1
Introduction to Epidemiology

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 *epidemiology* in the English language dates to around the time the London Epidemiological Society was established in the mid-19th century. Since then, *epidemiology* has been defined in many ways, including

- the study of the distribution and determinants of diseases and injuries in populations (Mausner & 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 disciplines 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 (*epidemic*) dates back to the time of Hippocrates (4th century BCE) and, until not too long ago, referred only to the rapid and extensive spread of an infectious disease within a group. Now, however, the term epidemic 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 all health-related determinants. In this non-limiting sense, epidemiology is still study of epidemics and their prevention (Kuller, 1991).

Unit of Concern

The main unit of concern of epidemiology is the group, or "an aggregate of human beings" (Greenwood (1935). Compare this to clinical medicine, whose main unit of concern is the individual. A metaphor that compares epidemiology to clinical medicine is as follows. Imagine 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 life jackets 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?

Public health is the set of disciplines, institutions, and practices that aim to reduce injury, disability, disease, and premature death. Epidemiology is one of the core disciplines of public health (Porta, 2008). Other disciplines in public health include biostatistics, environmental health sciences, health policy and management, and social and behavioral sciences. The practice of public health also requires cross-cutting interdisciplinary competencies in areas such as communication and informatics, culture and diversity, public health biology, and so on (Calhoun et al., 2008).

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 elements of *quality of life*, an area of increasing interest to epidemiologists.

Other Useful Terms

Some sources differentiate between *disease*, *illness*, and *sickness* (e.g., see Susser, 1973 or Miettinen & Flegel, 2003). However, for simplicity’s sake, we will use these terms interchangeably to mean any form of ill-health, including injury. We will use the term *morbidity* to refer to events and factors related to or caused by ill-health. The term *mortality* will simply refer to death.

An *epidemic* is the occurrences of disease in clear excess of normalcy, while a *pandemic* is an epidemic that affect several countries or continents. The term *endemic* refers to the constant or usual prevalence of a given disease or agent within a region or group.

Uses Of Epidemiology

Epidemiologic practice is characterized by a close connection between the scientific study of disease causality and the application of this knowledge to prevent illness and improve health. The discipline thus 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 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 general uses of epidemiology. These seven uses have stood the test of time and are listed in Table 1.1. The seventh use, search for causes, is perhaps the most important contemporary application because of its importance in disease prevention efforts.

TABLE 1.1. 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 is changing 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.

1.2 EVOLVING PATTERNS OF MORBIDITY AND MORTALITY

Epidemiologic Transition and Demographic Transition

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 acute infectious causes to chronic noninfectious diseases as the predominant causes of morbidity and mortality in developed nations (Table 1.2). This transition has resulted from changes in society at large and improvements in medical knowledge and technology.

TABLE 1.2. 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 heart (heart disease) [204.3]
2.	Tuberculosis (all forms) [194.4]	Malignant neoplasms (cancer) [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 disease) [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.

In addition, steady economic development has led to better living conditions, improved nutrition, decreased childhood mortality, diminished fertility rates, and technological advances in medicine. This has led to a substantial shift in the age distribution of populations—especially in industrialized societies—a phenomenon known as demographic transition (Fig. 1.1).

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)* [Figure0101.eps]

With the now familiar demographic shift came a concomitant rise in age-related diseases such as atherosclerotic cardiovascular and cerebrovascular diseases, cancer, chronic lung disease, diabetes and other metabolic diseases, liver disease, musculoskeletal disorders, and neurological disorders. Many of these 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 ("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 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 many chronic ailments. Out of this awareness arose development of new investigatory tools for epidemiologists, as we will soon discuss. Using these newly developed methods, epidemiology has identified many of the factors that cause these chronic conditions (Table 1.3).

TABLE 1.3. Chronic Diseases and Their Relation to Selected, Modifiable Risk Factors. + = Established risk factor ± = Possible risk factor

	Cardiovascular Disease	Cancer	Chronic Lung Disease	Diabetes	Cirrhosis	Musculoskeleta 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).

Mortality Trends Since 1950

Figure 1.2 displays age-adjusted mortality rates for the 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 absolute terms. 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.

Figure 1.2. Age-adjusted death rates from 1950 – 2006, the United States, for the six leading causes of death in 2006. Source: CDC/NCHS 2010, Figure 18 [Figure0102.psd]

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 expectancy at birth in the United States was 47.3 years. By 2006, life expectancy was 77.7 years. Life expectancy for men was 75.1 years. For women, it was 80.2 years. The higher life expectancy in women compared to men is phenomenon that has been noticed since the 17th century (Graunt, 1662).

