CHAPTER

1

INTRODUCTION TO COST-EFFECTIVENESS

OVERVIEW

IMAGINE THAT you are the director of a large cancer society. Your day-to-day duties require you to conduct some research and oversee employees whose job is to compile data and make health recommendations. One morning you sit down with a cup of coffee and toast, and when you open the morning paper, you find that one of your society's recommendations—that women between the ages of forty and sixty receive screening mammography for breast cancer—has made the headline news: an elderly-rights group is suing your society. This group argues that your recommendation unfairly discriminates against the elderly because you have implied that women over the age of sixty should not be screened for breast cancer.

You rush to the office and find that the teams that made the recommendation are already in a heated meeting. They have split into two factions, and each group is now accusing the other of making bad decisions. But did they? You manage to calm everyone down and review the process they used to arrive at their recommendation. You learn that both groups were concerned that recommending mammograms for women over a wider age range might become very costly, thereby jeopardizing screening for women who might benefit from screening mammography the most.

One group argued that it made sense to screen older rather than younger women: mammography works better in older women, who have less dense breast tissue. Older women, they reasoned, were less likely to have a falsely positive mammogram and therefore would be less likely to suffer unnecessary procedures or surgery. Unnecessary interventions, they noted, place women at risk for surgical complications, are psychologically traumatic, are costly, and may do more harm than good.

The other group argued that it was unwise to actively screen all elderly women with mammography, because women who had breast cancer would die from other natural causes before the cancer had a chance to spread. After all, breast cancer can take over a decade to kill, and the life expectancy of older people is limited. Therefore, they reasoned, elderly women would be subjected to an uncomfortable and expensive screening test that would have little impact on the length of their lives. Besides, who would want to undergo chemotherapy in the precious remaining years of their lives?

Both factions made arguments based on sound scientific, economic, and social research, but which group was right? You and your employees decide to conduct a more extensive analysis of the costs and benefits of breast cancer screening and plan to send out a press release to this effect. But where do you start?

You might start by having a team estimate the likelihood that older women will die of breast cancer if they are not screened and have another team estimate the number of women who are likely to have false-positive mammograms at different ages. You might also wish to obtain information on the number of years of life that mammography will save, the quality of life for women who have different stages of breast cancer, and the psychological impact of a positive test result among women who do not in fact have breast cancer **(false-positive test results).** Because both teams were concerned about the costs of mammography, you may also wish to calculate the cost of screening mammography and the cost of all of the medical care that might be averted by detecting breast cancer at an early stage. Finally, because each team is interested in knowing whether women in both age groups might benefit from mammography, you decide that the costs and health benefits of screening each group should be compared to not screening women at all. If all of these factors were put together in a systematic manner, you would have conducted a cost-effectiveness analysis.

WHY COST-EFFECTIVENESS IS USEFUL

Now let's take a step back and consider why all of this is important in the first place. Certainly you want to know whether mammography is going to lead to net improvements or net declines in health. If it's only going to hurt people, we certainly don't want to do it. But if we know it helps, we also want to know whether it is affordable.

What does "affordable" mean when you are talking about human life? Take a moment to imagine what the society we live in could do with an infinite amount of money. We could build a huge public transportation system that eliminates car accidents, pollution, and noise. We could use only solar power and switch to 100 percent recycling, eliminating the major remaining causes of pollution; this would greatly reduce environmental carcinogens and oxidizing agents that cause cancer, heart disease, and premature aging. In addition, it would delay global warming, which threatens to put much of civilization under water, leading to countless deaths in the process. We could completely mechanize industry, eliminating occupational accidents. Finally, we could create a highly advanced health system that provides full MRI body scans and comprehensive laboratory screening tests for everyone in the population to ensure that cancers and other disorders are detected at the earliest possible stage.

As it is, there are very few nations that can even provide safe drinking water to all their citizens. The challenge, then, is to figure out how best to spend the money we have so that the quantity and quality of life can be maximized.

Thus, even if mammography screening for breast cancer is on the whole effective, it is conceivable that the money spent on it could save more lives if it went toward something else. Cost-effectiveness analysis helps determine how to maximize the quality and quantity of life in a particular society that is constrained by a particular budget.

