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Relationship Between Acute and Chronic Disease Epidemiology

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Epidemiology is the study of epidemics. The primary goal of epidemiological studies should be the identification of the determinants of disease in order to decrease morbidity and mortality. Epidemiological studies evolve through descriptive, analytical, and experimental approaches. The traditional infectious disease epidemiology studies were primarily concerned with identification of an agent, incubation period, mode of transmission, population at risk, and methods of disease control. Chronic disease epidemiology has tended to emphasize a more complex interaction of independent and dependent disease variables that resulted in a greater need for statistical methodology. There has been relatively little interest in chronic disease epidemiology either in modes of disease transmission or in incubation periods. Chronic disease epidemiology has also focused more on analytical epidemiology than on experimental, clinical trials.

Many chronic diseases are probably caused by living organisms such as viruses. The fundamental difference in methodology may relate to length of incubation period. Chronic disease epidemiology should probably build more on successful methods of infectious disease epidemiology, especially modes of disease transmission, host susceptibility, incubation periods, and clinical trials. The concept of multifactorial etiology of many chronic diseases may be a measure of our ignorance of causality rather than a biological principle.

Epidemiology is a popular term. It is sometimes difficult to recognize an epidemiological study. The traditional epidemic investigation of an infectious disease may have little resemblance to the complex multivariate analysis in chronic disease epidemiology, or the clinical epidemiologist evaluating the efficacy of some specific therapy, the utilization of a drug, or the behaviors of physicians in the practice of medicine. Epidemiology is becoming synonymous with any health or medical studies in humans which include both a numerator and a denominator.

A clinician may describe 30 cases of a specific disease in great detail. When this description is defined in relation to a specific hospital population over a defined time period, it becomes clinical epidemiology. A variety of interesting and probably important statistical tools, widely used in the social science fields, have been rediscovered by the epidemiologist and have become part of the jargon of epidemiological methods. Even in our best epidemiological journals, papers appear in which the simple rate of an event or proportion is no longer presented, but only the result of regression analysis. The reader generally hopes and tries to believe that the simple rates and proportions common to epidemiological studies, a logical first step in any analysis, have been done prior to the regression analysis, and that the editors of these journals are attempting to save space by excluding much if not all of the basic analyses.

There should be a common thread in the epidemiological investigation (Table 1). Infectious disease epidemiology is not remarkably different from chronic or clinical

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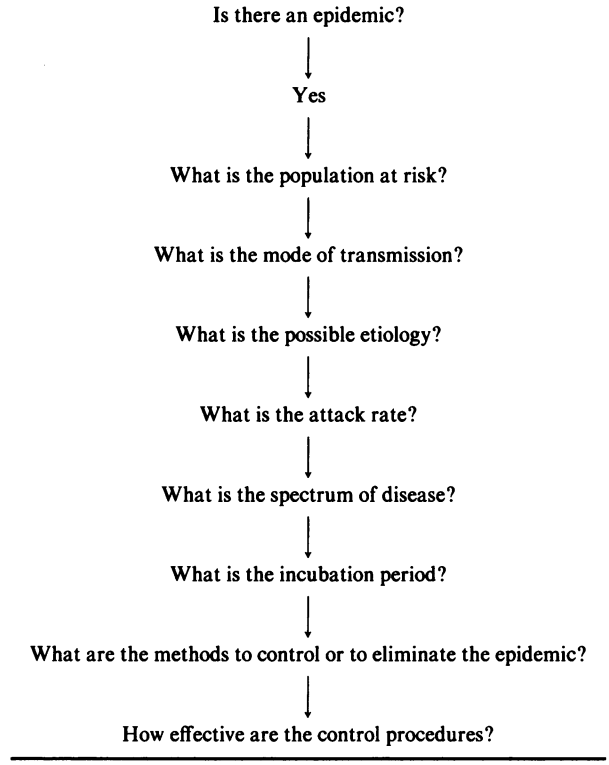
TABLE 1
The Epidemiology Investigation



epidemiology when this common approach to epidemiology is followed. Table 1 describes what I believe is the common base of the epidemiology investigation. Epidemiology is the study of epidemics. The definition of an epidemic is the increase above an expected value for an event. That event can be an infectious disease, a higher incidence of mortality from a chronic disease, a greater frequency of hospitalization for a certain disease, a higher case-fatality percentage, or even the greater utilization of a diagnostic procedure. The first step in any investigation or in any epidemiological study, however, should be a statement as to the definition of the epidemic.