Figure 1.3 charts the dramatic increases in life expectancy that occurred during the 20^{th} century in the United States. During the early part of the 20^{th} century, increases in life expectancy can be traced to decreases in mortality at younger ages. This was 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).

Figure 1.3. Life expectancy at birth and at age 65 by sex, United States, 1900–2003. Source: CDC/NCHS, 2006, Figure 24 [Figure0103.psd]

From the mid-century onward, life expectancy at older ages started to show significant increases. In 1950, a 65-year-old man had a life expectancy of 12.8 remaining years; by 2000, this value increased to 16.0 years; and by 2006, this value was 17.0 years (CDC/NCHS, 2010). For women, the comparable values for expected number of years remaining at age 65 were 15.0 (in 1950), 19.0 (in 2000), and 19.7 (in 2006). These increases can be traced to technological improvements in medical care, dietary changes, avoidance of smoking, reductions in vascular disease and the pharmacologic control of high blood pressure and hyperlipidemia (Doll, 1992).

1.3 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

Roots of Epidemiology

Epidemiological insights into health and disease are probably as old as civilization itself. The Old Testament refers to the benefits of a certain diet, the Greeks had theories that linked febrile illnesses to environmental conditions ("marsh fever"), and the Romans recognized the toxic effects of consuming wine from lead-glazed pottery. However, Hippocrates (circa 460–388 bce) is often given credit for preparing 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 1.4), 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 1.4. Part I of *On Air, Waters, and Places*, full text available http://classics.mit.edu/Hippocrates/airwatpl.html

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 reawakened, coinciding with the Age of Enlightenment, a period 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.

The reawakening of scientific observation in medicine during the Age of Enlightenment is exemplified by the work of the “English Hippocrates,” Thomas Sydenham (1624– 1689). Like Hippocrates, Sydenham stressed the need for careful observation and recordings for the advancement of health and health care. Using information combed from his 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 on Diseases of Workers (De Morbis Artificum Diatriba) which discussed the hazards of various irritating chemicals, dust, metals, and abrasive agents encountered in 52 different occupations (Ramazzini, 1713). 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’s work, the Englishman Percival Pott (1713–1788) identified chimney soot as the cause of enormously elevated rates of scrotal cancer in chimney sweeps (Pott, 1775).

John Graunt

The development of vital statistics systems was key to studying disease on a population basis. The earliest tallying of deaths dates 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 demographic approach to studying disease took a major step forward when an intellectually curious London haberdasher by the name of John Graunt (1620–1674; Fig. 1.4) tallied mortality statistics and made many forward-looking and insightful interpretations based on these tables in his publication entitled Natural and Political Observations... Made upon the Bills of Mortality (1662).

Figure 1.4. *John Graunt (1620–1674). (Source: O’Donnell, 1936, p. 147. Verity of the likeliness could not be confirmed.)* [Figure0104.eps]

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. 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.

By starting with a hypothetical group of 100 people, Graunt constructed one of the first known life tables. Out of 100 people born, Graunt projected the following expectations for survival at various ages:

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

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) hints at the seeds of disease passing from healthy to sick individuals in the poem De Rerum Natura. However, the first cogent germ theory of disease was presented by Girolamo Fracastoro in 1546 (Saracci, 2001). Despite this early theory, the microbial theory of contagion was not accepted for some time to come. As of the 1820s and 1830s, the doctrine of contagion was in decline and the prevailing theory of epidemics was expressed in terms of “spontaneous generation” and “miasma atmospheres,” with major attention devoted to environmental conditions, particularly poor sanitation. This began to change midcentury when, in 1840, Jakob Henle (1809–1885) presented his treatise of the contagium animatum—a living substance that multiplied within the body where it was excreted by sick individuals and communicated to healthy individuals. John Snow (1813–1858) had similar ideas about contagion, basing his theories on the clinical features of cholera, its responsiveness to therapy, and its spread along the routes of human commerce and war (discussed in more detail below). The French chemist Louis Pasteur (1822–1895) refuted the doctrine of spontaneous generation by demonstrating that decay was produced by microorganisms. Pasteur was also able to isolate the agent responsible for an epidemic disease in silkworms in 1865, found that septicemia was caused by anaerobic bacterium, and developed the process for killing germs by heating or boiling that bears his name (“pasteurization”). Henle’s student Robert Koch’s (1843–1910) breakthrough came when he decided to stain microbes with dye, enabling him to visualize the microbe that caused tuberculosis (in 1882) and discover the cholera bacillus (in 1883).