We'll get deeper into this later in the book, but let's examine the specifics of the example to illustrate how resource allocation might work. Assume that the U.S. Congress decided to allocate $1 trillion to the competing health projects mentioned above. It could choose public transportation, greatly reducing pollution (a cause of pneumonia, cancer, and heart disease) and motor vehicle accidents (the fifth leading cause of death). It could invest in clean energy, reducing dependence on oil while reducing air pollution. Or it could choose the universal MRI strategy, detecting more tumor-producing cancers, some of which can be cured if detected early. If Congress knew the cost per year of life saved, it would know how to maximize the number of lives saved with the $1 trillion investment.

One thing that might strike some readers as a bit strange about this hypothetical situation is that we are essentially deciding who lives and who dies. If we save the mothers and fathers with cancerous tumors by opting for universal MRI examinations, many sons and daughters will die in car accidents as a result. Behind these numbers are real people affected by whatever decision is ultimately made. The more tangible the lives affected are, the more difficult the decision becomes.

As one famous physician, Paul Farmer (2004), points out, you cannot let a person die in front of you when you know that an effective treatment exists. Is the solution therefore to start a medical clinic, even if it comes at the expense of a more effective vaccination campaign? We might know that one intervention saves more lives than the other. However, when the most cost-effective intervention saves lives we will never see—lives that lie abstracted in numbers—it is more difficult to rationalize the choice.

Nevertheless, policymakers must often make abstracted decisions based on data from cost-effectiveness analysis, and these sometimes involve decisions that improve survival for one group at the cost survival for another. (We'll see an actual example of this later in the book.) These decisions become more abstract when quality-of-life issues are added to the mix of life-and-death issues.

ELEMENTS OF COST-EFFECTIVENESS ANALYSIS

Just as a driver really only needs to know about the accelerator, brake, and gearshift before driving a car for the first time, this section provides the basic parts of a cost-effectiveness analysis that you need to have in your head before you can start getting down to business.

Health Interventions

A **health intervention** can be a treatment, screening test, or primary prevention technique (for example, vaccinating children to prevent measles). Health interventions typically reduce the incidence rate of disease or its complications, improve the quality of life lived with disease, or improve life expectancy. Most produce some combination of these benefits. The benefits of a health intervention are referred to as **outcomes**. Health outcomes can assume any form, but the most common health outcomes are big picture items, such as hospitalizations prevented, illnesses avoided, or deaths averted (as opposed to little picture items, such as stomachaches reduced).

The first question that should pop into mind when speaking of the cost-effectiveness of a particular intervention such as mammography aimed at improving a health outcome is, Relative to what? Mammography will certainly appear cost-effective if we compare it to a total body scan for breast cancer. But it might not be cost-effective relative to educating women to perform breast self-examination in the shower on a regular basis. The intervention to which you are comparing the intervention of interest is called the **competing alternative**.

The Competing Alternative

Improvements in health states and improvements in length of life do not always go hand-in-hand. For instance, we perform mammography even though the procedure produces discomfort. Likewise, we provide steroids to patients with asthma even though this medication can be harmful over the long term. Such complications shouldn't be a deterrent. The whole point of cost-effectiveness, after all, is to examine the optimal course of action when there is considerable uncertainty. (Otherwise why bother with the analysis in the first place?)

Uncertainty also arises when one intervention is slightly more effective but costs considerably more than the competing alternative. In these instances, one cannot know whether more lives will be saved by spending the money on the more effective intervention or by purchasing the cheaper, less effective alternative and then spending the money saved on another lifesaving modality.

Virtually all health interventions cost something up front. But they also affect the amount of money spent on future medical care. For instance, a woman who is found to have breast cancer at an early stage will likely incur the cost of hospitalization and surgery in addition to the mammography, but the cancer may be cured, averting the future cost of more severe disease. Thus, mammography can produce value by averting disease and future costs. In short, the overall cost and overall effectiveness of any given alternative strategy are not often apparent on first glance.

So what is the net (overall) cost of mammography, and how much benefit can we expect? To answer this question, we first want a sense of how much of an improvement in health states we'll get from mammography over the long term.

Health States

While health outcomes such as deaths are concrete overarching measures of health, it is also important to examine more specific improvements in one's state of health, such as reduced pain or improved ability to walk. Specific states of health are quite logically referred to as **health states**. (Whoever said cost-effectiveness was difficult?)

