

## Chapter 1

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# Introducing the history of epidemiology

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Nature cannot know its own history, humans can

## Introduction

### Why teach the history of epidemiology?

'Know yourself': this Socratic maxim expresses the rationale for learning the history of epidemiology. Self-knowledge and a critical but positive attitude towards the discipline is fostered by the study of the historical development of epidemiology, which enables the epidemiologist/teacher to highlight several salient features. (A professional historian of science may adopt a more personalized view arising from his/her research.) These salient features include:

- ♦ The common elements unifying all branches of epidemiology as a population health science beyond today's subdivision into specialized areas.
- ♦ The relationship of epidemiology to other scientific disciplines and its methodological specificities, strengths and weaknesses in respect to them.
- ♦ The emergence of key concepts, either methodological as 'risk', or substantive as the modes of diffusion of pathogens in the community. This cumulative but irregular accrual of knowledge is characterized by controversies, blind alleys, and sheer errors as well as by material hurdles and personal and institutional conflicts. It may appear long when time is measured in years but is much less when a generation of scientists is, more appropriately, taken as the time unit.
- ♦ The influence of the demographic, health, social, cultural, and economic context on the development of epidemiology and of epidemiological methods.
- ♦ The role of epidemiology in society through its impact in the health field, largely mediated through the essential functions of epidemiology within public health.
- ♦ The roots and dynamics of present trends in epidemiology and the options for reinforcing, contrasting, or inflecting them.

None of these features are going to be entirely missed by anyone working in epidemiology without much concern for remote or proximate historical antecedents. However, as in epidemiology follow-up studies – which explicitly embody the time dimension – are much more informative than cross-sectional studies, so the historical dimension can provide a wider and clearer perspective on the nature of the discipline and on the role of its practitioners in society. At a time when all scientific activities have increased (and increasingly recognized and debated) the implications of an economic, social, and ethical nature of the historical perspective may become more of a necessity than a curiosity.

As history can be learnt so it can be taught. In this respect a basic consideration is that historical knowledge changes in time not only because of cumulative advances, as for all theoretical or empirical sciences, but also because the point of observation of the historical past moves continuously forward with time and the landscape that becomes visible to the eye of the observer changes in consequence. As a reconstruction of the past, history is to a non-negligible extent a function of the present and of what the present allows or does not allow us to discern. This unavoidable bias may be grossly amplified when the past is reconstructed primarily to justify particular aspects and views of the present: for instance, rudimentary and lopsided reconstructions of mankind's evolutionary history have been abundantly and tragically employed to support racist theories and practices.

## **Whom to teach?**

The teaching as outlined here is primarily addressed to students following Master and PhD courses who intend to become full-time epidemiologists or make a large use of epidemiology in their professional work; for example, public health practitioners, clinicians, and occupational physicians.

This teaching can only be regarded as preliminary for students who may wish to proceed in one of two directions: first, historical epidemiology as a description and analysis of health and diseases in given areas and past periods of time; second, the history of epidemiology as the reconstruction of the development of theories, concepts, methods, and practices, including the study of the role of individuals and institutions.

At a number of medical schools students follow a course in epidemiology or epidemiological methods lasting 20–40 hours: in this context a short (1-hour) historical overview should be offered.

## **How and when to teach?**

This chapter is a guide for the preparation of a short introductory module of 8–10 hours within a Master or PhD programme; it does not provide a script for lectures. In many epidemiology programmes historical notes are confined to occasional (if any) comments within the body of other modules. This module aims instead at presenting structured material as an individualized teaching block to students provided they have already followed at least one or more modules in general epidemiology and epidemiological methods. Important points to which the teacher should pay attention are features in the development of epidemiology particular to their country. An effort

should be made to take these into account, lest elements essential to the understanding of the present situation are missed.

## Teaching objectives

The objective of the module is to focus and raise the motivation of students for the historical perspective in epidemiology, promoting the exercise of asking and answering – when confronted with a methodological or substantive issue – questions such as: How has the issue developed overall? Was it recognizable and in what form, for example, at the beginning of the twentieth century? What were its antecedent and related issues? How was it tackled within the framework of existing knowledge? Did it induce critical advancements in knowledge? Was it instrumental for the development of approaches and methods more widely applicable? Were there any social, economic, political, and ethical factors which had non-trivial influences on it? Were any social, economic, political, and ethical consequences derived from its treatment within epidemiology? What can a historical exploration tell us about the present status and future evolution of the issue?

Of course, similar questions arise in daily work, typically when reviewing the literature on a specific research topic. Looking at these historically means expanding questions and answers in two ways: first, in time, going back not only a few years or a couple of decades (which may, however, be perfectly adequate for the strict needs of the research topic at hand); and second, in extent, tracing connections of the issue internally within epidemiology and other sciences, and externally to the societal context.

## Structure of course

The module includes five parts:

1. An overview of the history of epidemiology (one lecture with brief discussion in plenary).
2. The modern history of tobacco and health: scientific aspects (one lecture with extended discussion in plenary).
3. The modern history of tobacco and health: societal aspects (one lecture with extended discussion in plenary).
4. A paper from the past (paper reading followed by extended discussion in plenary).
5. Present trends linking past and future (reading of papers followed by extended discussion in plenary).

The total time required for the module is between 8 and 10 hours, to be split over 2 or more days. Papers for reading can be distributed in advance. A class of more than ten to fifteen students should be split into smaller subgroups. Reading can be completed and some discussion developed within subgroups in preparation for a plenary session in which each subgroup presents for general discussion the issues they have identified as important. A written outline of each part with essential references should be prepared for distribution.

