

AN INTRODUCTION TO EPIDEMIOLOGY



Michael Alderson

An Introduction to Epidemiology

Michael Alderson

*Professor of Epidemiology, Institute of
Cancer Research, University of London
Honorary Consultant, Royal Marsden Hospital*



© Michael Alderson 1976

All rights reserved. No part of this publication may be reproduced or transmitted, in any form or by any means, without permission

First edition 1976

Reprinted with corrections 1980

Published by

THE MACMILLAN PRESS LTD

London and Basingstoke

Associated companies in Delhi Dublin

Hong Kong Johannesburg Lagos Melbourne

New York Singapore and Tokyo

ISBN 0 333 16564 0 (paper cover)

Printed in Hong Kong

This book is sold subject to the standard conditions of the Net Book Agreement

The paperback edition of this book is sold subject to the condition that it shall not, by way of trade or otherwise, be lent, resold, hired out, or otherwise circulated without the publisher's prior consent in any form of binding or cover other than that in which it is published and without a similar condition including this condition being imposed on the subsequent purchaser

An Introduction to Epidemiology

Preface

Epidemiology has three main aims: to describe the distribution and size of disease problems in human populations; to identify aetiological factors in the pathogenesis of disease; to provide the data essential for the management, evaluation and planning of services for the prevention, control and treatment of disease. In order to fulfil these aims, three rather different classes of epidemiological study may be mounted.

- (1) Descriptive studies concerned with observing the distribution and progression of disease in populations;
- (2) Analytical studies concerned with investigating hypotheses suggested by the descriptive studies;
- (3) Experimental or intervention studies concerned with measuring the effect on the population of manipulating environmental influences thought to be harmful, or by introducing in a controlled way preventive, curative and ameliorative services.

This book describes the various approaches that can be made in following such paths of investigation.

Since routine mortality and morbidity statistics may provide background information for many studies and may be the sole source of data for some, two chapters are devoted to these issues. There follow chapters on the use of cross-sectional, retrospective and prospective studies, with examples in each of particular studies, the principles involved and some of the advantages and disadvantages of the different approaches. A further chapter deals with intervention studies, including preventive, clinical and medical-care trials. The final chapter discusses the use of all these approaches to the study of medical care in this country.

Considerable emphasis is placed on study design in each chapter and attention is also paid to methods of analysis and the interpretation of data, particularly to certain statistical techniques that are used predominantly in the field of epidemiology. The intention is to indicate the relevance of these approaches, and to provide a guide to the literature and textbooks on statistics for readers wishing to explore these aspects further. The examples of published work that are quoted have been chosen to illustrate the methods of epidemiology. It is hoped that each example will help to stimulate interest in the subject, but no attempt has been made to provide a comprehensive cover of all the findings of epidemiological studies. The examples deal predominantly with the methods used in the study of chronic disease, the main field of work of epidemiologists in developed countries, together with an application of these methods to medical-care studies.

Epidemiology will be one of the sources of fresh data that may be of concern to everyone involved in the health-care field, whether these data relate to aetiology, means of prevention or modes of delivery of health care. It is suggested that many entrants into the health-care field (doctors, nurses,

PREFACE

administrators and ancillary staff) should have some appreciation of the role of epidemiology and the underlying methods used in order to be able to read published work and interpret it. It is also hoped that a clear exposition of the various approaches used in epidemiology may stimulate a wider range of individuals to carry out their own, however limited, studies. In addition to the general acceptance that undergraduates should be introduced to this subject, there is a growing tendency to acknowledge that administrators in the health service should be trained in disciplines such as epidemiology. It is hoped that this book will provide a basic introduction to the subject suitable for this general readership who may not wish to study the subject any further. In addition the text should act as a useful basis for a more detailed course suitable for those entering into community medicine, and should also provide guidance for individuals in any branch of medicine who wish to carry out their own studies.

The stimulus to write this book came from the involvement in the teaching of medical and other students in the health field. This was reinforced by individuals bringing a range of fascinating problems for discussion. Each of these problems from the different branches of medicine has indicated the growing interest of many individuals working in the health service to carry out their own projects. It is hoped that this book will give assistance to such persons. These people are not named in the text, but a debt of gratitude is owed to them for the way in which the presentation of practical issues has stimulated thought. A recent note by Hubble* has drawn attention to the relatively fine dividing line that separates plagiarism from correctly attributed quotation, and original thought. It is obvious that the bulk of the ideas in this text have been distilled from contact with many colleagues over the past fifteen years; in particular a debt of gratitude is owed to Robert Wofinden, Jerry Morris and Alwyn Smith. It is also a pleasure to acknowledge the help from staff in the Medical Information Unit, especially Sue Collins and Shirley Kingsley-Thomas who prepared the typescript. I have benefited from comments of Dr David Jones, Dr Ragunath Nayak, Mr Michael Slattery and my wife who have each read a draft.