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

Figure 1.5. Distribution of the Boophilus tick before eradication. [Figure0105.eps]

Médecine d'observation

Due 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. A few landmark figures will be cited.

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 $3\frac{3}{4}$-year 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 claimed 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; Fig. 1.6) wrote: "I conceive that without the aid of statistics nothing like real medical science is possible."

Although PCA 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 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 4 days of symptoms) and in those who received later treatment (no untreated control group was available). Some of Louis's recordings are shown in Figures 1.7 and 1.8 in their original format. Using these data, Louis found that mortality was greater in the earlier treated group than in the later treated group (44 vs. 25%, respectively). This type of observation led to the eventual end of this antiquated form of treatment. Just as important, it demonstrated the need for rigorous evaluation of conventional clinical practices. Medical systems that could not withstand a test of observation were to be discredited.

Figure 1.6. Pierre-Charles Alexandre Louis (1787–1872). (*Source*: Wikipedia Commons) [Figure0106.psd]

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. [Figure0107.eps]

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.) [Figure0108.eps]

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 & 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 defined discipline united by its belief that health could be advanced by the scientific study of diseases 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; Fig. 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" (1885, p. 234). His anatomically based system of disease classification is the antecedent to the International Classification of Disease currently in use.

Figure 1.9. William Farr (1807–1883). (Source: Lilienfeld & Lilienfeld, 1977; reprinted by permission of Oxford University Press and the Society for Epidemiologic Research.) [Figure0109.eps]

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" (1885, p. 187). Figure 1.10 is a replica of one of Farr's tabulations.

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.) [Figure0110.eps]

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 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 & 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; Fig. 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.

Figure 1.11. John Snow (1813—1858). [Figure0111.eps]

Cholera in Victorian England Some background will further this discussion. 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.

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” (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” (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 recognized as these distinct epidemiologic methods (Winkelstein, 1995):

Comparison of cholera mortality rates by geographic region. We now recognize this as the basis of the ecological study design.

Comparison of cholera mortality rates in groups defined by exposure to possibly causal agents and factors. We now recognize this as the basis of the cohort study design.

Comparison of potentially causal exposures in cholera cases and non-cases. We now recognize this as the basis of the case–control study design.

Ecological study Water distribution in 19th century London was the purview of private water companies. The two major companies the 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 (Fig. 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.

Figure 1.12. Snow’s ecological data of cholera rates. (Source: Snow, l855, p. 73.) [Figure0112.eps]

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.

Cohort study 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 calculate cholera mortality rates according to water supplier. He found 1,263 cholera deaths in the 40,046 households exposed solely to water from the Southwark & Vauxhall (S&V) Company. Thus, household supplied by S&V had a choler mortality rate of $\frac{1263}{40{,}046 \text{ households}} = .0315$ per household or, equivalently, 315 per 10,000 household. In households served solely by the Lambeth Company, 98 cholera deaths occurred in 26,107 households, for a rate of $\frac{98}{26{,}107 \text{ households}} = .0038$ or 38 per 10,000 households. Thus, the households supplied by the S&V water company experienced cholera at 8-times the rate of those supplied by the Lambeth water company. This type of study in which the exposure and disease status of individuals is compared forms the basis of the cohort study design.

Case–Control comparisons In contrast the cohort method in which rates are compared in various exposure groups, case-control methods compare the exposure status in cases and non-cases (controls). As part of Snow's inquiry into the terrible outbreak of cholera that effected in 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 (Fig. 1.13).

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.) [Figure0113.eps]

Snow found that 61 of the fatalities during this outbreak had used water from the Broad Street pump, 6 had reportedly not drunk water from the pump, and 6 could not determine whether or not they had used water from the pump. In contrast, use of Broad Street pump water by noncases had been infrequent. For example, of the brewery near the pump where no worker's had died of cholera, Snow remarked, "The men are allowed 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). Thus, cases were much more likely than non-cases to have consumed the contaminated pump water. Comparison of exposure histories of cases and non-cases forms the basis of the case-control study design.

Case by case analysis Sometimes overlooked in these investigations is Snow's scrutiny of cases that seemed to contradict the normal pattern of infection. One such observation came when investigating a couple of cases from the town 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.