## Teaching contents

Material for the five components of the module can be found and selected for assemblage and teaching in:

1. The historical sketch.
2. The key references listed at the end of the chapter.
3. The other references reported at the chapter end.

Following the historical sketch (pp. 4–15), content indications (with specific references) for each of the five parts are provided (pp. 15–17). *The key references should be readily available to the teacher as they are a primary source of material for all parts of the module.*

### A historical sketch

As the name implies this ‘sketch’ is not a synthesis of an analytical and scholarly work; more simply, and much less ambitiously, it aims to offer the teacher a broad framework and some illustrative material for the module.

To review the yesterday, today, and tomorrow of epidemiology (here seen with a bias towards Europe) it may be convenient, though somewhat arbitrary, to consider three periods: (1) early epidemiology, extending from the fifth century BC to around 1830; (2) classical epidemiology, from around 1830 to the 1940s; (3) new epidemiology, from the 1940s to the present.

#### Yesterday: a bird’s eye view

**Early epidemiology** This long stretch of time ran for more than two millennia, from Hippocrates (c.470–c.400 BC) to the first third of the nineteenth century. Numerous and keen epidemiological observations were made and have been handed down in surviving documents, based at best on simple or crude methods of investigation (when unfairly judged by our contemporary methodological standards). Epidemiological theories were also elaborated to explain the spreading of diseases, notably those recurrently striking and decimating populations (‘epidemics’).

Hippocrates developed the medical approach by providing concise, accurate, and complete descriptions of actual clinical cases, including diseases such as tetanus, typhus, and phthisis. This remained ‘without parallel until the late seventeenth century’ (Singer and Underwood, 1962). However, in his book on *Air, Waters and Places*, he clearly identified – as a seminal environmental scientist – the general dependence of health not on magical influences but on an identifiable array of natural external factors (Table 1.1).

The reawakening of *clinical observation* in the seventeenth century, epitomized by the ‘English Hippocrates’ Thomas Sydenham (1624–1689), brought attention back to the circumstances surrounding the occurrence of clinical cases, thus not only reviving the Hippocratic tradition but adding to it. In the year 1700, Bernardino Ramazzini (1633–1714) wrote in his *De Morbis Artificum Diatriba* (Ramazzini, 1982):

The physician has to ask many questions of the patients. Hippocrates states in *De Affectionibus* ‘When you face a sick person you should ask him from what he is suffering, for what reason, for how many days, what he eats and what are his bowel movements’. To all these questions one should be added ‘What work does he do?’

**Table 1.1**

Whoever wishes to investigate medicine properly should proceed thus: in the first place to consider the seasons of the year, and what effects each of them produces. Then the winds, the hot and the cold, especially such as are common to all countries, and then such as are peculiar to each locality. In the same manner, when one comes into a city to which he is a stranger, he should consider its situation, how it lies as to the winds and the rising of the sun; for its influence is not the same whether it lies to the north or the south, to the rising or to the setting sun. One should consider most attentively the waters which the inhabitants use, whether they be marshy and soft, or hard and running from elevated and rocky situations, and then if saltish and unfit for cooking; and the ground, whether it be naked and deficient in water, or wooded and well watered, and whether it lies in a hollow, confined situation, or it elevated and cold; and the mode in which the inhabitants live, and what are their pursuits, whether they are fond of drinking and eating to excess, and given to indolence, or are fond of exercise and labor.

Hippocrates

On Airs, Waters and Places

Besides being an acute clinician Ramazzini moved from the observation of individual cases to the consideration of similar cases sharing work circumstances.

Ramazzini is today regarded as the founder of occupational medicine, a key section of the larger field of environmental medicine and epidemiology. A contemporary of Ramazzini was Giovanni Maria Lancisi (1654–1720), anatomist and clinician, whose *De Subitaneis Mortibus* (1707), in which he reports a detailed pathological investigation of a series of sudden deaths in Rome, is probably the first epidemiological study of a non-communicable condition (Lebowitz, 1970). The study was commissioned by the Pope, to whom Lancisi was the personal physician (there were no grant applications!).

On a rather different, essentially *demographic* approach, are the developments that were already taking place in the late Middle Ages and Renaissance Italy in the latter part of the fourteenth and in the fifteenth centuries. For instance, in Florence and Venice the counting of deaths and some early form of death certification specifying the cause in broad terms (e.g. ‘plague’ or ‘not plague’ during such epidemics) were current and established practices (Carmichael, 1986). The major step forward from recording, counting, and accounting to a quantitative analysis of the data was the later accomplishment of John Graunt (1620–1674) in London, who can be regarded as the founder of demography. His *Natural and Political Observations Upon the Bills of Mortality* (1662) was based on a series of weekly bills covering individual deaths and their causes in the London area back to 1603. His treatment of the data included three key innovations (Dupaquier and Dupaquier, 1985): (1) a critical examination of the sources, attempting to address issues of biased recording; (2) the use of frequencies, e.g. of deaths and ratios rather than absolute numbers in his analysis, which allowed several correct comparisons to be made; (3) the application of methods to tackle concrete problems which prompted him, for instance, to conclude that homicides were indeed rather rare, that mortality rates in the first year of life were higher in males than in females, thus compensating the slightly higher number of males at birth; and that, apart from plague, chronic conditions were killing more people than were acute conditions. After Graunt, demographic studies progressed with the invention of the

first empirical life tables (E. Halley, 1656–1742), while, particularly in France, mathematical tools were being developed for dealing with chance events and probabilities (initially arising out of games), which were soon seen as equally applicable to the study of such collective phenomena as births, deaths, etc.