In infectious disease epidemiology, this descriptive epidemiological phase depends predominantly on surveillance of either geographic or temporal variations in disease (Table 2). Because of the relatively short incubation periods of many infectious diseases, wide oscillations in disease frequency over relatively short periods of time are often noted in the community, and thus the surveillance of disease in defined communities over time is the cornerstone of descriptive infectious disease epidemiology.

The study of chronic disease also depends on a measurement of geographic or temporal distributions of disease. Unfortunately, available morbidity data is often absent, incomplete, or inaccurate; thus, until recently much of chronic disease descriptive epidemiology depended on quantification of mortality statistics in relation to time, place, and person. Mortality statistics depend on both the incidence of a disease and the case-fatality percentage. The chronic disease epidemiologist spends an

TABLE 2
Is There an Epidemic?

Descriptive Epidemiology	
Acute Diseases	Chronic Diseases
1. Surveillance of geographic or temporal variations a. Short incubation periods often lead to wide oscillation of disease measured by incidence or attack rates in community.	1. Geographic distribution of morbidity and mortality by host characteristics 2. Temporal trends in disease a. Long incubation periods and absence of morbidity data result in emphasis on mortality statistics dependent on both incidence and case fatality. b. Prevalent rather than incident cases usually studied

inordinate amount of time and effort trying to interpret both the geographic variations and trends in specific diseases. Has cancer increased in the population during the past 30 or 40 years because of the introduction of many environmental carcinogens, or has the apparent incidence increased only because of better diagnosis and ascertainment of cases, while the mortality statistics have remained relatively flat [1]? Possibly the incidence has increased, but with improved treatment the case-fatality rate has fallen. The modern chronic disease epidemiologist has, unfortunately, spent too little time improving methods of collecting descriptive epidemiology and attempting to define the epidemic clearly. The only chronic disease that is well defined in terms of descriptive epidemiology in the United States and in other countries is cancer [2]. Only in selected communities such as Rochester, Minnesota, and the like, have serious attempts been made to quantify the epidemic of chronic disease [3].

The second key question in an epidemiological investigation is the determinants of the population at risk (Table 3). The infectious disease model tries to identify the population at risk in relation to the probability of exposure to the suspected vehicle of disease transmission, such as food, water, air, insect, and so on, and the host susceptibility to infectious disease, often based on prior immunity or selected social demographic characteristics and, more recently, on certain genetic markers. These measures of susceptibility have broken down as we recognize the increasing latency of infection and the incorporation of the viral genotype into the host DNA.

In chronic disease epidemiology, the populations at risk are more difficult to identify and generally are defined in very broad terms, usually social demographic characteristics, specific occupational groups, and so forth. Often, in infectious disease epidemiology, the population at risk is defined prior to disease onset either through the identification of a historical cohort, such as all the individuals attending a specific event, or individuals exposed to a specific water supply. In chronic disease epidemiology, the population is defined either at the time of disease, that is, as a measure of the mortality rates, or the prevalence of disease in a defined community. The probability of exposure to a potential etiological agent or vehicle of transmission of disease is much more difficult to define in chronic diseases. For example, until recent years much of our occupational and environmental epidemiology depended predominantly on the measurement of specific occupations with a large group of individuals and comparison of mortality rates within that occupational group either to the general population or to

TABLE 3
What Is the Population at Risk?