Public action As a result of his investigations, 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.[*] Thus, Snow's lucid combination of observation and reasoning serves to inspire epidemiologists, while his efforts to have the pump handle removed serves as a symbol of public health action.

Twentieth-Century Epidemiology

Many social and scientific events 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, 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, and 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 established as one of its core disciplines (Gordon, 1952).

At about mid-century, Wade Hampton Frost (1880–1938), the first professor of epidemiology in America, declared that 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). Some sources accordingly refer to post-WW II epidemiology as "modern epidemiology." However, before getting into modern epidemiology, let us consider a couple of early century epidemiologic events that led the way to transitions in the disciopline.

Emile Durkheim

Emile Durkheim (1858–1917) was a French sociologist known for his compelling scientific approach to studying sociologic problems. In his *Rules of Sociological Method* (1895), he sets forth that social explanations require comparisons, comparisons require classification, and classification requires the definition of those facts to be classified, compared, and ultimately explained. Consistent with these rules, Durkheim warns against *notiones vulgares*—the idea that

[*] It is now apparent that the cholera outbreak in the Golden Square Area was receding on its own and the removal of the pump handle was probably not crucial (see Figure 4.5). However, the discovery of cholera as a waterborne caused by an infectious has undoubtedly saved numerous lives.

crudely formed concepts of natural phenomena without scientific reflection produce only false knowledge: just as alchemy had preceded chemistry and astrology had preceded astronomy, social reflection merely foreshadows true social science.

Durkheim's seminal work *Le Suicide* (1897) considers many potential determinants of suicide, including psychopathological states, race, heredity, climate, season, imitative behavior, religion, social instability, and a host of other social phenomena. Table 1.6, a replica of a table from *Le Suicide*, shows suicide rates per 1,000,000 person-years by age and marital status in France for the years 1889–1891. From these data, Durkheim concludes: (1) Marriage before the age of 20 ("too early marriages") has an aggravating influence on suicide, especially in men; (2) after age 20, married persons of both sexes enjoy some protection from suicide in comparison with unmarried people; (3) the protective effect of marriage is greater in men; and (4) widowhood diminishes the protective effects of marriage but does not entirely eliminate it. Durkheim reflects on whether the apparent protective effects of marriage are 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 foreshadows the modern epidemiologic approach.

TABLE 1.6. Suicides per 1,000,000 Person per Year by Age and Marital Status, France, 1889–1891

				Coefficients of Preservation [Rate Ratios]		
Ages	Unmarried	Married	Widowed	Married With Reference to Unmarried	Married With Reference to Widowed	Widowed With Reference to Unmarried
Men						
15–20	113	500	…	0.22	…	…
20–25	237	97	142	2.40	1.45	1.66
25–30	394	122	412	3.20	3.37	0.95
30–40	627	226	560	2.77	2.47	1.12
40–50	975	340	721	2.86	2.12	1.35
50–60	1,434	520	979	2.75	1.88	1.46
60–70	1,768	635	1,166	2.78	1.83	1.51
70–80	1,983	704	1,288	2.81	1.82	1.54
Above 80	1,571	770	1,154	2.04	1.49	1.36
Women						
15–20	79.4	33	333	2.39	10.00	0.23
20–25	106	53	66	2.00	1.05	1.60
25–30	151	68	178	2.22	2.61	0.84
30–40	126	82	205	1.53	2.50	0.61
40–50	171	106	168	1.61	1.58	1.01
50–60	204	151	199	1.35	1.81	1.02
60–70	189	158	257	1.19	1.62	0.77
70–80	206	209	248	0.98	1.18	0.83
Above 80	176	110	240	1.60	2.18	0.79

Source: Durkheim, (1897, p. 174, 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, when they 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. The U.S. Marine Hospital Service was established in 1798 to care for seamen and to serve as a bulkhead against incoming infectious agents. In 1902, the Marine Hospital Service was renamed the Public Health Service, soon after expanding its mission to protect the public by investigating a wide variety of infectious and noninfectious diseases.

