CHAPTER 1
Epidemiology Past and Present

1.1 Epidemiology and its uses
- What is epidemiology?
- What is public health?
- What is health?
- Additional useful terms
- Uses of epidemiology

1.2 Evolving patterns of morbidity and mortality
- Twentieth century changes in demographics and disease patterns
- Mortality trends since 1950
- Trends in life expectancy

1.3 Selected historical figures and events
- Roots of epidemiology
- John Graunt
- Germ theory
- Médecine d'observation and La Méthode Numerique (Pinel and Louis)
- The London Epidemiological Society
- William Farr
- John Snow
  - Cholera in Victorian England
  - Miasma theory of transmission
  - Snow's theory
  - Snow's ecological analysis
  - Snow's retrospective cohort analysis
  - Snow's case series
  - Publication
- Twentieth-century epidemiology
- Emile Durkheim
- Joseph Goldberger
- The British Doctors Study

1.4 Chapter summary
- Epidemiology and its uses
- Evolving patterns of morbidity and mortality
- Selected historical figures and events

Review questions

References

Epidemiology Kept Simple: An Introduction to Traditional and Modern Epidemiology, Third Edition.
B. Burt Gerstman.

1.1 Epidemiology and its uses

What is epidemiology?

The word **epidemiology** is based on the Greek roots *epi* (upon), *demos* (the people, as in ''democracy'' and ''demography''), and *logia* (''speaking of,'' ''the study of''). Specific use of the term in the English language dates to the mid-19th century (*Oxford English Dictionary*), around the time the London Epidemiological Society was founded in 1850. Since then, *epidemiology* has defined itself in many ways, including:

- the study of the distribution and determinants of diseases and injuries in populations (Mausner and Baum, 1974);
- the study of the occurrence of illness (Gaylord Anderson cited in Cole, 1979, p. 15);
- a method of reasoning about disease that deals with biological inferences derived from observations of disease phenomena in population groups (Lilienfeld, 1978b, p. 89);
- the quantitative analysis of the circumstances under which disease processes, including trauma, occur in population groups, and factors affecting their incidence, distribution, and host responses, and the use of this knowledge in prevention and control (Evans, 1979, p. 381).

A widely accepted contemporary definition of epidemiology identifies the discipline as ''the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to control of health problems'' (Last, 2001).

The word *epidemiology* is, of course, based on the word **epidemic**. This term dates back to the time of Hippocrates, circa 400 BCE. Until not too long ago, *epidemic* referred only to the rapid and extensive spread of an infectious disease within a population. Now, however, the term applies to any health-related condition that occurs in clear excess of normal expectancy. For example, one may hear mention of an ''epidemic of teen pregnancy'' or an ''epidemic of violence.'' This broader use of the term reflects epidemiology's expansion into areas beyond infectious disease control to include the study of health and health-related determinants in general. In this non-limiting sense, epidemiology is still the study of epidemics and their prevention (Kuller, 1991).

In addition, epidemiology is becoming increasingly integrated in biomedical research and health care. Note, however, that the main distinction between *epidemiology* and *clinical medicine* is their primary **unit of concern**. The primary unit of concern for the epidemiologist is ''an aggregate of human beings'' (Greenwood, 1935). Compare this with clinical medicine, whose main unit of concern is the individual. A metaphor that compares epidemiology with clinical medicine discusses a torrential storm that causes a break in the levees. People are being washed away in record numbers. Under such circumstances, the physician's task is to offer lifejackets to people one at a time. In contrast, the epidemiologist's task is to stem the tide of the flood to mitigate the problem and prevent future occurrences.

What is public health?

Like epidemiology, public health has been defined in many different ways including ''organized community effort to prevent disease and promote health (Institute of

Medicine, 1988) and ''one of the efforts organized by society to protect, promote, and restore the people's health (Last 2001). By any definition, the aim of public health is to reduce injury, disability, disease, and premature death in the population. Public health is thus a mission comprising many activities, including but not limited to epidemiology. Epidemiology is a ''study of'' with many applications, while public health is an undertaking.

Note that epidemiology is one of the core disciplines of public health. Other core disciplines in public health include biostatistics, environmental health sciences, health policy and management, and social and behavioral sciences (Calhoun *et al*., 2008). The practice of public health also requires cross-cutting interdisciplinary competencies in areas such as communication, informatics, culture and diversity, and public health biology.

What is health?

Health itself is not easily defined. The standard medical definition of health is ''the absence of disease.'' Dis-ease, literally the absence of ''ease,'' is when something is wrong with a bodily or mental function. The World Health Organization in the preamble to its 1948 constitution defined health as ''a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity.''

Walt Whitman (1954, p. 513), in his poetic way, defined health as:

> the condition [in which] the whole body is elevated to a state by other unknown—inwardly and outwardly illuminated, purified, made solid, strong, yet buoyant. A singular charm, more than beauty, flickers out of, and over, the face—a curious transparency beams in the eyes, both in the iris and the white—temper partakes also. The play of the body in motion takes a previously unknown grace. Merely to move is then a happiness, a pleasure—to breathe, to see, is also. All the before hand gratifications, drink, spirits, coffee, grease, stimulants, mixtures, late hours, luxuries, deeds of the night seem as vexatious dreams, and now the awakening; many fall into their natural places, wholesome, conveying diviner joys.

This passage from Whitman address *quality of life*, an area of increasing interest to epidemiologists.

Additional useful terms

One of the ten American Schools of Public Health MPH Epidemiology competencies is to ''apply the basic terminology and definitions of epidemiology'' (Calhoun *et al*., 2008). Therefore, terminology will be introduced throughout this book. Table 1.1 lists definitions for several standard terms. For example, an **epidemic** is the occurrences of disease in clear excess of normalcy, while a **pandemic** is an epidemic that affects several countries or continents. An **endemic** disease is one that is consistently present in the environment. The term endemic is also used to refer to a normal or usual rate of disease. An excellent source for epidemiologic definitions is *The Dictionary of Epidemiology* (Porta, 2008), which is updated periodically.

Some terms used in the field are not readily defined in a singular way. For example, some sources differentiate between disease, illness, and sickness. Susser (1973) defines

Table 1.1 Selected terms briefly defined.

Epidemiology: the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems
Public health: organized effort to prevent disease and promote health
Endemic: occurring at a consistent or regular rate
Epidemic: occurring in clear excess of normalcy
Pandemic: an epidemic that affects several countries or continents
Morbidity: related to or caused by disease or disability
Mortality: related to death

disease as the medically applied term for a physiological or psychological dysfunction; **illness** is what the patient experiences; and **sickness** is the state of dysfunction of the social role of an ill person. In contrast, one source considers ''disease'' a subtype of ''illness'' (Miettinen and Flegel, 2003). While yet in other contexts, ''disease'' is merely a general term used to refer to any health-related outcome or condition. Thus, the use of epidemiologic terminology is context specific and is, at times, controversial.

Uses of epidemiology

Epidemiologic practice is characterized by a close connection between the scientific study of the causes of disease, and the application of this knowledge to treatment and prevention (especially the later). The discipline covers a broad range of activities, including conducting biomedical research, communicating research findings, and participating with other disciplines and sectors in deciding on public health practices and interventions.

A sample of epidemiology's varied concerns include studies of the effects of environmental and industrial hazards, studies of the safety and efficacy of medicines and medical procedures, studies of maternal and child health, studies of food safety and nutrition, studies of the long-term effects of diet and lifestyle, surveillance and

Table 1.2 General uses of epidemiology (Morris, 1957).

1	In **historical study** of the health of the community and of the rise and fall of diseases in the population; useful ''projections'' into the future may also be possible.
2	For **community diagnosis** of the presence, nature, and distribution of health and disease among the population, and the dimensions of these in incidence, prevalence, and mortality; taking into account that society and health problems are changing.
3	To study the **workings of health services**. This begins with the determination of needs and resources, proceeds to analysis of services in action and, finally, attempts to appraise. Such studies can be comparative between various populations.
4	To estimate, from the common experience, the **individual's chances and risks of disease**.
5	To help **complete the clinical picture**: by including all types of cases in proportion; by relating clinical disease to subclinical; by observing secular changes in the character of disease, and its picture in other countries.
6	In **identifying syndromes** from the distribution of clinical phenomena among sections of the population.
7	In the **search for causes of health and disease**, starting with the discovery of groups with high and low rates, studying these differences in relation to differences in ways of living; and, where possible, testing these notions in actual practice among populations.

control of communicable and noncommunicable diseases, ascertainment of personal and social determinants of health and ill-health, medico-legal attribution of risk and responsibility, screening and early detection of the population for disease, and the study of health-care services. Because findings from epidemiologic investigations are linked to health policy, epidemiologic studies often have important legal, financial, and political consequences.

More than half a century ago, Morris (1957) described seven uses of epidemiology. These seven uses, listed in Table 1.2, have stood the test of time. The seventh use, search for causes, is perhaps the most important current application because of its essential role in effective disease prevention.

1.2 Evolving patterns of morbidity and mortality

Twentieth century changes in demographics and disease patterns

The theory of **epidemiologic transition** focuses on the dramatic changes in morbidity and mortality that have occurred in relation to demographic, biologic, and socioeconomic factors during the 20th century (Omran, 1971). Ample evidence exists to document a transition from infectious diseases as the predominant causes of morbidity and mortality to a predominance of noninfectious diseases (Table 1.3). The transition from predominantly infectious to noninfectious causes resulted from changes in society at large and improvements in medical technology. Steady economic development led to better living conditions, improved nutrition, decreases in childhood mortality, diminished fertility rates, and technological advances in medicine.