Descriptive Epidemiology	
Acute Diseases	Chronic Diseases
1. Population at risk often defined in terms of probability of exposure to suspected vehicle of disease transmission and host susceptibility based on prior immunity 2. Population at risk usually defined prior to disease onset	1. Population at risk defined in broad terms, usually social demographic characteristics, occupation 2. Population at risk usually defined at time of disease as prevalence or mortality 3. Probability of exposure usually defined in very general terms

another occupational population. The degree of exposure within the specific occupation was only loosely defined, and specific measurements of exposure were not of high priority. More recently, chronic disease epidemiologists have become more aware of the need better to define the specific populations at risk in relation to potential exposures. Greater emphasis is now placed on actual measurement of exposure of workers or of potentially exposed individuals to an environmental hazard by utilizing classical industrial hygiene methods or, more preferably, by direct quantification of individual exposures [4,5]. We can expect a substantial improvement in the identification of specific environmental exposure and better determination of risk as new techniques are applied to identify individual as opposed to aggregate estimates of exposure.

The third step in the epidemiological investigation is the analysis of the mode of transmission of the etiological agent or vehicle in the population (Table 4). In infectious disease epidemiology, this component is of primary importance. Epidemics are defined in terms of common source, person-to-person, indirect or vector-borne, and vertical transmission. The primary emphasis in analytical infectious disease epidemiology is often in the study of the mode of transmission of the disease. Cases will be compared to controls by potential exposure to a common source, to individuals who are infectious, or to an indirect vector of transmission. Analysis of disease distributions in relation to geographic area, time, and personal characteristics aim primarily to understand the mode of transmission as an important clue in the search for the etiological agent.

Surprisingly, in chronic disease epidemiology, almost no emphasis is placed on the mode of transmission. Few of the modern textbooks, primarily on chronic disease epidemiology, even discuss the concept of mode of transmission in relation to the epidemiological investigation. The primary emphasis in chronic disease epidemiology has been on the attempt to identify the relationships between selected independent and dependent variables such as disease. Remarkably, the chronic disease epidemiologist has spent relatively little time attempting to understand how these independent variables may relate to the dependent variable with respect to mode of disease transmission. Yet clearly we can classify chronic disease by mode of transmission of either the vehicle or the etiological agent in exactly the same way as in infectious diseases. Coronary atherosclerotic heart disease is most likely a classical example of a common source epidemic (diet, cholesterol, and saturated fat), and insulin-dependent

TABLE 4
What Is the Mode of Transmission?

Analytical Epidemiology	
Acute Diseases	Chronic Diseases
1. Method of disease transmission is of primary importance: —common source —person to person —indirect: vector —vertical 2. Primary emphasis in analytical epidemiology is on mode of transmission: a. Case-control studies seek mode of transmission as clue to vehicle and etiology.	1. Little emphasis on mode of transmission 2. Primary emphasis in chronic disease epidemiology is to identify relationships between independent and dependent variables such as disease.

diabetes, a person-to-person transmitted infectious disease, a virus or viruses [6,7]. Lung cancer can be considered to be an example of a common source, continuous exposure epidemic (cigarette smoking); cervical cancer (and AIDS), venereal diseases [8,9,10]. Chronic disease epidemiology methods would be substantially improved if a new emphasis on the mode of transmission of the disease became a cornerstone of the research effort.

The next step in the epidemiological investigation is the attempt to identify the possible etiology of disease (Table 5). Infectious disease epidemiology evolved in the era of a single agent for a single disease. The classical case-control studies in infectious disease epidemiology were generally a comparison of serological evidence of infection or some tissue fingerprint or marker of the agent between defined cases versus suitable controls. The controls were usually selected on the basis of probability of being exposed to the agent of interest. Relative risks were usually substantial if the specific agent that was causal had been properly identified, which was especially true in those situations in which not only clinical but also subclinical disease could be identified.

The second approach in infectious disease epidemiology was to compare exposure to the possible vehicle of transmission, such as a common water supply, food chain, insect vector, and so on, between cases and controls. For example, in the study of the epidemiology of acquired immune deficiency syndrome, the two key components of the case-control studies have been, first, the evidence of infection with human immune deficiency virus, i.e., serological comparison between cases and controls; and, second, the comparison of possible mode of transmission such as receptive anal intercourse, blood transfusions, and contaminated blood factors between cases and controls.

