CHAPTER 2

Evidence-Based Public Health

LEARNING OBJECTIVES

- Explain the steps in the evidence-based public health process.
- Describe a public health problem in terms of morbidity and mortality.
- Describe the course of a disease in terms of incidence, prevalence, and case-fatality.
- Describe how the distribution of disease may be used to generate hypotheses about the cause of a disease.
- Describe an approach used in public health to identify a contributory cause of a disease or other condition and establish the efficacy of an intervention.
- Identify types of intervention approaches used when implementing interventions.
- Describe uses of qualitative data that complement quantitative data.
- Describe the process of grading evidence-based recommendations.
- Explain the role that evaluation plays in establishing effectiveness as part of evidence-based public health.
- Describe the uses and limitations of predicting population outcomes.

Tobacco was introduced to Europe as a new world crop in the early 1600s. Despite the availability of pipe tobacco and, later, cigars, the mass production and consumption of tobacco through cigarette smoking did not begin until the development of the cigarette rolling machine by James Duke in the 1880s. This invention allowed mass production and distribution of cigarettes for the first time. Men were the first mass consumers of cigarettes. During World War I, cigarettes were widely distributed free of charge to U.S. soldiers.

Cigarette smoking first became popular among women in the 1920s—an era noted for changes in the role and attitudes of women—and at this time, advertising of cigarettes began to focus on women. The mass consumption of cigarettes by women, however, trailed that of men by at least two decades. By the 1950s, over 50% of adult males and approximately 25% of adult females were regular cigarette smokers.

The health problems of cigarette smoking were not fully recognized until decades after the habit became widespread. As late as the 1940s, R.J. Reynolds advertised that "more doctors smoke Camels than any other cigarette."

Epidemiologists observed that lung cancer deaths were increasing in frequency in the 1930s and 1940s. The increase in cases did not appear to be due to changes in efforts to recognize the disease, the ability to recognize the disease, or the definition of the disease. Even after the increasing average life span and aging of the population were taken into account, it was evident that the rate of death from lung cancer was increasing—and more rapidly

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for men than women. In addition, it was noted that residents of states with higher rates of smoking had higher rates of lung cancer. In the 1950s, the number of lung cancer deaths in females also began to increase, and by the 1960s, the disease had become the most common cause of cancer-related death in males and was still rising among women.[1,2]

This type of information was the basis for describing the problems of cigarette smoking and lung cancer and developing ideas or hypotheses about its etiology, or cause. Let us take a look at how the evidence-based public health approach has been used to address the problem of cigarette smoking. There are five basic questions that we need to ask that together make up what we will call the evidence-based public health approach:[3]

1. **P**roblem: What is the health problem?
2. **E**tiology: What is/are the contributory cause(s)?
3. **R**ecommendations: What works to reduce the health impacts?
4. **I**mplementation: How can we get the job done?
5. **E**valuation: How well does/do the intervention(s) work in practice?

These five questions provide a framework for defining, analyzing, and addressing a wide range of public health issues and can be applied to cigarette smoking for the purposes of this chapter.[4] We will call this framework the **P.E.R.I.E. process**. This process is actually circular, as illustrated in **Figure 2.1**. If the evaluation suggests that more needs to be done, the cycle can and should be repeated. Thus, it is an ongoing process.

Using cigarette smoking as an example, we will illustrate the steps needed to apply the evidence-based public health approach.

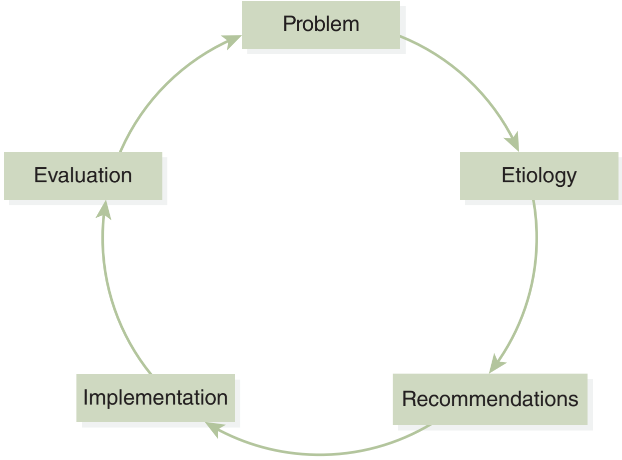

Figure 2.1 Evidence-Based Public Health: The P.E.R.I.E. Approach

How Can We Describe a Health Problem?

In describing a health problem, we need to address the burden, the course, and the distribution of disease. The first step in addressing a health problem is to describe its **burden of disease**, which is the occurrence of disability and death due to a disease. In public heath, disability is often called **morbidity** and death is called **mortality**. We will want to know the current burden of disease and whether there has been a recent change in the burden of the disease.

In addition to describing the burden of disease, it is important to describe what we call the **course of a disease**. The course of a disease asks how often the disease occurs, how likely it is to be present currently, and what happens once it occurs. Describing the course of a disease as well as the burden of disease requires us to use measurements known as rates. **Box 2.1** discusses what we mean by "rates" and how we can use them to describe the burden and course of disease.

In addition to describing the burden and the course of a disease or other health problem, we need to ask: What is the **distribution of disease**? Distribution of disease asks such questions as: Who gets the disease? Where are they located? When does the disease occur? Let us see how understanding the distribution of disease may help generate ideas or hypotheses about the disease's etiology (cause).

Box 2.1 Rates and the Description of a Health Problem

The term "**rate**" is often used to describe any type of measurement that has a numerator and a denominator where the numerator is a subset of the denominator—that is, the numerator includes only individuals who are also included in the denominator. In a rate, the numerator measures the number of times an event, such as lung cancer, occurs. Epidemiologists need to define the criteria they are using to measure the occurrence of the disease. This is known as the **case definition**.

The denominator measures the number of times the event could occur. We often use the entire population in the denominator, but at times, we may only use a smaller **at-risk population**. For instance, when measuring the rate of cervical cancer, we would only use the population of females in the denominator, and when measuring rates of prostate cancer, we would only use the population of males in the denominator.[a]

There are two basic types of rates that are key to describing a disease.[5,6] These are called **incidence** rates and **prevalence**. Incidence rates measure the chances of developing a disease over a period of time—usually 1 year. That is, incidence rates are the number of new cases of a disease that develop during a year divided by the number of people in the at-risk population at the beginning of the year, as in the following equation:

$$\textit{Incidence rate} = \frac{\textit{\# of new cases of a disease in a year}}{\textit{\# of people in the at-risk population}}$$

We often express incidence rates as the number of events per 100,000 people in the denominator. For instance, the incidence rate of lung cancer might be 100 per 100,000 per year. In evidence-based public health, comparing incidence rates is often a useful starting point when trying to establish the **etiology**, or cause, of a problem.

Mortality rates are a special type of incidence rate that measure the incidence of death due to a disease during a particular year. Mortality rates are often used to measure the burden of disease. When most people who develop a disease die from the disease, as is the situation with lung cancer, the mortality rate and the incidence rates are very similar. Thus, if the incidence rate of lung cancer is 100 per 100,000 per year, the mortality rate might be 95 per 100,000 per year. When mortality rates and incidence rates are similar and mortality rates are more easily or reliably obtained, epidemiologists may substitute mortality rates for incidence rates.[b]

The relationship between the incidence rate and the mortality rate is important because it estimates the chances of dying from the disease once it is diagnosed. We call this the **case-fatality** rate. In our example, the chances of dying from lung cancer—the mortality rate divided by the incidence rate—is 95%, which indicates that lung cancer results in a very poor prognosis once it is diagnosed.

Prevalence is the number of individuals who have a disease at a particular time divided by the number of individuals who could potentially have the disease. It can be represented by the following equation:

$$\textit{Prevalence} = \frac{\textit{\# living with a particular diease}}{\textit{\# of people in the at-risk population}}$$

Thus, prevalence tells us the **proportion** or percentage of individuals who have the disease at a point in time.[5,6]

Despite the fact that lung cancer has become the most common cancer, the prevalence will be low because those who develop lung cancer do not generally live for a long period of time. Therefore, you will rarely see people with lung cancer. The prevalence of chronic lung diseases of prolonged duration, such as asthma or chronic obstructive pulmonary disease (COPD), is often relatively high; hence you will often see people with these diseases.[c]

Prevalence is often useful when trying to assess the total impact or burden of a health problem in a population and can help identify the need for

(continues)

a When talking about the term "rate," many epidemiologists also include a unit of time, such as a day or a year, over which the number of events in the numerator is measured. This may also be called a **true rate**. The term "rate" as used in this text includes true rates, as well as proportions. A proportion is a fraction in which the numerator is a subset of the denominator. A time period is not required for a proportion; however, it often reflects the situation at one point in time.

b This is an example of the pragmatic approach that is often taken by epidemiologists when they are limited by the available data. The question facing epidemiologists is frequently: Are the data good enough to address the question? Thus, epidemiology can be thought of as an approximation science.

c The relationship between incidence and prevalence rates is approximately the incidence rate × average duration of the disease = the prevalence rate. Both the incidence rate and the average duration affect the prevalence of the disease. Together, the incidence, prevalence, and case-fatality rates provide a population-based summary of the course of a disease. Incidence reflects the chance of developing the disease, prevalence indicates the chances of having the disease, and case-fatality indicates the prognosis or chance of dying from the disease.

Box 2.1 Rates and the Description of a Health Problem *(continued)*

services. For example, knowledge that there is a high prevalence of lung cancer in a certain region may indicate that there is a need for special types of healthcare services in that area. Prevalence, as we will see, is also very useful in clinical medicine as the starting point for screening and diagnosis.

When using rates to describe a problem, we often use the rates of mortality and morbidity to describe the burden of disease. We use the incidence, prevalence, and case-fatality as the three key rates or measures that together provide a description of the course of disease. Together, these three measures address the key issues that we need to know in describing the course of a health problem: How likely it is to occur? How likely it is to be present currently? What happens once it occurs? Thus, understanding the burden of disease and the course of disease requires us to understand and use rates. As we will see, rates are also key to understanding the distribution of disease.

How Can Understanding the Distribution of Disease Help Us Generate Ideas or Hypotheses About the Cause Of Disease?

Public health professionals called **epidemiologists** investigate factors known as "person" and "place" to see if they can find patterns or **associations** in the frequency of a disease. We call these **group associations** or ecological associations. Group associations may suggest ideas or hypotheses about the cause, or etiology, of a disease.

"Person" includes demographic characteristics that describe people, such as age, sex, race, and socioeconomic factors. It also includes behaviors or exposures, such as cigarette smoking, exercise, radiation exposure, and use of medications.

"Place" traditionally implies geographic location, such as a city or state. Place matters in the occurrence of disease. The term "healthography" has recently been introduced to reflect the importance of geographic location to health. Place also includes nonphysical connections between people, such as a university community or a shared Internet site. When these types of factors occur more frequently among groups with the disease than among groups without the disease, we call them **risk indicators** or risk markers.[d]

Box 2.2 illustrates how person and place can be used to generate hypotheses about the cause of a disease.

In looking at the distribution of lung cancer and the potential risk factors, epidemiologists found some important relationships. In terms of person, the increases in lung cancer mortality observed in the 1930s–1950s were far more dramatic among men than among women, though by the 1950s, the mortality rate among women had begun to increase as well. It was noted that cigarette use had increased first in men and later among women. There appeared to be a delay of several decades between the increase in cigarette smoking and the increase in lung cancer mortality among both men and women. This illustrates that "time" along with "person" and "place" is important in generating hypotheses.

In terms of place, it was found that the relationship between cigarette smoking and lung cancer mortality was present throughout the United States, but was strongest in those states where cigarette smoking was most common. Therefore, changes over time and the distribution of disease using person and place led epidemiologists to the conclusion that there was an association between groups of people who smoked more frequently and the same group's mortality rates due to lung cancer. These relationships generated the idea that cigarettes might be a cause of lung cancer.

It is important to realize that these mortality rates are group rates. These data did not include any information about whether those who died from lung cancer were smokers. It merely indicated that groups who smoked more, such as men, also had higher mortality rates from lung cancer. The most that we can hope to achieve from these data is to generate hypotheses based on associations between groups, or group associations. When we try to establish causation or etiology, we will need to go beyond group association and focus on associations at the individual level.