Decreases in mortality and fertility led to a substantial shift in the age distribution of populations, especially in industrialized societies, a phenomenon known as the **demographic transition** (Figure 1.1). With this now familiar demographic shift

Table 1.3 Leading causes of death in the United States, 1900 and 2007.[a]

Rank	1900[b]	2007[c]
1.	Pneumonia (all forms) and influenza [202.2]	Diseases of the heart [204.3]
2.	Tuberculosis (all forms) [194.4]	Malignant neoplasms (cancers) [186.6]
3.	Diarrhea, enteritis, and ulceration of the intestines [142.7]	Cerebrovascular diseases (stroke) [45.1]
4.	Diseases of the heart [137.4]	Chronic lower respiratory diseases [42.4]
5.	Intracranial lesions of vascular origin [106.9]	Accidents (unintentional injuries) [41.0]
6.	Nephritis (all forms) [88.6]	Alzheimer's disease [24.7]
7.	All accidents [72.3]	Diabetes mellitus (diabetes) [23.7]
8.	Cancer and other malignant tumors [64.0]	Influenza and pneumonia [17.5]
9.	Senility [50.2]	Nephritis, nephrotic syndrome and nephrosis (kidney diseases) [15.4]
10.	Diphtheria [40.3]	Septicemia [11.5]

[a] Crude death rates per 100 000 are listed in square brackets. Rates have not been adjusted for age differences in the population and, therefore, should not be compared between time periods.
[b] Source: National Office of Vital Statistics, 1947.
[c] Source: Xu *et al*., 2010.

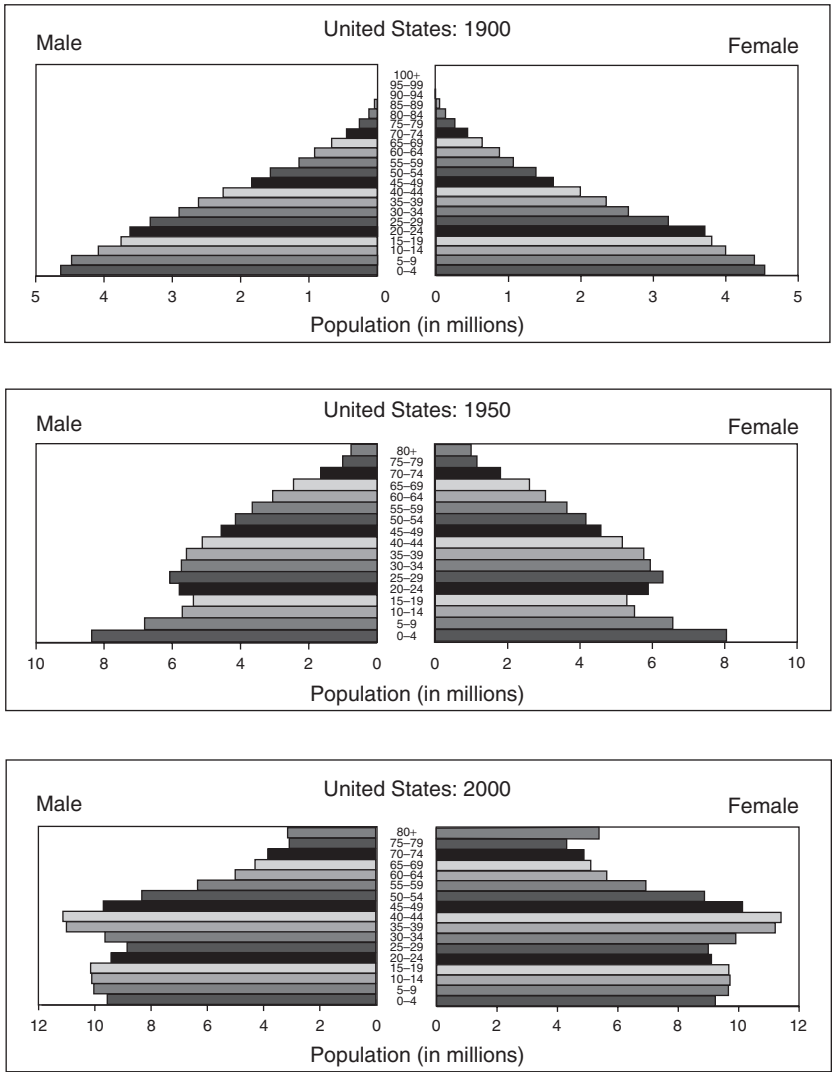

Figure 1.1 Population pyramids for the United States, 1900, 1950, and 2000 (Sources: Bureau of the Census, 1904; U.S. Census Bureau International Data Base, 2002).

came a concomitant rise in age-related diseases such as atherosclerotic cardiovascular and cerebrovascular disease, cancer, chronic lung disease, diabetes and other metabolic diseases, liver disease, musculoskeletal disorders, and neurological disorders. Many of these noncontagious diseases are thought to have important lifestyle components rooted in behaviors such as smoking, dietary excesses, and physical inactivity (''diseases of civilization''). As of the mid-20th century, these prevalent chronic diseases were viewed primarily as an intrinsic property of aging (so-called degenerative diseases). Now, however, these diseases are regarded as a diverse group of pathologies with varied and complex etiologies. What brings them together as a

Table 1.4 Chronic diseases and their relation to selected, modifiable risk factors: + = established risk factor and ± = possible risk factor.

Cause	Cardiovascular disease	Cancer	Chronic lung disease	Diabetes	Cirrhosis	Musculoskeletal diseases	Neurologic disorders
Tobacco use	+	+	+			+	±
Alcohol use	±	+			+	+	+
High cholesterol	+						
High blood pressure	+						
Diet	+	+	±	±		+	±
Physical inactivity	+	+		+		+	
Obesity	+	+		+		+	+
Stress	±	±					
Environ. tobacco smoke	±	±	+				
Occupation		+	+		±	+	±
Pollution		+	+				+
Low socioeconomic status	+	+	+	+	+	+	

Based on Brownson *et al*. (1993, p. 4).

group is their insidious onset, long duration, and the fact that they seldom resolve spontaneously.

By the middle of the 20th century, epidemiologists came to realize that the limited tools they had developed to address acute infectious diseases were no longer sufficient in studying chronic ailments. Out of this awareness arose development of new investigatory tools—field surveys, cohort studies, case–control studies, and clinical trial—as will be addressed later in this book. Using these newly developed methods, epidemiologists identified risk factors that influence the incidence of many chronic conditions (Table 1.4).

Mortality trends since 1950

Figure 1.2 displays age-adjusted mortality rates for all causes combined and the six leading causes of death in the United States in 2006 for the years 1950 through 2006. Rates are plotted on a logarithmic scale, so even modest downward slopes represent large changes in the rates of occurrence. During this period, age-adjusted mortality for all causes combined decreased from 1446.0 per 100 000 in 1950 to 776.5 per 100 000, a 47% decline. An important component of this decline came from advances in preventing cardiovascular and cerebrovascular mortality. In 1950, mortality from heart disease occurred at the adjusted rate of 588.8 per 100 000. By 1992, this rate was cut by two-thirds, to 200.2 per 100 000.

Trends in life expectancy

Life expectancy is the average number of years of life a person is expected to live if current mortality rates in the population were to remain constant. In 1900, life

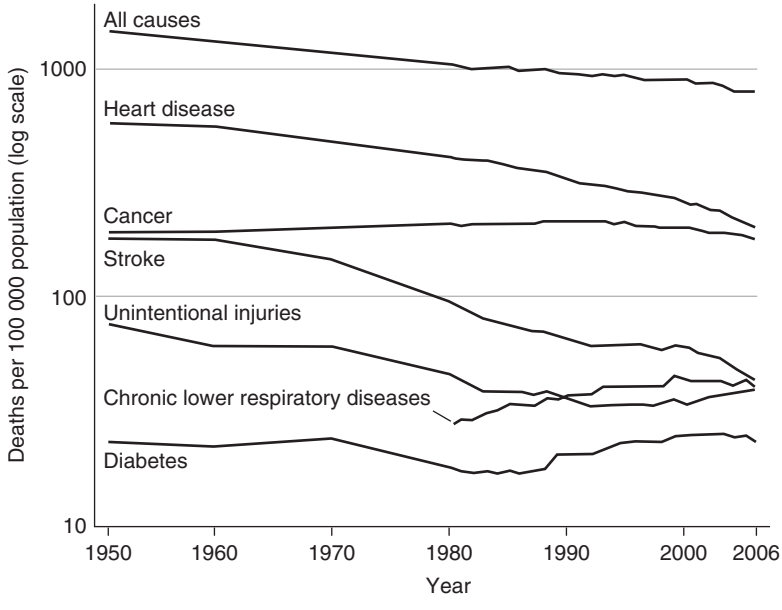

Figure 1.2 Age-adjusted death rates from 1950 to 2006, the United States, for the six leading causes of death in 2006 (Source: CDC/NCHS 2010).

expectancy at birth in the United States was 47.3 years. By 2006, life expectancy was 77.7 years (75.1 years for men and 80.2 years for women). Figure 1.3 charts this dramatic progress.

During the early part of the 20th century, increases in life expectancy can be traced to decreases in mortality at younger ages due primarily to improved sanitization and hygiene, improved nutrition, smaller family size, better provision of uncontaminated water, control of infectious disease vectors, pasteurization of milk, better infant and child care, and immunization (Doll, 1992). Since the middle of the century 20th century, life expectancy at older ages has shown significant increases. In 1950, a 65 year old man had a life expectancy of 12.8 remaining years; by 2000 this has increased to 16.0 years; by 2006 this had increased to 17.0 years (CDC/NCHS, 2010). For women, comparable increases have occurred. These increases can be traced to technological improvements in medical care (e.g., antibiotics, improvements in the safety of surgery, treatment of hypertension, etc.), dietary changes, avoidance of smoking, reductions in vascular diseases, and the pharmacologic control of high blood pressure and hyperlipidemia (Doll, 1992).