In chronic disease epidemiology, on the other hand, the emphasis has often not been on the identification of a specific etiological agent, but rather primary emphasis on host environmental relationships. The identification of the specific etiological agent has been difficult because of the potential complex interrelationships between the host and a variety of factors that may lead to disease. The relative risks that are identified in case-control studies are usually at relatively low magnitude. The reason for this fact is that most of these measures are either a surrogate marker of the true etiological agent or are not determined accurately. We may compare an occupational history (that is, farmers versus non-farmers among individuals with non-Hodgkin's lymphoma) and

TABLE 5
What Is the Possible Etiology of the Disease?

Study Design	
Acute Diseases	Chronic Diseases
1. Primary emphasis on agent: Case-Control: a. Comparison of prevalence of serological marker of agent or tissue fingerprint of agent between defined cases vs. controls 2. Comparison of history of exposure to possible vehicle of transmission among cases vs. controls	1. Primary emphasis on host environment: Case-Control: a. Classical—case-control studies: 1. Usually low-order relative risks because of identification of surrogate measure of etiology 2. Difficult to separate exposure between cases and controls 3. Emphasis on statistical methods to evaluate multiple independent variables

find a slightly elevated (at most twofold) excess relative risk among farmers. Similarly, we may then evaluate exposure to pesticides between cases and controls [11]. The degree of exposure to the pesticide or the specific chemical that may be the causal agent for non-Hodgkin's lymphoma is often difficult, if not impossible, to identify.

In chronic disease epidemiology, because of the long incubation period, it is often difficult truly to separate exposure between cases and controls. Thus, chronic disease epidemiology depends on a probability estimate of the likelihood of exposure of the cases versus the controls, and such measures as duration of exposure and possible dose. Markers of individual exposure, such as serological evidence of prior viral infection or actual identification of individual measurement of exposure to a specific vehicle, are often lacking. It is possible that without good measures of exposure between cases and controls the success of chronic disease epidemiology studies is substantially limited. A primary goal in chronic disease epidemiology may, therefore, be an attempt to improve our methods of measuring prior exposure to the possible etiological agent. The studies of exposures to Agent Orange in Vietnam are probably a classic example [12]. The failures initially to be able actually to measure dioxin among potentially exposed troops has substantially limited studies of possible Agent Orange exposure to disease. Only recently has it become apparent that the measurement of dioxin levels in tissues many years after the exposure may provide the most important step in the epidemiological evaluation of the relationship between possible Agent Orange, dioxin exposure, and selected diseases.

The use of surrogate measures of exposure to a specific etiological agent often results in difficult analytical problems that require sophisticated statistical methods in order to evaluate the independent effects of multiple variables. Many times in these analyses more than one of the independent variables is acting as a surrogate measure of the specific etiological agent. For example, a simple measure such as level of education is a surrogate marker for a variety of health habits which are either directly or inversely correlated with level of education, such as cigarette smoking, alcohol intake, dietary factors, and the like. Level of education is also often a marker for income and degree of and availability of medical care, which could be a primary determinant of the likelihood that the disease of interest could be identified. The evaluation of confounding, variables which in some way are affecting both the distribution of the independent

TABLE 6
What Is the Possible Etiology of the Disease?

Study Design[a]	
Acute Diseases: Longitudinal	Chronic Diseases: Longitudinal
1. Sero-epidemiology: a. Risk of disease over time sero-negative—sero-positive b. Relationship between sero-conversion and disease c. Family studies—secondary attack rates	1. Prospective or historical cohort studies to evaluate risk of disease. Major problems include stability of risk factors, low incidence of disease, long incubation period, difficulty of measuring prior exposure, especially dose.

[a]Continued from Table 5

and dependent outcomes, has become one of the most important and controversial components of chronic disease epidemiological methodology. Unfortunately, relatively few studies have evaluated whether such statistical techniques have added to our understanding of the etiology of disease or only to a refinement of statistical methodology for the analysis of independent variables.

