Epidemiological research methods

Part I. Why epidemiology?

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In the first article in a series on epidemiological research methods, we describe the origins and uses of epidemiology and introduce the different types of epidemiological study design.

The origins of epidemiology

Epidemiology is derived from the Greek words επι 'upon' and δεμος 'people', in other words the study of people. It was first associated with the study of outbreaks of contagious disease in humans ('epidemics'). The earlier investigators' attempts to find the cause of the infection meant that they had to follow a community-based approach. For this reason, epidemiology is often associated with public health, community medicine and infectious diseases. The original concepts and methods of epidemiology were derived from the investigation of infectious disease outbreaks such as the cholera outbreak in London in the middle of the last century. John Snow's observations during the 1853 - 1854 outbreak marked the scientific beginnings of both epidemiology and environmental health.[1] He challenged the prevailing view that cholera was primarily an air-borne cause of disease and water a mere contributing cause. He traced the source of the infection (the cholera *Vibrio* was first identified in 1883) to the Broad Street pump after carefully mapping out the distribution of cases and their source of water. Not satisfied with only describing the course and cause of the epidemic, he removed the pump handle to prevent further contamination (however, the epidemic was already declining by the time he took action!).

At about the same time that John Snow was conducting research, William Farr,[2] the first compiler of abstracts in the Registrar-General's Office in London, was laying down the basis for the collection and analysis of vital events (births and deaths). Farr was well aware of the relationship between prevalence and incidence of disease and the differences between retrospective and prospective studies. His work and that of Nightingale[3] and Chadwick[4] laid the foundation for the quantification and interpretation of causes of mortality. Nightingale was one of the first health professionals to analyse hospital causes of death. She did her pioneering work during the Crimean War and on her return was the first person to use pie-charts as a method of data display. Chadwick, in contrast, investigated the relationship between mortality and morbidity on the one hand and the social environment on the other. His investigation[4] into 'sanitary conditions' in London in 1842 resulted in far-reaching public health legislation.

From the middle of the 20th century, epidemiologists have increasingly focused their attention on non-infectious causes of death. The 'epidemic transition', which occurred over the last century in Europe and North America, has seen infectious diseases giving way to chronic diseases such as cancer and ischaemic heart disease as major causes of death. This transition has been associated with profound economic and social transformations in these societies and epidemiologists have had to contend with multiple environmental factors or agents, often acting together with unknown factors in chronic disease causation.[5]

In more recent years, epidemiologists have increasingly focused their attention on features other than deaths and have shown that epidemiological methods are critical to the diagnostic, prognostic, therapeutic and overall management approach needed in clinical medicine.[6-8] These developments are also reflected in modern definitions of epidemiology, three of which are: (*i*) the study of the occurrence of illness;[9] (*ii*) the study of the distribution and causes of health impairment in human populations and the evaluation of actions taken to improve health (L. M. Irwig — unpublished internal document; Institute for Biostatistics); and (*iii*) the quantitative study of the distribution and determinants of health and disease in organisms, with the objective of maximizing health (definition developed by the 1978 M.Sc. (Clin. Epid.) class, McMaster University, Toronto, Canada).

These definitions share some common ideas, whether expressed explicitly or implicitly: epidemiology is concerned with the health of populations rather than individuals. It is used to study relationships between people, their diseases, the agents that cause or prevent or cure these diseases, and the environment.

Epidemiology in South Africa

In South Africa, the first reported epidemiological study was the description of the prevalence of syphilis in the black population by Dr W. R. Harrhy, District Surgeon of Barkly West, published in the *South African Medical Journal* in 1888.[10] In a subsequent report[11] it was stated that the drop in the prevalence of syphilis in troops in Cape Town from 207 cases per 1 000 in 1888 to 27 cases per 1 000 in 1896 could be attributed to the 1889 decision of the Colonial Parliament to pass the Contagious Disease Act. Even before these studies, a community-based epidemiological study could be discerned in the large settlement at the Cape of Good Hope in 1652 to provide sailors en route to the East with fresh provisions to prevent scurvy.[12] The effect of scurvy at the time was so devastating that most ships reported losses of half or more of their crew. Vasco da Gama reported that 100 of his crew of 168 died of scurvy in their 1498 Cape trip. With the provision of fresh food from the Cape to seafarers, the death rate of scurvy decreased, even though it was almost a century later that James Lind, in a clinical trial on board HMS *Salisbury*, demonstrated the efficacy of citrus fruit and the worthlessness of other remedies such as cider, salt water or elixir vitriol.