1.3 Selected historical figures and events

> A knowledge of epidemiological history, combined with a firm grasp of the statistical method were as essential parts of the outfit of the investigator in the field as was a grounding in bacteriology.
>
> *Major Greenwood*

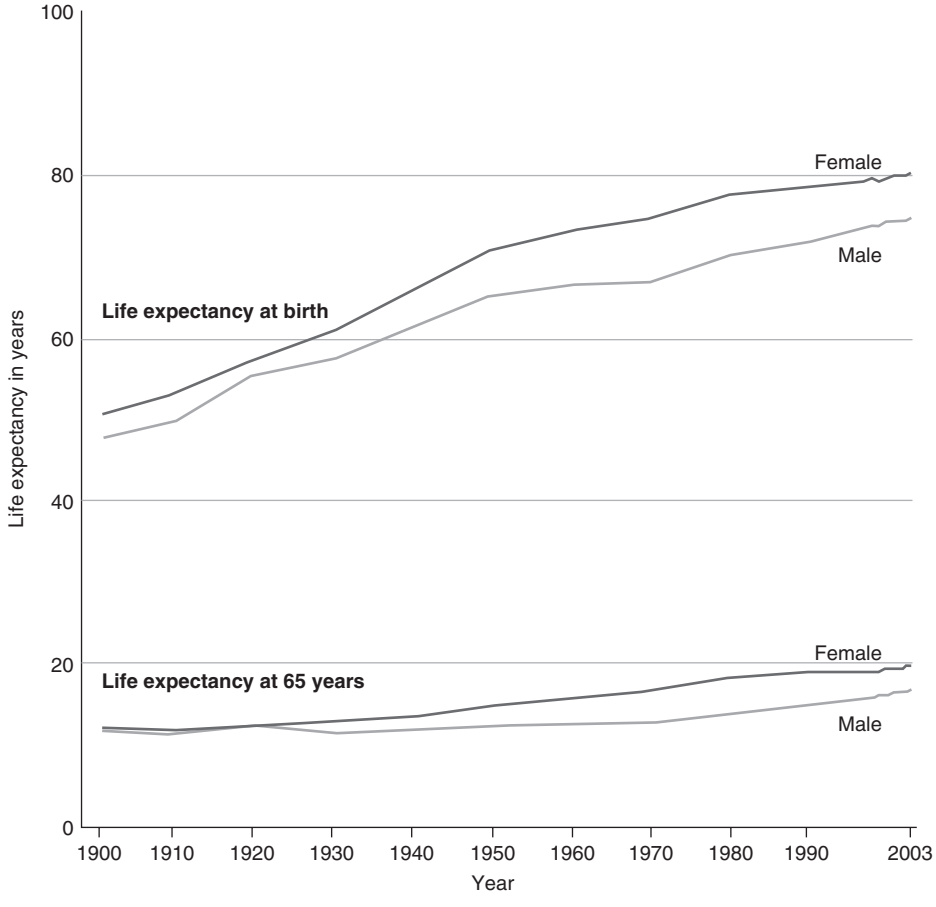

Figure 1.3 Life expectancy at birth and at age 65 by sex, United States, 1900–2003 (Source: CDC/NCHS, 2006).

Roots of epidemiology

Epidemiological insights into health and disease are probably as old as civilization itself. The Old Testament refers to the benefits of certain diets, the Greeks linked febrile illnesses to environmental conditions (''marsh fever''), and the Romans recognized the toxic effects of consuming wine from lead-glazed pottery.

Hippocrates (circa 460–388 BCE) is said to have prepared the groundwork for the scientific study of disease by freeing the practice of medicine from the constraints of philosophical speculation, superstition, and religion, while stressing the importance of careful observation in identifying natural factors that influenced health. In *Air, Waters, and Places* (Table 1.5), Hippocrates refers to environmental, dietary, behavioral, and constitutional determinants of disease. ''From these things, we must proceed to investigate everything else.'' Elsewhere, Hippocrates provides accurate descriptions of various clinical ailments, including tetanus, typhus, and tuberculosis.

Table 1.5 Part I of *On Air, Waters, and Places* (Hippocrates, 400 BCE).

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 for they are not at all alike, but differ much from themselves in regard to their changes. 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. We must also consider the qualities of the waters, for as they differ from one another in taste and weight, so also do they differ much in their qualities. In the same manner, when one comes into a city to which he is a stranger, he ought to 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. These things one ought to consider most attentively, and concerning 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 is 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, and not given to excess in eating and drinking.

A long period of relative quiescence in scientific medicine followed the Hippocratic era. In the 17th century scientific observation in medicine began to reawaken, dawning an upcoming Age of Enlightenment in the 18th century. This period is credited with the development of scientific methods based on systematized observation, experimentation, measurement, and a multistep process that advanced from theory to conclusion by testing and revising causal hypotheses. In summarizing the profound impact brought about by these changes, Ariel and Will Durant (1961, p. 601) wrote:

> Science now began to liberate itself from the placenta of its mother, philosophy. It developed its own distinctive methods, and looked to improve the life of man on the earth. This movement belonged to the heart of the Age of Reason, but it did not put its faith in ''pure reason''—reason independent of experience and experiment. Reason, as well as tradition and authority was now to be checked by the study and record of lowly facts; and whatever logic might say, science would aspire to accept only what could be quantitatively measured, mathematically expressed, and experimentally proved.

The features of scientific work—measuring, sequencing, classifying, grouping, confirming, observing, formulating, questioning, identifying, generalizing, experimenting, modeling, and testing—now took prominence.

A very early reawakening came with the work of the ''English Hippocrates'' **Thomas Sydenham** (1624–1689). Like Hippocrates, Sydenham stressed the need for careful observation for the advancement of health care. Using information combed from patients' records, Sydenham wrote about the prevalent diseases of his day. In a similar vein, Sydenham's contemporary **Bernardino Ramazzini** (1633–1714) published his comprehensive work *The Diseases of Workers* (*De Morbis Artificum Diatriba*). *The Diseases of Workers* discussed the hazards of various environmental irritants (chemicals, dust, metals, and abrasive agents) encountered in 52 different occupations. Renowned as an early expositor of specificity in linking environment cause to disease, Ramazzini set the stage for occupational medicine and environmental epidemiology. Not long after Ramazzini, the Englishman **Percival Pott** (1713–1788) identified chimney soot as the cause of enormously elevated rates of scrotal cancer in chimney sweeps (Pott,

1775/1790). This may have been the first link demonstrating a causal association between a malignancy and an environmental carcinogen.

John Graunt

The development of systems to collect the causes of death on a population basis was key to the development of epidemiology. The earliest tallying of deaths dates back to the reign of the Black Death (bubonic plague), when in the 14th and 15th centuries officials in Florence and Venice began keeping records of the number of persons dying, specifying cause of death in broad terms, such as plague/not plague (Saracci, 2001).

In England, the collection of death certificates began in selected parishes in 1592. However, it was not until the middle of the 17th century that this resource started to be used in an epidemiologic way by an intellectually curious London haberdasher by the name of **John Graunt** (1620–1674; Figure 1.4). Graunt tallied mortality

Figure 1.4 John Graunt (1620–1674).

statistics and made many forward-looking and insightful interpretations based these tallies in his publication *Natural And Political Observations Mentioned In A Following Index And Made Upon The Bills Of Mortality* (1662). Among his many observations, Graunt noted regional differences in mortality, high mortality in children (one-third of the population died before the age of 5), and greater mortality in men than women despite higher rates of physician visits in women (a phenomenon that still exists today). He noted that more boys than girls were born, debunked inflated estimates of London's population size, noted that population growth in London was due mostly to immigration, determined that plague claimed more deaths than originally thought, and documented an epidemic of rickets.

By starting with a hypothetical group of 100 people, Graunt constructed one of the first known life tables as follows. Out of 100 people born, Graunt projected the following expectations for survival (O'Donnell, 1936):

At the end of 6 years	64 of the initial 100 would be alive
At the end of 16 years	40 of the initial 100 would be alive
At the end of 26 years	25 of the initial 100 would be alive
At the end of 36 years	16 of the initial 100 would be alive
At the end of 46 years	10 of the initial 100 would be alive
At the end of 56 years	6 of the initial 100 would be alive
At the end of 60 years	3 of the initial 100 would be alive
At the end of 76 years	1 of the initial 100 would be alive
At the end of 80 years	0 of the initial 100 would be alive

Graunt recognized the importance of systematized record collection, was fastidious in his concern for accuracy, and took great care in scrutinizing the origins of data while being aware that certain forms of death tended to be misclassified. Given the period in which he lived and the limitations of its data, these are remarkable insights. It is therefore not surprising that many modern epidemiologists trace the birth of their discipline to Graunt's remarkable work. Rothman (1996) proffers the following lessons modern epidemiologists can learn from Graunt:

- He was brief.
- He made his reasoning clear.
- He subjected his theories to repeated and varied tests.
- He invited criticism of his work.
- He was willing to revise his ideas when faced with contradictory evidence.
- He avoided mechanical interpretations of data.

Despite his brilliance with numbers, John Graunt was not a good money manager. He died bankrupt on Easter-eve 1674 and was buried under what was then a pigsty in St. Dunstan's Church in Fleet Street. His eulogy read, ''what pitty 'tis so great an ornament of the city should be buryed so obscurely!'' (Aubrey, 1949).

Germ theory

The notion of a living agent as a cause of disease had been around since ancient times. For instance, the Roman poet Lucretius (circa 100 BC) refers to the seeds

of disease passing from healthy to sick individuals in the poem *De Rerum Natura*. However, the first cogent germ theory was presented by **Girolamo Fracastoro** in 1546 (Saracci, 2001).

Despite early theories of contagion, the prevailing theories of epidemics in the 19th century were expressed in terms of ''spontaneous generation'' and ''miasma atmospheres.'' This manner of thinking began to change midcentury when in 1840 **Jakob Henle** (1809–1885) presented his treatise of the *contagium animatum* in which he theorized that a living substance multiplied within the body where it was excreted by sick individuals and communicated to healthy individuals.

During the same era, **John Snow** (1813–1858) was independently developing similar ideas about contagion, basing his theories on the epidemiologic and pathophysiologic features of cholera. Among Snow's early epidemiologic observations was how cholera spread along the routes of human commerce and war and was propagated from human to human. Among his pathophysiologic observations was the cholera was primarily a gastrointestinal disease and that the loss of fluids caused its systemic effect by means of ''internal congestion'' (sludging of the blood and hypovolemic shock). Snow's theory of contagion recognized that infection with a stabile living organism was necessary for transmission to occur and that the infectious agent multiplies after infections to produce its effects (Winkelstein, 1995). Later in this chapter we will discuss three of Snow's seminal epidemiologic studies.

The French chemist **Louis Pasteur** (1822–1895) ultimately put the doctrine of spontaneous generation to rest by demonstrating that fermentation and organic decay were produced by microorganisms. Pasteur was also the first to isolate an agent responsible for an epidemic disease (in silk worms, in 1865), found that septicemia was caused by anaerobic bacterium, and developed the process for killing germs by heating that still bears his name (''pasteurization'').