Figure 1.1 shows how a health intervention improves health states. Here, we see that people having an asthma attack arrive at the emergency room with difficulty breathing (health state 1). The health intervention is to provide intravenous steroids and aerosolized medications to help such patients breathe. Typically, patients experience dramatic improvements in breathing once treated (health state 2).

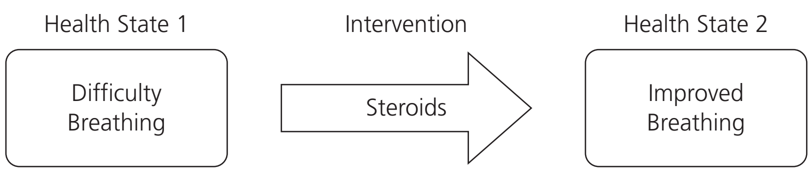

FIGURE 1.1. *Example of the Effect of a Health Intervention on the Health States of Patients Admitted to the Emergency Room for an Acute Asthma Attack*

Simple. So why the fuss? We wish to first think about this in very simplistic terms because we will later need to think about the various ways in which health states change when a medical intervention occurs, which can be somewhat complex. Collectively, improvements in health states add up to improvements in one's **health status**.

Health Status

A person's health status is the sum of his or her health states. If someone can jog and isn't anxious or depressed, we might say that the person has an excellent health status based on those two health states alone.

In a cost-effectiveness analysis, a researcher gathers information on the ways in which a health intervention changes the average health status of a group of people alongside costs (Figure 1.2). Imagine for a moment you are evaluating a treatment for bacterial pneumonia and comparing it to no treatment at all. In Figure 1.2, "health status 1" represents the collective health states of untreated people, and "health status 2" represents the collective health states of treated people.

Suppose were looking at treatment of bacterial pneumonia with antibiotics. Someone with bacterial pneumonia might have pain with breathing and a fever and be confined to bed. Someone who has been treated would have less pain and less fever and might be able to get around. In other words, the treated person would experience an improvement in health status.

Because health status is an amorphous concept, there is no direct way to measure it. Instead, cost-effectiveness analysis examines the quantity of life alongside a measure of the quality of life associated with a given health status. The point of a cost-effectiveness analysis is therefore to estimate what an improvement in health status will produce in terms of quality and quantity of life and how much it will cost to achieve these improvements.

We must also look at how health status (the collection of health states) changes over time. For instance, suppose you are again at your job at a major cancer society, and you are trying to decide whether to recommend screening mammography. Cancer evolves over many years. So we'll want to know how it will affect everything from a patient's ability to perform daily activities to her mental health as time goes on.

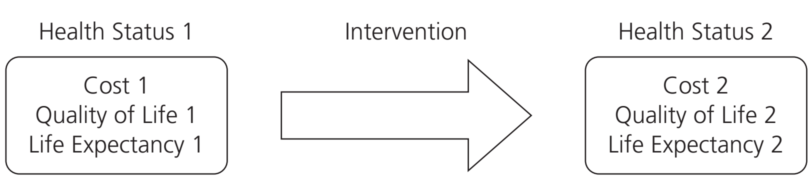

FIGURE 1.2. *Components of a Cost-Effectiveness Analysis*

Take another look at Figure 1.2 The quality of life in health status 1 for women screened for breast cancer is higher over the short term than it is in health status 2. Women in health status 1 have not undergone the pain of having their breast squeezed between two metal plates and do not have to face the pain and suffering associated with the diagnosis (or a misdiagnosis) of breast cancer if it is detected. In fact, since the cancer is producing no symptoms and the women do not know that they have breast cancer, they will be as subjectively healthy as anyone else over the short term. But the women in health state 2 (undetected cancer) may not have to face the pain and suffering associated with advanced breast cancer in the future.

Finally, the length of life is shorter for women who have not received a mammogram (life expectancy 1) than those who have (life expectancy 2). This is a critical factor that must be considered in any cost-effectiveness analysis. But what do we do with all this information on health status and life expectancy? Enter the **quality-adjusted life year (QALY)**.