Longitudinal, prospective studies in infectious disease epidemiology have been relatively limited until recent years (Table 6). The most interesting and important longitudinal studies have been the use of serum banks to evaluate the risks of disease among sero-negative or sero-positive individuals to a specific agent over time or the relationship between sero-conversion to a specific agent and subsequent risk of disease [13]. These studies have also been expanded to look at other serological, cellular, and tissue markers of possible infection and subsequent risks of disease. The relatively short incubation period of many of the infectious diseases and the successful ability to store at least serum and, perhaps, now cells have offered an excellent opportunity for these types of longitudinal studies. Another interesting and important component of longitudinal studies in infectious disease epidemiology has been the family studies or the attempt to measure secondary attack rates within families as a way of determining the transmission of the agent, infectivity, pathogenicity of the agent, and the incubation period [14].

Longitudinal studies in chronic disease epidemiology are very limited by the long incubation period of many of the diseases, their relatively low incidence, and the difficulties of maintaining surveillance. Thus, many of the true longitudinal studies have been restricted to cardiovascular disease, especially coronary heart disease. Longitudinal studies in coronary artery disease have many similarities to the sero-epidemiological longitudinal studies in infectious diseases. Risk factors, in this case levels of some factor in the blood such as blood cholesterol, are measured at a specific point in time or repeatedly over time, and the subsequent risk of disease is determined in relation to the levels of the risk factors. In recent years, sero-epidemiological approaches, including development of serum banks of stored specimens for subsequent analysis, have become useful in chronic disease epidemiological studies as well [15]. The longitudinal studies of the etiology of breast cancer are now collecting and storing blood, cells, and other tissue markers among healthy high-risk women with the hope of subsequently analyzing selected specimens among new cases of breast cancer and selected controls [16,17]. This approach should receive the highest priority in

subsequent chronic disease epidemiological studies. These techniques, directly carried over from infectious disease epidemiology, have great potential in chronic disease epidemiology, especially as improved methodology evolves for the storage of serum, cells, and so on.

The classical historical cohort evolved from occupational epidemiology in an attempt to utilize information that had not been previously collected for epidemiological study purposes. Such studies have proven extremely important in many of our occupational investigations. The data, however, have been substantially restricted by the paucity of information about individual exposures and the identification of specific etiological agents among a mixture of various chemicals and other environmental factors that may be related to subsequent disease.

Once a disease has been identified and there is some evidence of the specific etiology, then a major concern in infectious disease epidemiology is the determination of the attack rate or the incidence of the disease (Table 7). Specific agents are defined in terms of their infectivity or the probability of causing infection, the pathogenicity in terms of causing disease, and the virulence or the severity of disease. Susceptibility to infection or to disease is often determined in relation to prior immunity and selected host and genetic characteristics. As noted, the secondary attack rate becomes an important measure of both estimation of risk, that is, the attack rate, and also an understanding of the modes of transmission and the incubation period. Concepts such as virulence and pathogenicity are rarely discussed in chronic disease epidemiology. Incidence rates are usually measured either cross-sectionally, i.e., from registries, or in specific, defined, longitudinal population studies. Cumulative incidence is a measure of an individual's risk of disease over a specific period of time and in some ways is more closely akin to an estimation of the attack rate over time in infectious disease epidemiology.

The measurement of secondary attack rate in chronic disease epidemiology, that is, secondary cases in the family, is usually equated with some genetic risk rather than the potential spread of an etiological agent within the family [18]. Clearly, secondary cases within a family are confounded by both the shared genes and environment. In many of the chronic disease studies, the environmental as compared to the genetic component have been difficult to separate. Genetic epidemiology has begun to evolve new techniques to look specifically at genotypic as opposed to phenotypic markers. The development of these new techniques, including restriction, fragment-length polymorphisms, and identification of the DNA of the specific genes, can provide very powerful tools for the study of genetic, environmental interactions such as the relationship between dietary intake of cholesterol and LDL, Apo-B levels and risk of heart attack, or specific immuno-genetic markers and response to infectious agents. The possible interaction of genetic and environmental factors within the family will become easier to study.