Henle's student **Robert Koch** (1843–1910) made a breakthrough when he decided to stain microbes with dye, enabling him to visualize the microbe that caused tuberculosis in 1882 and the cholera bacillus in 1883. Koch is also known for his Postulates, which he developed in 1890.

Until the discovery of arthropod (insect borne) transmission of Texas cattle fever, the only known modes of transmission for infectious agents were by water and air. In 1882, **Daniel E. Salmon** (1850–1914) realized that Texas cattle fever presented something unusual—the disease stayed below a geographic line that extended through the southern United States and Mexico (Figure 1.5) and was not conveyed from bovine to bovine directly or through the atmosphere. Using various epidemiologic and laboratory methods, he and a team of workers at the U.S. Department of Agriculture conducted a series of experiments that demonstrated the vector-borne transmission of the disease. This was the first demonstration of a complex web of causation involving an agent (*Babesia bigeminal*) being transmitted to a mammalian host (cattle) through an invertebrate vector (the tick *Boophilus angulatus*). Discoveries of invertebrate vectors for other diseases (e.g. malaria, yellow fever) soon followed. The complex interactions involved in the maintenance and transmission of an agent in the environment provided the first theories of **medical ecology**.

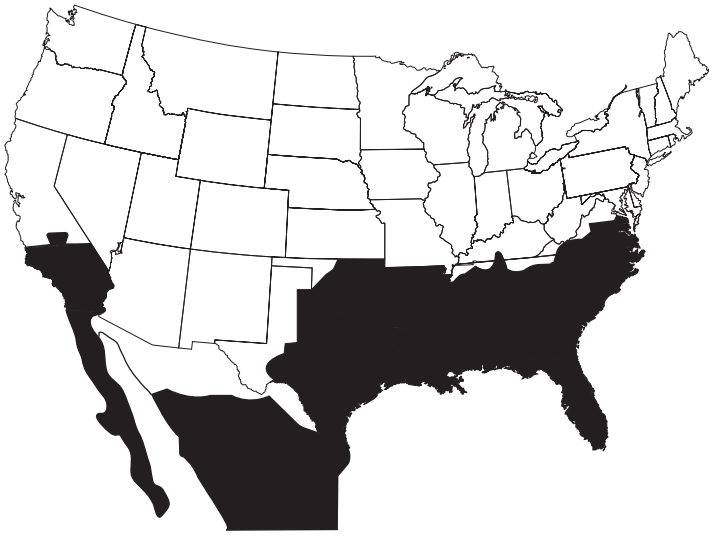

Figure 1.5 Distribution of the *Boophilus* tick before eradication.

Médecine d'observation and La Méthode Numerique (Pinel and Louis)

Owing to a confluence of strong social changes and the consolidation of statistical and probability theory, 18th century France was the incubator of many modern statistical principles and ideas. While the *Academie Royales des Sciences de Paris* were debating Laplace's theory of probability, a parallel movement emphasizing clinical quantification was brewing in the Parisian schools of medicine. The best known of these French physicians were Philippe Pinel and Pierre Charles Alexandre Louis.

Philippe Pinel (1745–1826), primarily known as a pioneer in the scientific and humane treatment of mental illness, also had a passion for medical statistics. Pinel's main statistical achievement was insistence on careful observation and refusal to get lost in undue reliance on unconfirmed theory and appeals to authority. In the introduction to his major work on mental illness published in 1809, he writes that ''a wise man has something better to do than to boast of his cures, namely to be always self-critical.'' After explaining his statistical approach, Pinel states that ''doctors who disapprove of my methods are at liberty to use the method they normally adopt, and a single comparison will suffice to show where the advantage lies'' (Armitage, 1983, p. 322).

In 1795, Pinel was appointed to administer a notorious women's asylum (the Salpêtrière). During his tenure in this position, he collected data on 1002 patients admitted during a 3 year and 9 month period. His studies at the Salpêtrière included cross-classifying cases by year of admission, clinical diagnoses, characteristics of patients at time of admission, and selected outcomes. Using this information, he demonstrated that his overall cure rates were better than those seen in institutions following less enlightened methods. This was true, he concluded, despite the fact that his patient mix tended to have more severe conditions than the comparable institutions. Thus, Pinel was aware of the statistical problem we now call confounding and was able to reason an enlightened approach to its consideration.

Often considered the ''father of clinical statistics,'' the influential French physician **Pierre-Charles Alexandre Louis** (1787–1872; Figure 1.6) wrote: ''I conceive that without the aid of statistics nothing like real medical science is possible.'' Although P.C.A. Louis made careful quantitative observations on many diseases, perhaps his best remembered research evaluated bloodletting as a treatment for various ailments (Louis, 1837).

Bloodletting, an extremely popular form of therapy at the time, required the removal of blood from the patient by lancet or through the placement of leeches on specific parts of the body. The procedure was so popular that 42 million leeches were imported into France in 1833. Louis was the first to call into question the effectiveness of this age-old remedy. Through attentive recordings of clinical observations (*médecine d'observation*), Louis tabulated the response to bloodletting in patients by carefully monitoring the outcome in various treatment groups.

In one analysis, Louis compared death rates and duration of disease in patients who received early treatment (within the first four days of symptoms) and in those

Figure 1.6 Pierre-Charles Alexandre Louis (1787–1872) (Source: Wikipedia Commons).

1		2		3		4		5		6		7		8		9	
10	3	7	3	19	3	19	3	28	2	13	1	24	2	19	2	35	1
12	2	10	2	29	3	12	2	17	3	16	2	12	4	12	1	11	2
14	2	12	2	20	2	15	2	40	2	23	3	19	2	18	1	17	2
				20		22	4	13	2	35	5	18	2	20	3	30	3
				16	3	12	4	21	2	17	2	15	2	13	2		
				17	4	21	2	13	2			27	2	21	2		
						25	3										
						28	4										
						40	2										
						16	2										
						12	4										
12	$2\frac{1}{3}$	10	$2\frac{1}{3}$	20	3	20	8	22	2	21	$2\frac{3}{5}$	19	$2\frac{1}{3}$	17	2	23	2

The figures upon the horizontal line above the columns indicate the day when the first bleeding was performed; the figures on the left in each column mark the duration of the diaease; those on the right, the number of bleedings; and those on the horizontal line below, show the mean duration of the disease and the average number of bleedings.

Figure 1.7 Duration of disease and number of bleeding in patients who survived according to day of first treatment. The original legend is reproduced in the figure.

1	2	3	4	5	6	7	8	9
6 5 18	53 5 65	4 1 57	29 2 19	16 4 58	62 4 20	20 2 68	25 1 40	22 1 50
	12 3 69	16 2 54	29 4 46	8 2 63	10 2 40			
	8 2 65	6 3 30	12 1 85	9 4 24	29 3 24			
	12 1 55	6 4 47	15 3 37					
	17 7 75	47 2 75	17 1 67					
		11 4 45	20 3 22					
6 5 18	20 $3\frac{3}{5}$ 66	15 3 51	20 $2\frac{1}{3}$ 49	11 3 48	33 3 28	20 2 68	25 1 40	22 1 50

Figure 1.8 Duration of disease, number of bleeding, and age of patients who died, according to day of first treatment (See Figure 1.7 for meaning of column headings).

who received later treatment (no untreated control group was available). Some of Louis's recordings are shown in Figures 1.7 and 1.8. Using these data, Louis found that mortality was greater in the earlier treated group than in the later treated group (44 versus 25%, respectively).

This type of observation led to the eventual end of this antiquated form of treatment and demonstrated the need for rigorous evaluation of conventional clinical practices. Medical systems that could not withstand a test of observation were to be discredited.

Louis attracted a large following, conveying his beliefs to many of the men who would establish modern medical and public health movements in England, the United States, and continental Europe (Osler, 1897; Lilienfeld and Lilienfeld, 1977). Some of these men were influential in establishing the epidemiologic movement in Victorian England.

The London Epidemiological Society

Urbanization and development of long-distance transportation (shipping and rail) in 19th century Europe led to repeated introductions of cholera, typhoid fever, smallpox, and other infectious diseases into the unsanitary housing conditions of densely populated metropolitan centers. This led to many dramatic outbreaks of ''crowd diseases.'' Driven by pragmatic concerns, a group of English physicians, who realized their obligation went beyond treating sick individuals, chartered the London Epidemiological Society on March 6, 1850 (Lilienfeld, 1978a). The stated objectives in the charter of this organization are remarkably insightful:

> . . . to endeavour, by the light of modern science, to review all those causes which result in the manifestation and spread of epidemic diseases—to discover causes at present unknown, and investigate those which are ill understood—to collect together facts, on which scientific researches may be securely based—to remove errors which impeded their progress—and thus, as far as we are able, having made ourselves thoroughly acquainted with the strongholds of our enemies, and their modes of attack, to suggest those means by which their invasion may either be prevented, or if, in spite of our existence, they may have broken in upon us, to seek how they may be most effectually combated and expelled.
>
> *Babington*, 1850, p. 640

Epidemiology thus came into being as a specific discipline united by its belief that health could be advanced by the scientific study of disease on a population level. One of the members of this new group was a former pupil of P.C.A. Louis: the physician William Farr.

William Farr

It had been nearly two centuries since John Graunt's Observations when, in 1837, the English Parliament created a centralized registration system for information on births, deaths, and marriages. In 1839, William Farr (1807–1883; Figure 1.9) was appointed to head the branch of this office involved with these statistics; he served in this post for the next 40 years. During his tenure, Farr established a national registration system for the collection, classification, analysis, and reporting of mortality statistics—the forerunner of the today's vital statistics and disease surveillance systems. Farr had an insatiable appetite for collecting, tabulating, and analyzing morbidity and mortality statistics. He recognized the importance of standardized nomenclatures of disease, remarking that ''[disease] nomenclature is of as much importance [in epidemiology] as weights and measures in the physical sciences'' (Farr, 1885, p. 234). His anatomically based system of disease classification is the antecedent to the International Classification of Disease currently in use.

Farr relied on comparisons of rates in which numerator data comprised deaths and denominator data comprised population size. Using these simple calculations, Farr compared mortality rates in people of different backgrounds, social classes, and occupations searching for ''causes that make the rates of mortality vary'' (Farr, 1885, p. 187). Figure 1.10 is a replica of one of Farr's tabulations.

Figure 1.9 William Farr (1807–1883).