Finally, epidemiologists take a scientific approach to addressing public health problems. They are often skeptical of initial answers to a question and ask: Could there be another explanation for the differences or changes in the distribution of disease?

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d The term "risk indicator" or "risk marker" needs to be distinguished from the term "risk factor." A risk factor is a candidate for being a contributory cause and implies that at least an association at the individual level has been established.

Box 2.2 Generating Hypotheses from Distributions of Person and Place

An increased frequency of disease based upon occupation has often provided the initial evidence of a group association based upon a combination of "person" and "place." The first recognized occupational disease was found among chimney sweeps, often exposed for long periods of time to large quantities of coal dust, and who were found to have a high incidence of testicular cancer.

The Mad Hatter described in *Alice's Adventures in Wonderland* by Lewis Carroll made infamous the 19th-century recognition that exposure to mercury fumes was associated with mental changes. Mercury fumes were created when making the felt used for hats, hence the term "mad as a hatter."

The high frequency of asbestos in the lungs and lung disease among those who worked in shipyards suggested a relationship between asbestos and lung disease decades before the dangers of asbestos were fully recognized and addressed. A lung disease known as silicosis among those who worked in the mining industry likewise suggested a relationship that led to an in-depth investigation and greater control of the risks.

More recently, a rare tumor called angiosarcoma was found to occur among those exposed over long periods to polyvinyl chloride (PVC), a plastic widely used in construction. The initial report of four cases of this unusual cancer among workers in one PVC plant was enough to strongly suggest a cause-and-effect relationship based upon place alone.

An important example of the impact that place can have on generating ideas or hypotheses about causation is the history of fluoride and cavities. In the early years of the 20th century, children in the town of Colorado Springs, Colorado, were found to have a very high incidence of brown discoloration of the teeth. It was soon recognized that this condition was limited to those who obtained their water from a common source. Ironically, those with brown teeth were also protected from cavities. This clear relationship to place was followed by over two decades of research that led to the understanding that fluoride in the water reduces the risk of cavities, while very high levels of the compound also lead to brown teeth. Examination of the levels of fluoride in other water systems eventually led to the establishment of levels of fluoride that could protect against cavities without producing brown teeth.

Such strong and clear-cut relationships are important, but relatively unusual. Often, examinations of the characteristics of person and place in populations suggest hypotheses that can be followed up among individuals to establish cause-and-effect relationships.[4,5]

How Do Epidemiologists Investigate Whether There Is Another Explanation for the Difference or Changes in the Distribution of Disease?

Epidemiologists ask: Are the differences or changes real or are they **artifactual**? There are three basic reasons that changes in rates may be artifactual rather than real:

- Differences or changes in the interest in identifying the disease
- Differences or changes in the ability to identify the disease
- Differences or changes in the definition of the disease

For some conditions, such as human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), these changes have all occurred. New and effective treatments have increased the interest in detecting the infection. Improved technology has increased the ability to detect HIV infections at an earlier point in time. In addition, there have been a number of modifications of the definition of AIDS based on new opportunistic infections and newly recognized complications. Therefore, with HIV/AIDS, we need to be especially attentive to the possibility that artifactual changes have occurred.[e]

In describing the distribution of a problem, epidemiologists ask: Are the differences or changes used to suggest group associations and generate hypotheses artifactual or real?

Let us see how this applies to our lung cancer example. As we have seen, lung cancer is a disease with a very poor prognosis; therefore, the burden of disease is high as measured by its high mortality rate. This was the situation in the past and to a large extent continues to be the situation.

e In the short run, artifactual changes need to be distinguished from real changes. Note, however, that artifactual changes such as the increased incidence due to increased effort can ultimately produce real changes if effective interventions exist to take advantage of the earlier detection of the disease.

Mortality rates have been obtained from death certificates for many years. The cause of death on death certificates is classified using a standardized coding system known as the International Classification of Diseases (ICD). No equally complete or accurate system has been available for collecting data on the incidence rates of diseases such as lung cancer. However, as we learned in our discussion of rates, the incidence rates and mortality rates for lung cancer are very similar. Therefore, we can use mortality data as a substitute for incidence data when evaluating the overall burden of lung cancer in a population.

By the 1930s, epidemiologists had concluded from the study of death certificates that lung cancer deaths were rapidly increasing. This increase continued through the 1950s—with the increase in lung cancer occurring two decades or more after the increase in consumption of cigarettes. Therefore, it was not immediately obvious that the two were related. In order to hypothesize that cigarettes are a cause of lung cancer, one needed to conclude that there was a long delay and/or a need for long-term exposure to cigarettes before lung cancer developed. There was a need for more **evidence** linking cigarettes and lung cancer among individuals.

From the 1930s through the 1950s, a large number of studies established that lung cancer deaths were increasing among men, but not among women. That is, there was a change over time and a difference between groups. Epidemiologists, therefore, considered whether the changes or differences in rates were real, or whether they could be artificial or artifactual.

With lung cancer, the diagnosis at the time of death has been of great interest for many years. The ability to diagnose the disease has not changed substantially over the years. In addition, the use of ICD codes on death certificates has helped standardize the definition of the disease. Epidemiologists concluded that it was unlikely that changes in interest, ability, or definition explained the changes in the rates of lung cancer observed in males, thus they concluded that the changes were not artifactual, but real.[f]

Box 2.3 discusses age adjustment, which is one additional step that epidemiologists frequently make when looking at rates.

What Is the Implication of a Group Association?

Group associations are established by investigations that use information on groups or a population without having information on the specific individuals within the group. These studies have been called **population comparisons** or ecological studies. Having established the existence of a group

Box 2.3 Age Adjustment

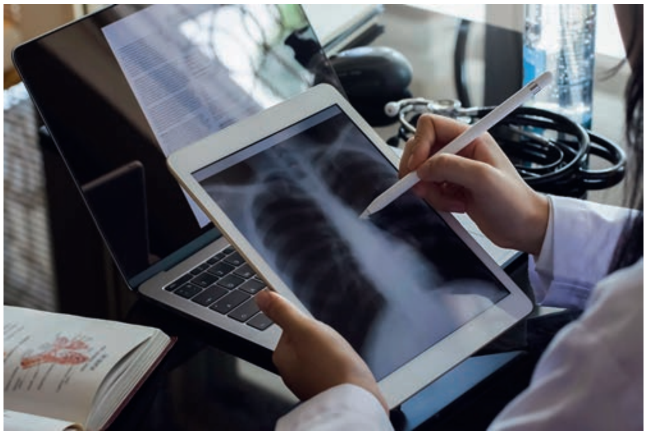
Despite the existence of a real change in the rates of lung cancer between 1930 and 1960, it was still possible that the increased mortality rates from lung cancer were due to the increasing life span that was occurring between 1930 and 1960, leading to the aging of the population and an older population on average. Since older people are more likely to develop lung cancer, the aging of the population itself could explain the real increase in the rates.

To address this issue, epidemiologists use what is called **age adjustment**. To conduct age adjustment, epidemiologists look at the rates of the disease in each age group and also the **age distribution**, or the number of people in each age group in the population. Then they combine the rates for each age group, taking into account or adjusting for the age distribution of a population.[g]

Taking into account the older average age of the population in 1960 compared to 1930 slightly reduced the apparent increase in lung cancer, but large differences between 1930 and 1960 remained. As a result, epidemiologists concluded that lung cancer mortality rates changed over this period, especially among men; the changes in rates were real; and the changes could not be explained simply by the aging of the population. Thus, epidemiologists had established the existence of a group association between groups that smoked more cigarettes and groups that developed lung cancer.

f There are actually several types of lung cancer defined by the ICD codes. Most, but not all, types of lung cancer are strongly associated with cigarette smoking.

g Adjustment for age is often performed by combining the rates in each age group using the age distribution of what is called a **standard population**. The age distribution of the U.S. population in 2000 is currently used as the standard population. Adjustment is not limited to age and may at times be conducted using other characteristics that may differ among the groups, such as gender or race, which may affect the probability of developing a disease.



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association, we still do not know if the individuals who smoke cigarettes are the same ones who develop lung cancer. We can think of a group association as a hypothesis that requires investigation at the individual level. The group association between cigarettes and lung cancer was the beginning of a long road to establish that cigarettes are a cause of lung cancer.

The existence of a group association or even an individual association does not ensure that a cause-and-effect relationship exists. Imagine the following situation: the mortality rates from drowning are higher in southern states than in northern states in the United States. The per capita consumption of ice cream is also higher in southern states than in northern states. Thus, a group association was established between ice cream consumption and drowning. In thinking about this relationship, you will soon realize that there is another difference between southern and northern states. The average temperature is higher in southern states, and higher temperatures are most likely associated with more swimming and also more ice cream consumption. Ice cream consumption is therefore related both to swimming and to drowning. We call this type of factor a possible **confounding variable**.

In addition, in this situation, there is no evidence that those who drown actually consumed ice cream. That is, there is no evidence of an association at the individual level. Thus, group associations can be misleading if they suggest relationships that do not exist at the individual level.

Epidemiology research studies that look at associations at the individual level are key to establishing etiology, or what we will call contributory cause. Etiology is the second component of the P.E.R.I.E. approach. Let us turn our attention to how to establish etiology.

Etiology: How Do We Establish Contributory Cause?

Understanding the reasons for disease is fundamental to the prevention of disability and death. We call these reasons etiology. In evidence-based public health, we use a very specific definition of etiology called **contributory cause**. The evidence-based public health approach relies on epidemiological research studies to establish a contributory cause. This requires that we go beyond group association and establish three definitive requirements:[6]

1. The "cause" is associated with the "effect" at the individual level. That is, the potential "cause" and the potential "effect" occur more frequently in the same individual than would be expected by chance. Therefore, we need to establish that individuals with lung cancer are more frequently smokers than individuals without lung cancer.
2. The "cause" precedes the "effect" in time. That is, the potential "cause" is present at an earlier time than the potential "effect." Therefore, we need to establish that cigarette smoking comes before the development of lung cancer.
3. Altering the "cause" alters the "effect." That is, when the potential "cause" is reduced or eliminated, the potential "effect" is also reduced or eliminated. Therefore, we need to establish that reducing cigarette smoking reduces lung cancer rates.

Box 2.4 illustrates the logic behind using these three criteria to establish a cause-and-effect relationship, as well as the implications of a contributory cause.

These three definitive requirements may be established using three different types of investigations, all of which relate potential "causes" to potential "effects" at the individual level. That is, they investigate whether individuals who smoke cigarettes are the same individuals who develop lung cancer.[5] The three basic types of investigations are called **case-control studies**, **cohort studies**, and **randomized controlled trials**.

Case-control studies are most useful for establishing requirement number one of contributory cause; that is, the "cause" is associated with the "effect" at the individual level. Case-control studies can demonstrate that cigarettes and lung cancer occur together more frequently than would be expected by chance alone. To accomplish this, cases with the disease (lung cancer) are compared to similar individuals without the disease, called controls.

Box 2.4 Lightning, Thunder, and Contributory Cause

The requirements for establishing the type of cause-and-effect relationship known as contributory cause used in evidence-based public health as well as clinical medicine can be illustrated by the cause-and-effect relationship between lightning and thunder that human beings have recognized from the earliest times of civilization.

First, lightning is generally associated with thunder; that is, the two occur together far more often than one would expect if there were no relationship. Second, with careful observation, it can be concluded that the lightning is seen a short time before the thunder is heard. That is, the potential "cause" (the lightning) precedes in time the "effect" (the thunder). Finally, when the lightning stops, so does the thunder—thus, altering the "cause" alters the "effect."

Notice that lightning is not always associated with thunder. Heat lightning may not produce audible thunder, or the lightning may be too far away for the thunder to be heard. Lightning is not sufficient in and of itself to guarantee that our ears will subsequently always hear thunder. Conversely, it has been found that the sound of thunder does not always require lightning. Other reasons for the rapid expansion of air, such as an explosion or volcanic eruption, can also create a sound similar or identical to thunder.

The recognition of lightning as a cause of thunder came many centuries before human beings had any understanding of electricity or today's appreciation for the science of light and sounds. Similarly, cause-and-effect relationships established by epidemiological investigations do not always depend on understanding the basic science behind the relationships.