It is, perhaps, surprising that comparative incidence measures among populations and various subgroups within populations are very important components of infectious disease epidemiology problems and have played a relatively small role in most chronic disease epidemiology. Clearly, part of the problem has been the difficulties of adequate ascertainment of incident disease across populations and both the low incidence and long incubation periods. Yet the striking differences in the incidence of both insulin-dependent and non-insulin-dependent diabetes, selected cancers, and coronary heart

TABLE 7
What Is the Attack Rate or Incidence of Disease?

Acute Diseases	Chronic Diseases
1. Attack rate usually measured in terms of incidence of new cases: Also measured by probability of infection—infectivity, pathogenicity, and virulence of agent Susceptibles often can be well defined.	1. Incidence measured either cross-sectionally, i.e., registries, or from defined longitudinal studies. Incomplete and biased ascertainment a major problem
2. Secondary attack rate important measure to estimate both risk and mode of transmission	2. Secondary attack rate usually considered a measure of genetic risk

disease have provided some of the strongest evidence for an understanding of the possible etiology of these diseases [19,20,21].

The understanding of the spectrum of disease from subclinical to clinical and fatal is an important component of infectious disease epidemiology (Table 8). Serological methods to identify subclinical disease have played an important role in infectious disease epidemiology in attempting to understand disease transmission and identification of the specific etiological agent.

In chronic disease epidemiology, the measurement of subclinical disease is very difficult and is often not evaluated. Many of the controls in the classical case-control studies have subclinical manifestations of the disease of interest. This fact is especially true in the studies of cardiovascular disease, diabetes, and probably many of the cancers among older individuals at least. The inability to differentiate subclinical from clinical disease, and from non-disease, may be one of the factors that lead to a conservative or reduced estimation of risk in many chronic disease studies. Interestingly, in infectious disease epidemiology the ability to identify the risk factors that determine subclinical versus clinical disease has not been very successful. Age at time of infection and certain general host characteristics have provided only weak markers of the determinant of the spectrum of disease. Searches for specific host or genetic characteristics as well as other environmental factors that may contribute to the severity of the disease process have not been a successful mainstream component of infectious disease epidemiology, at least until recent times.

In chronic disease epidemiology, on the other hand, the determinants of the natural

TABLE 8
What Is the Spectrum of Disease?

Acute Diseases	Chronic Diseases
1. Spectrum from subclinical to clinical—very important—serological methods played an important role in epidemiological studies.	1. Measurement of subclinical disease very difficult and often not evaluated. Many controls have subclinical disease, reducing risk estimates of studies.
2. Ability to determine risk factors for subclinical vs. clinical disease not very successful	2. Determinants of natural history of disease, i.e., from mild to severe to death, and efficacy of therapies are often a very important component of research (clinical epidemiology).

history of the disease from mild, to severe, to death, and the efficacies of specific therapies have been a very important component of research and, in fact, form the basis of clinical epidemiology. The use of epidemiological methods in the evaluation of clinical care has probably substantially enhanced the field of clinical medicine.

The early infectious disease epidemiologist evolved out of the concerns for control of the spread of infectious diseases in the community, with a primary emphasis on modifying the modes of disease transmission and, subsequently, prevention of disease by active and passive immunization or by environmental controls. The new breed of chronic disease epidemiologists may be evolving out of the clinical concerns about the effective treatment of chronic diseases and the need for an active preventive approach which depends on understanding of the specific etiologies and modes of transmission.