POPULATION, DEATHS, AND MORTALITY per 1,000 at TWELVE DIFFERENT PERIODS of AGE, in LONDON and in ENGLAND, 1861–70.

AGES.	LONDON. MEAN POPULATION, 1861–1871.		LONDON. ANNUAL DEATHS in 10 Years 1861–70.		LONDON. ANNUAL MORTALITY Per 1,000 living during the Years 1861–70.		ENGLAND. ANNUAL MORTALITY Per 1,000 living during the Years 1861–70.	
	Males.	Females.	Males.	Females.	Males.	Females.	Males.	Females.
All Ages -	1,415,466	1,613,659	37,581	36,053	26•55	22•34	23•61	21•28
0—	195,963	196,500	17,032	14,997	86•91	76•32	73•16	63•43
5—	161,151	163,821	1,509	1,449	9•37	8•85	8•15	7•76
10—	141,969	145,035	603	590	4•24	4•07	4•46	4•48
15—	131,585	151,530	766	773	5•82	5•10	6•16	6•62
20—	133,185	166,302	1,096	1,034	8•23	6•22	8•45	7•96
25—	233,714	280,674	2,538	2,470	10•86	8•80	9•90	9•69
35—	178,860	206,826	3,066	2,656	17•14	12•84	13•46	12•03
45—	124,417	144,530	3,195	2,676	25•68	18•52	19•17	15•56
55—	71,145	90,739	3,120	3,035	43•85	33•45	33•00	27•77
65—	33,097	49,021	2,741	3,296	82•83	67•23	66•90	58•80
75—	9,325	16,338	1,576	2,394	169•02	146•54	146•58	134•43
85 & upds.	1,055	2,343	339	683	321•42	291•42	313•57	283•64

Figure 1.10 Mortality statistics for London and England in the 19th century. ''The death-rate is a fact; anything beyond this is an inference'' (Source: Farr, 1885, p. 123).

A self-taught mathematician, Farr used actuarial techniques to address questions of mortality and survival. He understood the relation between incidence and prevalence, and was ahead of his time in distinguishing the calculation of risks and rates (Vandenbrouke, 1985). He compared mortality in subgroups to help identify risk factor for morbidity and mortality.

Farr was open-minded about theories of disease etiology. In studying cholera, he initially believed in miasma theory—the false notion that the cholera agent was nonliving and spread through the atmosphere, being ''most fatal at low places.'' However, by 1866, it was clear to Farr that cholera was not transmitted by air but was instead spread by contaminated water (Eyler, 2001).

Farr's theories about the causes of disease included such modern concepts as ''indulgences in excess, by idleness, or by improvidence . . . conflicts with each other . . . organized parasites in the body . . . and molecules which, though of no recognized form, evidently thrive, propagate, die in the bodies of men'' (Farr, 1885, p. 117). The effects of population density on transmission of agents were described, as were properties of herd immunity. Farr also understood the importance of follow-up in evaluating prognosis and the effectiveness of medical treatment (Farr, 1838, 1862). Therefore, it is not surprising to find that Farr has been identified as one of the founders of modern epidemiology (Susser and Adelstein, 1975, p. iii). Farr also provided data and exerted influence on the man who many consider to be the essential hero of modern epidemiology—John Snow.

John Snow

John Snow (1813–1858; Figure 1.11) was a Victorian surgeon with varied scientific and social interests. In addition to being a pioneer in epidemiology, he was a recognized expert in the development and administration of inhaled anesthesia such that he attended the birth of two royal children to administer chloroform gas to Queen Victoria for the purpose of childbirth in 1853 and again in 1857 (Richardson, 1887). Our interests, however, center on his role in epidemiology through his investigations of cholera.

Cholera in Victorian England

Cholera hit Great Britain in 1831–1832, coming from India via the British seaports. As an apprentice to a Newcastle surgeon, Snow attended patients suffering from these early cholera epidemics (Richardson, 1887). When the epidemic resurfaced in 1848, Snow formulated his theories about the disease publishing his views as an article (Snow, 1849a) and booklet (Snow, 1849b). These articles laid out his ideas of cholera as a disease primarily affecting the gastrointestinal tract with the agent entering directly into the alimentary canal orally. Snow theorized that the source of the agent was fecal-contaminated water. This theory contradicted the predominant theory of the time—miasma (''bad air'') theory—which instead professed that cholera arouse from the emanations of inorganic material in the form of foul smelling gases.

Figure 1.11 John Snow (1813—1858). (Source: Wikipedia Commons.)

Miasma theory of transmission

With our current knowledge about infectious diseases transmission, it is difficult to distance ourselves adequately in order to understand the miasma theory of epidemics. In broad strokes however, miasma theory placed emphasis on the noxious vapors produced from ordinary organic decay and decomposition without the presence of prior contagion. This theory was mixed with concepts of ''localizing influences'' which promoted the propagation of the cholera poison, ''predisposing causes,'' ''spontaneous generation,'' and ''cholera atmospheres.'' In contrast to this predominant view of transmission, Snow maintained that ''no mere emanation arising from evolution of foul smelling gases can, *per se*, . . . , originate a specific disease'' (Richardson, 1887, p. xxxix).

Snow's theory

Snow based his theory of cholera pathogenesis on both the clinical and epidemiologic features of the disease. Cholera begins with symptoms specific to the gastrointestinal tract, without the fever and the whole-body signs associated with other epidemic diseases. This caused Snow to postulate ''cholera is, in the first instance at least, a local affection of the mucous membrane of the alimentary canal'' (Snow, 1849a, p. 745). From this, Snow inferred ''the disease must be caused by something which passes from the mucous membrane of the alimentary canal of one patient to that of the other, which it can only do by being swallowed and as the disease grows in a community by what it feeds upon, attacking a few people in a town first, and then becoming more prevalent, it is clear that the cholera poison must multiply itself by a kind of growth'' (Snow, 1849a, p. 746).

Snow also noted that the course of cholera could be traced along with troop movements from India, stating ''one feature immediately strikes the inquirer—viz., the evidence of its communication in human intercourse'' (Snow, 1849a, p. 746). These ideas ultimately coalesced in the form a theory in which Snow proposed that cholera was a self-propagating agent spread from person to person through contaminated water and food.

The London cholera epidemics of 1853–1854 allowed Snow to test these theories using what we now recognize as three distinct epidemiologic methods (Winkelstein, 1995). These are:

- Comparisons of cholera mortality rates using regional aggregate-level data. We now recognize this as the basis of the *ecological study design*.
- Comparison of cholera rates in groups defined by exposure to various water sources. We now recognize this as the basis of the *retrospective cohort study design*.
- Comparison of the characteristics of cholera cases and non-cases in a method that bears some semblance to a case–control study but is really *a case series analysis*.[a]

Snow's ecological analysis

Water distribution in 19th century London was the purview of private water companies. The two major companies that distributed water were the Southwark & Vauxhall Company and the Lambeth Company. During the epidemic of 1849, roughly the same number of deaths occurred in London districts served by either company. However, during the 1853 epidemic, Snow noted that cholera mortality was higher in regions served by the Southwark & Vauxhall Company than in regions served by the Lambeth Company (Figure 1.12), suggesting that water provided by the Southwark & Vauxhall Company served as the vehicle for the dissemination of the cholera agent. This is an ecological comparison because rates are compared by region and there is little or no follow-up of individual experience.

Further investigations led Snow to discover that Southwark & Vauxhall derived its water from downstream sources that were polluted with sewage. In contrast, the Lambeth Company had moved its water source upstream away from the primary sources of sewage pollution, explaining its superior safety.

---

[a] A true case–control study would require a random or at least representative sample of noncases from the population that begat the cases.

Sub-Districts.	Popula-tion in 1851.	Deaths from Cholera in 1853.	Deaths by Cho-lera in each 100,000 living.	Water Supply.
St. Saviour, Southwark	19,709	45	227	Southwark and Vauxhall Water Company only.
St. Olave . . .	8,015	19	237	
St. John. Horsleydown	11,360	7	61	
St. James, Bermondsey	18,899	21	111	
St. Mary Magdalen .	13,934	27	193	
Leather Market .	15,295	23	153	
Rotherhithe* . .	17,805	20	112	
Wandsworth . .	9,611	3	31	
Battersea . . .	10,560	11	104	
Putney . . .	5,280	—	—	
Camberwell . .	17,742	9	50	
Peckham . . .	19,444	7	36	
Christchurch, Southwk	16,022	7	43	Lambeth Water Company, and Southwark and Vauxhall Com-pany.
Kent Road . .	18,126	37	204	
Borough Road . .	15,862	26	163	
London Road . .	17,836	9	50	
Trinity, Newington .	20,922	11	52	
St. Peter, Walworth .	29,861	23	77	
St. Mary, Newington .	14,033	5	35	
Waterloo (1st part) .	14,088	1	7	
Waterloo (2st part) .	18,348	7	38	
Lambeth Church (1st part) . . .	18,409	9	48	
Lambeth Church (2nd part) . . .	26,784	11	41	
Kennington (1st part)	24,261	12	49	
Kennington (2nd part)	18,848	6	31	
Brixton . . .	14,610	2	13	
Clapham	16,290	10	61	
St. George, Chamberwell	15,849	6	37	
Norwood . . .	3,977	—	—	Lambeth Water Company only.
Streatham. . .	9,023	—	—	
Dulwich . . .	1,632	—	—	
First 12 sub-districts .	167,654	192	114	Southwk. & Vaux.
Next 16 sub-districts .	301,149	182	60	Both Companies.
Last 3 sub-districts .	14,632	—	—	Lambeth Comp.

* A part of Rotherhithe was supplied by the Kent Water Company: but there was no cholera in this part.

Figure 1.12 Snow's ecological data on cholera rates by water district, 1853. (Source: Snow, l855, p. 73.)

