II.1.1 Type of study* ..... 44

*II.1.2 Sample specifications* ..... 44
II.1.2.1 Sample characteristics ..... 44
II.1.2.2 Sample size ..... 45
II.1.2.3 Sampling method ..... 46

*II.1.3 Derivation of methods* ..... 47

**II.2 Study procedure** ..... 49

*II.2.1 The sampling process* ..... 49
II.2.1.1 Identification of schools ..... 49
II.2.1.2 Classes and ethnic breakdown ..... 49
II.2.1.3 Coding and stratification ..... 50
II.2.1.4 Random sampling, stage 1 ..... 51
II.2.1.5 Random sampling, stage 2 ..... 53
II.2.1.6 Follow-up of non-participants ..... 54

*II.2.2 The Questionnaire* ..... 57
II.2.2.1 Content ..... 57
II.2.2.2 Repeatability in Europeans ..... 57
II.2.2.3 Repeatability in Polynesians ..... 58

*II.2.3 Bronchial challenge testing: materials* ..... 60
II.2.3.1 Histamine preparation and assay ..... 60
II.2.3.2 Nebuliser type and calibration ..... 62
II.2.3.3 Spirometer type and calibration ..... 64

*II.2.4 Bronchial challenge testing: procedure* ..... 67
II.2.4.1 Baseline measures ..... 67
II.2.4.2 Histamine dosing schedule ..... 68
II.2.4.3 Calculations and classification of bronchial responsiveness ..... 70
II.2.4.4 Reproducibility of bronchial challenge testing ..... 71

*II.2.5 Other recordings* ..... 72

*II.2.6 Communications and ethical considerations* ..... 74
II.2.6.1 Approval ..... 74
II.2.6.2 Explanatory letters and consent ..... 74
II.2.6.3 Letters to parents and general practitioners ..... 75

**II.3 Analysis of the study** ..... 76

*II.3.1 Data handling* ..... 76
II.3.1.1 Coding and entering data ..... 76
II.3.1.2 Statistical analysis ..... 76

*II.3.2 Definitions and classification* ..... 77
II.3.2.1 Race and ethnicity ..... 77
II.3.2.2 Socio-economic status and residential status ..... 77
II.3.2.3 Symptoms, diagnosis and medication ..... 78
II.3.2.4 Asthma prevalence ..... 79

*Chapter III*
**CHARACTERISTICS OF SAMPLED CHILDREN** ..... 80
*Outline* ..... 82

**III.1 Methods of data analysis** ..... 84

**III.2 Participation** ..... 85
III.2.1 Schools participating ..... 85
III.2.2 Children participating ..... 85

**III.3 Characteristics of participants** ..... 87
III.3.1 Age, gender and ethnic group ..... 87
III.3.2 Race, ethnic group and socio-economic status ..... 87
III.3.3 Birthplace and residence in Auckland ..... 91
III.3.4 Residence outside Auckland ..... 94
III.3.5 Smoking in the home ..... 98
III.3.6 Socio-economic status and smoking in the home ..... 102
III.3.7 Mean age, height and baseline lung function ..... 102

**III.4 Characteristics of non-participants** ..... 107
III.4.1 Age, gender and ethnicity ..... 107
III.4.2 Known asthma and reasons for non-participation ..... 107

**III.5 Summary** ..... 114

*Results: Section A*
*Asthma Prevalence in Auckland Children* .....115

*Chapter IV*
**COMPARISON OF ASTHMA PREVALENCE AMONG EUROPEAN CHILDREN IN AUCKLAND AND AUSTRALIA**.....116
*Outline*.....118

**IV.1 Comparison of the towns and study methods**.....121
IV.1.1 General features of the study towns.....121
IV.1.2 Comparison of methods.....121
IV.1.3 Method of data analysis.....123

**IV.2 Results**.....124
IV.2.1 Characteristics of children in the three towns.....124
IV.2.2 Respiratory symptoms.....124
IV.2.3 Bronchial hyperresponsiveness.....124
IV.2.4 Symptoms combined with BHR.....130
IV.2.5 Asthma diagnosis and medication use.....130
IV.2.6 Other indices: maternal asthma, and early bronchitis.....130
IV.2.7 BHR in symptomatic children.....132
IV.2.8 BHR, recent respiratory infection, and asthma symptoms.....132
IV.2.9 Effect of recent medication on BHR in symptomatic children.....132