The third approach, *theorization*, concerning in particular the fact that the most frequent and murderous diseases appeared obviously ‘communicable’, either from person to person or from fomites, has a forerunner in the Latin poet Lucretius (first–second century BC). In his poem *De Rerum Natura* he hints that ‘seeds’ of disease can pass from a sick to a healthy individual. It was, however, only much later that Gerolamo Fracastoro (1478–1553), in his *De Contagione et Contagiosis Morbis* (1546), presented the first clear and coherent germ theory of disease, ‘a mountain peak in the history of aetiology, perhaps unequalled by any other writer between Hippocrates and Pasteur’ (Winslow, 1980). Fracastoro theorized that a variety of diseases are caused by transmissible, self-propagating entities (germs) which, however, were conceived more as substances akin to present day viruses than to bacteria. Correctly, he thought that these agents were specific to each disease and could spread from person to person or through infected articles (fomites) or at a distance. He went as far as arguing that treatment should consist of the destruction of the germs by either heat or cold (which is obviously correct), or of their evacuation from the body, or by checking the putrefaction processes caused by these germs, or by neutralizing them by antagonistic substances (which again was correct, but unfortunately these were not available). He is also on record as having not only described, but also given the name to a new disease making ravages in his time – syphilis (1530).

The three streams in early epidemiology, medical, demographic and theoretical, coalesced in an effective way only towards the end of the eighteenth and beginning of the nineteenth centuries, giving rise to epidemiology as we recognize it today, an investigation of diseases and their aetiology at the population level. What had been missing during the very long early phase was not so much the individual components of the epidemiological approach as the integrated and systematic process of empirical observations, quantitative description, hypothesis formulation, deductive reasoning and empirical testing on new observational or experimental data. This started in science with Galileo Galilei (1564–1642) at the beginning of the seventeenth century and gradually spread from physics to other branches of study. In biology an early high point in this combination of observation, experiment and quantitative reasoning was the discovery of the circulation of blood by Willliam Harvey (1578–1657), a contemporary of Galilei.

**Classical epidemiology** With the advent of the industrial transformation of western Europe, starting in Great Britain and propagating from the mid-eighteenth century to the continent in the next decades, ‘crowd diseases’ emerged which struck the populations amassed in the slums of the fast-growing centers of industrial development: London, Glasgow, Manchester, Paris, Lyon, Berlin, etc. This provided the decisive stimulus and at the same time the observational field for epidemiology, which developed as the investigation facet of a vast public health movement. Only a few landmarks and figures can be briefly cited.

In Great Britain medical registration of deaths had been introduced in 1801 and in 1838 William Farr (1807–1883) introduced a national system of recording causes of death. Once the mechanism started to work it provided a wealth of data which Farr himself first analyzed with great skill, making full use of life table techniques (close in most details to those in present day use) and of procedures for standardizing rates. He was also instrumental in building up a classification of diseases for statistical purposes, both national and international. His analyses, published from the Registrar General's Office at regular intervals, gave a picture of the evolving health condition of the population of Great Britain and drew the attention of all social investigators during the Victorian period, including Marx and Engels. The work of John Snow (1813–1858), a contemporary of William Farr, is generally quoted as an example of a brilliant analytical investigation which can lead to the identification of a pathogenic agent and its elimination from the environment. Cholera (Asiatic cholera) had started to rage in India and then moved westwards, the first epidemic hitting Great Britain in 1831–32, causing at least 60 000 deaths. Snow directly investigated the subsequent major epidemic episodes in London in 1849 and 1854, focusing attention on the role that polluted water might have played in the spread of the disease. Among a number of other observations he noted (Table 1.2) that, while in 1849 and 1854 roughly the same number of deaths had occurred in the London districts supplied by the water company of Southwark and Vauxhall, a marked reduction in deaths had occurred in those districts supplied by the Lambeth company. No major change in population had occurred between 1849 and 1854 but, unlike Southwark and Vauxhall, the Lambeth company had changed its sources of water supply, moving higher up the Thames, probably above, as Snow conjectured, the greatest source of contamination by city sewage. Indeed, when he computed death rates from cholera (Table 1.3), they were more than 20 times lower for the districts supplied by the Lambeth company in respect to those supplied by Southwark and Vauxhall. Strong corroboration of these findings came from a more refined investigation: in some areas the water supplies for the two companies happened to be closely intermixed, some houses receiving their water from the Lambeth company and others from Southwark and Vauxhall. The number of houses and the size of the pertinent populations belonging to each company were known, but a door to door inquiry was needed, and was indeed carried out by Snow, on all cholera cases to ascertain to which company the water supply of their

**Table 1.2** Mortality from cholera in the areas of London supplied by the Southwark and Vauxhall, and Lambeth Water Companies in 1849 and 1854\*

Districts with water supplied by	Number of deaths attributed to cholera	
	1849	1854
Southwark and Vauxhall Company	2261	2458
Lambeth Company	162	37
Both companies	3905	2547

\* From Snow, 1853

**Table 1.3** Mortality from cholera in the districts of London supplied by the Southwark and Vauxhall, and the Lambeth Companies, July 8 to August 26, 1854\*