Michael Alderson

* Hubble, D. (1974). Personal view. *Br. med. J.*, 3, 623

Contents

<i>Preface</i>	ix
1 The Role of Epidemiology	1
1.1 Who Practises Epidemiology?	1
1.2 Development of Epidemiology	2
1.3 Four Categories of Study	3
1.4 Need for Numeracy	4
1.5 Different Approaches to the Consideration of Epidemiology	4
References	6
2 The Use of Mortality Statistics	7
2.1 Basic Example of the Use of Mortality Statistics	7
2.2 Principles	10
2.2.1 Variation in persons, places and time	13
2.2.2 Generation of hunches	16
2.2.3 Testing hypotheses	17
2.2.4 Monitoring the public's health	19
2.3 Advantages and Disadvantages of Mortality Statistics	21
2.4 Extensions of the Use of Mortality Data	23
2.4.1 International comparisons	25
2.5 Statistical Techniques	27
2.5.1 Cohort analysis	27
2.5.2 Standardisation	29
2.5.3 Do differences in numbers of deaths or death rates mean anything?	31
2.5.4 Proportional mortality	33
2.5.5 Multivariate analyses	35
References	35
3 Other Sources of Routine Data	38
3.1 Use of Hospital Discharge Data	39
3.1.1 Abortion statistics	43
3.1.2 Cancer registration	46
3.1.3 Congenital abnormalities	48
3.1.4 The General Household Survey	50
3.1.5 Infectious diseases	51
3.1.6 Mental Health Enquiry	54
3.1.7 Morbidity statistics from general practice	56

CONTENTS

3.1.8	Sickness-absence statistics	58
3.1.9	Other sources of routine data	60
3.1.10	Data from other countries	61
3.2	Principles of the Use of Routine Data	62
3.3	Advantages and Disadvantages of Routine Data	63
3.4	Extensions of the Use of Routine Data	66
3.4.1	Simultaneous examination of data from two different sources	67
3.4.2	<i>Ad hoc</i> linkage of routine data	69
3.4.3	Registers	70
3.4.4	Record linkage	72
3.4.5	Use of retrievable data	74
3.5	Statistical Techniques	76
3.5.1	Cusums	76
3.5.2	Man years at risk	77
3.5.3	Space-time clustering	78
	References	79
4	Cross-sectional Studies	83
4.1	Basic Examples	83
4.2	Principles Involved in Cross-sectional Studies	86
4.2.1	Choice of study population	86
4.2.2	Categories of data	87
4.2.3	Sampling	88
4.2.4	Factors affecting the response rate in surveys	89
4.2.5	Motivation of subjects	93
4.3	Advantages and Disadvantages of Cross-sectional Studies	94
4.3.1	Importance of accurate data	95
4.3.2	Accuracy of subjects' responses	97
4.3.3	Accuracy of examination findings	99
4.3.4	Accuracy of investigation results	100
4.3.5	Bias introduced by nonresponse	101
4.4	Extension of the Method of Cross-sectional Studies	103
4.5	Analysis of Survey Data	107
4.5.1	Preliminary analysis of survey data	107
4.5.2	Association between two or more variates	109
4.5.3	Quantification of validity of data	111
4.5.4	How large a study is required?	113
	References	114
5	Retrospective Studies	119
5.1	Basic Example of a Retrospective Study	119
5.2	Principles of Retrospective Studies	121