**IV.3 Discussion**.....137

**IV.4 Conclusions**.....141

**IV.5 Summary**.....142

*Chapter V*
**COMPARISON OF ASTHMA PREVALENCE AMONG EUROPEAN, MAORI AND PACIFIC ISLAND CHILDREN IN AUCKLAND**.....143
*Outline*.....145

**V.1 Method of data analysis**.....147

**V.2 Results**.....149
V.2.1 Individual respiratory symptoms.....149
V.2.2 Bronchial hyperresponsiveness (BHR).....149
V.2.3 Criteria of asthma prevalence.....153
V.2.4 Interaction with socio-economic group.....157
V.2.5 Interaction with smoking in the home.....157

V.2.6 Interaction with residence and birthplace ..... 157
V.2.7 Multiple logistic regression analysis of interactions ..... 165
V.2.8 Related conditions ..... 165
V.2.9 Diagnosis and treatment of symptomatic children ..... 167

**V.3 Discussion** ..... 170

**V.4 Conclusions** ..... 175

**V.5 Summary** ..... 176

*Chapter VI*
**DIAGNOSIS AND TREATMENT OF CHILDREN WITH ASTHMA SYMPTOMS IN AUCKLAND** ..... 177
*Outline* ..... 179

**VI.1 Methods of analysis** ..... 182

**VI.2 Results** ..... 183
VI.1.1 Diagnosis of children with asthma symptoms ..... 183
VI.2.2 Treatment of children with a diagnosis of asthma or asthma symptoms ..... 186
VI.2.3 Clinical associations with bronchodilator and prophylactic use ..... 192

**VI.3 Discussion** ..... 194

**VI.4 Conclusions** ..... 197

**VI.5 Summary** ..... 198

*Results: Section B*
*Epidemiological Correlates of Bronchial Hyperresponsiveness in a Random Field Study* ..... 199

*Chapter VII*
**THE INTER-RELATIONSHIP AMONG BRONCHIAL HYPERRESPONSIVENESS, THE DIAGNOSIS OF ASTHMA, AND ASTHMA SYMPTOMS** ..... 200
*Outline* ..... 202

**VII.1 Method of analysis** ..... 205
VII.1.1 Analytical approach ..... 205
VII.1.2 Definitions ..... 205
VII.1.3 Analysis of distribution of histamine response ..... 208

**VII.2 Results** ..... 210
VII.2.1 Distribution of the response to histamine ..... 210
VII.2.2 The relationship of BHR to diagnosed asthma ..... 214
VII.2.3 The relationship of BHR to current symptoms ..... 219
VII.2.4 BHR and diagnosis compared as screening tests for current symptoms ..... 222
VII.2.5 Overlap of BHR, diagnosed asthma, and asthma symptoms ..... 227

**VII.3 Discussion** ..... 230

**VII.4 Conclusions** ..... 240

**VII.5 Summary** ..... 241

*Chapter VIII*
**ASSOCIATIONS OF BRONCHIAL HYPERRESPONSIVENESS WITH PERSONAL AND ENVIRONMENTAL VARIABLES** ..... 242
*Outline* ..... 244

**VIII.1 Methods of analysis** ..... 248
VIII.1.1 Analysis of the relationship of personal variables to BHR ..... 248
VIII.1.2 Analysis of the relationship of environmental variables to BHR ..... 248
VIII.1.3 Multivariate analysis of bronchial responsiveness ..... 252

**VIII.2 Results** ..... 255

***VIII.2.1 The relationship of BHR to personal variables*** ..... 255
VIII.2.1.1 Demographic variables ..... 255
VIII.2.1.2 Bronchitis in infancy and atopic conditions in children or parents ..... 262
VIII.2.1.3 Past or current respiratory symptoms ..... 265
VIII.2.1.4 Maintenance medication ..... 265
VIII.2.1.5 Passive and active smoking and glue sniffing ..... 265
VIII.2.1.6 Factors operating prior to bronchial challenge testing ..... 269
VIII.2.1.7 Height and baseline lung function ..... 271

***VIII.2.2 The relationship of BHR to environmental variables*** ..... 271
VIII.2.2.1 Temporal trends in BHR rates and comparison with asthma admission rates ..... 271
VIII.2.2.2 Weather conditions and BHR rate on half-day of testing ..... 275

***VIII.2.3 Summary of univariate analyses of risks*** ..... 280

***VIII.2.4 Multivariate analysis of bronchial responsiveness*** ..... 285

VIII.2.4.1 Development of the models ..... 285
VIII.2.4.2 Variables and interactions within the logistic model ..... 290
VIII.2.4.3 Comparative effects of variables in the logistic model ..... 293
VIII.2.4.4 Predictive value of the logistic model ..... 296
VIII.2.4.5 Multiple linear regression model ..... 302