In the past century there were a number of important landmarks with epidemiological relevance in South Africa, including: (*i*) the Public Health Act of 1897; (*ii*) the great Spanish influenza epidemic of 1918; (*iii*) the Gluckman Commission of 1944; (*iv*) the development of the Institute for Biostatistics of the South African Medical Research Council

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(MRC); (*v*) the establishment of an epidemiology unit at the Department of Health in Pretoria; and (*vi*) the founding of the Epidemiological Society of Southern Africa (ESSA) in August 1983. We hope that the establishment of the B.Sc. Honours course in epidemiology at the University of Stellenbosch (the first of its kind in the RSA) will have a national impact on epidemiological work in South Africa through the achievements of its graduates.

The Public Health Act of 1897 introduced by-laws that gave urban authorities power in their districts to register births and deaths and notify authorities of infectious diseases.[13] The Act was designed to cover all 'Europeans' and 'Coloureds' in the country.[14] It was recognized that there would be problems in the rural areas where doctors were scarce, and that the system would take time to implement. However, it was felt that the procedures would yield important statistics 'regarding social questions'. This Act has subsequently been revised, but vital statistics and statistics on notifiable diseases are still regarded as the backbone of epidemiological studies. In recent years, epidemiologists have stressed the importance of obtaining reliable and accurate statistics from all parts of South Africa and have highlighted the extent of current inadequacies in basic data collection.[15,16]

The influenza epidemic of 1918 resulted in considerable mortality and morbidity, affected many people between 25 and 45 years, was associated with a high prevalence of fatal lobar pneumonia and caused widespread panic.[17] The pandemic did, however, provide the impetus for the *Volksgezondheidswet*, No. 36 of 1919, that laid the foundation for public health in South Africa.[18]

The task given the National Health Services Commission of 1944 (chaired by Henry Gluckman) was to 'investigate and recommend the best measures to be adopted for ensuring adequate health services for all sections of the people of the Union'.[19] Over a 21-month period the Commission carried out the most extensive study ever undertaken of South Africa's overall health status, and found that the health services were mainly concerned with 'care of ill health and very little with prevention of diseases', and were disjointed and haphazard in that they were maldistributed and available only to a small section of the population. The quality of health statistics (registration of births and deaths and disease notification) was found to be extremely poor and incomplete. Chapter 5 of the report detailed results of a nutritional survey of 'Europeans' in which it was found that 31,5% of children in the Cape were malnourished and that 28% received no milk.

In general, the Gluckman Report painted a bleak picture of South Africa's health status, which should have provided the impetus for the creation of a national health department for the support of community-based health centres and for recognition of the need for preventive medicine and the critical role of social and economic factors. The report recommended that 'the mere provision of doctoring would not be enough to secure health for all the people of South Africa, but that there would have to be fundamental cuttings at the roots of ill health'.[20] Only a few recommendations were immediately implemented. The health-centre approach was experimentally tested in Bulwer, Natal. From 1942 a form of primary health care was practised there.[21] The centre stressed the need for integrating curative and promotive services, including the role of non-health factors such as soil erosion and migrant labour in causing gross nutritional failure. During the period 1942-1950, the local infant mortality rate dropped from 275/1 000 to 101/1 000 and the incidence of gross nutritional disorders virtually disappeared.[22] Unfortunately this type of community intervention was not widely practised in South Africa and many of the recommendations were not implemented in the ensuing decades. In 1976, the then Secretary of Health wrote that the existing health services were 'bewildering in complexity and diversity...and fragmentation'.[18] The 1950s and 1960s saw the emigration of many South Africans, who were to become eminent epidemiologists in the USA, Canada, Israel and the UK. This same period saw South Africa play a leading role in the development of the yellow fever and pneumococcal vaccine.[23]

In the 1960s the Division of Medical Statistics and Epidemiology of the National Nutrition Research Institute of the CSIR (which subsequently became the National Research Institute for Nutritional Diseases of the MRC) was formed, and developed into the Institute for Biostatistics of the MRC under the directorship of Dr S. A. Fellingham. In this institute the opportunity existed for the first time in South Africa to bring epidemiological and biostatistical expertise jointly to bear on, *inter alia,* planning epidemiological studies.