Snow's retrospective cohort analysis

Snow noticed that there were sub-districts in London where water pipes traveled side-by-side down streets supplying water to households of various sorts. By determining the water supplies for each house and the household of each case, Snow was able to tabulate cholera mortality rates according to water supplier. He found 1263 cholera deaths in the 40 046 households exposed solely to water from the Southwark & Vauxhall (S&V) Company. Thus, households supplied by S&V had a cholera mortality rate of:

$$\frac{1263 \text{ cases}}{40\,046 \text{ households}}$$

$$= 0.0315 \text{ per household or, equivalently, } 315 \text{ per } 10\,000 \text{ household}$$

In households served solely by the Lambeth Company, 98 cholera deaths occurred in 26 107 households, for a rate of:

$$\frac{98 \text{ cases}}{26\,107 \text{ households}} = 0.0038 \text{ or } 38 \text{ per } 10\,000 \text{ households}$$

The rest of London experienced

$$\frac{1422 \text{ cases}}{256\,423 \text{ households}} = 0.0055 \text{ or } 55 \text{ per } 10\,000 \text{ households}$$

Thus, the households supplied by the S&V water company experienced cholera at eight-times the rate of those supplied by the Lambeth water company and more than five-times the rate of the rest of London. This type of analysis of rates according to exposure status forms the basis of the cohort study design.

Snow's case series

In contrast to the cohort method in which rates are compared according to exposure status, case–control studies compare the characteristics of diseased and non-diseased individuals. As part of Snow's inquiry into the terrible outbreak of cholera that affected the Golden Square Area of London in August and September of 1854, he prepared a map showing the distribution of cases in relation to the infamous Broad Street pump (Figure 1.13).

Snow's case series analysis

Snow found that 61 of the fatalities during this outbreak had used water from the Broad Street pump, six had reportedly not drunk water from the pump, and six could not determine whether or not they had used water from the pump. Thus, exposure to Broad Street pump water, if not universal, was very common.

Snow also interviewed cases that seemed to contradict the normal pattern of infection. One interesting observation came when investigating a couple of cases from the suburb of Hampstead, whereby Snow wrote:

> I was informed by this lady's son that she had not been in the neighbourhood of Broad Street for many months. A cart went from Broad Street to West End every day, and it was the custom to take out a large bottle of the water from the pump in Broad Street, as she preferred it. The water was taken on Thursday, 31st August, and she drank of it in the evening, and also on Friday. She was seized with cholera on the evening of the latter day, and died on Saturday, as the above quotation from the register shows. A niece, who was on a visit to this lady, also drank of the water; she returned to her residence, in a high and healthy part of Islington, was attacked with cholera, and died also. There was no cholera at the time, either at West End or in the neighbourhood where the niece died.
>
> *Snow*, 1855; 1936 reprint, pp. 45–46

Thus, although residing outside of the epidemic area, these two cases were discovered to have imbibed water from the Broad Street pump after all.

Snow also interviewed noncases from subpopulations in which cholera had been surprisingly infrequent. For example, in the brewery near the Broad Street pump (see map), no workers had died of cholera. Snow remarked, ''The men are allowed

Figure 1.13 Snow's map of the 1854 Golden Square cholera outbreak. Each horizontal line represents a cholera death. Public water pumps are shown as enclosed dots (⊙). The Broad Street pump is in the center of the map. (Source: Snow, 1855, 1936 reprint, pp. 44 and 45.)

a certain quantity of malt liquor, and Mr. Huggins [the proprietor] believes they do not drink water at all; and he is quite certain that the workmen never obtained water from the pump in the street'' (Snow, 1855, 1936 reprint p. 42).

Publication

As a result of his investigation of the Golden Square (''Broad Street Pump'') outbreak, Snow was able to convince the vestrymen of the parish to remove the handle from the offensive pump. The pump handle was removed, and the plague recessed. More importantly, Snow's lucid observations and reasoning continue to inspire epidemiologists, while his efforts to remove the pump handle serves as a symbol of public health action.

Twentieth-century epidemiology

Many social and scientific events have influenced the development of epidemiology in the 20th century. Industrialization and economic development accelerated greatly, two world wars occurred, the 1918–1919 influenza pandemic claimed between 20 and 40 million lives, European colonialism dissolved, the stock market crashed and a great economic depression ensued, capitalism and communism clashed in a cold war, communism collapsed, world population growth accelerated, medical technology entered into a new stage, communication evolved, networks expanded, life expectancy increased dramatically, and the age structure of populations in industrialized countries transitioned. Concurrent with these trends, epidemiology developed from a descriptive field to an analytic discipline, with biostatistics increasingly serving as an essential discipline (Gordon, 1952).

About mid-century, Wade Hampton Frost, the first professor of epidemiology in the USA, declared that contemporary events had ''extended the meaning of [the word] epidemiology beyond its original limits, to extend not merely the doctrine of epidemics but a science of broader scope in relation to the mass phenomena of disease in their usual or endemic as well as their epidemic occurrence'' (Frost, 1941). Let us consider several early 20th century epidemiologists that led the way in the transition of the discipline.

Emile Durkheim

Emile Durkheim (1858–1917) was a French sociologist known for his compelling scientific approach to studying social phenomena. In his *Rules of Sociological Method* (1895), he sets forth that (a) social explanations require comparisons, (b) comparisons require classification, and (c) classification requires the definition of those facts to be classified, compared, and ultimately explained. Consistent with these rules, Durkheim warned against *notiones vulgares*—the idea that crudely formed concepts of social phenomena without scientific reflection produce only false knowledge: as alchemy had preceded chemistry and astrology had preceded astronomy, untested thoughts on social phenomena merely foreshadows true social science.

Durkheim's seminal work *Le Suicide* (1897) considered many potential risk factors for suicide, including psychopathological states, race, heredity, climate, season, imitative behavior, religion, social instability, and a host of other social phenomena. Table 1.6 is based on Table XXI from *Le Suicide*. From these data, Durkheim concluded: (a) marriage before the age of 20 (''too early marriages'') has an aggravating influence on suicide, especially in men; (b) after age 20, married persons of both sexes enjoy some protection from suicide in comparison with unmarried people; (c) the protective effect of marriage is greater in men; and (d) widowhood diminishes the protective effects of marriage but does not entirely eliminate it. Durkheim reflected on whether the apparent protective effects of marriage were due to the influence of the married domestic environment or whether this ''immunity'' is due to some sort of ''matrimonial selection'' (i.e. people who marry have certain physical and moral constitutions that make them less likely to commit suicide). This type of reflective reasoning and careful interpretation of empirical data foreshadowed the modern epidemiologic approach.

Table 1.6 Rates (per million per year) and relative risks of suicide by age and marital status, France, 1889–1891.

Ages	Rate per million/year			Relative risk	
	Unmarried	Married	Widowed	Unmarried with reference to married	Unmarried with reference to widowed
Men					
15–20	113	500	—	0.22	—
20–25	237	97	142	2.40	1.66
25–30	394	122	412	3.20	0.95
30–40	627	226	560	2.77	1.12
40–50	975	340	721	2.86	1.35
50–60	1434	520	979	2.75	1.46
60–70	1768	635	1166	2.78	1.51
70–80	1983	704	1288	2.81	1.54
Above 80	1571	770	1154	2.04	1.36
Women					
15–20	79.4	33	333	2.39	0.23
20–25	106	53	66	2.00	1.60
25–30	151	68	178	2.22	0.84
30–40	126	82	205	1.53	0.61
40–50	171	106	168	1.61	1.01
50–60	204	151	199	1.35	1.02
60–70	189	158	257	1.19	0.77
70–80	206	209	248	0.98	0.83
Above 80	176	110	240	1.60	0.79

Source: Durkheim, (1897, p. 178, Table XXI).

Joseph Goldberger

Joseph Goldberger (1874–1929; Figure 1.14) was born in the Austrian–Hungarian Empire in a town now located in the Czech Republic. His family emigrated to the United States when he was 6, and settled in Manhattan's Lower East Side. After obtaining his medical degree in 1895 and a brief stint in private practice, he entered the Marine Hospital Service in 1899.[b]

As a young public health officer, Goldberger was assigned to investigate various tropical diseases such as yellow fever, typhoid, and dengue fever, which were the main concerns of the Public Health Service at that time. In 1914, the Surgeon General of the United States appointed Goldberger to investigate the crisis of pellagra which was raging in the southern United States. We now know that pellagra is a nutritional disease caused by severe deficiencies of niacin and the amino acid tryptophan. (The body can synthesize niacin using tryptophan as a precursor.) However, at the time, pellagra was thought to be contagious. Goldberger contradicted this commonly held belief, basing his understanding on the observation that pellagra demonstrated a preference for inmates in hospitals and orphanages, leaving employees of the

[b] The U.S. Marine Hospital Service was established in 1798 to care for seamen and to serve as a bulkhead against infectious agents. It is the forerunner of the Public Health Service, which was established in 1902.

Figure 1.14 Joseph Goldberger (1874–1929).

institutions largely unaffected. Since germs would not distinguish between inmates and employees, Goldberger searched for an alternative cause.

By the spring of 1914, Goldberger had begun his investigations on nutrition and pellagra. Among Goldberger's many studies were nutritional analyses of affected and unaffected households. Table 1.7 is based on a table from Goldberger's 1918 article. This table documents the relative paucity of meats, dairy products, and green vegetables in households with pellagra. Goldberger's work led to nutritional interventions that were effective in treating and preventing pellagra. Note that the bulk of Goldberger's work occurred one to two decades before Elvehjem *et al*. (1937) identified niacin as the specific nutritional deficiency that causes pellagra.

Table 1.7 Caloric intake of foods constituting the average daily supply in nonpellagrous and pellagrous households in seven cotton mill villages, 15-day period in 1916.

Groups of foods	Nonpellagrous households		Pellagrous households	
	Highest income	Lowest income	Lowest income one or more cases	Low-income two or more cases
Meats (exclusive of salt pork), eggs, milk, butter, cheese	762	639	338	270
Dried and canned peas and beans (exclusive of canned string beans)	126	113	115	123
Wheaten flour, bread, cakes and crackers, cornmeal, grits, canned corn, rice	2162	2082	1752	1840
Salt pork, lard, and lard substitutes	741	673	748	745
Green and canned vegetables (exclusive of corn), green and canned string beans, fruits of all kinds	131	71	60	69
Irish and sweet potatoes	55	53	53	46
Sugar, syrup, jellies and jams	250	205	222	217
All foods . . .	4267	3836	3288	3310

Source: Goldberger *et al*. (1918).

By midcentury, epidemiologic theory and methods took major steps forward in order to study the non-infectious causes of diseases that comprised the major causes of morbidity and mortality as the century progressed. Major advancements were made first in the study of cigarette-related diseases, heart disease, mental disorders, cancers, and medical safety and effectiveness. One of the studies that signaled the reckoning of this new era of ''modern epidemiology'' is the British Doctors Study.