When a factor such as cigarettes has been demonstrated to be associated on an individual basis with an outcome such as lung cancer, we often refer to that factor as a **risk factor**.[h]

During the 1940s and early 1950s, a number of case-control studies established that individuals who developed lung cancer were far more likely to be regular cigarette smokers compared to similar individuals who did not smoke cigarettes. These case-control studies established requirement number one—the "cause" is associated with the "effect" at the individual level. They established that cigarettes are a risk factor for lung cancer.

Cohort studies are most useful for establishing requirement number two—the "cause" precedes the "effect." Those with the potential "cause" or risk factor (cigarette smoking) and those without the potential "cause" are followed over time to determine who develops the "effect" (lung cancer).[i]

Several large scale cohort studies were conducted in the late 1950s and early 1960s. One conducted by the American Cancer Society followed nearly 200,000 individuals over 3 or more years to determine the chances that smokers and nonsmokers would develop lung cancer. Those who smoked regularly at the beginning of the study had a greatly increased chance of developing lung cancer over the course of the study, thus establishing requirement number two, the "cause" precedes the "effect" in time.

Randomized controlled trials are most useful for establishing requirement number three—altering the "cause" alters the "effect." Using a chance process known as **randomization** or random assignment, individuals are assigned to be exposed or not exposed to the potential "cause" (cigarette smoking). Individuals with and without the potential "cause" are then followed over time to determine who develops the "effect."

Conducting a randomized controlled trial of cigarettes and lung cancer would require investigators to randomize individuals to smoke cigarettes or not smoke cigarettes and follow them over many years. This illustrates the obstacles that can occur in seeking to definitively establish contributory cause. Once there was a strong suspicion that cigarettes might cause lung cancer, randomized controlled trials were not practical or ethical as a method for establishing cigarette smoking as a contributory cause of lung cancer. Therefore, we need to look at additional **supportive**

h A risk factor, as we just discussed, usually implies that the factor is associated with the disease at the individual level. At times, it may be used to imply that the factor not only is associated with the disease at the individual level, but that it precedes the disease in time. Despite the multiple uses of the term, a risk factor does not in and of itself imply that a cause-and-effect relationship is present, though it may be considered a possible cause.

i It may seem obvious that cigarette smoking precedes the development of lung cancer. However, the sequence of events is not always so clear. For instance, those who have recently quit smoking cigarettes have an increased chance of being diagnosed with lung cancer. This may lead to the erroneous conclusion that stopping cigarette smoking is a cause of lung cancer. It is more likely that early symptoms of lung cancer lead individuals to quit smoking. The conclusion that stopping cigarette smoking causes lung cancer is called **reverse causality**. Thus, it was important that cohort studies followed smokers and nonsmokers for several years to establish that the cigarette smoking came first.

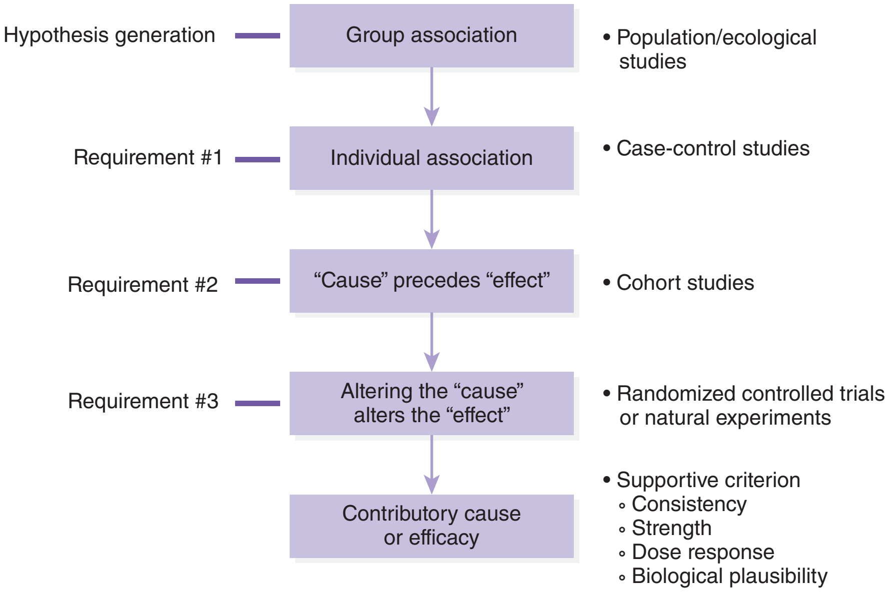

Figure 2.2 Fulfilling Requirements for Establishing Contributory Cause or Efficacy

criteria, or ancillary criteria, that we can use to help us establish the existence of contributory cause.[j]

Figure 2.2 illustrates the requirements for definitively establishing contributory cause and the types of studies that may be used to satisfy each of the requirements. Notice that the requirements for establishing contributory cause are the same as the requirements for establishing **efficacy**. Efficacy implies that an intervention works; that is, it increases positive outcomes or benefits in the study group compared to the control group being investigated.

What Can We Do If We Cannot Demonstrate All Three Requirements to Definitively Establish Contributory Cause?

When we cannot definitively establish a contributory cause, we often need to look for additional supportive evidence.[6] In evidence-based public health we often utilize what have been called supportive or ancillary criteria to make scientific judgments about cause and effect. A large number of these criteria have been used and debated. However, four of them are widely used and pose little controversy. They are:

- Strength of the relationship
- Dose-response relationship
- Consistency of the relationship
- Biological plausibility

Let us examine what we mean by each of these criteria.

The **strength of the relationship** implies that we are interested in knowing how closely related the risk factor (cigarette smoking) is to the disease (lung cancer). In other words, we want to know the probability of lung cancer among those who smoke cigarettes compared to the probability of lung cancer among those who do not smoke cigarettes. To measure the strength of the relationship, we calculate what we call the **relative risk**. The relative risk is the probability of developing the disease if the risk factor is present compared to the probability of developing the disease if the risk factor is not present. Therefore, the relative risk for cigarette smoking is calculated as:

j At times, a special form of a cohort study called a **natural experiment** can help establish that altering the cause alters the effect. A natural experiment implies that an investigator studies the results of a change in one group, but not in another similar group, that was produced by forces outside the investigator's control. For instance, after the surgeon general's 1964 *Report on Smoking and Health* was released, approximately 100,000 physicians stopped smoking. This did not happen among similar professionals such as lawyers. Over the next decade, the rates of lung cancer among physicians dropped dramatically, but not among similar professionals. Despite the fact that natural experiments can be very useful, they are not considered as reliable as randomized controlled trials. Randomization, especially in large studies, eliminates differences between groups or potential confounding differences, even when these differences in characteristics are not recognized by the investigators.

$$\text{Relative risk} = \frac{\text{Probability of lung cancer for cigarette smokers}}{\text{Probability of lung cancer for nonsmokers}}$$

The relative risk for the average level of cigarette smoking and lung cancer is approximately 10. A relative risk of 10 is very large. It tells us that the chances or probability of developing lung cancer are 10 times as great for the average smoker compared to the average nonsmoker.[k]

In addition to looking at the strength of the overall relationship between smoking cigarettes and lung cancer, we can ask whether smoking increasing quantities of cigarettes is associated with a greater chance of developing lung cancer. If it is, then we say there is a **dose-response relationship**. For instance, smoking one pack of cigarettes per day over many years increases the chances of developing lung cancer compared to smoking half a pack per day. Similarly, smoking two packs per day increases the chances of developing the disease compared to smoking one pack per day. These examples show that a dose-response relationship is present.[l]

Consistency implies that studies in different geographic areas and among a wide range of groups produce similar results. A very large number of studies of cigarettes and lung cancer in many countries and among those of nearly every race and socioeconomic group have consistently demonstrated a strong individual association between cigarette smoking and lung cancer.

The final supportive criterion is **biological plausibility**. This term implies that we can explain the occurrence of disease based upon known and accepted biological mechanisms. We can explain the occurrence of lung cancer by the fact that cigarette smoke contains a wide range of potentially toxic chemicals that reach the locations in the body where lung cancer occurs.

The supportive criteria add support to the argument that cigarette smoking is a contributory cause of lung cancer. **Table 2.1** summarizes the use of supportive criteria in making scientific judgments about contributory cause and illustrates these principles using the cigarette smoking and lung cancer scenario. It also cautions us to use these criteria carefully because a cause-and-effect relationship may be present even when some or all of these criteria are not fulfilled.[6]

We have now summarized the approach used in evidence-based public health to establish a contributory cause. We started with the development of group associations that generate hypotheses and moved on to look at the definitive requirements for establishing contributory cause. We also looked at the supportive criteria that are often needed to make scientific judgments about contributory cause. **Table 2.2** summarizes this process and applies it to cigarette smoking and lung cancer.

What Does Contributory Cause Imply?

Establishing a contributory cause on the basis of evidence is a complicated and often time-consuming job. In practice, our minds often too quickly jump to the conclusion that a cause-and-effect relationship exists. Our language has a large number of words that may subtly imply a cause-and-effect relationship, even in the absence of evidence. **Box 2.5** illustrates how we often rapidly draw conclusions about cause and effect.

It is important to understand what the existence of a contributory cause implies and what it does not imply. Despite the convincing evidence that cigarette smoking is a contributory cause of lung cancer, some individuals never smoke and still develop lung cancer. Therefore, cigarettes are not what we call a **necessary cause** of lung cancer. Some individuals smoke cigarettes all their lives and do not develop lung cancer. Thus, cigarettes are not what we call a **sufficient cause** of lung cancer.

k A relative risk of 10 does not tell us the **absolute risk**. The absolute risk is the actual chance or probability of developing the disease (lung cancer) in the presence of the risk factor (cigarette smoking), expressed numerically—for example, as 0.03 or 3%. A relative risk of 10 might imply an increase from 1 in 1000 individuals to 1 in 100 individuals. Alternatively, it might imply an increase from 1 in 100 individuals to 1 in 10 individuals. A relative risk can be calculated whenever we have data on groups of individuals; therefore, it does not in and of itself imply that a contributory cause is present. We need to be careful not to imply that the risk factor will increase the chances of developing the disease or that reducing or eliminating the risk factor will reduce or eliminate the disease unless we have evidence of contributory cause. For case-control studies, a measure known as the **odds ratio** can be calculated and is often used as an approximation of relative risk.

l A dose-response relationship may also imply that greater exposure to a factor is associated with reduced probability of developing the disease, such as with exercise and coronary artery disease. In this case, the factor may be called a **protective factor** rather than a risk factor. Note that a dose-response relationship may occur only within a limited range of exposure. For instance, smoking a small number of cigarettes per day may not lead to lung cancer. In addition, there may be an upper limit such as three packs per day, beyond which the probability of lung cancer does not increase.

Table 2.1 Supportive or Ancillary Criteria—Cigarettes and Lung Cancer

Criteria	Meaning of the criteria	Evidence for cigarettes and lung cancer	Cautions in using criteria
Strength of the relationship	The risk for those with the risk factor is greatly increased compared to those without the risk factor.	The relative risk is large or substantial. The relative risk is greater than 10 for the average smoker, implying that the average smoker has more than 10 times the probability of developing lung cancer compared to nonsmokers.	Even relatively modest relative risks may make important contributions to disease when the risk factor is frequently present. A relative risk of 2, for instance, implies a doubling of the probability of developing a disease.
Dose-response relationship	Higher levels of exposure and/or longer duration of exposure to the "cause" are associated with increased probability of the "effect."	Studies of cigarettes and lung cancer establish that smoking half a pack a day over an extended period of time increases the risk compared to not smoking. Smoking one pack per day and two packs per day further increase the risk.	No dose-response relationship may be evident between no smoking and smoking a small number of cigarettes per day or between smoking three and four packs per day.
Consistency of the relationship	Studies at the individual level produce similar results in multiple locations among populations of varying socioeconomic and cultural backgrounds.	Hundreds of studies in multiple locations and populations consistently establish an individual association between cigarettes and lung cancer.	Consistency requires the availability of numerous studies that may not have been conducted.
Biological plausibility	Known biological mechanisms can convincingly explain a cause-and-effect relationship.	Cigarette smoke directly reaches the areas where lung cancer appears.	Exactly which component(s) of cigarette smoking produce lung cancer are just beginning to be understood.