CONTENTS

5.2.1	Categories of data	121
5.2.2	Relation to cross-sectional studies	123
5.2.3	Other sources of 'index' cases	123
5.2.4	Choice of controls	124
5.3	Advantages and Disadvantages of Retrospective Studies	125
5.4	Extension of Retrospective Studies	127
5.5	Statistical Analysis of Data from Retrospective Studies	128
5.5.1	Relative risk	128
5.5.2	Relative risk and absolute difference	132
5.5.3	Combination of two or more aetiological factors	132
5.5.4	Analysis of matched case-control studies	133
	References	135
6	Prospective Studies	138
6.1	Basic Example	138
6.2	Principles of Prospective Studies	142
6.3	Advantages and Disadvantages of Prospective Studies	145
6.4	Extension of the Method of Prospective Studies	146
6.4.1	Initial survey plus automatic end-point	146
6.4.2	<i>Ad hoc</i> follow up	147
6.4.3	Resurvey	148
6.4.4	Longitudinal study	149
6.4.5	Automatic entry and end-point	150
6.4.6	Automatic entry and survey	151
6.5	Statistical Techniques	152
6.5.1	Life tables	152
6.5.2	Assessment of cure	155
6.5.3	Prediction	157
6.5.4	Derivation of inferences	158
	References	160
7	Intervention Studies	163
7.1	Basic Example	163
7.2	Principles of Intervention Studies	164
7.2.1	Definition of the study population	164
7.2.2	Methods of allocation	165
7.2.3	Standardisation of intervention	166
7.2.4	Collection of outcome data	166
7.3	Advantages and Disadvantages of Intervention Studies	168
7.4	Extension of the Method of Intervention Trials	171
7.4.1	Preventive trials	172
7.4.2	Clinical trials	176
7.4.3	Medical-care intervention studies	177

CONTENTS

7.5 Statistical Techniques	179
7.5.1 Numbers required in a fixed-size trial	180
7.5.2 Random allocation	181
7.5.3 Sequential analysis	183
References	186
8 Medical-care Studies	189
8.1 Assessment of Need	190
8.2 Demand	192
8.3 Use of Health Service Facilities	195
8.3.1 Use of primary medical-care facilities	196
8.3.2 Use of outpatient facilities	197
8.3.3 Use of inpatient facilities	197
8.4 Outcome	200
8.5 Functioning of the Health Service	203
8.6 Planning	205
8.7 Evaluation	208
8.8 Mathematical Models	213
References	216
<i>Recommended further reading</i>	222
<i>Index</i>	223

1 The Role of Epidemiology

Epidemiology may be defined as the study of the determinants of the incidence and prevalence of disease. This relatively simple definition has some extremely widespread implications. It immediately suggests that epidemiology may be used to identify the cause of disease, but it must be remembered that it is most unusual that there is a single cause for a disease without any other confounding or intervening factors playing a part. Thus the examination of the causation of disease may involve investigators in an extremely wide range of studies unravelling a complex tangle of factors. The consideration of factors influencing the prevalence of disease adds a different perspective to the role of epidemiology; the prevalence of disease (the measure of the extent to which a disease exists in a population at a point in time) is a combination of the incidence of the condition, the cure rate and the fatality from this condition. In order, therefore, to study the determinants of the prevalence of a condition, information about the incidence, the natural history of the disease and the impact of the health-care system on the disease is required. This involves studying the cause of disease, the identification of disease patterns, the population's attitudes to disease, their tendency to seek cure, the range of care provided and the impact of such care on the disease. The above definition thus acknowledges the activities of epidemiologists in a range of studies throughout the medical-care field in examining the functioning of the health-care system and its impact on the health of a population.

1.1 Who Practises Epidemiology?

There is a very small but steadily growing proportion of the total manpower in the health field identifying themselves as trained epidemiologists. Although many of the studies discussed in this book have been carried out by 'professional epidemiologists', it is important to point out that many studies have been done by individuals working primarily in other branches of medicine. Recently, classic work has been carried out in general practice and by hospital staff. Pickles (1939) described a whole series of studies carried out in a rural practice in the Yorkshire dales. By the use of relatively simple methods relying on careful documentation and analysis of observations, he provided unique contributions on the spread of a number of infectious diseases. Fry (1966, 1974) has patiently documented the health problems of patients in an urban practice and reported on the natural history of a range of acute and chronic diseases. A major extension of such work in general practice has been the large-scale study on oral contraceptives involving 23 000 users, an equal number of controls and records provided by 1400 general practitioners whose activity was co-ordinated by Dr Clifford Kay (1974). Gregg (1941) noticed a change in the proportion of children referred to his clinic in Australia with certain eye defects; this stimulated him to

initiate studies on the association between maternal rubella and congenital abnormality of the subsequently born child. More recently Burkitt (1962), while working as a surgeon in East Africa, was responsible for the identification of a new form of malignant disease; he then launched studies of its epidemiology.

These examples are arbitrarily selected from a wide range of studies that have been carried out by clinicians either in the primary medical-care or in the hospital field. They indicate that there is no need to consider that epidemiology is a branch of medical science only practised by a restricted group of specially trained individuals. Over the past few years increasing emphasis has been placed on the need for administrators in the health service to be trained in disciplines such as epidemiology. This is an indication of the acceptance of the application of these techniques to the study of medical problems and the contribution that such studies can make to the management and planning of the delivery of health-care services.