The British Doctors Study

The work of the British team of **Austin Bradford Hill** (1897–1991) and **Richard Doll** (1912–2005) extended many epidemiologic methods in the years following World War II. Bradford Hill's contributions included the introduction of the randomized clinical trial for measuring the benefits of medical interventions, advancements in case–control and cohort methods for the study of exposure–disease relations in observational studies, and articulation of a framework for judging causality using nonexperimental data. Richard Doll's work has been important in transforming our understanding of smoking and other environmental causes of cancer.

As an example, Doll and Hill published an early case–control study linking cigarette smoking to lung cancer in 1950, in which they found a significantly higher proportion of heavy smokers in their case series than in their control series. For instance, 26% of the male lung cancer patients smoked 25 cigarettes a day or more, in comparison to 13% of their control group (Figure 1.15). A similar pattern was found in female cases and controls.

Not long after publishing their case–control study, Doll and Hill sent out inquiries to medical doctors in the United Kingdom asking them to classify their smoking status and quantify the approximate amount they smoked. This brief questionnaire was

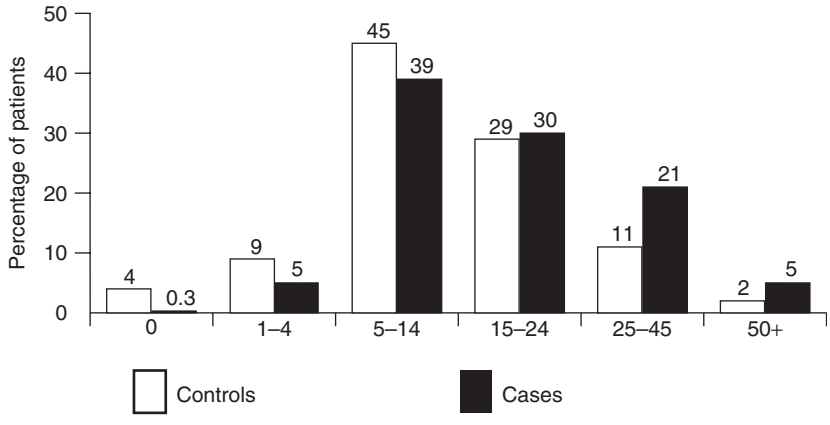

Figure 1.15 Smoking experience of male cases and controls in an early case–control study of lung cancer and smoking (Doll and Hill, 1950).

Table 1.8 Age-adjusted mortality per 1000 person-years according to amount smoked, British Doctors Study.

		Death rates of men smoking a daily average of:			
Cause of death	No. of deaths	Nonsmokers	1–14 g	15–24 g	25+ g
Lung cancer	36	0.00	0.48	0.67	1.14
Other cancers	92	2.32	1.41	1.50	1.91
Respiratory diseases other than cancers	54	0.86	0.88	1.01	0.77
Coronary thrombosis	235	3.89	3.91	4.71	5.15
Other cardiovascular disease	126	2.23	2.07	1.58	2.78
Other diseases	247	4.27	4.67	3.91	4.52
All causes	789	13.61	13.42	13.38	16.30

Source: Doll and Hill (1954).

sent to 59 600 physicians, of which 40 564 replies that were sufficiently complete for analysis were returned. The first report from this cohort study, published in 1954, showed that lung cancer mortality paralleled the amount smoked (Table 1.8). It also showed higher rates of coronary heart disease and other cancers in smokers.

A follow-up report published in 1956 confirmed these smoking-related associations while demonstrating additional associations for chronic obstructive pulmonary disease, peptic ulcer, and pulmonary tuberculosis. After 40 years of follow-up, the British Doctors Study is still ongoing. Figure 1.16 exhibits survival curves for the cohort, demonstrating that 50% of heavy smokers died before age 70 compared with only 20% of nonsmokers; 8% of heavy smokers have survived to age 85, compared with 33% of nonsmokers.

These and other developments following World War II have occurred in the context of rapid growth in understandings of disease etiology. A new age of *modern epidemiology* was thus born, with epidemiology as a discipline distinct from other scientific endeavors with its own concepts and theories, yet still intimately attached to these other disciplines in the study of disease etiology.

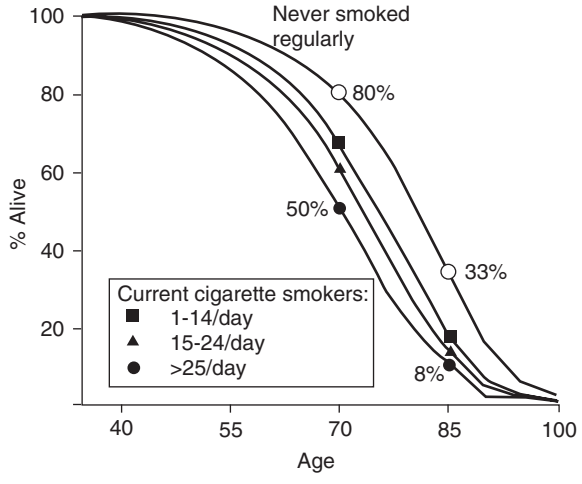

Figure 1.16 Survival in the British Doctors cohort according to amount smoked (Based on data in Doll *et al.*, 1994).

1.4 Chapter summary

Because this is a long chapter with a lot of detail, this summary is provided for review.

Epidemiology and its uses

Epidemiology is the study of the distribution and determinants of health and disease in populations. It is one of the core disciplines of public health, with its objective *to learn* about those factors the prevent disease and injury and promote health. In contrast to clinical medicine, epidemiology focuses primarily on aggregates as opposed to individual patients. Epidemiology is characterized by a close connection between the scientific study of disease causation and application of this knowledge to prevent disease and improve health. It thus covers a broad range of activities, including conducting biomedical research, communicating research findings, and participating with other disciplines in public health interventions. Applications of epidemiology include studying population-based trends in morbidity and mortality, diagnosing health problems in communities, studying the effectiveness of health care, estimating individual chances of disease recovery, identifying new syndromes and characterization of the full spectrum of known ailments, and, most importantly, elucidating the causes of ill-health.

Evolving patterns of morbidity and mortality

Whereas morbidity and mortality in the 19th and early 20th centuries were dominated by acute and infectious causes, the major health problems of today are largely chronic and non-infectious. This shift is known as the *epidemiologic transition*. Accompanying this transition has been a change in population age structure known as the

demographic transition. In 1900, life expectancy at birth in the USA was 47 years. In 2007, life expectancy was almost 78 years. Increases in life expectancy have occurred in all groups, with improvements during the first part of the 20th century mostly during childhood, and improvement during the second half of the century largely during middle- and late-age. Concomitant with these changes has been a decrease in birthrates, resulting in an aging of the population.

Selected historical figures and events

Epidemiological insights into health and disease are probably as old as civilization itself. The scientific roots of epidemiology can be traced to Hippocratic principles developed in the 4th century BCE. However, the central tenants of modern epidemiology can be attributed to the renaissance of scientific and artistic ideas starting in the 16th century and developed in the Age of Enlightenment starting in the 18th century. Epidemiology emerged as a unique discipline in Victorian England with the establishment of the London Epidemiological Society in 1850, with the work of many individuals, notably William Farr and John Snow. In the 19th century and first half of the 20th century, epidemiology was concerned primarily with the control of infectious diseases. Beginning in the early 20th century, as the burden of disease shifted from acute infectious diseases to chronic ''lifestyle diseases,'' developments in the epidemiologic study of chronic diseases and medical safety and effectiveness took on greater importance. Rapid growth in understanding the epidemiologic study all types of diseases encouraged a modern form of epidemiology, with its own distinct scientific practices and theories.

Review questions

R.1.1 The word epidemiology is based on the Greek terms *epi*, *demos*, and *ology*. Define each of these terms.

R.1.2 Select your favorite definition of epidemiology. What appeals to you about this particular definition?

R.1.3 How does *epidemiology* differ from *clinical medicine*? How does it differ from *public health*?

R.1.4 The preamble to the 1948 constitution of the World Health Organization addresses three elements of health and well-being. Name these three elements.

R.1.5 Define these terms: *epidemic*, *pandemic*, *endemic*, *morbidity*, *mortality*.

R.1.6 Is it the responsibility of the epidemiologist to effectively communicate their findings? Explain.

R.1.7 List Morris's (1957) seven general uses of epidemiology.

R.1.8 One of Morris's (1957) uses of epidemiology is *community diagnosis*. What does this mean in plain terms?

R.1.9 Describe the demographic transition of the 20th century.

R.1.10 Describe the epidemiologic transition of the 20th century.

R.1.11 Age-adjusted mortality decreased by approximately 40% from 1950 to 2000. Which major causes of death demonstrated the steepest declines?

R.1.12 Describe the change in the shape of the population pyramid that occurred during the 20th century.

R.1.13 List several examples of modifiable risk factors for chronic diseases.

R.1.14 True or false? Overall age-adjusted cancer mortality rates increased dramatically during the second half of the 20th century. Explain your response.

R.1.15 True or false? Age-adjusted cardiovascular mortality rates continued to increase dramatically during the second half of the 20th century. Explain your response.

R.1.16 List the three current most popular causes of death in the USA in rank order.

R.1.17 True or false? Life expectancy at birth increased by about 30 years during the 20th century.

R.1.18 In what century was epidemiology first recognized as a unique discipline?

R.1.19 Which ancient philosopher/physician is said to have initially freed the study of health and disease from philosophical speculation, superstition, and religion?

R.1.20 List features of scientific work.

R.1.21 Match each of these historical figures with their brief biographical descriptions.
Historical figures: William Farr, Fracastoro, John Graunt, Pierre-Charles Alexandre Louis, Philippe Pinel, Percival Pott, Daniel Salmon, John Snow, Thomas Syndenham
Brief descriptions:

(A) The ''English Hippocrates,'' in the 1600s.
(B) Identified soot as the cause of scrotal cancer in 18th century chimney sweeps.
(C) 17th century physician who used population-based vital statistics to derive early epidemiologic observations.
(D) Presented first cogent germ theory of disease in 1545.
(E) 19th century American veterinarian who led the team that discovered the first vector-borne ecology of a disease.
(F) 18th/19th century French physician who pioneered the humane treatment of mental illness and said ''a wise man has something better to do than to boast of his cures, namely to be always self-critical.''
(G) 19th century French physician whose studies led him to believe that bloodletting was infective in the treatment of pneumonia; known as a proponent of ''the numerical method.''
(H) 19th century British physician who was the first registrar of mortality statistics nationally; pioneer in the use of vital statistics and epidemiologic methods in Victorian England.
(I) Victorian surgeon who studied the transmission of cholera; best known for convincing authorities to remove the handle from the Broad Street pump.