Table 2.2 Cigarettes and Lung Cancer—Establishing Cause and Effect

Requirements for contributory cause	Meaning of the requirements	Types of studies that can establish the requirement	Evidence for cigarette smoking and lung cancer
Associated at a population level (group association)	A group relationship between a "cause" and an "effect."	Ecological study or population comparison study: a comparison of population rates between an exposure and a disease.	Men began mass consumption of cigarettes decades before women and their rates of lung cancer increased decades before those of women.
Individual association: "requirement one"	Individuals with a disease ("effect") also have an increased chance of having a potential risk factor ("cause").	Case-control studies: cases with the disease are compared to similar controls without the disease to see who had the exposure.	Lung cancer patients were found to have approximately 10 times the chance of smoking cigarettes regularly compared to those without lung cancer.
Prior association: "requirement two"	The potential risk factor precedes—in time—the outcome.	Cohort studies: exposed and similar unexposed individuals are followed over time to determine who develops the disease.	Large cohort studies found that those who smoke the average amount of cigarettes have approximately 10 times the chance of subsequently developing lung cancer.
Altering the "cause" alters the "effect": "requirement three"	Active intervention to expose one group to the risk factor results in a greater chance of the outcome.	Randomized controlled trials allocating individuals by chance to be exposed or not exposed are needed to definitively establish contributory cause. Note: these studies are not always ethical or practical.	Alternatives to randomized controlled trials, such as "natural experiments," established that those who quit smoking have greatly reduced chances of developing lung cancer. In addition, the four supportive criteria also suggest contributory cause.

Box 2.5 Words that Imply Causation

Often, when reading the newspaper, watching television, or looking at social media, you will find that conclusions about cause and effect are made based upon far less rigorous examination of the data than we have indicated is needed to definitively establish cause and effect. In fact, we often draw conclusions about cause and effect without even consciously recognizing we have done so. Our language has a large number of words that imply a cause-and-effect relationship, some of which we use rather casually.

Let us take a look at the many ways that a hypothetical newspaper article might imply the existence of a cause-and-effect relationship or a contributory cause even when the evidence is based only upon a group association or upon speculation about the possible relationships.

> Over several decades, the mortality rates from breast cancer in the United States were observed to increase each year. This trend was due to and can be blamed on a variety of factors, including the increased use of estrogens and exposure to estrogens in food. The recent reduction in breast cancer resulted from and can be attributed to the declining use of estrogens for menopausal and postmenopausal women. The declining mortality rate was also produced by the increased use of screening tests for breast cancer that were responsible for early detection and treatment. These trends demonstrate that reduced use of estrogens and increased use of screening tests have contributed to and explain the reduction in breast cancer.

While these conclusions sound reasonable and may well be cause-and-effect relationships, note that they rely heavily on assertions for which there is no direct evidence provided. For instance, the following words are often used to imply a cause-and-effect relationship when evidence is not or cannot be presented to support the relationship:

- due to
- blamed on
- result from
- attributable to
- produced by
- responsible for
- contributed to
- explained by

It is important to be aware of conscious or unconscious efforts to imply cause-and-effect relationships when the data suggest only group associations and do not meet our more stringent criteria establishing cause and effect.

The fact that not every smoker develops lung cancer implies that there must be factors that protect some individuals from lung cancer. The fact that some nonsmokers develop lung cancer implies that there must be additional contributory causes of lung cancer. Thus, the existence of a contributory cause implies that the "cause" increases the chances that the "effect" will develop. Its presence does not guarantee that the disease will develop. In addition, the absence of cigarette smoking does not guarantee that the disease will not develop.

Despite the fact that cigarettes have been established as a contributory cause of lung cancer, cigarette smoking is not a necessary or a sufficient cause of lung cancer. In fact, the use of the concept of "necessary and sufficient cause" is not considered useful in the evidence-based public health approach because so few, if any, diseases fulfill the definitions of necessary and sufficient cause. These criteria are too demanding to be used as standards of proof in public health or medicine.

By 1964, the evidence that cigarette smoking was a contributory cause of lung cancer was persuasive enough for the Surgeon General of the United States to produce the first Surgeon General's *Report on Smoking and Health*. The report concluded that cigarettes are an important cause of lung cancer.

Over the following decades, the Surgeon General's reports documented the evidence that cigarette smoking causes not only lung cancer, but also other cancers—including cancer of the throat and larynx. Cigarette smoking is also a contributory cause of COPD and coronary artery disease. Smoking during pregnancy poses risks to the unborn child, and passive or secondhand smoke creates increased risks to those exposed—especially children.[7] Based on the Surgeon General's findings, there is clearly overwhelming evidence that cigarette smoking is a contributory cause of lung cancer and a growing list of other diseases. Thus, let us turn our attention to the third component of the P.E.R.I.E. process: recommendations.

Recommendations: What Works to Reduce the Health Impact?

The evidence for cigarette smoking as a cause of lung cancer, as well as other diseases, was so strong that it cried out for action. In evidence-based public health, however, action should be grounded in **recommendations** that incorporate evidence. That is, evidence serves not only to establish contributory cause, but is also central to determining whether or not specific interventions work.[8,9]

Evidence-based recommendations are built upon the evidence from studies of interventions. Thus, recommendations are summaries of the evidence about which interventions work to improve health outcomes. They indicate whether action should be taken. Evidence-based recommendations utilize the same types of investigations we discussed for contributory cause. In fact, the requirements of contributory cause are the same as those for establishing that an intervention works or has efficacy for the particular population that was studied. Evidence-based recommendations, however, go beyond efficacy or benefits and also take into account harms or safety.

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In the decades since the Surgeon General's initial report, a long list of interventions has been implemented and evaluated. The results of these interventions and evaluations can then be integrated into evidence-based recommendations.[m]

Recommendations for action have been part of public health and medicine for many years. Evidence-based recommendations, however, are relatively new. They have been contrasted with the traditional eminence-based recommendation, which uses the opinion of a respected authority as its foundation. Evidence-based recommendations ask about the research evidence supporting the benefits and harms of potential interventions. In evidence-based recommendations, the opinions of experts are most important when research evidence does not or cannot provide answers.

Before looking at the evidence-based recommendations on cigarette smoking made by the Centers for Disease Control and Prevention (CDC), let us look at how they are developed and graded. Evidence-based recommendations are based upon two types of criteria: the quality of the evidence and the magnitude of the impact. Each of these criteria is given what is called a **score**.[8,9] The quality of the evidence is scored based in large part upon the types of investigations and how well the investigation was conducted. Well-conducted randomized controlled trials that fully address the health problem are considered the highest quality evidence. Often, however, cohort and case-control studies are needed and are used as part of an evidence-based recommendation.

Expert opinion, though lowest on the hierarchy of evidence, is often essential to fill in the holes in the research evidence.[8,9] The quality of the evidence also includes determining whether the data collected during an intervention are relevant to their use in a particular population or setting. Data from young adults may not be relevant to children or the elderly. Data from severely ill patients may not be relevant to mildly ill patients. Thus, high-quality evidence needs to be based not only on the research, which can establish efficacy in one particular population, but also on how well the intervention works in the specific population in which it will be used.

In evidence-based public health, the quality of the evidence is often scored as good, fair, or poor. Good quality implies that the evidence fulfills all the criteria for quality. Poor quality evidence implies that there are fatal flaws in the evidence and recommendations cannot be made. Fair quality lies in between, having no fatal flaws and sufficient, but limited, evidence.[n]

In addition to looking at the quality of the evidence, it is also important to look at the magnitude of the impact of the intervention. The magnitude of the impact asks the question: How much of the disability and/or death due to the disease can be potentially removed by the intervention? In measuring the

m The term **intervention** is a very broad term in public health. Interventions range from individual counseling and prescription of pharmaceutical drugs that aid smoking cessation; to group efforts, such as peer support groups; to social interventions, such as cigarette taxes and legal restrictions on smoking in restaurants.

n To fulfill the criteria for good quality data, evidence is also needed to show that the outcome being measured is a clinically important outcome. Short-term outcomes called **surrogate endpoints**, or surrogate outcomes, such as changes in laboratory tests, may not reliably indicate longer term or clinically important outcomes.

magnitude of the impact, evidence-based recommendations take into account the potential benefits of an intervention, as well as the potential harms. Therefore, we can regard the magnitude of the impact as the benefits minus the harms, or the "net benefits."[o]

The magnitude of the impact, like the quality of the evidence, is scored based upon a limited number of potential categories. In one commonly used system, the magnitude of the impact is scored as substantial, moderate, small, and zero/negative.[8] A substantial impact may imply that the intervention works extremely well for a small number of people, such as a drug treatment for cigarette cessation. A substantial impact may also imply that the intervention has a modest net benefit for any one individual, but can be applied to large numbers of people, such as through media advertising or taxes on cigarettes.

Evidence-based recommendations combine the score for the quality of the evidence with the score for the impact of the intervention.[9] **Table 2.3** summarizes how these aspects can be combined to produce a classification of the strength of the recommendation, graded as A, B, C, D, and I as used by the U.S. Preventive Services Task Force.

It may be useful to think of these grades as indicating the following:

- A = Must—A strong recommendation.
- B = Should—In general, the intervention should be used unless there are good reasons or contraindications for not doing so.
- C = May—The use of judgment is often needed on an individual-by-individual basis. Individual recommendations depend on the specifics of an individual's situation, risk-taking attitudes, and values as is often the situation in clinical medicine.
- D = Don't—There is strong evidence to recommend against using the intervention.
- I = Indeterminant, insufficient, or "I don't know"—The evidence is inadequate to make a recommendation for or against the use of the intervention at the present time.

Notice that evidence-based public health and medicine rely primarily on considerations of benefits and harms. However, recently, issues of financial cost have begun to be integrated into evidence-based recommendations. At this point, however, cost considerations are generally only taken into account for "close calls." Close calls are often situations where the net benefits are small to moderate and the costs are large.

The evidence-based public health approach increasingly relies on the use of evidence-based recommendations that are graded based on the quality of the evidence and the expected impact of the intervention. The recommendations are made by a wide array of organizations, as discussed in **Box 2.6**. It is important to appreciate the source of the recommendations, as well as the methods used to develop them.[6]

Let us take a look at some examples of how interventions to prevent smoking, detect lung cancer early, or cure lung cancer have been graded. The CDC publishes "The Guide to Community Preventive Services," commonly referred to as "The Community Guide."[9]

Table 2.3 Classification of Recommendations

Magnitude of the impact				
Quality of the evidence	**Net benefit: substantial**	**Net benefit: moderate**	**Net benefit: small**	**Net benefit: zero/negative**
Good	A	B	C	D
Fair	B	B	C	D
Poor (insufficient evidence)	I	I	I	I

Data from Agency for Healthcare Research and Quality, U.S. Preventive Services Task Force. *The Guide to Clinical Preventive Services 2014.* AHRQ Pub. No. 14-05158. 2014.

o The magnitude of the impact can be measured using the relative risk calculation. When dealing with interventions, the people who receive the intervention are often placed in the numerator. Thus, an intervention that reduces the bad outcomes by half would have a relative risk of 0.5. The smaller the relative risk is, the greater the measured impact of the intervention. If the relative risk is 0.20, then those with the intervention have only 20% of the risk remaining. Their risk of a bad outcome has been reduced by 80%. The reduction in a bad outcome is called the **attributable risk percentage** or, if a contributory cause is present, the percent efficacy. The intervention can only be expected to accomplish this potential reduction in risk when a contributory cause is present and the impact of the "cause" can be immediately and completely eliminated.

Box 2.6 Who Develops Evidence-Based Recommendations?

Evidence-based recommendations may be developed by a range of groups, including the government, practitioner-oriented organizations, consumer-oriented organizations, organized healthcare systems, and even for-profit organizations. Organizations developing evidence-based recommendations, however, are expected to acknowledge their authorship and identify the individuals who participated in the process, as well as their potential conflicts of interest. In addition, regardless of the organization, the evidence-based recommendations should include a description of the process used to collect the data and make the recommendations.

For-profit organizations may make evidence-based recommendations. However, their obvious conflicts of interest often lead them to fund other groups to make recommendations. Thus, the funding source(s) supporting the development of evidence-based recommendations should also be acknowledged as part of the report.