The determination of the incubation period of a specific disease is also an important component of infectious disease epidemiological research (Table 9). Knowledge of the incubation period is important in understanding the etiology of disease and the mode of transmission. Knowledge of the period of infectivity in relation to the incubation period is of critical importance in disease control and prevention. Dr. Philip Sartwell published a series of interesting and important papers describing methods of estimating the distribution of the incubation period and pointed out that usually there was a log-normal distribution, that the median rather than the mean was the best measure of the incubation period, and that there seemed to be a specific, and often constant, dispersion factor of the antilog of the log standard deviation for the specific infectious diseases [22]. Lilienfeld et al. further utilized Sartwell's methods to evaluate the incubation periods of selected chronic diseases and showed also that the incubation periods for some of the chronic diseases were also log-normally distributed with specific dispersion factors [23]. Surprisingly, however, the incubation period has really not been a major focus of chronic disease epidemiology, except in cases of common source events such as unique radiation exposures in Hiroshima or Nagasaki. The incubation period is hardly discussed in major textbooks of epidemiology.

In chronic disease epidemiology there appears to be much greater interest in modeling the evolution of disease and trying to evaluate the interaction between initiating agents and those that may promote subsequent progression from an earlier stage to a subsequent clinical disease. Numerous mathematical models have been generated to study the possible progression of cancer, based on the number of changes at the cellular level that are necessary for progression from neoplasia to clinical disease [24].

A lack of understanding of the concepts of incubation periods may have resulted in misinterpretation of the relationship between current exposure and disease. Peto and Doll have pointed out that the modeling of the incubation period of lung cancer from age at onset of cigarette smoking to the development of disease probably explains much of the geographic variations and trends in lung cancer among populations [25]. The absence of any knowledge of incubation period of a chronic disease often makes it practically impossible to identify the specific etiological agent. Further research in chronic disease epidemiology on ways to measure the incubation period of disease may be an important priority in etiological research.

Infectious disease epidemiology evolved out of the need to control or eliminate epidemics (Table 10). The clinical trials of vaccines, of drug therapy, or of other prophylactic approaches were the gold standard of infectious disease research.

TABLE 9
What Is the Incubation Period?

Acute Diseases	Chronic Diseases
1. Incubation period is an important component of epidemiological research for identifying specific agent and mode of transmission.	1. Little interest in incubation periods of disease. Primary emphasis in common source events, i.e., radiation exposure
2. Incubation period usually defined as median and log-normal distribution with specific dispersion factor	2. Much interest in modeling evolution of disease, evaluation of initiation and promoters, and multi-stage progression of disease
3. Family studies important	3. Family studies usually related to genetic epidemiology

Without good clinical trials to determine the efficacy of a specific intervention, the infectious disease epidemic model was often suspect. The natural experiments in which the potential vehicle or mode of transmission was modified by non-experimental changes in the environment have played a role in testing causal hypothesis of a specific agent of disease but have not really replaced the carefully well-done randomized clinical trials.

In chronic disease epidemiology, on the other hand, observational epidemiology appears to have a higher priority than clinical trials. In fact, except perhaps in cardiovascular diseases, the clinical trials area has been left to the purview of the clinicians and the biostatisticians. It is, perhaps, only in cardiovascular diseases that the epidemiologist has played a role similar to that in infectious diseases. Natural experiments such as migrant studies, observation of temporal trends, and selected and unusual changes in risk factors because of religious preferences, or social pressures, and the like have played a much more important role in studying the etiology of disease [26,27,28,29]. There appears to be some reluctance or even hostility toward randomized clinical trials among chronic disease epidemiologists. The costs and the complexities of these trials and the need for collaborative efforts often are not recognized within the academic community and have probably provided some of the reasons for the failure of chronic disease epidemiologists to pursue experimental epidemiology more aggressively. There has never been and probably never will be a specific randomized clinical trial in the United States to determine the effects of smoking cessation on the reduction of risks of lung and other cancers. Dietary recommendations for the

TABLE 10
What Are the Methods to Control or Eliminate the Epidemic?