Districts with water supplied by	Population 1851	Deaths from cholera	Cholera death rate per 1000 population
Southwark and Vauxhall Company	167,654	844	5.0
Lambeth Company	19,133	18	0.9
Both companies	300,149	652	2.2

\* From Snow, 1853

homes belonged. This allowed the correct calculation of valid rates of cholera occurrence. The results are shown in Table 1.4, which clearly demonstrates that even within the same physical area the origin of the water supply separates in a clearcut way those populations with high and low rates of disease occurrence. All of these observations can be seen, in fact (Winkelstein, 1995), as the test of a lucid theory of the etiology of communicable diseases that Snow had elaborated and presented in 1853 in a paper entitled 'On continuous molecular changes' along the lines of previous work by the German pathologist Jacob Henle (1809–1885).

In France the influence of great mathematicians such as D'Alembert, Condorcet, the Swiss Euler and Bernoulli family, Lagrange and Laplace who worked to various extents on probability and statistics during the eighteenth and early nineteenth century was strongly felt in the medical field. A central figure in this development was the physician Pierre Louis (1787–1872), who introduced the 'numerical method' in medicine and produced statistical evidence that the then widespread practice of bloodletting was virtually ineffective or even dangerous. That the scientific climate in the first half of the

**Table 1.4** Mortality from cholera in London, July 8 to August 26, 1854, related to source of individual water supply in three groups of districts\*

Group of districts with water supplied by	Water supply of individual houses	Population 1851	Deaths from cholera	Cholera death-rate per 1000 population
Southwark and Vauxhall Company	Southwark and Vauxhall Company	167,654**	738	4.4
Lambeth Company	Lambeth Company	19,133**	4	0.2
Both companies	Southwark and Vauxhall Company	98,862	419	4.2
	Lambeth Company	154,615	80	0.5
Rest of London		1,921,972	1,422	0.7

\* From Snow, 1853

\*\* Overestimated by a small amount, since this figure includes population with no water supply

nineteenth century had become favorable to a quantitative study of medical phenomena is shown by the substantial number of articles published in most of the European countries dealing with problems in quantitative biology or in the clinical or public health domains (Buck *et al.*, 1988). Even in a country like Italy, which by that time had become, after an illustrious past, rather peripheral in scientific development, one finds evident traces of this atmosphere. For instance, at the first Congress of Italian Scientists, in Pisa in 1838 (*Atti della prima riumione degli scienziati italiani* 1939), it was proposed that to compare different treatments the best method would be to administer them in different wards of large hospitals to which access of patients would be on a strict rotation basis without any possibility of choice on the part of the physicians. The outcome of each treatment would then be carefully recorded and counted and the whole process, as well as the interpretation of the results identifying the superior treatment (if any), would be strictly monitored and reported by a steering committee.

The highest degree of synthesis between experimental science, medicine, simple but penetrating demographic investigation, and public health concern was probably achieved in the unique personality of the German scientist Rudolf Virchow (1821–1902). His work in pathology is regarded as a cornerstone of modern medicine. Not only is he the acknowledged founder of (microscopic) cellular pathology, but he also wrote and was very active in the field of public health, based on his belief that ‘medicine is a social science’. It is interesting to see how the flow of communication took place at that time and how, for instance, an agreed system of classification of diseases, basic to any epidemiological work, was shaping up. At the International Congress of Statistics in 1855, Rudolf Virchow stated (Virchow, 1985):

The form of the bulletin indicated by Mr. Farr can be recommended from the practical and medical point of view, because it contains one column for the disease, and another for the consequences of the diseases that have been the immediate cause of death; for it is one of the most important aims of statistics to know not only the direct causes of death but also the indirect ones, i.e. the pathological state which produces the truly lethal alterations. The mechanism itself of death is of interest for practical statistics only in the case of crime, or of a lesion due to violence, or of accident. In contrast, practical hygiene is most interested in appraising the aetiology of mortality.

One can clearly recognize here the basic concept and structure of current death certification, separating underlying causes from proximate causes, as well as the separate classification of accidents and traumatic events even now present in the International Classification of Diseases (ICD). It fell to another German scientist, Robert Koch (1843–1910), in the wake of the fundamental discovery of microorganisms by Louis Pasteur (1822–1895), not only to contribute to the discovery of the agents of several diseases (including the actual identification of the major disease tuberculosis), but also to formulate a set of criteria for establishing causality in epidemiological studies. With the new ability to isolate from healthy and diseased people a wide variety of microorganisms, an entirely new problem arose at that time of sorting out the few capable of causing a disease from the majority of innocent passengers. Koch's criteria, among others, addressed this issue in a sharp way, stating that, to be regarded as a causative agent of a disease, a microorganism:

- (a) should be found in all subjects with the disease;
- (b) should be grown *in vitro* (in a suitable medium);
- (c) should be capable of reproducing the disease in some animal species.