The points argue for a wide range of individuals being familiar with the general principles of epidemiological studies. Epidemiology will be one of the sources of fresh data that will be of concern to everyone in the health field whether these data relate to aetiology, means of prevention or modes of delivery of health care. It is on these grounds therefore that all categories of health-service staff should have some appreciation of the role of epidemiology and the underlying methods in order to be able to read published work and interpret it. The medical field undergoes continuous change and therefore the most important aspect of training is not the accumulation of facts, but the acquisition of the ability to accept fresh information, and judge whether the findings warrant change in practice.

Apart from facilitating the interpretation of other people's findings, it is possible that a description of the methods of epidemiology may stimulate the use of these techniques by a wider range of individuals. Some of the work discussed in later chapters has been carried out using the minimum of facilities. Useful studies can be done either by examining the routinely available data, or by collecting a restricted amount of information and analysing this in a relatively simple way; the resources required for many worthwhile studies are slight compared with research in other fields. The emphasis is mainly on the need for careful planning and consideration of the issues involved, the collection of observations of known accuracy and the careful interpretation of such material.

1.2 Development of Epidemiology

The foundations of epidemiology were laid in the nineteenth century, when a few classic studies made a major contribution to the saving of life. This work was particularly concerned with infectious diseases. However, even at that time there was an awareness of the need to look at the influence of the environment. Other studies early in the nineteenth century demonstrated the influence of occupation on morbidity and mortality, and also the effect on health of the general environment and social conditions. Thackrah (1832)

produced a lengthy book on the effects of arts, trades and professions on health, while Chadwick (1842) in his report on the sanitary condition of the labouring population in Great Britain discussed the influence on health of drainage, ventilation, overcrowding in dwellings, low income and poor diet.

A misconception that has lingered too long is that epidemiology is primarily concerned with infectious diseases. From the start it was recognised that the onset of disease can be due to an infective agent; this was associated with an awareness of the important influence of physical, emotional, social and genetic factors. In developed countries the majority of health-care problems now stem from chronic disease and the bulk of the examples in the following chapters are related to studies on chronic disease. The basic techniques for studying infectious disease are similar. However, due consideration must always be given to the relative influence of the prime aetiological agent, the 'vehicle' for transmitting it, the associated factors affecting risk of development of a disease and the host's response to the disease.

1.3 Four Categories of Study

Epidemiology involves four different categories of study. The first one is descriptive: for example, 'Who gets heart disease?' National data have been used to examine the mortality from heart disease in different countries in relation to some of the characteristics of the individuals who died and other basic items available in the mortality data (for instance the fatality rates in relation to age, sex, time of year and secular trend). This limited material has then been supplemented by population surveys, which have looked at the prevalence of identified heart disease.

A second category of study is hypothesis testing, for instance exploring the question 'Does diet influence heart disease?'. National mortality rates have been contrasted with estimates of intake *per capita* of various nutrients. This has been followed by the examination of the reported diets of persons with heart disease and of control subjects. A more precise examination may occur with the measurement of the habitual diet in a large number of subjects and their follow up to determine which individuals develop heart disease in relation to initial categorisation of diet.

If the descriptive and hypothesis-testing studies point to a particular factor being of importance in the development of the disease, these studies may be followed by a third phase—an intervention study. For example, work has been carried out to test whether an actual alteration of diet in individuals has any effect on the incidence, recurrence rate or fatality from heart disease.

These three main categories of epidemiological study may each require, as a preliminary phase, a fourth and rather different approach—that is, a method study. As with any other research work, before embarking on a definitive study there may be a need to refine the techniques required in the applied study. For example, in order to examine the diet of a large number of individuals, there is the need to develop a technique for assessing diet that is

reliable and valid, and yet sufficiently simple to be applied in the field to a large number of subjects.

Method studies involving the development of data-collection techniques may also lead to improved disease categorisation. For example, epidemiological, clinical and pathological work has indicated that Hodgkin's disease may be a heterogeneous collection of conditions. The ability to distinguish between these types of Hodgkin's disease may be a necessary preliminary to aetiological studies (MacMahon, 1966). Other work may suggest that a 'condition' does not really exist. Examination of the X-rays of 132 subjects with dysphagia by eight observers resulted in variation of between 6 and 59 per cent of the subjects being reported as having a web (Elwood and Pitman, 1966). This suggests that the Patterson-Kelly syndrome may be nothing more than a variation in observers' interpretations of barium swallows.