One well-regarded model for the development of evidence-based recommendations is the task force model used by the United States Preventive Services Task Force of the Agency for Healthcare Research and Quality (AHRQ), as well as by the Task Force on Community Preventive Services of the CDC.[8,9] The task force model aims to balance potential conflicts of interest and ensures a range of expertise by selecting a variety of experts, as well as community participants, based upon a public nomination process. Once the task force members are appointed, their recommendations are made by a vote of the task force and do not require approval by the government agency.

As a reader of evidence-based recommendations, it is important that you begin by looking at which group developed the recommendations; whether they have disclosed their membership, including potential conflicts of interest; and the groups' procedures for developing the recommendations.

This guide indicates that the following interventions are recommended, implying a grade of A or B:

- Clean indoor air legislation, prohibiting tobacco use in indoor public and private workplaces
- Federal, state, and local efforts to increase taxes on tobacco products as an effective public health intervention to promote tobacco use cessation and to reduce the initiation of tobacco use among youths
- The funding and implementation of long-term, high-intensity mass media campaigns using paid broadcast times and media messages developed through formative research
- Proactive telephone cessation support services (quit lines)
- Reduced or eliminated copayments for effective cessation therapies
- Reminder systems for healthcare providers (encouraging them to reinforce the importance of cigarette cessation)
- Efforts to mobilize communities to identify and reduce the commercial availability of tobacco products to youths

Additional recommendations encourage clinicians to specifically counsel patients against smoking, prescribe medications for adults, encourage support groups for smoking cessation, and treat lung cancer with the best available treatments when detected.

Of interest is the grade of D for recommending against screening for early detection of lung cancer using traditional chest X-rays. The evidence strongly suggests that screening using this method may detect cancer at a slightly earlier stage, but not early enough to alter the course of the disease. Therefore, early detection does not alter the outcome of the disease. Research has identified improved screening methods that may detect lung cancer in time to make a difference.

Evidence-based recommendations are not the end of the process. There may be a large number of recommendations among which we may need to choose. In addition, we need to decide the best way(s) to put the recommendations into practice. Thus, implementation is not an automatic process. Issues of ethics, culture, politics, and risk-taking attitudes can and should have major impacts on implementation. A fourth step in the evidence-based public health approach requires us to look at the options for implementation and to develop a strategy for getting the job done.

Implementation: How Do We Get the Job Done?

Strong recommendations based upon the evidence are ideally the basis of implementation. At times, however, it may not be practical or ethical to obtain the evidence needed to establish contributory cause and develop evidence-based recommendations. The process of implementation itself may be part of the process of establishing causation, as it was for cigarette smoking in the 1960s when 100,000 physicians stopped smoking and their rates of lung cancer declined rapidly, as compared to other similar professionals who did not stop smoking.

Today, there are often a large number of interventions with adequate data to consider implementation. Many of the interventions have potential harms, as well as potential benefits. The large and growing array of possible interventions means that health decisions require a systematic method for deciding which interventions to use and how to combine them in the most effective and efficient ways. One method for examining the options for implementation uses a structure we will call the "When-Who-How" approach.

"When" asks about the timing in the course of disease in which an intervention occurs. This timing allows us to categorize interventions as primary, secondary, and tertiary. **Primary interventions** take place before the onset of the disease. They aim to prevent the disease from occurring. **Secondary interventions** occur after the development of a disease or risk factor, but before symptoms appear. They are aimed at early detection of disease or reducing risk factors while the individual is asymptomatic. **Tertiary interventions** occur after the initial occurrence of symptoms, but before irreversible disability. They aim to prevent irreversible consequences of the disease. In the cigarette smoking and lung cancer example, primary interventions aim to prevent cigarette smoking. Secondary interventions aim to reverse the course of disease by smoking cessation efforts or screening to detect early disease. Tertiary interventions diagnose and treat diseases caused by smoking in order to prevent permanent disability and death.[p]

"Who" asks: At whom should we direct the intervention? Should it be directed at individuals one at a time as part of clinical care? Alternatively, should it be directed at groups of people, such as vulnerable populations, or should it be directed at everyone in a community or population?[q]

Finally, we need to ask: How should we implement interventions? There are three basic types of interventions when addressing the need for behavioral change. These interventions can be classified as information (education), motivation (incentives), and obligation (requirements).

An information or education strategy aims to change behavior through individual encounters, group interactions, or social and mass media, etc. Motivation implies use of incentives for changing or maintaining behavior. It implies more than strong or enthusiastic encouragement—it implies tangible reward. Obligation relies on laws and regulations requiring specific behaviors.

Box 2.7 Technological Innovation as a Method of Implementation

Technological innovation implies the use of technology as a method of implementation. Technology is attractive because it may circumvent the need to change behavior. For instance, airbags are easier to implement than the use of seat belts, which is easier to implement than changing driving habits.

Technology may not always be effective, at least for all groups. The introduction of e-cigarettes represented a major technological innovation. E-cigarettes allowed nicotine to be administered as a vapor much like it is delivered via cigarettes but without the large number of other harmful chemicals. Nicotine consumed as e-cigarettes has been shown to be effective in reducing withdrawal among chronic smokers. Unfortunately, because e-cigarettes allow nicotine to rapidly and effectively enter the brain, they also lead to nicotine addiction among those not previously addicted. Thus, the technological innovation of e-cigarettes has led to more, not less, addiction, especially among adolescents.

The development of technology may be expensive. Its use may require the user to learn technical skills such as computer skills. These limitations of technology may fall most heavily on those with low levels of income and education, thereby increasing the impact of inequalities in a society.

The use of technology to solve many health problems is attractive, but the limitations of technology must also be kept in mind.

In addition to information, motivation, and obligation, at times it may be possible to use a fourth strategy which we will call technological innovation. To learn more about the pros and cons of technological innovation see **Box 2.7**.

Table 2.4 illustrates how options for implementation for cigarette smoking might be organized using the "When-Who-How" approach. To better understand the "who" and "how" of the options for intervention when behavior change is needed, refer to **Table 2.5**, which outlines nine different options.

p Determining whether an intervention is primary, secondary, or tertiary depends on the individual's situation. For instance, an intervention to stop smoking may be secondary or tertiary for the smoker. However, by preventing secondhand smoke, it may be primary for those in close contact with the smoker. Thus, a single intervention may be classified in more than one way.

q The CDC defines four levels of intervention: the individual, the relationship (for example, the family), the community, and society or the population as a whole. This framework has the advantage of separating immediate family interventions from community interventions. The group or at-risk group relationship used here may at times refer to the family unit or geographic communities. It may also refer to institutions or at-risk vulnerable groups within the community. The use of group or at-risk group relationship provides greater flexibility, allowing application to a wider range of situations. In addition, the three levels used here correlate with the measurements of relative risk, attributable risk percentage, and population attributable percentage, which are the fundamental epidemiological measurements applied to the magnitude of the impact of an intervention.

Table 2.4 Framework of Options for Implementation

	When	Who	How
Levels	1. Primary—prior to disease or condition 2. Secondary—prior to symptoms 3. Tertiary—prior to irreversible complications	1. Individual 2. At-risk group 3. General population/ community	1. Information (education) 2. Motivation (incentives) 3. Obligation (requirement)
Meaning of levels	1. Primary—remove underlying cause, increase resistance, or reduce exposure 2. Secondary—postexposure intervention, identify and treat risk factors or screen for asymptomatic disease 3. Tertiary—reverse the course of disease (cure), prevent complications, restore function	1. Individual often equals patient care 2. At-risk implies groups with common risk factors 3. General population includes defined populations with and without the risk factor	1. Information—efforts to communicate information and change behavior on basis of information 2. Motivation—rewards or penalties to encourage or discourage without legal requirement 3. Obligation—required by law or institutional sanction
Cigarette smoking example	1. Primary—prevention of smoking, reduction in secondhand exposure 2. Secondary—assistance in quitting, screening for cancer if recommended 3. Tertiary—health care to minimize disease impact	1. Individual smoker 2. At-risk—groups at risk of smoking or disease caused by smoking (e.g., adolescents as well as current and ex-smokers) 3. Population—entire population, including those who never have or never will smoke	1. Information—stop smoking campaigns, advertising, warning on package, clinician advice 2. Motivation—taxes on cigarettes, increased cost of insurance 3. Obligation—prohibition on sales to minors, exclusion from athletic eligibility, legal restrictions on indoor public smoking

Table 2.5 Examples of "Who" and "How" Related to Cigarette Smoking

	Information	Motivation	Obligation
Individual	Clinician provides patient with information explaining reasons for changing behavior	Clinician encourages patient to change behavior in order to qualify for a service or gain a benefit (e.g., status or financial)	Clinician denies patient a service unless patient changes behavior
	Example: clinician distributes educational packet to a smoker and discusses his or her own smoking habit	Example: clinician suggests that the financial savings from not buying cigarettes be used to buy a desired item	Example: clinician implements recommendation to refuse birth control pills to women older than 35 years who smoke cigarettes
High-risk group	Information is made available to all those who engage in a behavior	Those who engage in a behavior are required to pay a higher price	Those who engage in a behavior are barred from an activity or job
	Example: warning labels on cigarette packages	Examples: taxes on cigarettes	Example: smokers banned from jobs that will expose them to fumes that may further damage their lungs
Population	Information is made available to the entire population, including those who do not engage in the behavior	Incentives are provided for those not at risk to discourage the behavior in those at risk	An activity is required or prohibited for those at risk and also for those not at risk of the condition
	Example: media information on the dangers of smoking	Example: lower healthcare costs for everyone results from reduced percentage of smokers	Example: cigarette sales banned for those younger than 18 years

Deciding when, who, and how to intervene depends in large part upon the available options and the evidence that they work. It also depends in part on our attitudes toward different types of interventions. In U.S. society, we often prefer to rely on informational or educational strategies. These approaches preserve freedom of choice, which we value in public, as well as private, decisions. Use of mass and social media informational strategies may be quite economical and efficient relative to the large number of individuals they reach through messages, but they often need to be tailored to different audiences. However, information is often ineffective in accomplishing behavioral change—at least on its own.

Strategies based upon motivation, such as taxation and other incentives, may at times be more effective than information alone, though educational strategies are still critical to justify and reinforce motivational interventions. Motivational interventions should be carefully constructed and judiciously used, or they may result in what has been called **victim blaming**. For example, victim blaming in the case of cigarette smoking implies that we regard the consequences of smoking as the smokers' own fault.

The use of obligation or legally required action can be quite effective if clear-cut behavior and relatively simple enforcement, such as restrictions on indoor public smoking, are used. These types of efforts may be regarded by some as a last resort, but others may see them as a key to effective use of other strategies. Obligation inevitably removes freedom of choice and if not effectively implemented with regard for individual rights, the strategy may undermine respect for the law. Enforcement may become invasive and expensive; thus, obligation requires careful consideration before use as a strategy.

Understanding the advantages and disadvantages of each type of approach is key to understanding many of the controversies we face in deciding how to implement programs to address public health problems; however, implementation is not the end of the evidence-based public health process. It is important to evaluate the success of an intervention in practice. Evaluation is the fifth and final component of the P.E.R.I.E. approach.

Evaluation: How Do We Evaluate Results?

Public health problems are rarely completely eliminated with one intervention—there are few magic bullets in public health. Therefore, it is important to evaluate whether an intervention or combination of interventions has been successful in reducing the problem. It is also critical to measure how much of the problem has been eliminated by the intervention(s) and what is the nature of the problem that remains. When evaluating how well an intervention works in public health or clinical practice we use the term **effectiveness**. The term efficacy, in contrast, is used when we address how well an intervention works under research conditions.

Traditionally, evaluation has asked before and after questions. For instance, studies of cigarette smoking between the mid-1960s, when cigarettes were first declared a cause of lung cancer, and the late 1990s demonstrated that there was nearly a 50% reduction in cigarette smoking in the United States and that the rates of lung cancer were beginning to fall—at least among men. However, much of the problem still existed because the rates among adolescent men and women remained high and smoking among adults was preceded by smoking as adolescents nearly 90% of the time. Thus, an evaluation of the success of cigarette smoking interventions led to a recycling of the P.E.R.I.E. process. It focused on how to address the issue of adolescent smoking and nicotine addiction among adults.