While the first criterion is formulated in a strictly deterministic way and therefore looks at a glance radically different from our contemporary probabilistic concepts, one may doubt whether it has ever been applied as such without in practice making allowance for a margin of error in what one would regard as 'all subjects' (99%? 95%?). Perhaps it is the third criterion which more sharply differs from those nowadays quoted in the literature, following the guidelines put forward by A. B. Hill, which include as one element supporting causality 'the biological plausibility'. This is much weaker and less strict than the ability to reproduce the disease in some animal species, which reflects an attitude of giving full weight to the result of experiments in animals, a feature which became somewhat blurred with the advent of the 'new epidemiology' in the 1940s. Indeed, while the further evolution of epidemiology after Pasteur and Koch throughout the last part of the nineteenth and first part of the twentieth centuries largely occurred hand in hand with parallel experimental and laboratory developments in the field of microbiology, the new epidemiology addressing the unknown causes of non-infectious diseases went back to rely, as for instance Snow had done before the microbiological era, pre-eminently on direct observations in human groups.

**The new epidemiology** Individual studies on cancer, non-rheumatic cardiovascular diseases, and psychiatric diseases, can be traced well back in time, but one can take as a convenient turning point for the rise of the new epidemiology the period around the Second World War. A major stream in the development of the new epidemiology is what could be labeled as the 'tobacco and health story'. Initial observations were either of a statistical nature or of a clinical one. Among the first one can mention is a short and remarkable paper by Pearl (Pearl, 1938) using insurance data showing that the expectation of life for smokers was substantially reduced in respect to non-smokers. Among the second, one might single out the observation by Ochsner and De Bakey (Ochsner and De Bakey, 1939) of high frequency of smokers among the lung cancer patients coming to their hospital in those early days of thoracic surgery. These were followed by still other statistical findings of a general nature pointing to a dramatic increase of lung cancer rates in men throughout the 1940s, in particular in the US and the UK. In 1950, three hospital-based case control studies were almost simultaneously published (Levin *et al.*, 1950; Wynder and Graham, 1950; Doll and Hill, 1950) which clearly showed an association 'most probably' (at that time) causal, between tobacco smoking and lung cancer. The paper by Levin *et al.* used information available in clinical records at one cancer center starting from 1938. The other two investigations collected *ad hoc* information on hospitalized cases and controls. Interestingly, when Doll and Hill set forth to investigate the etiology of lung cancer, which had become a common disease in the UK, they were thinking of air pollution, at that time very severe in London (the 'London Fog'), as an even more plausible candidate than tobacco smoke. As it turned out, the results of their study neatly caused

the role of tobacco smoke to emerge, with that of air pollution much less evident. These three studies were the first in a long sequence of case control and cohort studies carried out in different countries relating tobacco smoking to various diseases. Doll and Hill themselves added another well known investigation, following a cohort of British doctors prospectively and reporting the results first in 1964 (Doll and Hill, 1964). This cohort, which has now been observed for 40 years (Doll *et al.* 1994), provided strong support to the etiological role of tobacco, not only on lung cancer but on a spectrum of neoplastic and non-neoplastic diseases. It is interesting to note (Saracci, 1995) that the survival curves from age 35 to 100 years for the 6813 subjects insured in the US observed by Pearl in the late thirties and for the cohort of 34 439 British doctors followed from 1951 to 1971 by Doll and coworkers show a closely similar loss in median survival (4.9 and 5 years, respectively). When lifetime smokers are compared to lifetime non-smokers, however, with the prolongation of the follow-up until 1991 the loss increased to 7.5 years in the British cohort.

One can safely state that by 1964, the date of publication of the results of the cohort study by Doll and Hill and of the first US Surgeon General's report on Smoking and Health (the 'Terry Report' from the name of the Surgeon General) (Smoking and Health, 1964), the role of smoking in the causation of a number of lethal diseases can be regarded as soundly established. The Terry Report is an extremely valuable document, which can still be read with profit by anyone interested in assessing large amounts of disparate data bearing on an etiological problem. It is interesting from the methodological viewpoint to know that the inability in the initial periods of study to reproduce neoplasms in animals by exposing them to tobacco smoke was regarded – in line with Koch's third criterion – as an important element for questioning the validity of the conclusions drawn from the epidemiological studies. It is certainly not coincidental that at about this time epidemiologists felt compelled to rethink the criteria used to infer causality in general (rather than in infectious diseases) and that A. B. Hill produced a set which can still be used as a reference (Hill, 1965). As already noted, this changes the requirement of an agent to be able to reproduce the disease in animals to the more general and optional requirement of biological plausibility. This perspective on causality had the unintended consequence of downplaying almost completely in some circumstances and epidemiological circles the value of animal experiments (incidentally, it can be noted that, using better experimental set-ups, tobacco smoke has produced cancers in experimental animals): this result was an unfortunate one and in flat contradiction to all thinking and practice in biology.

This phase of the development of epidemiology received new input from the two-way exchange between epidemiology and clinical medicine, which has been a constant feature in the history of the subject. As previously exemplified Ramazzini, a clinician, and Snow, a physician (pioneering anesthesia), had enlarged clinical observations by looking for causes of disease at the population level; conversely, Louis had brought the methods of population studies into the clinical domain to evaluate the effects of medical acts in patient populations. The 'new epidemiology' clearly highlights this dual exchange. In Great Britain, John Ryle (1899–1950), Professor of Medicine at Cambridge, moved from the clinic to become the first director of the Institute of

Social Medicine at Oxford, established at the time of the Second World War to investigate the influence of social, genetic, environmental, and domestic factors on the incidence of human diseases and morbidity. He was a key motivator of the work of the post-war generation of British epidemiologists, who made crucial contributions to the identification of causal factors of chronic diseases. In a parallel and opposite move, epidemiological methods were showing their value for clinical research and were increasingly incorporated into a growing stream of 'clinical epidemiology', namely studies of diagnostic, prognostic, therapeutic, and rehabilitative procedures in populations of sick subjects. A yardstick in this development was the publication in 1972 by Archie Cochrane (1909–1988); (Cochrane, 1972) of a brilliant essay advocating a systematic use of the randomized trial method to evaluate procedures in the areas of clinical and health services.