1.4 Need for Numeracy

Considerable emphasis is placed on study design in each of the chapters and attention is also paid to the methods of analysis and interpretation of collected data. Epidemiology is essentially a multidisciplinary approach, and in particular relies heavily on numerical techniques. Each chapter ends with brief consideration of some of the relevant statistical techniques. This is not intended to serve as a text of statistical techniques, but merely to indicate the relevance of statistical method and in particular to emphasise those methods that are of special use in epidemiological studies. Some of the techniques, such as the calculation of relative risk or proportional mortality, are not generally dealt with in the standard books on statistics. These techniques are therefore given more emphasis, and only the most cursory mention is made of those statistical approaches that have been fully dealt with elsewhere. One of the reasons for including the sections on statistics is to indicate the specific methods appropriate in the various categories of epidemiological study. This should facilitate communication between the research worker and the statistician. It must be emphasised that when statistical advice is required, this should be sought at an early stage in planning a study and not when the material has all been collected and an attempt is being made to interpret it. Armitage (1971) has suggested that 'statisticians are in too short a supply to act as collaborators in more than a fraction of all statistically orientated studies in medical research'. There is a need therefore for those mounting epidemiological studies or attempting to interpret the work of others to appreciate the relevance of certain statistical techniques in the handling of material.

1.5 Different Approaches to the Consideration of Epidemiology

Epidemiology could be considered under the applications it may have, such as the definition of disease groups, the unravelling of primary and associated

aetiological factors in the causation of disease, and the delineation of the natural history of disease. Another approach is to describe the findings of epidemiology in relation to disease entities, such as malignant, heart and respiratory diseases. A third approach is to describe the methods of epidemiology illustrating these by the different categories of use (thereby indicating some selected findings from the application of such methods).

This is the approach that has been used in this book, but this should in no way suggest that a study of the methods of epidemiology in isolation is of merit. The approach has been deliberately chosen, however, in an attempt to interest a wide range of individuals in the use of such methods, whatever their particular field of work. In this book, there has not been any attempt to provide a comprehensive account of the findings of epidemiology in relation to every major category of disease problem. This is chiefly because the approach selected only provides a discussion of the findings as part of a consideration of particular problems of study design and interpretation of results; also it is felt that the findings of epidemiology cannot be looked at in isolation. For instance, when considering malignant diseases, epidemiology can provide background information and some extremely interesting pointers to the causes of various malignant diseases and the steps that can be taken to prevent these diseases. Even the descriptive data on the disease in question requires support from clinical and pathological studies to indicate the specific nature of the condition. A discussion of the natural history of the disease should not really be divorced from the consideration of the various methods of treatment for each particular malignant disease, and a detailed assessment of the outcome of treatment. Such an approach calls for integrated topic teaching rather than the isolated presentation of the findings of epidemiological studies. Factual information is provided in a number of books (see further reading lists) on the epidemiology of particular diseases, and data are being augmented all the time by fresh studies reported in the literature.

Even in the absence of any clear knowledge of the underlying cause of disease, epidemiology may help to unravel the 'vehicle' responsible for the transmission of the disease (whether this is due to infection, exposure to physical and/or chemical factors, or is genetically determined). Such studies are pursued not merely to add to the general body of medical knowledge, but in the hope that the relationship between aetiology and the development of the disease may be sufficiently clarified that preventive measures can be suggested. For many conditions, whether these are acute or chronic diseases, there is a growing awareness that the individual's level of recognition of diseases varies. In medical-care studies an important aspect of the work involves not only identifying the determinants of disease, but also the factors associated with seeking care. Such studies lead to a consideration of who gets treatment and the results of treatment. A standard treatment given to a number of patients with a disease of particular severity results in a variation in response; epidemiological methods may be used to identify the factors associated with this variation in response. Such information may be useful in improving the selection of patients for each type of treatment. The techniques used for the examination of the results of treatment are closely aligned to some of the general methods of epidemiology and are covered in

chapter 7. Work on the examination of the natural history of the disease and of response to the treatment requires measurement of outcome of such care. Such studies may be part of a general examination of the functioning of the health service. This involves consideration of facilities required for care, variation in type of care provided, factors affecting uptake of care and the outcome from such care. Attention is paid to these issues in the final chapter of the book.