The Quality-Adjusted Life Year

Consider the nuanced changes in the quality of life that occur when a person with diabetes is given a medication to lower blood sugar. At first, the patient has to take a pill and may think of herself as sicker than she did before being given the prescription. But over time, this pill might prevent a myocardial infarction, which would have a grave impact on the person's perception of her health and her ability to get around or to do other things she enjoys. In other words, it affects many different dimensions of this person's health, or many different health states. Together, real-world improvements in these health states, along with their effect on life expectancy that occur when a health intervention is applied, constitute the effectiveness of that intervention.

Just to drill the point home, a health outcome (such as a myocardial infarction) leads to changes in one's health states (ability to walk, work, or even to have sex), which in turn affect the person's quantity and quality of life. If we could somehow combine a measure of quality of life with a measure of quantity of life, we would be just about set in terms of measuring the effectiveness of any given health intervention.

As it turns out, we have just such a thing: the quality-adjusted life year, more affectionately known as a QALY, is a year of life lived in perfect health. At any given age, the average number of years we can expect to live is our life expectancy. Therefore, the average number of QALYs we can expect to live is our **quality-adjusted life expectancy (QALE)**. QALE is the average number of years one can expect to live in a state of perfect health. Throughout this book, you'll become increasingly familiar with what a QALY is, how it is calculated, and how it is used. For now, just accept that it is a year of perfect health.

Costs

For a moment, let's consider the changes in costs associated with mammography. The total cost of mammography includes those costs associated with the mammogram as well as future medical costs incurred as a result of this screening test. These future costs will include the value of lost work and the medical costs associated with treating cancer that was detected early.

Failing to provide a screening test also costs something. These costs include those associated with treating breast cancer that is so advanced that it is self-evident to the patient or is easily detectable on physical examination. People with advanced breast cancer will incur higher medical costs and miss more work than will those who were diagnosed early in the course of illness. All of these costs must ultimately be considered.

When comparing mammography to no mammography, the difference in costs, morbidity, and mortality is captured in the *incremental cost-effectiveness ratio*. This tells you how much you will need to spend to realize a unit gain in effectiveness.

THE COST-EFFECTIVENESS RATIO

Ratios put medical information into perspective. For instance, if a physician knows that there are 180,000 new cases of breast cancer a year in the United States, she will not be able to provide much information to a woman worried about developing that disease. If the physician knows that there are 11 new cases per 10,000 women each year, she will have a much better idea of how to communicate the risk.

Similarly, the cost-effectiveness ratio provides the consumers of our research with information that more readily allows comparisons. In fact, it provides a ton of information in one single number. The cost-effectiveness ratio not only provides information on cost, improvements in health status, and changes in life expectancy, but it also has a built-in comparison: it tells you how much you will spend to buy additional health relative to the competing alternative.

Let's take an example. Suppose you are working for a pharmaceutical company that just came out with a powerful new antibiotic for treating staphylococcus infection, Staphbegone. It is more effective than other antibiotics at saving life, but it's also much more expensive than what is now being used, Staphbeilln. But it will also get people out of the hospital faster, so it will reduce hospitalization costs and produce improvements in health-related quality of life.

We want to compare Staphbegone to Staphbeilln. We put Staphbeilln on the right-hand side of the equation because it is less effective. (This ensures that the ratio will be positive if the intervention costs money but improves health and negative if the intervention saves money and improves health.) If we call the old drug "intervention 1" and the new drug "intervention 2," the incremental cost-effectiveness ratio takes the form:

$$\frac{(\text{Cost of intervention 2} - \text{Cost of intervention 1})}{(\text{Quality-adjusted life expectancy 2} - \text{Quality-adjusted life expectancy 1})} \quad (1.1)$$

Here, quality-adjusted life expectancy is used in the denominator because this is the standard unit of effectiveness (more on standardization in the next chapter). However, in some cases (also discussed in the next chapter), other measures of effectiveness might be used. Some economists call these additional costs and effectiveness values

marginal values. In cost-effectiveness speak, they are generally referred to as **incremental values**.

Now, you should have a general idea of what cost-effectiveness is. You should also have an idea of what the incremental cost-effectiveness ratio means. In the next section, we move from what cost-effectiveness is to why cost-effectiveness analysis is a critical part of any well-functioning society.