### Today: epidemiology in the making

Today, as yesterday, epidemiology as a population approach to health and disease embraces two bodies of knowledge: first, epidemiological methods of investigation (which are part of scientific methodology), and, second, epidemiological substantive notions developed by application of such methods (these notions become part of medicine in its biological and social facets).

Both bodies of knowledge have undergone substantial expansion since World War II with the development of the 'new epidemiology'. A simple comparison of early with recent editions of any one of the classical textbooks of medicine (*Cecil Textbook of Medicine*, 9th edition, 1955, 19th edition, 1992, Philadelphia, Saunders) shows how epidemiology has contributed to change and increased, sometimes dramatically, our understanding of the time and space evolution, etiology, and opportunities for control (preventive or therapeutic), of major classes of diseases such as ischemic heart disease, chronic obstructive lung disease, asthma, cancers at several sites, not to mention newer entities like toxic shock syndrome, AIDS, Legionnaires' disease, or *Helicobacter* infections. This progress has been matched by the emergence, *de facto* or formally recognized, of a wide spectrum of subspecialties (cancer epidemiology, pediatric epidemiology, genetic epidemiology, clinical epidemiology, etc.) within epidemiology itself. On the methodological side it is sufficient to remember that no text specifically devoted to epidemiological methods was available before 1960, when the book by MacMahon and coworkers was published (MacMahon *et al.*, 1960), whereas today methodology provides enough matter for 10 or 20 major books with different degrees of completeness and complexity. Study design methods and statistical methods of analysis have been developed in and from the context of problems in epidemiology, rather than by borrowing them from other areas of applied methodology and statistics. Also, in recent years, a unified approach to the analysis of occurrence data (incidence and mortality rates), which has implications for study design, has been developed based on the unifying principle of likelihood inference. These developments have taken place concurrently within an accelerated evolution in the whole field of biology and health, and one can single out four traits, particularly salient in Europe and other economically developed areas of the world.

1. The unprecedented advances of research in some domains, fundamental to all other fields of biology and medicine, like immunology, the neurosciences, and, most prominently, molecular genetics and cell and developmental biology. Clearly, switching the study of higher organisms, including humans, from the anatomy and physiology of the phenotype (as has been the case until recently) to the direct study of the anatomy and physiology of the genotype opens an entirely new perspective, the implications of which (preventive, therapeutic, and ethical) are not yet fully perceptible.
2. The advances in clinical medicine at the diagnostic and therapeutic levels. Until 60 or 70 years ago effective treatments could be counted on the figures of one hand, so that the only way open for disease control – in many cases effective – was prevention. Nowadays, treatments capable of effectively influencing length and quality of survival are available for a number of serious conditions, both infectious and non-infectious. As a consequence, the balance and the competition between the preventive and curative approach needs to be seen in a fresh light and critically reassessed. A relevant example is mortality rates from ischaemic heart disease, the marked decrease of which in several western countries appears to be in part due to decreased incidence and in part to decreased lethality because of better treatment options.
3. The escalating costs of all health care delivery systems, whether private, public or mixed, have brought to the forefront issues of effective and efficient use of available resources which were of negligible importance, or almost unknown, three or four decades ago.
4. The renewed awareness among professionals and the general public of the dependence of health (of humans as well as of other living organisms) on the environment, material and social, personal, local or general. In parallel with this goes the realization that tangible deterioration of the environment does take place because of shortsighted human activities.

These developments and their interrelationship change the pattern of the factors capable of promoting, damaging or restoring health, and impose a virtually continuous reappraisal and adaptation of the health care system and, more generally, of all plans of action aimed at influencing health.

### Tomorrow's horizon

Three major challenges stand on the horizon of epidemiology and epidemiologists in the coming decades entailing, as with any challenge, both opportunities and risks.

**The challenge of evolving biology** Few would disagree with a comment by Sir Richard Doll (Doll, 1993):

Classical methods of epidemiological research are proving less and less productive as the simple problems are being successfully solved. They will doubtless continue to be used to make new discoveries from time to time ... but without some brilliant new inspirations, the rate of discovery of new facts of any importance by the use of these classical methods must be expected to slow down.

A major way to maintain momentum is certainly to incorporate concepts and techniques evolving at an impressive pace from such basic disciplines as immunology and molecular biology and genetics. For instance, epidemiology can improve its resolving power by using biological markers of exposures (e.g. DNA or protein adducts with toxic xenobiotics) rather than continue to rely in the future mostly on questionnaire assessment of exposure. The study of individual susceptibility, genetic or acquired, can help to identify the most vulnerable subgroups. More generally, the mechanistic study (pathogenetic study) of how different factors cooperate in producing a disease can be of help in identification of specific etiological agents (etiological study). For instance, if an investigation combining epidemiology with immunology and biochemistry isolates a specific air pollutant as responsible for the induction of asthma attacks, control measures can be addressed specifically to the sources of that pollutant (a more generic approach to all pollutants in the air may simply not be possible). There is, however, the danger that studies of pathogenesis may become attractive *per se* (indeed, they are) rather than as one more way of elucidating controllable etiological factors. It will be for epidemiologists to bring back to the level of etiology and prevention the wealth of investigations that the convergence of epidemiology and modern biology is now making possible.