Many of the examples given in the following chapters relate to classic examples of particular studies. These have been chosen because they illustrate the particular methods used and not in order to give a systematic catalogue of the various findings of epidemiological studies. A number of the examples stem from the personal experience of the author; again these have been used as an indication of method rather than having been selected because of the specific value of their findings. Some of the problems discussed will be well known to the general reader, while others relate to problems affecting a relatively small segment of the population and involving quite rare diseases. Although the chapters do not provide a systematic or comprehensive documentation of the findings of epidemiology over the complete range of health problems, relatively generous provision of cross-references in the index goes some way to overcoming this issue. The text introduces a number of key terms used in epidemiology, particularly relating to methods of study design and data handling. Definitions of these terms have been collected into a list, which is to be found at the end of the book (pp. 223–226).

References

Recommended reading

- Armitage, P. (1971). *Statistical Methods in Medical Research*, Blackwell, Oxford
 Pickles, W. N. (1939). *Epidemiology in County Practice*, Wright, Bristol

Other references

- Burkitt, D. (1962). A tumour syndrome affecting children in tropical Africa. *Postgrad. med. J.*, **38**, 71–9
 Chadwick, E. (1842). *Report on an Enquiry into the Sanitary Condition of the Labouring Population of Great Britain* (reprinted, 1965, University Press, Edinburgh)
 Elwood, P. C., and Pitman, R. D. (1966). Observer error in the radiological diagnosis of Patterson–Kelly web. *Br. J. Radiol.*, **39**, 587–9
 Fry, J. (1966). *Profiles of Disease*, Livingstone, Edinburgh
 Fry, J. (1974). *Common Diseases: Their Native Incidence and Care*, Medical and Technical Publishing, London
 Gregg, N. M. (1941). Congenital cataract following german measles in the mother. *Trans. ophthalm. Soc. Aust.*, **3**, 35–46
 Kay, C. (1974). *Oral Contraceptives and Health—Interim Report on the Oral Contraception Study of the Royal College of General Practitioners*, Pitman Medical, London
 MacMahon, B. (1966). Epidemiology of Hodgkin's disease. *Cancer Res.*, **26**, 1189–200
 Thackrah, C. T. (1832). *The Effects of Arts, Trades and Professions, and of Civic States and Habits of Living, on Health and Longevity: with Suggestions for the Removal of Many of the Agents which Produce Disease, and Shorten the Duration of Life* (reprinted, 1957, Livingstone, Edinburgh)

2 The Use of Mortality Statistics

Mortality returns have been collected in England and Wales since 1839, and an annual publication of statistics produced. Soon after their introduction they were used in a number of special studies on the cause of disease. Hill (1955) suggested that perhaps the most important feature in Snow's argument about the transmission of cholera was his adept handling of the vital statistics for London, which were provided by the Registrar General in the mid-nineteenth century. Since then, these statistics have continued to serve as a ready source of background information for many health problems. Partly because of their extensive history, they form a suitable starting point for the consideration of the methods of epidemiology. Their use is chiefly as a constant source of descriptive material, although subsection 2.2.3 provides an example of their use in hypothesis testing. An additional reason for commencing with a consideration of mortality statistics is that they provide an introduction to the consideration of the steadily expanding range of morbidity statistics now becoming available in both developing and developed countries.

2.1 Basic Example of the Use of Mortality Statistics

A dense fog engulfed the Greater London area during the four days, 5–8 December, 1952. Although the fog was exceptionally severe, its grave effects were only recognised as information was accumulated from a number of sources. Newspapers carried stories about the fog, and a heavy demand for hospital beds was noted. The public appeared to expect that the main mortality would occur in the elderly; only those intimately concerned with deaths, such as coroners and registrars of deaths, were able to realise, and then only on a local basis, the true extent of the mortality. Not until all the death certificates had been assembled and analysed did the excess mortality become apparent. The figures were immediately made known to parliament by the Minister of Health. On 18 December, in answer to a written question, the Minister replied that the number of deaths from all causes occurring in Greater London during the week ending 13 December had been 4703; this compared with 1852 in the corresponding week of the previous year. It was suggested that the cold weather had caused some of the increase in the number of deaths, but that a large part of the increase must be attributed to the fog. Since the Minister of Health replied in writing, there was no discussion and no reference was made to the need for a special study. However, the information produced an immediate reaction and it was apparent that the problem of preventing further disasters of this nature was urgent. It was decided that a special study, concentrating primarily on the fatalities, and in particular a statistical investigation of the material available to the Registrar General, would try to discover the factors responsible for the increased mortality.