**VIII.3 Discussion** ..... 304
VIII.3.1 Genetic determinants ..... 305
VIII.3.2 Determinants in infancy ..... 307
VIII.3.3 Continuing influences during childhood ..... 309
VIII.3.4 Short-term determinants: environmental correlates ..... 312
VIII.3.5 Short term determinants: physiologic correlates ..... 315
VIII.3.6 Short-term determinants: clinical correlates ..... 317
VIII.3.7 Prediction of bronchial response to histamine ..... 320

**VIII.4 Conclusions** ..... 323

**VIII.5 Summary** ..... 325

**EPILOGUE** ..... 326

**LIST OF REFERENCES** ..... 333

**APPENDICES** ..... 360
*Appendix A:* List of classes coded in the sampling frame ..... 361
*Appendix B:* Explanatory letters and the Questionnaire ..... 370
*Appendix C:* Predicted values of FEV1 and FVC ..... 383
*Appendix D:* Bronchial challenge test recording form ..... 385
*Appendix E:* Letters of support for the study ..... 389
*Appendix F:* Letters explaining results of bronchial challenge ..... 402
*Appendix G:* Hospital board area admission rates for asthma in NZ ..... 405

# *List of Tables*


*Chapter II*

Table II.1 Stratification of sample....52
Table II.2 Numbers in the sampling process....55
Table II.3 Agreement between Samoan & English questionnaires: main questions....59
Table II.4 Agreement between Samoan & English questionnaires: derived variables....59
Table II.5 Assay of histamine solutions....61
Table II.6 Bronchial challenge reproducibility....72

*Chapter III*

Table III.1 Age and gender by ethnic group....88
Table III.2 Participants: ethnic group....89
Table III.3 Participants: socio-economic group....89
Table III.4 Ethnic composition of study population compared to Auckland & NZ....90
Table III.6 Socio-economic group: comparison of Europeans, Maoris and Pacific Islanders in sample....92
Table III.7 Birthplace and residence in Auckland by ethnic group....93
Table III.8 Birthplace by ethnic group: significance....95
Table III.9 Lifelong residence by ethnic group: significance....96
Table III.10 Residence outside Auckland....97
Table III.11 Proportions living in high asthma admission rate areas: by ethnic group....99
Table III.12 Smoking in the home: quantities....100
Table III.13 Smoking in the home: ethnic differences....101
Table III.14 Comparison betweeen ethnic groups of means for age, height and baseline lung function....106
Table III.15 Non-participants by ethnic group, gender and age....108
Table III.16 Comparison of participants and non-participants: gender....109
Table III.17 Comparison of participants and non-participants: age....110
Table III.18 Non-participants: breakdown by presence/absence of asthma and reason for non-participation....111
Table III.19 Comparison of participants and non-participants for presence of known/diagnosed asthma....113

*Chapter IV*

Table IV.1 Characteristics of children in the three towns....125
Table IV.2 Prevalence of respiratory symptoms....126
Table IV.3 Prevalence and severity of BHR....128
Table IV.4 Prevalence of symptoms combined with BHR....131
Table IV.5 Asthma diagnosis and medication use....131
Table IV.6 BHR rates among children in different symptom categories....133
Table IV.7 The relationship of BHR to recent URTI and asthma symptoms....135

*Chapter V*

Table V.1 Prevalence of individual symptoms....150
Table V.2 Prevalence of BHR and distribution by PD20 value....152
Table V.3 Asthma prevalence criteria irrespective of BHR status....154
Table V.4 Asthma prevalence criteria with concurrent BHR....155
Table V.5 Effect of socio-economic status on symptoms and on BHR....158

Table V.6 Ethnic differences in symptom and BHR rates: effect of controlling for socio-economic group ..... 159
Table V.7 Effect of smoking in the home on symptom and BHR rates ..... 160
Table V.8 Ethnic differences in rates of *any symptom ever*: effect of controlling for various smokers in the home ..... 161
Table V.9 Ethnic differences in rates of *any current symptom*: effect of controlling for various smokers in the home ..... 162
Table V.10 Ethnic differences in BHR rates: effect of controlling for various smokers in the home ..... 163
Table V.11 Effect of residence and birthplace on symptom and BHR rates..... 164
Table V.12 Prevalence of related conditions in children and their parents..... 166
Table V.13 Diagnosis and treatment of symptomatic children ..... 168