Since the 1970s the Department of Health's Epidemiology Unit in Pretoria has under Dr H. Küstner's guidance followed the approach of the US Centers for Disease Control in making epidemiological information (e.g. notification, trends) available to relevant health professionals through the publication of *Epidemiological Comments.* He has emphasized, both in a thesis[24] and in the monthly reports, the need for field epidemiology and surveillance based on epidemiological methods. Over the last few years there has been a reawakening to the need to conduct innovative epidemiological studies of relevance to the RSA. Watermeyer[25] in 1976 called for new epidemiological methods to investigate the problems of tuberculosis, gastro-enteritis and malnutrition, and stressed the need for research findings to be implementable. Community-based descriptive studies in recent years[26,27] and even a few hospital-based studies[28-30] have attempted to do this. Many of the published reports have methodological problems which limit their usefulness. In addition to descriptive studies, Mann[31] in 1982 stressed the need for more epidemiological research in the RSA which took advantage of the range of lifestyles, diets, work habits and the presence of the scientific means to be able to study the effect of risk factors on chronic diseases. Selected studies have addressed these issues in analytical and intervention studies.[32] Some of the above will be used to illustrate methodological points in subsequent articles in this series. Such illustrative material will be derived from public health and from clinical medicine, amplifying the notion that epidemiology is a flexible methodological discipline useful in all areas of health care.

The founding of ESSA in 1983 is the latest event leading to increased awareness of the uses of epidemiology. Membership is open to all interested people involved in epidemiological work and one of its objectives is to advance knowledge and to promote teaching, research and involvement in epidemiology and its applications. To achieve this the Society organizes meetings, conferences and workshops, and publishes a scientific journal (in collaboration with the Infectious Disease and Sexually Transmitted Disease Societies).

The uses of epidemiology

Epidemiological research methods are commonly used to: (*i*) determine the extent of health problems in the community; (*ii*) investigate the cause of disease and roles of transmission; (*iii*) study the natural history of disease; (*iv*) develop the basis for prevention programmes; and (*v*) evaluate the effectiveness of preventive or therapeutic programmes.

The relevance of these applications of epidemiological methods is evident from the triad of host, agent and environmental factors used to model the distribution of diseases and their determinants. Important host factors include intrinsic factors such as genetic, racial, constitutional and physiological status, earlier immunological and medical experience as well as age and sex. Typical agents include infectious, chemical and physical agents. The absence of an agent, for example essential nutrients, also has an effect on disease. Environmental or extrinsic factors include the hazards of intra-uterine life and the perinatal period, hygiene conditions, geographical, seasonal, and climatic factors, the degree of crowding, work conditions, dietary factors, herd immunity (for infectious diseases) and other conditions imposed by sociological, cultural and economic patterns of life.

The presence, excessive presence, or relative lack of an agent is essential for the occurrence of a disease. A disease may have a single agent, a number of independent agents, or a complex of two or more agents, the combined presence of which is essential for disease. Agents interact dynamically both with the host (potential patient) and the environment. A simple example of the agent-host-environment relationship is measles. Age, earlier immunization and physiological status are host determinants of the probability of disease-given infection. The measles virus (the agent) is transmitted by droplet spread. An increased concentration of infectious droplets will increase a susceptible host's risk of infection and disease. Environmental factors, such as degree of crowding, herd immunity or season, are all determinants of the likelihood of infection in individuals. This is a highly schematized example. In reality, changes occur in two or all members of the triad, disease being the outcome of any disequilibrium. This model is applicable not only to acute infectious diseases, but also to chronic infectious diseases, ischaemic heart disease and cancer. In the latter two diseases, agents may be of diverse origins, e.g. cigarette smoke, asbestos, stress, or occupational hazards.

The epidemiological research methods to be discussed later in this series will relate mostly to studies of chronic diseases, even though epidemiology started off with infectious diseases. The foundation of chronic disease research methods is to select an appropriate study design for a given research question (Table I), and the different study designs obviously reflect different uses of epidemiological research methods. Each study design will be closely scrutinized later, but a few comments on important principles are justified here.

A *descriptive study* is used to quantify the size or extent of a health problem in terms of time (when did it occur?), place (where did it occur?) and person (which groups are affected?), i.e. the aim of the study is to describe certain attributes in the population. A typical question answered by a descriptive study in biological research would be: 'What are the age-specific mortality rates for tuberculosis in South Africa?' A similar study in the field of health services research may attempt to answer the question: 'How good or poor is compliance with treatment of hypertension?'