EXERCISES 1 AND 2

1. Suppose that a complete course of Staphbegone costs $12,000 and a complete course of Staphbeilln costs $4,000. The average hospitalization costs $1,000 per day. Patients given Staphbegone have an average length of hospitalization of 5 days and Staphbeilln have an average hospitalization of 10 days. What is the incremental cost of Staphbegone?
2. Persons given Staphbegone have a higher survival rate than those given Staphbeilln. On average, those given Staphbegone can expect to go on to have a quality-adjusted life expectancy of 35 QALYs, while those given Staphbeilln go on to live 34.5 QALYs. Using the answer from exercise 1.2, what is the incremental cost-effectiveness of Staphbegone?

TIPS AND TRICKS

Answers to all self-study questions are presented in Appendix A.

WHY CONDUCT COST-EFFECTIVENESS ANALYSIS?

There are a number of ways to prevent or treat most diseases. For instance, breast cancer can be detected by self-examination, examination by a medical practitioner, screening mammography, ultrasound, spiral CT, or MRI. It is also possible to compare different levels of intensity of a single health intervention. For example, screening mammography might be performed every six months, every year, or every two years. Each of these competing alternatives is associated with a different effectiveness and a different cost. In the real world, many different approaches are used to diagnose or treat disease (Wennberg and Gittelsohn, 1982), some by crackpot medical practitioners.

Many students of cost-effectiveness analysis rightly question the logic of choosing interventions based on both cost and effectiveness criteria rather than effectiveness alone. After all, it is often argued, shouldn't we purchase the best treatments regardless of their costs? In the first section of this chapter, we saw that there is an almost infinite number of life-saving expenditures, including some combination of screening modalities. The question, then, is, Which ones can we afford? To answer this question, let's first consider what we mean by *cost* and what we mean by *effectiveness*.

Costs Matter

Even when the most effective modality is known, it may have unforeseen effects on human life if its use takes vital resources from other social programs. First, consider your personal budget. Suppose that you make $2,000 a month. Now suppose that your rent, minimum food purchases, basic utilities, and transportation come to $1,800. You could spend some of the $200 on going out to the movies and save the rest. Alternatively, you could live it up and go out to a fancy dinner and the theater five nights a month and live without electricity; go on an expensive vacation and not pay your rent; or blow the whole wad on that haute couture suit you've always wanted. Some of us can accept that it's not possible to consume everything we want. But when the goods and services we are consuming define who lives and who dies, the choices become much more difficult.

Consider the case of a tiny country with 100 people and a total health budget of $10,000 per year. If the country paid for expensive organ transplants, it could spend its entire budget on one person, leaving nothing for clean water, vaccinations, primary care, or other medical services that greatly prolong the quality and quantity of life for everyone in the country. If it instead spent $1,000 per year to keep vaccinations up to date, $7,000 per year for all needed antibiotics and basic primary care, and $2,000 per year on emergency surgery, many more lives would be saved. The value of goods and services in their best alternative use is the **opportunity cost** of an investment, such as a medical intervention.

Thus, just as your electricity bill has an opportunity cost, so too does vaccination.

FOR EXAMPLE

The Case for Education as a Health Expenditure

Basic schooling is thought to greatly reduce morbidity and mortality in both the industrialized and developing context. Education provides the cognitive skills and the social credentials needed for survival and adaptation to any ecological niche (Wilkinson, 1999). For instance, middle-class neighborhoods tend to have lower rates of crime victimization, access to healthier foods, and better housing. None of this is likely without an adequate education. Similarly, cognitive skills allow people to better assess hazards (such as taking the train instead of a bus in India), and may even reduce errors in medication dosage or compliance with medical prescriptions. As it turns out, education not only saves lives; it saves money (Muennig and Woolf, 2007). Therefore, it can be argued that basic education should be prioritized over the provision of basic medical services when resources are slim (Muennig and Woolf, 2007).

In circumstances where health funds are budgeted (and therefore fixed), cost-effectiveness analysis can provide information on how to realize the largest health gains with the money that you have (Gold, Siegel, Russell, and Weinstein, 1996; Ubel, DeKay, Baron, and Asch 1996). For instance, in a country with a national health system, interventions can be ranked in order of their cost-effectiveness. If we know how much will be spent on each health intervention in total, it becomes possible to go down the list until the money runs out. This is also known as **appropriate technology utilization**; if a government barely has money to pay for vaccination (an appropriate technology), it does not make sense to pay for heart-lung transplants (a technology that is inappropriate given the budgetary constraints).