*Chapter VI*
Table VI.1 Percentage ever diagnosed as asthma, by ethnic group & symptom ..... 184
Table VI.2 Percentage of children on different asthma medication, by ethnic gp ..... 187

*Chapter VII*
Table VII.1 BHR as a screening test for diagnosed asthma in different subgroups ..... 216
Table VII.2 Characteristics of groups in which diagnosis and BHR do not match versus those that do ..... 218
Table VII.3 BHR and frequency of current symptoms in each ethnic group ..... 221
Table VII.4 BHR as a test for diagnosed asthma..... 233
Table VII.5 BHR as a screening test for symptoms ..... 235

*Chapter VIII*
Table VIII.1 Percent of children with BHR in different categories, broken down by ethnic group ..... 256
Table VIII.2 Effect of birthplace and residential history on rates of BHR ..... 260
Table VIII.3 Risks of BHR associated with certain demographic variables ..... 261
Table VIII.4 Risks of BHR associated with bronchitis in infancy and atopic conditions..... 263
Table VIII.5 Risks of BHR associated with various symptom categories ..... 266
Table VIII.6 Risks of BHR associated with taking maintenance asthma medications..... 267
Table VIII.7 Risks of BHR associated with substance use by parents and child ..... 268
Table VIII.8 Risks of BHR associated with factors at or prior to the challenge ..... 270
Table VIII.9 Risks of BHR associated with values below the median of height and baseline lung function..... 272
Table VIII.10 Risks of BHR associated with values below the median of environmental variables at the time of testing ..... 281
Table VIII.11 Risks of BHR associated with values below the median of environmental variables before or after testing..... 282
Table VIII.12 List of starting variables in procedures 1 and 3..... 286
Table VIII.13 Comparison of the three initial logistic regression models..... 288
Table VIII.14 Comparison of Model 4 with parameter estimates from individual ..... regressions and from the 78-variable starting model..... 291
Table VIII.15 Odds ratios of BHR risk associated with variables in Model 4 ..... 294
Table VIII.16 The ability of various cut-off points of the DFP to identify children with BHR, compared to three clinical variables..... 300
Table VIII.17 Multiple linear regression model ..... 303
Table VIII.18 Postulated determinants of bronchial responsiveness to histamine ..... 322

# *List of Illustrations*

## Colour plates


| | | |
|---|---|---|
| Frontispiece | A child performing spirometry in the classroom | iii |
| Chapter I | International trends in asthma mortality among 5-34 year olds (reproduced, with permission, from Rea, Sears *et al* 1987a) | 2 |
| Chapter 2 | Map of Auckland | 41 |
| Chapter 3 | A child being measured before testing | 81 |
| Chapter 4 | A European child performing spirometry | 117 |
| Chapter 5 | A Polynesian child performing spirometry | 144 |
| Chapter 6 | A child receiving an inhaled bronchodilator after testing | 178 |
| Chapter 7 | A child receiving nebulised histamine in the classroom | 201 |
| Chapter 8 | The research vehicle in a school playground | 243 |


## Black and white illustrations


| | | |
|---|---|---|
| Chapter II | | |
| Figure II.1 | Sampling exclusions at each stage | 56 |
| Figure II.2 | Proportion of all Std 2 & 3 children sampled, by ethnic group | 56 |
| Figure II.3 | De Vilbiss no. 40 glass nebuliser | 63 |
| Figure II.4 | Vitalograph calibration | 66 |
| Figure II.5 | Histamine dosing schedule | 69 |
| Chapter III | | |
| Figure III.1 | Participation within the definitive sample | 86 |
| Figure III.2 | Smoking in the home and socio-economic group: EUROPEANS | 103 |
| Figure III.3 | Smoking in the home and socio-economic group: MAORIS | 104 |
| Figure III.4 | Smoking in the home and socio-economic group: PACIFIC ISLANDERS | 105 |
| Chapter IV | | |
| Figure IV.1 | Map of Australia and NZ, showing the study sites | 122 |
| Figure IV.2 | Prevalence of symptoms in the three towns | 127 |
| Figure IV.3 | Prevalence and severity of BHR in the three towns | 129 |
| Figure IV.4 | BHR rate in different symptom categories | 134 |
| Chapter V | | |
| Figure V.1 | Prevalence of symptoms, by ethnic group | 151 |
| Figure V.2 | Criteria of asthma prevalence, by ethnic group | 156 |
| Chapter VI | | |
| Figure VI.1 | The diagnosis of asthma, by ethnic group and number of current symptoms | 185 |
| Figure VI.2 | The diagnosis of asthma, by ethnic group and frequency of current wheeze | 185 |
| Figure VI.3 | Treatment with bronchodilators, by ethnic group and symptom category | 189 |
| Figure VI.4 | Treatment with prophylactics, by ethnic group and symptom category | 189 |
| Figure VI.5 | Frequency of use of asthma medication in the last 12 months | 190 |