Many of the interventions being used today grew out of this effort to cycle once again through the evidence-based public health process and look for a new understanding of the problem, its etiology, evidence-based recommendations, and options for implementation.

The advent of e-cigarettes is again requiring us to utilize the P.E.R.I.E. framework to better understand their benefits and harms. E-cigarette research illustrates how public health

Box 2.8 Qualitative Data and Their Importance to Public Health

Qualitative data can serve a variety of functions in public health. It can generate ideas or hypotheses for further study, provide key information on the reasons for success or failure of an intervention, and provide explanations for findings of quantitative research.

Quantitative research often includes a large sample and focuses on either/or outcomes, whereas qualitative research often looks in depth at a small sample, producing descriptions and allowing for a thorough exploration of the phenomenon of interest. Qualitative research on e-cigarettes may provide examples of the range of uses of qualitative research.

Focus groups and interviews are increasingly important forms of qualitative research that are being used to gain insight into how and why people come to conclusions or hold opinions on issues such as e-cigarettes. The opinions examined increasingly include issues such as perceptions of the benefits and harms of e-cigarettes, access to e-cigarettes, and what interventions would be effective in controlling use of e-cigarettes in children.

Qualitative research may also help explain quantitative research findings. For instance, quantitative research might conclude that e-cigarette use is growing among 16- to 18-year-olds but not among 12- to 16-year-olds. The insights provided by individuals of these ages may help explain these findings.

The ideas put forward by these types of qualitative research may generate new hypotheses to be examined using quantitative studies. They may also help assess barriers to implementation and suggest new approaches.

These and other approaches to qualitative research help generate new ideas or hypotheses, predict responses to new interventions, and help us better understand the reasons for the observed results of quantitative research. Qualitative and quantitative research should be seen as complementary, not competitive, as they can work together to provide greater insight and understanding.

research is being broadened to include not only traditional quantitative research but new methods of qualitative research. Roles of qualitative methods in public health research using e-cigarettes as an example is discussed in **Box 2.8**.

In recent years, this process of evaluation has been extended to attempt to address how well specific interventions work and are accepted in practice. A new framework, called the **RE-AIM** framework, is increasingly being used to evaluate these factors.[11] RE-AIM is a mnemonic that stands for **r**each, **e**ffectiveness, **a**doption, **i**mplementation, and **m**aintenance. You can think of the "RE" factors as evaluating the potential of the intervention for those it is designed to include or reach as well as those it has the potential to reach in practice. It is important to recognize that interventions are often applied far beyond the groups for whom they have been designed or investigated.

The "AIM" factors examine the acceptance of the intervention in clinical or public health practice in the short and long term. **Table 2.6** defines the meaning of each of these components and illustrates how a new hypothetical intervention for cigarette cessation might be evaluated using the RE-AIM framework.

A recent addition to evaluation methods in evidence-based public health, as a result of the COVID-19 pandemic, has been the use of modeling to forecast or predict the future course of a communicable disease or non-communicable disease epidemic or pandemic. **Box 2.9** introduces the concepts and uses of modeling to forecast the course of an epidemic or pandemic and to predict the impact of potential interventions.

Deciding the best combination of approaches to address a public health problem remains an important part of the judgment needed for the practice of public health. In general, multiple approaches are often needed to effectively address a complex problem like cigarette smoking. Population and high-risk group approaches, often used by public health professionals, and individual approaches, often used as part of health care, should be seen as complementary. Often, using both types of interventions is more effective than either approach alone. Social interventions, such as cigarette taxes and restrictions on public smoking, are also important interventions to consider.

Today, an enormous body of evidence exists on the relationship between tobacco and health. Understanding the nature of the problems, the etiology or cause-and-effect relationships, the evidence-based recommendations, and the approaches for implementing and evaluating the options for interventions remains key to the public health approach to smoking and health.[4] **Figure 2.3** diagrams the full P.E.R.I.E. approach.

Table 2.7 summarizes the questions to ask in the evidence-based public health approach.

Table 2.6 **Evaluation: RE-AIM Framework**

RE-AIM component	Meaning	Example
How well does the intervention work in practice?		
Reach	Asks: Who is the intervention being applied to in practice? May be groups or populations that are different than those on which it was investigated or intended for (i.e., the target population).	New prescription smoking cessation drug to be used along with behavioral intervention approved by FDA and given evidence-based rating of A for long-standing adult smokers. Adverse events include depression and liver disease that is reversible with cessation of medication. Should not be used in teenagers who experience increased incidence of suicidal ideas.
Effectiveness	Asks: What is the impact in practice on the intended or target population, including beneficial outcomes as well as harm?	When used for long-term adult smokers, follow-up studies demonstrate substantial long-term quit rates similar to those observed in randomized controlled trials with no serious adverse events not identified in preapproval studies. Benefits exceed harms when used on intended target population.
How well is the intervention accepted in practice?		
Adoption	Asks: How well is the intervention accepted by individuals and providers of services?	The drug is being widely used for long-term adult smokers. The drug is also being widely used for teenagers.
Implementation	Asks: How should the intervention be modified to reach target population and providers of services, but not those for whom the benefits do not exceed the harms?	A "black box" warning is placed on the prescribing information, warning clinicians of the potential suicide risk when used for teenagers.
Maintenance	Asks: How can we ensure long-term continuation of use and success of intervention among individuals and providers of services?	Long-term use of smoking cessation drug and behavioral change interventions are needed and are encouraged by coverage by health insurance plans.

Abbreviation: FDA, U.S. Food and Drug Administration
Data from Virginia Tech. *RE-AIM.* http://www.re-aim.org/. Accessed January 18, 2021.

Box 2.9 Using Evidence to Predict the Future in Populations

The impact of interventions on a large population is increasingly being evaluated using what are called **population prediction models**. Population prediction models aim to predict the future and also enhance understanding of how that future can be improved by potential interventions. Population prediction models gained considerable visibility during the COVID-19 pandemic when they were used to predict new cases, hospitalizations, deaths, etc. However, prediction models can be used for a range of conditions, including the impact of new interventions such as restrictions on e-cigarettes on cigarette smoking.

Modeling a communicable or noncommunicable disease epidemic or pandemic is similar to hurricane forecasting, but even more difficult because the outcome of a communicable disease can be fundamentally altered by changes in human behavior. Hurricane forecasting is rarely totally accurate. Nonetheless, it can help groups take action even if it misses the mark on important details. Modeling, like hurricane forecasting, often uses more than one model. These models may be based on different theories of how hurricanes develop, move, and act when they hit land. Combining the predictions made by alternative models often turns out to be better at prediction than use of only one model.

The farther a hurricane is from the point of landfall, the more the models tend to make different predictions. As landfall nears, the models tend to come together, having continued to incorporate new data along the way. The same is true of many public health prediction models since predicting the future is among the most difficult of human undertakings, especially long-term prediction. Therefore, COVID-19 predictions were most accurate when making predictions measured in days, weeks, or months rather than years.

Predicting the future begins by choosing a theory of how a communicable disease epidemic or noncommunicable disease epidemic spreads in a population. This theory is incorporated into a mathematical formula producing what is called a model. The model provides a step-by-step framework for integrating data to predict the future. The framework itself is called a model and the overall process has been called modeling.[r]

Before a model can be used for prediction, it needs to be validated by comparing the outcome predicted by the model and the actual observed outcomes. Once a model has been shown to be able to adequately predict the future, the model can also be used to predict the impact of a range of possible interventions.

For COVID-19, these have included stay-at-home policies and a range of health policies from mask usage, to opening schools or restaurants, to implementing vaccines with variable levels of effectiveness and acceptance. For cigarette smoking, they might include existing and new methods for addressing addiction.[12]

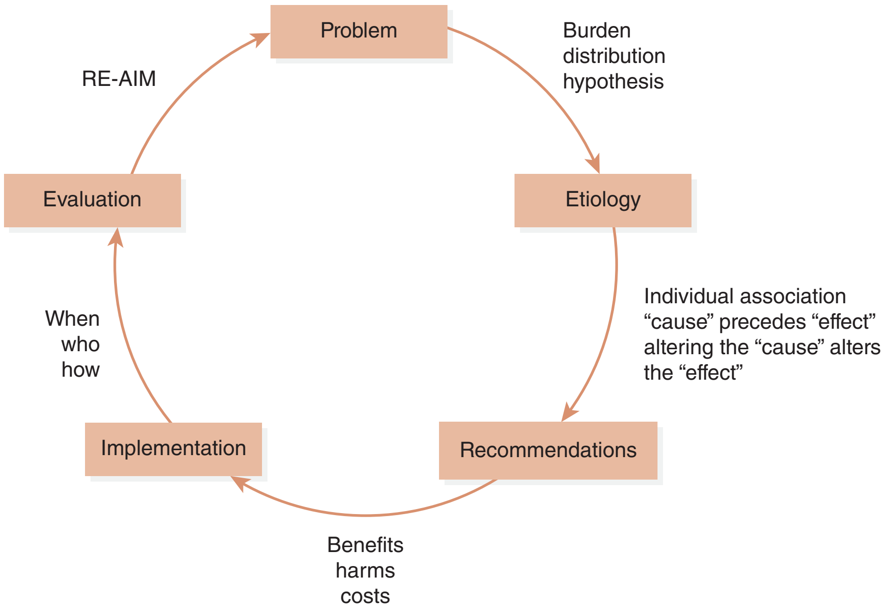

Figure 2.3 Evidence-Based Public Health: The Complete P.E.R.I.E. Approach

The P.E.R.I.E. process summarizes the steps in evidence-based public health. It emphasizes the need to understand the nature of the problem and its underlying causes. It also helps structure the use of evidence to make recommendations and decide on which options to put into practice. Finally, the circular nature of the P.E.R.I.E. process reminds us that the job of improving health goes on, often requiring multiple efforts to understand and address the problem.[10]

Now that we have an understanding of the basic approach of evidence-based public health, we can turn our attention to the fundamental tools at our disposal for addressing public health problems. First, however, take a look at the following Discussion Questions as well as the Cases and Discussion Questions for Section 1.

r For communicable diseases such as COVID-19, the SEIR model is commonly used. SEIR stands for Susceptible, Exposed, Infectious, and Removed. For COVID-19, the SEIR model assumes that everyone starts out as susceptible to COVID-19. They then have a probability of being exposed for each period of time. This leads to a probability of being infected and a subsequent probability of being hospitalized, dying, or being removed from the population by death or recovery. The SEIR model can be modified to include the potential for reinfection, asymptomatic transmission, etc.

Table 2.7 Questions to Ask—Evidence-Based Public Health Approach

Problem—What is the health problem? What is the burden of a disease or other health problem? What is the course of a disease or other health problem? Does the distribution of the health problem help generate hypotheses?
Etiology—What are the contributory causes? Has an association been established at the individual level? Does the "cause" precede the "effect"? Has altering the "cause" been shown to alter the "effect"? (If not, use ancillary criteria.)
Recommendations—What works to reduce the health impacts? What is the quality of the evidence for the intervention? What is the impact of the intervention in terms of benefits and harms? What grade should be given to indicate the strength of the recommendation?
Implementation—How can we get the job done? When should the implementation occur? At whom should the implementation be directed? How should the intervention(s) be implemented?
Evaluation—How well does the intervention work in practice? How well does the intervention work in practice on the intended or target population? How well does the intervention work in practice as actually used? How well is the intervention accepted in practice?

WRAP-UP

Key Words

Age adjustment
Age distribution
Artifactual
Associations
At-risk population
Biological plausibility
Burden of disease
Case-control studies
Case definition
Case-fatality
Cohort studies
Confounding variable
Consistency
Contributory cause
Course of a disease
Distribution of disease
Dose-response relationship
Effectiveness
Efficacy
Epidemiologists
Etiology
Evidence
Group associations
Incidence
Morbidity
Mortality
Necessary cause
P.E.R.I.E. process
Population comparisons
Population prediction models
Prevalence
Primary interventions
Proportion
Randomization
Randomized controlled trials
Rate
RE-AIM
Recommendations
Relative risk
Risk factor
Risk indicators
Score
Secondary interventions
Strength of the relationship
Sufficient cause
Supportive criteria
Tertiary interventions
Victim blaming

Discussion Questions

1. Use the P.E.R.I.E. framework and the list of questions to outline how each step in the P.E.R.I.E. process was accomplished for cigarette smoking.
2. How would you use the P.E.R.I.E. process to address the remaining problem of cigarette smoking in the United States?