**The challenge of evolving society** Society in most developed countries, and particularly in Europe, is characterized by an ageing population, reproduction rates that are below the population replacement rates, current flow of immigration from less developed countries (which is likely to continue in the coming decades), and persistent inequalities in health conditions between different sections of society, in particular gender, occupation, and socioeconomic categories. Monitoring trends and identifying causal factors in this area, which could be labeled 'social epidemiology', has been a longstanding concern of epidemiologists, characterizing in a major way their involvement in public health, both from the scientific and, when required, from the campaigning for health viewpoint. Whether this will retain substantial and sustained attention in epidemiological research or be left mostly to other professionals (e.g. sociologists) while epidemiologists become almost exclusively concentrated in the biomedical area, is an open issue.

**The challenge of diversification versus integration** As in all other scientific and technical branches of activity, epidemiology has been recently, and continues to, specialize along different axes. A first axis is methodology *versus* substantive studies; areas of current and future development in methodology are, for example, the treatment of exposure measurements and errors of measurement to reduce misclassification and improve study power, methods in genetic epidemiology, modeling of the exposure-response relationship with multiple longitudinal measurements. A second axis is diversification of different fields of substantive interest; for instance, cancer epidemiology, epidemiology of ageing, etc. A whole area of specialization is 'clinical epidemiology', the application of epidemiological methods within the clinical domain, both for studies evaluating diagnostic, prognostic, therapeutic, and rehabilitative procedures and for evolving formal methods of optimal clinical decision-making.

Stemming from this is the rapidly growing branch of ‘evidence-based medicine’ (EBM), which employs formal methods to assemble and evaluate the existing evidence on the effects of medical interventions. A final axis of diversification tends to separate those who specialize in investigative aspects for routine or research purposes from those who plan and implement interventions. In clinical medicine this has produced a variety of specialists in purely diagnostic activities (clinical chemists, clinical pathologists, diagnostic radiologists, imaging specialists), different from the therapist who decides and acts on the basis of the diagnosis; similarly, in the public health area the epidemiologist may become more and more a pure specialist in etiological and evaluative investigations, leaving others to decide what to do.

This unavoidable trend raises three major issues : (1) to what extent a global view can be preserved jointly with specialized or ‘subspecialized’ technical skills; (2) to what extent, side by side with epidemiologists specializing in different areas, the figure of the generalist can be maintained (again, the analogy with clinical medicine is pertinent, with one of the most difficult present day problems being the survival and role of the general physician or of the internist); (3) how epidemiologists can best cooperate in teams of specialists (epidemiologists with special skills and other professionals), including those in charge of taking public health decisions.

In its historical evolution epidemiology’s successes have largely derived from its working as the investigative component of public health, studying the distribution and determinants of health and diseases in populations. This essence should continue to be preserved in the foreseeable future by incorporating into epidemiological research the new opportunities currently arising in particular from the fields of genetics, environmental sciences, clinical medicine, and health care.

## **Content indications for the five parts of the module**

### **Overview of the history of epidemiology**

The historical sketch can be used as a basis for this overview. The interest of the students is heightened if examples are produced from the national and local context. The bulk of significant scientific advances in epidemiology has been concentrated in a relatively small number of countries. However, isolated but important discoveries – often related to special traits of local health and diseases – have come from many more countries and there is virtually no country in which the echo of scientific advance has not been received in some form. It is these aspects which can be exploited for illustrative purposes.

### **The modern history of tobacco and health: scientific aspects**

The identification of the causal role of tobacco smoking in a variety of diseases is a prime success of the new post-World War II epidemiology. The historical sketch (see The new epidemiology, above) contains an outline to be fleshed out using material from the quoted sources. The focus can be on the controversy on the etiological role of tobacco smoking, in particular on lung cancer, and on the emergence, under the stimulus of the controversy, of methodology for data analysis and of criteria for inferring causation in epidemiology. These aspects are covered in the ‘Smoking and Health

' report (1964), especially in Chapters 8 and 9 and in some of the publications, cited in the report, by eminent critics of the smoking causal hypothesis such as R. A. Fisher, a founder of modern statistical methodology, and J. Berkson, a leading medical statistician.

### The modern history of tobacco and health: societal aspects

The direct link between epidemiology and prevention is commonly stated as one of the merits of the epidemiological approach. Once causation has been established, as from the early 1960s for tobacco smoking and various pathological conditions, preventive actions can be implemented even without knowledge of the biological mechanisms leading to the condition. This logical sequence often breaks down in practice as the transition from sufficient knowledge for action to actual action is strongly influenced by a number of social, economic, cultural, and psychological factors. First, simply comparing the local or national tobacco smoking patterns and trends with the available established knowledge on health effects over time, and also comparing these with legislative and health promoting-actions is instructive. Second, as documented and discussed by Proctor (1999), the crucial role played in prevention by factors other than sound science and epidemiology is highlighted by the case of Nazi Germany, where vigorous anti-smoking campaigns were conducted, inspired by strong ideological reasons. Moreover, informative epidemiological evidence gathered during the Nazi period went ignored until recently for reasons mostly foreign to science. Third, the adverse health effects of passive exposure to environmental tobacco smoke (ETS), particularly lung cancer (Hackshaw *et al.* 1997; Boffetta *et al.*, 1998), have radically changed the prospects of preventive measures. Unlike (partially) voluntary active smoking, ETS exposure is wholly involuntary and there is general agreement that involuntary exposure should be controlled, mainly through legal restrictions. Hence, simply denying any material health effect of ETS became a major priority for tobacco producers, fought with organized and often unscrupulous means, as documented by Ong and Glantz (Ong and Glantz, 2000). This offers a lesson first on how powerful and well structured economic interests can lead to misinterpretation of scientific evidence to the point of active disinformation and, second, on how inherently liable to distortion by extrascientific forces the judgement of experts (who think of themselves as independent) may in fact be (Maggi, 2000).