Figure VI.6 Percentage of children taking any daily medications who were on bronchodilators and prophylactics ..... 191
Figure VI.7 Percentage of children taking any medication more than once per month who were on bronchodilators and prophylactics ..... 191

Chpater VII
Figure VII.1 Temporal relationship of the main variables examined ..... 207
Figure VII.2 Log linear extrapolation ..... 209
Figure VII.3 Frequency distribution of ΔFEV1 after cumulative doses of 0.24 and 3.9 μmol histamine ..... 211
Figure VII.4 Diagnosed children within the distribution of ΔFEV1 ..... 212
Figure VII.5 Symptomatic children within the distribution of ΔFEV1 ..... 213
Figure VII.6 Proportionate overlap of diagnosis and BHR ..... 215
Figure VII.7 Proportion with BHR, and PD20 range of responders, by frequency of wheezing ..... 220
Figure VII.8 BHR & diagnosis compared as screening tests for current symptoms ..... 223
Figure VII.9 BHR as a screening test: effect of varying PD20 criterion ..... 225
Figure VII.10 BHR as a screening test: effect of varying "symptomatic" criterion ..... 226
Figure VII.11 BHR & diagnosis as screening tests, by each ethnic group ..... 228
Figure VII.12 Overlap of BHR, diagnosed asthma, and asthma symptoms ..... 229

Chapter VIII
Figure VIII.1 The North Island of New Zealand ..... 249
Figure VIII.2 Auckland Urban Area Map ..... 250
Figure VIII.3 BHR rates by ethnic sub-group, in descending order of rate ..... 257
Figure VIII.4 Month of birth, BHR, atopy and asthma symptoms ..... 258
Figure VIII.5 BHR rate and month of birth, by ethnic group ..... 258
Figure VIII.6 BHR rates: interaction of family history and atopy in the child ..... 264
Figure VIII.7 Temporal variation in BHR rates over the study period ..... 273
Figure VIII.8 Comparison of weekly BHR rates and weekly asthma admission rates for children ..... 274
Figure VIII.9 Variation in temperature and absolute humidity, compared to weekly BHR rates ..... 276
Figure VIII.10 Variation in barometric pressure, horizontal visibility and rain, cf weekly BHR rates ..... 277
Figure VIII.11 BHR rate for half-days regressed against a) barometric pressure on the test-day b) barometric pressure one week previous to the study ..... 278
Figure VIII.12 Variation of BHR rates with wind direction ..... 279
Figure VIII.13 Variables associated with BHR: risks in order of decreasing significance ..... 283
Figure VIII.14 Sensitivity and specificity for different cut-off values of the DFP ..... 298
Figure VIII.15 Positive and negative predictive value for different cut-off values of the DFP ..... 298
Figure VIII.16 Accuracy and Youden's index for different cut-off values of the DFP ..... 299
Figure VIII.17 Sensitivity and positive predictive value for different cut-off values of the DFP ..... 299

# *List of Abbreviations*

| | |
|---|---|
| BHR | Bronchial hyperresponsiveness, measured by a challenge test |
| DFP | Discriminant function predictor (for derivation see Section VIII.2.4.4, page 296). |
| FEV1 | Forced expiratory volume in one second |
| ΔFEV1 | Percentage change in FEV1 by a given dose of histamine |
| $\Delta FEV1_{3.9}$ | Percentage change in FEV1 by 3.9 μmol of histamine |
| FVC | Forced vital capacity |
| NPV | Negative predictive value |
| NSW | New South Wales |
| NZ | New Zealand |
| NZ1 | Hospital board area of New Zealand with higher than average admission rate for asthma |
| NZ2 | Hospital board area of New Zealand with average admission rate for asthma |
| NZ3 | Hospital board area of New Zealand with lower than average admission rate for asthma |
| PD20 | Interpolated provocative dose of histamine resulting in a 20% fall in FEV1 from the post-saline value |
| PPV | Positive predictive value |
| URTI | Upper respiratory tract infection |