To explain why a health problem exists in terms of its genetic and/or environmental determinants an *analytical study* is usually conducted. In analytical studies at least two different populations or communities or groups are studied and compared with one another. These groups are usually selected so that they differ either in terms of the distribution of determinants or the distribution of disease, and these distributions are the result of processes outside the control of the investigator. On the basis of such a comparison differences among communities that have or do not have a certain health problem may indicate possible explanations or possible causes for the health problem. A typical question answered by an analytical study is: 'How much of South Africa's high cardiovascular mortality rates can be explained by lifestyle?' In health services research a typical question answered by an analytical study is: 'What factors (e.g. age, sex, knowledge) affect the likelihood of a patient not complying with hypertensive treatment?'

Once the disease has been fully characterized in terms of its distribution, course and cause, modification of the 'cause' should be attempted to control, treat or prevent disease in a population. To evaluate whether a proposed modification or treatment works, epidemiologists use *intervention studies.* In intervention studies two or more groups are also compared with one another, but they differ from analytical studies in that the researcher intervenes with a defined strategy, and ideally the allocation of patients to the two groups is under the control of the investigator. This is important, because by doing this the investigator can take steps to ensure that the groups are comparable in other important respects. Often, in practice, such a randomized controlled trial is not possible, in which case a group of patients may be observed before the intervention is instituted and again thereafter. Measurements in these two time periods are then compared. Such a before-after study has the weakness of having no contemporaneous control group. In biological research a typical question answered in an intervention study is: 'Does a proposed new anti-hypertension drug lower blood pressure?' In health services research a typical question answered in an intervention study is: 'Does a proposed compliance improving strategy (for example reminders about appointments) improve compliance?'

TABLE I. TYPES OF EPIDEMIOLOGICAL STUDY AND EXAMPLES OF QUESTIONS WHICH THEY CAN ANSWER

	Biological research	Health services research
Descriptive study	**What are the age-specific mortality rates in the RSA?**	**How good or poor is compliance with treatment for hyper-tension?**
Analytical study	**How much of the RSA's high cardio-vascular mortality rates can be explained on a genetic basis?**	**What factors (e.g. age, sex, knowledge) affect the likelihood of a patient not complying with treatment?**
Intervention study	**Does a proposed new antihypertensive drug lower blood pressure?**	**Does a proposed compliance-improving strategy (e.g. reminders about appointments) improve compliance?**

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Review Article

Socio-environmental factors and lung function

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Summary

The literature was reviewed to assess whether the evidence implicating socio-environmental (SE) factors as determinants of adult lung function was sufficient to require that they be taken into account in epidemiological studies, together with other factors, such as age and smoking. In six studies involving 11 000 adults resident in the USA, France and Denmark forced expiratory volume in 1 second was related to social class and/or one of a number of other factors including education, area of residence and housing status. Trends in three other studies involving approximately 15 000 children resident in the UK and the USA were similar. The consistency of the findings makes it difficult to escape the conclusion that SE factors should be taken into account in comparisons of lung function between populations when the purpose is to assess the role of other environmental factors such as occupational exposure.

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Lung function tests are an important part of the clinical assessment of respiratory illness, in particular when degree of impairment or disability needs to be evaluated, for instance for compensation purposes. Comparison of measured lung functions with reference values derived from published data on healthy populations is necessary given the many factors other than disease, the focus of clinical assessment, which contribute to between-individual variation in lung function.[1] Identical considerations apply to the use of lung function tests to assess the respiratory status of populations. Thus in examining work forces subject to particular occupational exposures, comparison with non-exposed or other healthy populations becomes a central issue.

Attention has recently been directed to the influence of socio-environmental (SE) factors on respiratory health status (including lung function) in the columns of this *Journal*.[2-4] The purpose of this study is to review the medical literature on the topic in order to evaluate three issues: (*i*) the role of SE factors *vis-à-vis* that of other determinants of lung function; (*ii*) whether they should be taken into account in epidemiological studies, in particular those focused on work forces; and, if so, (*iii*) the operational guidelines for so doing. This is particularly relevant in the RSA where SE factors are linked to ethnicity (Table I).[5] In addition, unanswered questions and future lines of research will be discussed.

Sources of variation in lung function

In order to assess the contribution of SE factors to variation in lung function, it is necessary to take into account the other known sources of variation.[6] These can conveniently be con-