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SECTION 1

Cases and Discussion Questions

HIV/AIDS Determinants and Control of the Epidemic

A report appeared in the CDC's *Morbidity and Mortality Weekly Report* (MMWR) on June 5, 1981, describing a previously unknown deadly disease in five young homosexual males, all in Los Angeles. The disease was characterized by dramatically reduced immunity, allowing otherwise innocuous organisms to become "opportunistic infections," rapidly producing fatal infections or cancer. Thus, acquired immunodeficiency syndrome (AIDS) first became known to the public health and medical communities. It was soon traced to rectal intercourse, blood transfusions, and reuse of injection needles as methods of transmission. Reuse of needles was then a common practice in poor nations. It was also widespread among intravenous drug abusers. Within several years, the disease was traced to a previously unknown retrovirus, which came to be called the human immunodeficiency virus (HIV).

A test was developed to detect the disease and was first used in testing blood for transfusion. Within a short period of time, the blood supply was protected by testing all donated blood, and transmission of HIV by blood transfusion became a rare event. Diagnostic tests for HIV/AIDS soon became available for testing individuals. For many years, these were used by clinicians only for high-risk individuals. In recent years, HIV testing has become more widely used, as the testing no longer requires blood drawing and the results are rapidly available. The CDC has put increasing emphasis on testing as part of routine health care.

In subsequent years, much has been learned about HIV/AIDS. Today, it is primarily a heterosexually transmitted disease with greater risk of transmission from male to females than females to males. In the United States, the Black population is at the greatest risk. Condoms have been demonstrated to reduce the risk of transmission. Abstinence and monogamous sexual relationships likewise eliminate or greatly reduce the risk. Even serial monogamy reduces the risk compared to multiple simultaneous partners. Male circumcision has been shown to reduce the potential to acquire HIV infection by approximately 50%.

In major U.S. cities, the frequency of HIV is often greater than 1% of the population, fulfilling the CDC definition of "high risk." In these geographic areas, the risk of unprotected intercourse is substantially greater than in most suburban or rural areas. Nearly everyone is susceptible to HIV infection, despite the fact that a small number of people have well-documented protection on a genetic basis.

Maternal-to-child transmission is quite frequent in the absence of treatment and has been shown to be largely preventable by treatments during pregnancy and at the time of delivery. CDC recommendations for universal testing of pregnant women and intervention for all HIV-positive patients have been widely implemented by clinicians and hospitals and have resulted in greatly reduced frequency of maternal-to-child transmissions in developed countries and in developing countries in recent years.

Medication is now available that greatly reduces or makes undetectable the load of HIV present in the blood. These medications delay the progression of HIV and also reduce the ease of spread of the disease. These treatments were rapidly applied to HIV/AIDS patients in developed countries, but it required about a decade before they were widely used in most developing countries. Inadequate funding from developed countries and controversies over patent protection for HIV/AIDS drugs delayed widespread use of these treatments in developing countries.

New and emerging approaches to HIV prevention include use of antiviral medications during breastfeeding and rapid diagnosis and follow-up to detect and treat those recently exposed. Identification and treatment of HIV-positive individuals who are unaware of their diagnosis plus the larger number of known HIV-positive individuals whose disease is not well controlled is key to addressing the ongoing epidemic. In addition, treatment of HIV-negative individuals at high risk of exposure is now routine. It includes prescribing medication as preexposure prophylaxis (PrEP).

The end of the HIV epidemic, if not the end of HIV, is now considered feasible using existing interventions by 2030. The U.S. government has set a goal of reducing new cases to 3000 per year from a level of approximately 30,000 per year a decade earlier.

Discussion Questions

1. Use the BIG GEMS framework to examine the factors in addition to infection that have affected the spread of HIV and the control or failure to control the HIV/AIDS epidemic.
2. What roles has health care played in controlling or failing to control the HIV/AIDS epidemic?
3. What roles has traditional public health played in controlling or failing to control the HIV/AIDS epidemic?
4. What roles have social factors (beyond the sphere of health care or public health) played in controlling or failing to control the HIV/AIDS epidemic?

The Aging Society

Harriet just turned 90 but all was not well. On the day before her birthday, she found herself lying on the bathroom floor in pain after slipping getting out of the shower. Fortunately, she was able to get help and she was soon on her way to the operating room to replace her hip. She was told that 40 years ago she would most likely have died from the fracture but now she was faced with months of rehabilitation and a long stay in a rehabilitative facility. She wondered what would come next.

The population of those older than 85 years is growing faster than those of any other age group. Those older than 85 have been called the "frail elderly" because they are far more vulnerable to a range of diseases from strokes and heart disease, to falls and fractures, to Alzheimer's and Parkinson's disease. There are currently less than 10 million people older than 85 in the United States. By 2050 that number is expected to exceed 20 million.

The life expectancy of those turning 65 today has grown to an average of approximately 20 years compared to less than 10 years when Medicare was begun in the mid-1960s. That means that about half those turning 65 today will be alive at age 85 and many will live well into their 90s.

Harriett was fortunate since her family did not have a history of Alzheimer's disease and Harriet's mind was quite clear despite her frailty. She was glad to take advantage of new systems of caring for the frail elderly, ranging from "aging in place," to senior day care, to family respite services, to efforts encouraging the elderly to remain active in their communities. These and other efforts have gained momentum as a result of the COVID-19 pandemic that most heavily affected the elderly, especially those in nursing homes.

The burdens of taking care of the frail elderly, however, are increasingly falling on family members as society seeks to limit costs. Family leave policies and tax benefits for caring for the elderly are policies that may help relieve this burden. Living alone can lead to loneliness, which is increasingly being recognized as a risk factor for deteriorating physical and mental status. Social interactions are key to good health in the elderly as well as their enjoyment of life.

Prevention takes on a different meaning for the frail elderly. Many traditional screening programs, such as routine Pap smears or routine testing for colon or breast cancer, no longer are being applied to the elderly, especially those older than 85. Control of low-density lipoprotein cholesterol, blood sugar, high blood pressure, and smoking cessation remain high priorities.

Efforts to prevent falls and respond quickly when they do occur have become a high priority for prevention in the frail elderly. Keeping physically active helps to prevent blood clots and worsening osteoporosis. As with Harriet, emergency treatment of these conditions, when they do occur, is now high on the list of common clinical procedures.

The healthcare system is gradually adjusting to the need to provide special services for the frail elderly who are often unable to navigate the increasingly complex world of community services, health care, and health insurance. Health navigators, sometimes called community health workers, patient navigators, or health insurance navigators, may become an important part of the healthcare and community health systems. Providing health services in the home or residence is increasingly recognized as an effective and efficient method for caring for the frail elderly.

Discussion Questions

1. What makes the frail elderly different from other older individuals? Explain.
2. What health professionals and nonhealth professionals are needed to care for the frail elderly? Explain.
3. How has the COVID-19 pandemic affected how we view the care of the elderly? Explain.
4. What services for the frail elderly do you think would be the most effective in improving their quality of life? Explain.

Smoking and Adolescents—The Continuing Problem

The rate of smoking in the United States has been reduced by over one-half since the 1960s. However, the rate of smoking among teenagers increased in the 1980s and 1990s, especially among teenage girls. This raised concerns that young women would continue smoking during pregnancy. In addition, it was found that nearly 90% of adults who smoked started before the age of 18, and in many cases at a considerably younger age.

In the 1980s and most of the 1990s, cigarette smoking was advertised to teenagers and even preteens, or "tweens," through campaigns such as Joe Camel. In the early 21st century, a series of interventions directed at teenagers and tweens was put into effect. These included elimination of cigarette vending machines, penalties for those who sell cigarettes to those younger than 18, and elimination of most cigarette advertising aimed at those younger than 18. In addition, the truth® campaign aimed to convince adolescents, who often see smoking as a sign of independence from their parents, that not smoking is actually a sign of independence from the tobacco companies who seek to control their behavior. Evaluation studies concluded that these interventions have worked to reduce adolescent smoking by about one-third.

Despite the successes of the early years of the 2000s in lowering the rates of cigarette smoking among adolescents, the rates have stabilized at approximately 20%. Evidence indicates that adolescents who smoke generally do not participate in athletics, more often live in rural areas, and are more often white and less often Black. Men and women smoke about the same amount overall, but white women smoke more and Asian women smoke less than their male counterparts.

New drugs taken as pills have recently been shown to increase the rates of success in smoking cessation among adults despite side effects. This is not the situation in adolescents because of increased potential for adverse effects, including suicide. A series of interventions has been suggested for addressing the continuing problem of adolescent smoking. These include:

- Eliminating flavored cigarettes, including the popular menthol-flavored cigarettes
- Expulsion from school for cigarette smoking
- Focus on adolescents in tobacco warning labels
- Selective use of nicotine gum and patches to help with withdrawal
- No-smoking rules for sporting events, music concerts, and other adolescent-oriented events
- Fines for adolescents who falsify their age and purchase cigarettes
- Higher taxes on tobacco products
- Rewards to students in schools with the lowest smoking rates in a geographic area
- Higher auto insurance premiums for adolescents who smoke
- Reduce the quantity of nicotine allowed in tobacco products to reduce the potential for addiction
- Testing of athletes for nicotine and exclusion from competition if they test positive

In addition, the National Academy of Medicine has recommended that the age for purchase of cigarettes be raised from 18 to 21 years.

Discussion Questions

1. How does this case illustrate the P.E.R.I.E. process?
2. Which of the previous interventions do you think would be most successful in reducing cigarette smoking among adolescents? Explain.
3. How would you classify each of these potential interventions as education (information), motivation (incentives), obligation (required), or innovation (technological change)?
4. What other interventions can you suggest to reduce adolescent smoking?

5. Do you agree with the National Academy of Medicine's recommendation to increase the age for sale of tobacco products to 21? Explain.

Reye's Syndrome: A Public Health Success Story

Reye's syndrome is a potentially fatal disease of childhood that typically occurs in the winter months at the end of an episode of influenza, chicken pox, or other acute viral infection. It is characterized by progressive stages of nausea and vomiting, liver dysfunction, and mental impairment that progress over hours to days and result in a range of symptoms, from irritability to confusion to deepening stages of loss of consciousness. Reye's syndrome is diagnosed by putting together a pattern of signs and symptoms. There is no definitive diagnostic test for the disease.

Reye's syndrome was first defined as a distinct condition using a case definition in the early 1960s. By the 1980s, over 500 cases per year were being diagnosed in the United States. When Reye's syndrome was first diagnosed, there was over a 30% case-fatality rate. Early diagnosis and aggressive efforts to prevent brain damage were shown to reduce the deaths and limit the mental complications, but there is no cure for Reye's syndrome.

In the late 1970s and early 1980s, a series of case-control studies compared children with Reye's syndrome and similar children who also had an acute viral infection, but did not develop the syndrome. These studies suggested that use of low-dose aspirin, then called "baby aspirin," was strongly associated with Reye's syndrome, with over 90% of those children afflicted with the syndrome having recently used aspirin.

Cohort studies were not practical because they would require observing very large numbers of children who might be given or not given aspirin by their caretakers. Randomized controlled trials were neither feasible nor ethical. Fortunately, it was considered safe and acceptable to reduce or eliminate aspirin use in children because there was a widely used alternative—acetaminophen (often sold under the brand name Tylenol)—that was not implicated in the studies of Reye's syndrome.

As early as 1980, the CDC cautioned physicians and parents about the potential dangers of aspirin. In 1982, the U.S. Surgeon General issued an advisory on the danger of aspirin for use in children. By 1986, the U.S. Food and Drug Administration required a Reye's syndrome warning be placed on all aspirin-containing medications. These efforts were coupled with public service announcements, informational brochures, and patient education by pediatricians and other health professionals who cared for children. The use of the term "baby aspirin" was strongly discouraged.