The use of appropriate technology isn't always popular. A person who needs a heart and lung transplant and is dying in the hospital evokes more sympathy than the unseen hundreds of people who might benefit from all of the vaccines that could be purchased with the same sum of cash. However, in the absence of sufficient funding to cover all known treatments for all known diseases, prioritizing expensive and less effective interventions will ultimately lead to more illness and death.

In the United States, medical care is almost never denied to anyone who can afford it, and there is no absolute cap on how much is spent on health care. In this setting, cost-effectiveness analysis provides clinicians, policymakers, and insurers with general guidelines on which interventions might generally be preferable. For instance, an intervention that costs $100,000 for each QALY it produces relative to the next most effective alternative might be seen as expensive by some, but might be purchased by others.

While highly anecdotal, this lack of an emphasis on cost-effectiveness likely provides a partial explanation for why the United States spends around twice as much on health care as the next biggest spender but ranks twenty-fifth among developing nations in terms of life expectancy (World Health Organization, 2006).

In developing nations, where government health budgets may be as low as five dollars per person, the need for cost-effectiveness analysis becomes critical (Attaran and Sachs, 2001). When budgets are small, the use of inappropriate technologies can greatly increase mortality in the population as a whole. Why more so than in industrialized nations? Simply because forgoing the least expensive and most effective interventions such as vaccinations produces more harm than forgoing interventions that produce less spectacular gains and cost more, such as dialysis. The basis for such decisions therefore has at least as much to do with its effectiveness at a population level as its cost.

Effectiveness Versus Efficacy

Usually tests, treatments, or interventions are measured in terms of their **efficacy**. Efficacy reveals how a test, treatment, or intervention works under experimental conditions. Experiments tend to work better under the watchful eye of researchers in a controlled laboratory setting than in the real world. Subjects are watched to make sure they take their medications and that laboratory specimens are properly frozen and shipped immediately for testing. In the real world, conditions tend to be less exacting.

Experiments that measure efficacy also tend to look at only short-term outcomes. There is usually one test that is known to detect the most cases, a treatment that has the highest cure rate, or public health interventions that are most likely to prevent a disease. Each of these is often thought of as the most efficacious option for preventing or treating disease. But can we say that the use of the most efficacious interventions will detect the most cases of disease, have the highest rate of treatment success, or prevent the most diseases in the real world?

Often the answer is no. Not only are tests performed differently or medications taken in different doses in the real world, but a number of other things happen as well. For instance, screening tests and treatments are sometimes associated with hidden dangers. As we saw in the screening mammography example, a false-positive mammogram can lead to unnecessary surgery and psychological stress.

Moreover, most treatments can produce debilitating or fatal side effects in a fraction of the people taking them. Therefore, when we examine the effectiveness of a treatment at extending human life expectancy, we have to consider that the treatment can prolong life in one way but reduce life expectancy in another way. Thus, the real-world effects may be smaller than the efficacy of the treatment would suggest. **Effectiveness** indicates how well such tests, treatments, or programs perform in the real world.

By providing data on effectiveness, cost-effectiveness analysis provides information on how interventions are likely to work in everyday use. While supplementing cereal grains with the vitamin folate may greatly reduce neural tube defects in newborns, it may also lead to the underdiagnosis of vitamin B_{12} deficiency among poor or elderly populations (Haddix, Teutsch, Shaffer, and Dunet, 1996). When vitamin B_{12} deficiency is not diagnosed and treated early, it too can lead to severe neurological complications. Thus, the efficacy of a given treatment in preventing a disease may not be representative of its overall effectiveness at preventing death due to that disease.

THE REFERENCE CASE ANALYSIS

Cost-effectiveness analyses can take many subtly different forms. Consider the case of a local health department that wishes to know the cost of screening people for tuberculosis in its clinics. It may examine the cost per case of active tuberculosis prevented when patients are screened in its clinics (relative to not providing these screening exams). This type of analysis would furnish the health department with information useful for making specific internal decisions, such as whether it is worthwhile to spend money on such programs. However, it would not provide a good deal of information on the overall benefits of screening to the population it serves because it does not provide any information on the ill effects of tuberculosis itself.

Or the health department may wish to expand the analysis in order to obtain information on both the cost-effectiveness of its operations and its broader mission of improving the longevity of the population it serves. For instance, it may wish to determine the cost of the program per year of life saved as well as the cost per case prevented. This would also provide information for internal decision making and on how the programs are benefiting the populations that they serve.