Acute Diseases	Chronic Diseases
1. Clinical trials often considered the "Gold Standard" of research	1. Observational epidemiology higher priority than clinical trials
2. Much epidemiological research related to testing specific intervention, i.e., vaccine trials, drug trials, elimination of vehicles of transmission	2. Acceptance of "causal" association much more likely without clinical trials
3. Natural experiments more of value in testing causal hypothesis and seeking specific agent of disease	3. Natural experiments of considerable value: migrant studies, temporal trends, selective change in risk factors

prevention of cancer are based on observational and some animal studies but, at the present time, not on the results of randomized clinical trials. Even in the cardiovascular field, the number of truly randomized double-blind primary prevention trials are relatively few, considering the extensive amount of research in this area.

Surveillance of disease in the population is an important component of infectious disease epidemiology (Table 11). The evaluation of the success of preventive programs depends on surveillance of infectious diseases. The Center for Disease Control has maintained an excellent and effective method of monitoring infectious diseases in the United States in order to determine the efficacy of various control procedures [30]. Monitoring systems of infectious diseases are often in place because of the traditional need to determine epidemics of disease as early as possible in order to reduce or prevent subsequent transmission of disease and larger epidemics within the community.

In the chronic disease area, surveillance and evaluation of control programs are just now being considered to be an important component. We are still dependent, however, predominantly on trends in mortality statistics rather than on any measures of morbidity. Long incubation periods for chronic diseases, changing criteria for definition of disease, and the confounding of mortality statistics by both changes in incidence and case-fatality have substantially limited our ability to monitor trends in disease. The failure to note substantial declines in cancer mortality over time has created a great deal of concern because it has suggested that our preventive and treatment efforts have failed. Good monitoring programs in chronic disease epidemiology are generally dependent on an active effort to measure the incidence, mortality, and changes in risk factors within limited areas. Such approaches have been both expensive and restricted to limited sub-segments of the population.

There unfortunately does not appear to be a ground swell of enthusiasm for effective surveillance of chronic diseases in the United States. The National Cancer for Health Statistics and, to a limited extent, several of the National Institutes of Health and the Center for Disease Control have provided a limited resource for the surveillance of chronic diseases [31]. In general, such surveillance has not been linked to tests of the evaluation of various control procedures.

Thus, there are substantial similarities and differences between chronic and infectious disease epidemiology in their approach to the study of disease. The infectious disease epidemiology model grew out of a need to control or eliminate epidemics. The approach was much more biological, active in the sense of seeking the specific etiology and vehicle of transmission based on the concepts of one agent for each disease, and on interactive models which separated risks into those related to the host, the specific characteristics of the agent, and the environments which increased or decreased the likelihood of transmission of disease.

Chronic disease epidemiology initially evolved out of interest in controlling diseases in the community. As investigators recognized the complex interaction of independent variables, a greater emphasis on the statistical methodology evolved. The longer incubation period, possible multiple etiological variables, and difficulties of defining subclinical disease have all contributed to our need to develop innovative methodology and approaches to analysis. It may be worthwhile for chronic disease epidemiology to rethink a parsimonious approach to the etiology of disease and again to consider that each disease is caused by one agent and to evaluate confounding in terms of host, agent, and the modes of transmission. The increasing interest of clinicians in the use of epidemiological methods to understand ways of reducing morbidity and mortality from

TABLE 11
How Effective Are Control Procedures?

Acute Diseases	Chronic Diseases
1. Surveillance of disease very important; shorter incubation periods and better definition of diseases enhance evaluation of control procedures.	1. Surveillance as evaluation of control usually based on trends in mortality rather than morbidity
2. Monitoring systems often in place. Disease reporting by medical community traditional component of control because of "transmission" of disease	2. Long incubation period and changing criteria of disease limit evaluations.
	3. Monitoring usually dependent upon a special program in limited areas

chronic diseases may again result in a greater emphasis on trying to understand the etiology and specific modes of transmission and on clinical trials to evaluate the prevention and control of disease. Epidemiology depends on an understanding of both human biology and on scientific methods. Chronic disease epidemiology should continue to emulate the best approaches developed by infectious disease epidemiologists—especially a primary goal of identifying an agent, mode of transmission, host susceptibility, and effective control and prevention. Every study with a numerator and a denominator is not epidemiology.

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