References

Armitage, P. (1983) Trials and errors: The emergence of clinical statistics. *Journal of the Royal Statistical Society. Series A (General)*, **146**, 321–334.

Aubrey, J. (1949) *Aubrey's Brief Lives*. Available: *http://www.york.ac.uk/depts/maths/histstat/aubrey.pdf* (accessed 23 March 2003).

Babington, B. G. (1850) Epidemiological Society. Monday, Dec. 2, 1850. Dr. Babington, President. *Lancet*, **2**, 639–642.

Brownson, R. C., Remington, P. L., and Davis, J. R. (1993) *Chronic Disease Epidemiology and Control*, American Public Health Association, Washington, D.C.

Bureau of the Census (1904) *Abstract of the Twelfth Census of the United States 1900*, 3rd edn, Government Printing Office, Washington, D.C.

CDC/NCHS (2006) Health, United States, 2006: chartbook on trends in the health of Americans. Available from *www.cdc.gov/nchs/data/hus/hus06.pdf*.

CDC/NCHS (2010) Health, United States, 2009: with special feature on medical technology. Available: *www.cdc.gov/nchs/data/hus/hus09.pdf*.

Calhoun, J. G., Ramiah, K., Weist, E. M., and Shortell, S. M. (2008) Development of a core competency model for the master of public health degree. *American Journal of Public Health*, **98** (9), 1598–1607.

Cole, P. (1979) The evolving case–control study. *Journal of Chronic Diseases*, **32**, 15–27.

Doll, R., and Hill, A. B. (1950) Smoking and carcinoma of the lung. *British Medical Journal*, **2**, 739–748.

Doll, R., and Hill, A. B. (1954) The mortality of doctors in relation to their smoking habits. *British Medical Journal*, **4877**, 1451–1455.

Doll, R., and Hill, A. B. (1956) Lung cancer and other causes of death in relation to smoking: a second report on the mortality of British doctors. *British Medical Journal*, ***ii***, 1071–1076.

Doll, R. (1992) Health and the environment in the 1990s. *American Journal of Public Health*, **82**, 933–941.

Doll, R., Peto, R., Wheatley, K., Gray, R., and Sutherland, I. (1994) Mortality in relation to smoking: 40 years' observations on male British doctors. *British Medical Journal*, **309** (6959), 901–911.

Durant, A., and Durant, W. (1961) *The Story of Civilization, 7, the Age of Reason Begins*, Simon & Shuster, New York.

Durkheim, E. (1895) *The Rules of the Sociological Method (I982 Reprint)* (ed. S. Lukes; transl. W. D. Halls), Free Press, New York.

Durkheim, E. (1897) *Suicide: A Study in Sociology (I951 Translation)* (transl. J. A. Spaulding and G. Simpson), Free Press, New York.

Elvehjem, C. A., Madden, R. J., Strong, F. M., and Woolley, D. W. (1937; 1974 reprint) The isolation and identification of the anti-black tongue factor 1937. *Nutrition Reviews*, **32** (2), 48–50.

Evans, A. S. (1979) Re: ''Definitions of Epidemiology.'' *American Journal of Epidemiology*, **109**, 379–382.

Eyler, J. M. (2001) The changing assessments of John Snow's and William Farr's cholera studies. *Sozialund Präventivmedizin*, **46**, 225–232.

Farr, W. (1838) On prognosis. *British Medical Almanac, Suppl*., 199–216.

Farr, W. (1862) A method of determining the effects of systems of treatment in certain diseases. *British Medical Journal*, **2**, 193–195.

Farr, W. (1885) *Vital Statistics: A Memorial Volume of Selections from the Reports and Writings of William Farr (1975 Reprint)*, Offices of the Sanitary Institute, Metuchen, NJ.

Frost, W. H. (1941) Risk of persons in familial contact with pulmonary tuberculosis (Reprint of *Am. J. Pub. Health*, 1933; **23**:426–432), in *Papers of Wade Hampton Frost, M.D.*: *A Contribution to Epidemiological Method* (ed. K. F. Maxcy), The Commonwealth Fund, New York, pp. 582–591.

Gordon, J. E. (1952) The twentieth century—yesterday, today and tomorrow (1920–), in *The History of American Epidemiology* (ed. C.-E. A. Winslow), CV Mosby; St. Louis, pp. 114–167.

Graunt, J. (1662) *Natural and Political Observations Mentioned in a Following Index and Made Upon the Bills of Mortality* (web reprint), *http://www.ac.wwu.edu/~stephan/Graunt/bills.html*.

Greenwood, M. (1935) *Epidemics and Crowd-Diseases: An Introduction to the Study of Epidemiology*, Williams & Norgate, London.

Hippocrates. (400 BCE) On airs, waters, and places, in *The Internet Classics Archive* (transl. F. Adams), retrieved 21 June 2012, from *http://classics.mit.edu/Hippocrates/airwatpl.html*.

Institute of Medicine (1988) The future of public health. Paper presented at the Committee for the Study of the Future of Public Health, Washington, D.C.

Kuller, L. H. (1991) Epidemiology is the study of ''epidemics'' and their prevention. *American Journal of Epidemiology*, **134**, 1051–1056.

Last, J. M. (ed.) (2001) *A Dictionary of Epidemiology* (4th edn), Oxford University Press, Oxford.

Lilienfeld, D. E., and Lilienfeld, A. M. (1977) Epidemiology: A retrospective study. *American Journal of Epidemiology*, **106**, 445–459.

Lilienfeld, D. E. (1978a) ''The greening of epidemiology'': Sanitary physicians and the London Epidemiological Society (1830–1870). *Bulletin of the History of Medicine*, **52**, 503–528.

Lilienfeld, D. E. (1978b) Definitions of epidemiology. *American Journal of Epidemiology*, **107**, 87–90.

Louis, P. C. A. (1837) *Researches on the Effects of Bloodletting in Some Inflammatory Diseases* (transl. C. G. Putnam), Hilliard, Gray, and Co., Boston.

Mausner, J. S., and Baum, A. K. (1974) *Epidemiology*, W.B. Saunders, Philadelphia.

Miettinen, O. S., and Flegel, K. M. (2003) Elementary concepts of medicine: V. Disease: one of the main subtypes of illness. *Journal of Evaluation in Clinical Practice*, **9** (3), 321–323.

Morris, J. N. (1957) *Uses of Epidemiology*, Livingstone, Edinburgh.

National Office of Vital Statistics (1947) *Deaths and Death Rates for Leading Causes of Death: Death Registration States, 1900–1940*. Photocopy received from National Center for Health Statistics, Hyattsville, MD (8 March 1996).

O'Donnell, T. (1936) *History of Life Insurance in its Formative Years; Compiled from Approved Sources*, American Conservation Company, Chicago.

Omran, A. R. (1971) The epidemiologic transition: A theory of the epidemiology of population change. *The Milbank Memorial Fund Quarterly*, **49**, 509–538.

Osler, W. (1897) Influence of Louis on American Medicine. *Bulletin of the Johns Hopkins Hospital*, **VIII**, 161–167.

Porta, M. S. (ed.) (2008) *A Dictionary of Epidemiology*, 5th edn, Oxford University Press, Oxford.

Pott, P. (1790) *The Chirurgical Works of Purcivall Pott*, Hanes W. Clark and R. Collins, London (original work published 1775).

Ramazzini, B. (1713; 2001) De morbis artificum diatriba [Diseases of workers]. Sections published in *American Journal of Public Health*, **91** (9), 1380–1382.

Richardson, B. W. (1887) John Snow, M.D. A representative of medical science and art of the Victorian era. (Reprinted in the 1936 text *Snow on cholera*). *The Asclepiad*, **IV**, 274–300.

Salmon, D. E. (1882) The dissemination of Texas fever, and how to control it. U.S.D.A Special Report 50.

Saracci, R. (2001) Introducing the history of epidemiology, in *Teaching Epidemiology—A Guide for Teachers in Epidemiology, Public Health and Clinical Medicine* (eds J. Olsen, R. Saracci, and D. Trichopoulos), Oxford University Press, New York, pp. 384.

Snow, J. (1849a) On the pathology and mode of communication of cholera. *London Medical Gazette*, **44**, 745–752.

Snow, J. (1849b) *On the Mode of Communication of Cholera*. John Churchill, London.

Snow, J. (1855) *On the Mode of Communication of Cholera*, 2nd edn, much enlarged, John Churchill, London.

Snow, J. (1855; reprint) *Snow on Cholera*, being a reprint of two papers by John Snow, M.D., together with a biographical memoir by B. W. Richardson, M.D., and an introduction by Wade Hampton Frost, M.D. (1936), The Commonwealth Fund, New York.

Susser, M. (1973) *Causal Thinking in the Health Sciences. Concepts and Strategies in Epidemiology*, Oxford University Press, New York.

Susser, M., and Adelstein, A. (1975) *Introduction, Vital statistics: A Memorial Volume of Selections from the Reports and Writings of William Farr (1885)*, Scarecrow Press, Metuchen, NJ, pp. iii–xiv.

Vandenbrouke, J.P. (1985) On the rediscovery of a distinction. *American Journal of Epidemiology*, **121** (5), 627–628.

Whitman, W. (1954) *The Complete Poetry and Prose of Walt Whitman*, vol. II, Garden City Books, Garden City, NY.

Winkelstein, W., Jr., (1995) A new perspective on John Snow's communicable disease theory. *American Journal of Epidemiology*, **142** (9 Suppl), S3–S9.

Xu J. Q, Kochanek K. D, Murphy S. L, Tejada-Vera B. (2010.) Deaths: Final data for 2007. *National Vital Statistics Reports*, vol. 58, No. 19, National Center for Health Statistics, Hyattsville, MD.