In the early 1980s, there were over 500 cases of Reye's syndrome per year in the United States. In recent years, there have often been fewer than five cases per year. The success of the efforts to reduce or eliminate the use of "baby aspirin" and the subsequent dramatic reduction in the frequency of Reye's syndrome provided convincing evidence that aspirin was a contributory cause of the condition and its removal from use was an effective intervention.

Discussion Questions

1. How does the Reye's syndrome history illustrate the use of each of the steps in the P.E.R.I.E. process?
2. What unique aspects of Reye's syndrome made it necessary and feasible to rely on case-control studies to provide the evidence to help reduce the frequency of the syndrome?
3. What types of methods for implementation were utilized as part of the implementation process? Can you classify them in terms of when, who, and how?
4. How does the Reye's syndrome history illustrate the use of evaluation to demonstrate whether the implementation process was successful?

Sudden Infant Death Syndrome (SIDS)

Sudden infant death syndrome, or SIDS, was first recognized as a distinct public health problem in the late 1960s when over 7000 infants each year were found to die suddenly and unexpectedly. "Crib deaths" have been recognized for centuries, but until they were formally recorded using a case definition and investigated, little was known about their cause, leading some to conclude that intentional or unintentional suffocation by parents or caregivers played an important role.

Data from the epidemiological investigations of SIDS indicated that the syndrome was very rare before babies' first month of life, increased during the second month, and peaked during the third month, before rapidly declining in frequency to again become rare after the fourth month of life. The timing of SIDS suggested that the condition occurs after infants begin to sleep for extended periods but prior to the time in which children can raise themselves up and roll over on their own. Additional evidence suggested a seasonal trend, with more cases of SIDS occurring during cold weather months than during warm weather months.

In the 1980s, several case-control studies of SIDS cases and similar infants without SIDS established that infants who slept on their stomachs were at substantially increased risk of dying from SIDS. The studies indicated that the chances increased 4 to 7 times, suggesting that if a cause-and-effect relationship exists, a clear majority of SIDS cases could be prevented if infants slept on their back.

Additional evidence of the effectiveness of a "back-to-sleep" intervention was provided by the experience of New Zealand, which was the first country to begin a program to encourage caretakers to put infants to sleep on their backs. The rates of SIDS in New Zealand declined rapidly in parallel with the increased rate at which infants were put to sleep on their back. Similar declines in SIDS did not occur in other countries that had not yet instituted similar back-to-sleep programs.

In 1992, the American Academy of Pediatrics made a recommendation that infants be placed on their back to sleep. The initial recommendations also endorsed side sleeping. In 1994, with the support of the American Academy of Pediatrics, the National Institutes of Health (NIH), and the U.S. Public Health Service, the Back-to-Sleep campaign was launched. The educational campaign included public service announcements; brochures and other publications, including information accompanying new cribs; plus efforts for pediatricians and others who care for infants to educate parents and caretakers about the importance of having infants sleep on their backs.

The frequency of infants sleeping prone in the United States was found by survey data to be reduced from approximately 70% to less than 15% during the years immediately following the initiation of the Back-to-Sleep campaign. During these years, the rates of SIDS fell by approximately 50%, an impressive change but less than expected by the initial data. The rate of prone sleeping among African Americans was found to be over twice as high as the rate among whites, and African American infants continued to have higher rates of SIDS than whites.

Continuing studies suggested that the side position was being commonly used. It was found that many infants moved from the side to the prone position, and movement from the side to the prone position carried a high risk of SIDS. Additional case-control studies suggested that soft objects and loose bedding as well as overheating with blankets were associated with SIDS. These relationships are consistent with the initial finding of an increase of SIDS in colder weather months.

Studies of the infants who slept on their back indicated an increasing in flattening of the head, or plagiocephaly. These changes were shown to be reduced by increasing the amount of "tummy time," or play periods in which infants are placed prone under supervision. Guidelines for tummy time are now part of the evidence-based recommendations.

SIDS continues to be an important cause of infant mortality, and new contributory causes continue to be investigated, including genetic factors that predispose to SIDS. SIDS reflects the use of evidence-based public health and the importance of continuing to study and develop new approaches to public health problems.

Discussion Questions

1. Discuss how the case study illustrates the problem component of the P.E.R.I.E. framework.
2. Discuss how the case study illustrates the etiology/efficacy component of the P.E.R.I.E. framework.
3. Discuss how the case study illustrates the recommendations component of the P.E.R.I.E. framework.
4. Discuss how the case study illustrates the implementation and evaluation components of the P.E.R.I.E. framework.
5. Discuss how this case study illustrates the recycling that is part of the P.E.R.I.E. framework.

Folic Acid and the Prevention of Spina Bifida and other Neural Tube Defects

Neural tube defects (NTD) are congenital birth defects that result from the failure of closure of the spinal column and skull or cranium. This closure normally occurs approximately 1 month after conception. This is before most women recognize that they are pregnant. The most severe form of NTD is anencephaly—partial or complete absence of the brain—and uniformly results either in fetal deaths or death soon after birth.

Spina bifida (see **Figure CSF 1.1**) is incomplete closure of the spinal column. In the most serious form of spina bifida, the unfused or open portion of the spinal column allows the spinal cord to protrude through an opening in the overlying vertebrae. The protruded nerves are usually damaged prior to birth, resulting in some degree of paralysis and loss of sensation below the level of the spinal cord defect. Many individuals experience bowel and bladder problems as well. In the late 20th century, spina bifida occurred in

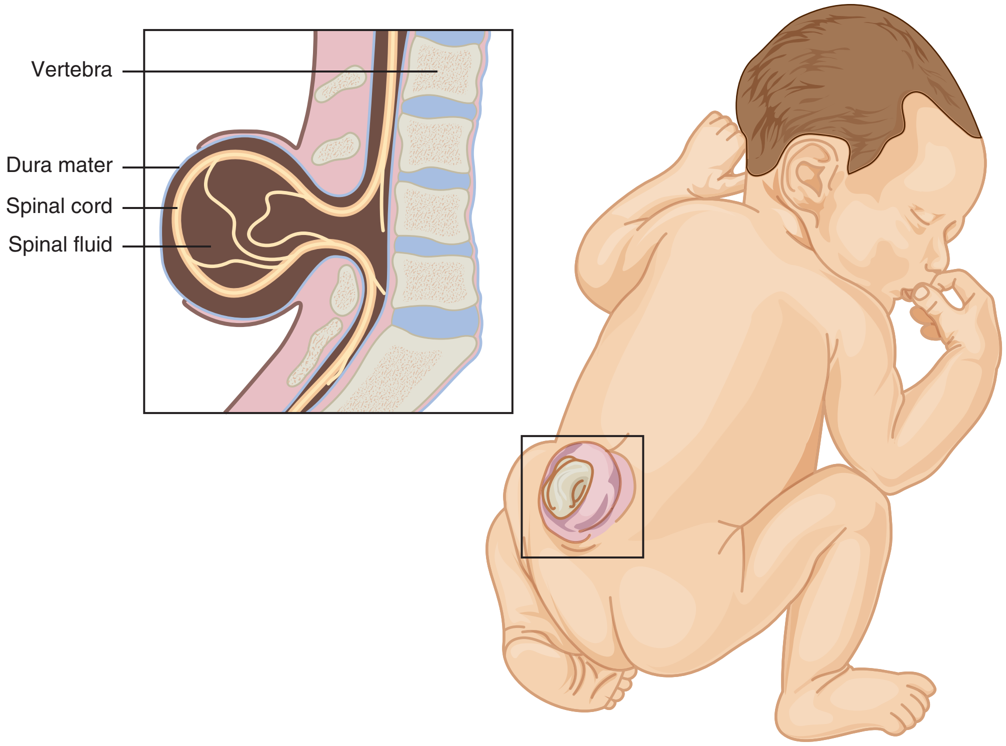

Figure CSF 1.1 Illustration of Location of Spina Bifida and Protrusion of Spinal Cord Outside the Spine.

Centers for Disease Control and Prevention. Available at https://en.wikipedia.org/wiki/Spina bifida. Accessed May 28, 2022.

approximately 1 in 2000 births in the United States. The rate of anencephaly, including fetal deaths after 20 weeks plus deaths soon after birth, was approximately two-thirds the rate for spina bifida. The chance of recurrence in a subsequent pregnancy once an NTD has occurred is approximately 5%.[1,2]

In recent years, a great deal has been learned about the causes of NTDs. As is often the case in health research, the earliest studies often compare rates in different groups or populations. These population comparisons or ecological studies are often designed to generate ideas or hypotheses. They can establish relationships or associations between groups, but not relationships based on individual-level data. As knowledge accumulates, investigators design more complex studies to test hypotheses using data from individuals. The following brief study synopses illustrate how the evidence was developed about an important contributory cause of neural tube defects.

In 1974 a population comparison (or ecological study) found that there was a substantial increase in NTDs (spina bifida and anencephaly) among those from lower socioeconomic groups compared to those in higher socioeconomic groups. This group association led investigators to suspect a range of causes, including nutritional factors.[3]

Several years later, a case-control study was published comparing pregnant women who gave birth to offspring with NTDs to a control group of pregnant women whose offspring were healthy. The investigators hypothesized that folic acid, which is present in many fresh fruits and vegetables, may not be readily available to women in lower socioeconomic groups. Red blood cell folate levels of study and control group participants were measured several months into pregnancy. Red blood cell folate is considered the best measurement of folic acid levels. The investigation demonstrated that the mothers of offspring with NTDs had substantially lower red blood cell folate levels compared to women whose offspring were healthy; this difference was statistically significant. As this was a case-control study, it was not possible to be sure whether the low red blood cell folate was the cause of the neural tube defect or was the result of the NTD.[4]

In 1981, a prospective cohort study was reported from five British health centers among women who had given birth to one or more infants with NTDs and were planning to become pregnant in the near future. All women were offered folic acid supplementation and chose whether or not to take the supplements. Among women who were fully supplemented, 1 out of 200 had a NTD recurrence. Among women who were unsupplemented, 13 out of 300 had a NTD recurrence. The results took into account differences between the groups and the results were statistically significant.[5]

Two randomized controlled trials were published in 1991 and 1992. In the first investigation, women with a previous NTD were randomized to receive either 4 mg of folic acid supplement per day or placebo pills. NTDs recurred in 6 out of approximately 600 women randomized to folic acid supplementation, versus 21 among the approximately 600 randomized to the placebo or comparison group. This difference in NTD rates was statistically significant.[6]

In the second randomized controlled trial, women planning a pregnancy (in most cases their first) were randomly assigned to either receive folic acid or alternatively to receive a trace element supplement not containing folic acid. Pregnancy was confirmed in 4753 women. There were six cases of NTD in those assigned to trace element supplement as compared to zero among those assigned to the vitamin supplement group. The results were statistically significant.[7]

In 1992, the U.S. Public Health Service recommended that all women of childbearing age increase consumption of folic acid and/or take vitamin supplements with folic acid to reduce spina bifida and anencephaly. Follow-up public health surveillance studies found little change over the next few years in the level of red blood cell folate among women of childbearing age. In 1996, the U.S. Food and Drug Administration authorized low-level fortification of all cereal grain products with folic acid. Fortification, which is very inexpensive, became mandatory in both the United States and Canada in 1998.

A study in Canada before and after fortification was introduced looked at the incidence rates of NTD. A total of 2,446 births with NTDs were recorded among 1.9 million births between 1993 and 2002. The incidence of NTDs decreased from 1.58 per 1000 births per year before fortification to 0.86 per 1000 births per year during the full-fortification period, a 46% reduction.[8]

The rate of spina bifida and other NTDs has remained at these lower rates but continues to occur, suggesting the need for additional folic acid or, alternatively, that there are other contributory causes of NTD. Additional research continues to explore new interventions to prevent, detect, and treat spina bifida and other neural tube defects.

Discussion Questions

1. How does this case illustrate the problem component of the P.E.R.I.E. framework?
2. How does this case illustrate the etiology/efficacy component of the P.E.R.I.E. framework? Explain how the requirements for efficacy of folic acid were established.
3. How does this case illustrate the recommendation component of the P.E.R.I.E. framework?
4. How does this case illustrate the implementation and evaluation components of the P.E.R.I.E. framework?
5. What limitation of case-control studies is illustrated in this case study? Why is it important to take into account differences between the study and control groups in a cohort study?

WRAP-UP

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