### A paper from the past

A paper addressing a substantive epidemiological issue with the methodological armamentarium available at the time of writing will provide a measure of the methodological gap separating the past from the present. Papers can be selected from those in the Key references: one example is the article on sickness and stress in operational flying in the Royal Air Force during World War II (Reid, 1948). In reading this article (or any other article selected for the exercise), students should focus in particular on:

- (a) key issues of design; whether and how issues of confounding, bias, and chance were dealt with at the design and analysis stages; how inferences about causation were developed;

- (b) how they would design today, within the limits of the database available to the author, a study addressing the same issue and how they would conduct and analyse it.

From a comparison of (a) and (b) the conclusions in the article may be assessed as: credible neither at the time of writing nor today; credible to a degree that one may even wish to specify (e.g. as 'moderately credible, credible, highly credible'), at the time of writing but not today in the light of new methodological criteria judged as non-dispensable; or credible at the time of writing as well as today, notwithstanding the inherent limitations deriving from the past status of the art.

#### Present trends linking past and future

This topic is discussed in the sections Today: epidemiology in the making and Tomorrow's horizon of the historical sketch. Taking as the occasion the turn of the century, many conferences and papers have been devoted to the role and future of epidemiology. At the international level a supplement of the *International Journal of Epidemiology* (The Future of Epidemiology, 1999) contains a series of papers providing a spectrum of views on the evolution of epidemiology. Two or three of these papers can be distributed to students for reading: each student should extract from each paper two lists of key points on which he or she agrees or disagrees. These points, with supporting arguments, will be discussed in plenary. An alternative way is to ask each student (before distributing any relevant paper) to prepare an outline of how they see, on one hand, the likely and, on the other, the desirable evolution of epidemiology as a scientific endeavour and as a practice within society. The outlines can then be presented to the class for discussion and compared with published essays.

Areas for consideration when looking from past and present into the future come under three main headings: (1) information sources (items such as population disease registries and stores of biological specimens: organization, access, use, protection, ethical and legal implications); (2) methodology (items such as methods to improve exposure and endpoint assessment, new study designs, multilevel analyses, pooled data analyses and meta-analyses, and risk modeling); (3) aims and uses of epidemiology (items such as the role of epidemiology in clinical medicine, environmental and occupational health, public health, prevention and reduction of inequalities in health between and within countries, priorities for research, communication of results and the role of epidemiologists in decision-making in the health area, responsibilities of epidemiologists).

### Assessing students' achievements

As stated, the objective of the module is to focus and raise the interest and motivation of students for the historical perspective on epidemiological themes, not to develop the skills necessary to gain this perspective (this would require a more sustained didactic endeavour). Students should be asked using a miniquestionnaire how they rate (on a 'poor, fair, good, excellent' scale) the module in respect to four aspects: increase in knowledge; usefulness for work; stimulation of interest for the historical perspective; motivation for personally engaging in historical exercises.

## Key references

### Books

- Porter, R.** (1997). *The greatest benefit to mankind: a medical history of humanity from antiquity to the present*. Fontana Press, London.  
 A history of health and medicine, seen both in its internal development and in its relationship to society, as a background to the history of epidemiology.
- Rosen, G.** (1993). *A history of public health* (Expanded edn). The Johns Hopkins University Press, Baltimore.  
 A standard reference, comprehensive and highly readable.

### Collections of articles and essays

- American Journal of Epidemiology* (1995), Vols 141 and 142. On the occasion of its 75th anniversary the journal has reprinted in the issues of 1995 a number of articles published from the late 1930s to the late 1970s which are regarded to be of historical relevance. Each is accompanied by a short commentary.
- Buck, C., Llopis, A., Najera, E. and Terris, M.** (1988). *The challenge of epidemiology: issues and selected readings*. Pan American Health Organization, Washington.  
 An indispensable collection of papers from Hippocrates to present day.
- Greenland, S., ed.** (1987). *Evolution of epidemiologic ideas: annotated readings on concepts and methods*. Epidemiology Resources Inc., Chestnut Hill.  
 A collection of methodological papers published between 1945 and 1977 covering issues of causal inference and developments in theory and quantitative methods. Each paper is accompanied by a commentary placing it in historical perspective.
- Lilienfield, A. M., ed.** (1980). *Times, places and persons. Aspects of the history of epidemiology*. The Johns Hopkins University Press, Baltimore.  
 A series of essays, most of them scholarly documented, by historians and epidemiologists: topics range from numerical methods in the 1830s to the history of eradication of small-pox.
- Smoking and Health** (1964). *Report of the Advisory Committee to the Surgeon General*, PHS, US Department of Health, Education & Welfare, Washington DC.  
 A landmark report: it establishes the etiological role of tobacco smoking in a number of diseases through a rigorous examination of the evidence, mostly epidemiological. Still instructive from a methodological angle.

### Other references

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