Figure 1.14. Joseph Goldberger (*1874–1929).* [Figure0114.eps}

As a young public health officer, Goldberger was assigned to investigate various tropical diseases such as yellow fever, typhoid, dengue fever, which were then 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 a severe deficiencies of niacin and the amino acid tryptophan. (The body can synthesize niacin using tryptophan as a precursor). However, Goldberger's work preceded this knowledge; pellagra was thought to be infectious at that time. Goldberger contradicted this commonly held belief, basing his understanding on the observation that pellagra demonstrated a preference for inmates in mental hospitals and orphanages, leaving employees of the 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 a replica of a table from a 1918 article published by Goldberger. This table documents the relative paucity of meats, dairy products, and green vegetables in households with pellagra. Goldberger's work lead to the nutritional interventions that were effective in treating and preventing pellagra. Note that most of Goldberger's work occurred one to two decades before Elvehjem and co-workers (1937) isolated 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

	Nonpellagrous Households		Pellagrous Households	
	With Highest	With Lowest	With Lowest Income and One or	With Two or More Cases (Mostly Low-Income

Groups of Foods	Income	Income	More Cases	Households)
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 to study many of non-infectious diseases that comprised the major causes of morbidity and mortality as the century progressed. Major advancement were made first in the study of cigarette-related diseases and later into other areas, including heart disease, mental disorders, cancers, and medical safety and effectiveness. Many examples can be used to illustrate these new methods. Here is one from the British team of Hill and Doll.

The British Doctors Study

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

Doll and Hill published one of the first case-control studies linking cigarette smoking to lung cancer in 1950. Not long after publishing their case–control study, they sent out inquiries to medical doctors in the United Kingdom asking them to classify their smoking status and qualify the approximate amount they smoked. The brief questionnaire was sent to 59,600 physicians of which 40,564 replies were received that were sufficiently complete to be used for analysis. The first report from this cohort study, published in 1954, showed that lung cancer mortality paralleled the amount smoked (Table 1.6). The report also showed higher rates of coronary heart disease in smokers.

TABLE 1.6. Age-Adjusted Mortality Rates 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).

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. It has identified 30 different causes of death associated with smoking. In addition, the data showed that 50% of heavy smokers died before age 70 compared with only 20% of nonsmokers. Moreover, 8% of heavy smokers have survived to age 85, compared with 33% of nonsmokers (Fig. 1.15).

Figure 1.15. British Doctors Cohort, Survival According to Amount Smoked. Based on data in Doll et al., 1994. {image = Figure0115.eps}

These and other developments have occurred in the context of rapid growth in understanding epidemiologic concepts and theories as a discipline distinct from other scientific endeavors. A new age of modern epidemiology was born, with epidemiology extended beyond its original limits.

CHAPTER SUMMARY

Because this is a long chapter, this summary is provided.

§1.1: 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, having as its objective the promotion of health and prevention of disease and injury. In contrast to clinical medicine, epidemiology focuses primarily on groups of individuals, as opposed to single individuals. Epidemiology is characterized by a close connection between the scientific study of disease causation and application of knowledge to prevent disease and improve health, and 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, elucidation of the causes of disease.

§1.2: Evolving Patterns of Morbidity and Mortality Whereas morbidity and mortality in the past were dominated by acute and infectious causes, the major health problems in industrialized societies today are primarily chronic and non-infectious. This shift is known as the epidemiologic transition. Accompanying this transition has been a change in demographics known as the demographic transition. In 1900, life expectancy at birth in the United States was approximately 47 years. In 2007, life expectancy was almost 78 years. Increases in life expectancy has occurred in all groups, with improvements during the first part of the 20th century focused on younger age, and improvement during the second half of the century more likely to come in middle and late age. Concomitant with these changes has been a decrease birthrates, resulting in an aging of the population.

§1.3: Historical Figures and Events Epidemiological insights into health and disease are probably as old as civilization itself. However, the scientific roots of epidemiology can be traced to Hippocratic principles developed in the 4th century BC. In addition, most of central tenants of modern epidemiology can be to the renaissance of empiricism and scientific ideas starting in the 16th century, with traces its roots medical statistics, occupational health, demography, medical sociology, and germ theory. Epidemiology emerged as a unique and organized discipline in Victorian England with the work of many individuals, notably William Farr and John Snow and the establishment of the London Epidemiological Society in 1850. 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 disease shifted in human populations, there were unprecedented developments in epidemiologic methods for studying chronic diseases (e.g., heart disease, cancer, mental disorders, chronic respiratory ailments) and medical safety and effectiveness took on greater importance. Rapid growth in understanding the epidemiologic study all types of diseases and outcomes has encouraged a modern form epidemiology with distinct scientific practices and theories.

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