Finally, tuberculosis is a severe disease that can require burdensome treatments and long stints in hospitals (sometimes in an isolated room), and it can have an impact on people's quality of life. The health department may therefore also wish to examine the cost of tuberculosis screening relative to improvements in the quality and quantity of life of the population it serves. This type of information would allow them to assess the impact of tuberculosis on mortality. It would also allow them to compare the cost of tuberculosis screening programs to programs that predominantly affect the quality of life, such as mental health programs.

While some health events, such as high-rise construction accidents, predominantly affect the quantity of life, others, such as repetitive stress injuries at work, predominantly affect the quality of life. When a measure of quality of life is added to a cost-effectiveness analysis, it becomes possible to compare health interventions across the spectrum of disease. (Recall that one QALY is a year of life lived in perfect health.)

The ability to make comparisons across different diseases opens up the possibility of standardizing cost-effectiveness analyses, so that the incremental gains associated with virtually any intervention can be compared with those of another. If the health department conducted its analysis based on the cost per active case of tuberculosis prevented, it would provide some information on how the new intervention compares with what it is doing now. But it wouldn't be able to compare its new intervention with other programs in the health department because the denominator is different. If it used life expectancy, the denominator would be the same. Therefore, it could compare the cost per life saved of the tuberculosis program with a program that aimed to prevent window falls.

But you would still miss the boat. A program designed to reduce repetitive stress injuries at work wouldn't save many lives. Therefore, no matter how good the program is, it will always seem less cost-effective than a program designed to prevent window falls. Here again, the QALY saves the day. By comparing interventions across a term that captures both quality and quantity of life, it becomes possible to measure the relative cost-effectiveness of each program in the health department—provided that costs, quality measures, and life years gained are all calculated in a similar way in each of the analyses. Under these conditions, it is possible to compare the incremental cost per QALY gained for health interventions as different as vaccination and migraine prevention. Of course, you need a standard set of methods to refer to if you are going to do this. This more or less standardized set of methods is called the **reference case analysis** (Gold, Siegel, Russell, and Weinstein, 1996).

The use of disparate approaches to cost-effectiveness analysis sometimes leads to widely different study results. For example, in the introduction to their book, the Panel on Cost-Effectiveness in Health and Medicine notes that the published cost-effectiveness of screening mammography for the detection of breast cancer varies from cost savings to $80,000 per life saved (Gold, Siegel, Russell, and Weinstein, 1996). The panel set methodological standards for conducting cost-effectiveness analyses in hopes of closing that gap. And the reference case was born.

The reference case is the most comprehensive type of cost-effectiveness analysis. It requires the use of QALYs as the unit of effectiveness to ensure that all studies have comparable outcomes. The reference case also requires that the study include all costs (regardless of who pays) that are likely to be relevant. In this book we focus on reference case analyses because it is important to know the rules of the reference case and because it provides the most comprehensive tool kit for conducting any type of cost-effectiveness analysis you wish.

FOR EXAMPLE

What's in a Name?

A lot of fuss is made over the distinction between *health* interventions and *medical* interventions (Gold, Siegel, Russell, and Weinstein, 1996). *Health* generally refers to public health programs, such as the provision of clean water or laws requiring grains to be fortified with vitamins. *Medical interventions* specifically refer to things that medical providers do, such as selecting the most appropriate antibiotic. In practice, the distinction is blurry. For instance, checking blood pressure might be considered a health intervention if it is done as part of a screening program, but a medical intervention if it is done to ensure that a patient is receiving the proper dosage of medication. In this book, we usually refer to both types of interventions under the general heading of "health."

Why would you want to conduct any type of cost-effectiveness analysis besides the reference case analysis? Consider the health department used as an example at the beginning of this section. If the department is interested only in internal decision making, a reference case analysis would provide superfluous information, such as private sector costs and patient costs. Therefore, a reference case analysis is not necessarily the best approach in all situations. (For more information, see "A Note on Methods" in the Preface to this book.)

You now should have a sense of what cost-effectiveness is, why it is important, and who it is important for. In the next section, we move on to how cost-effectiveness analysis is used to make policy decisions in health.

COST-EFFECTIVENESS ANALYSIS AND POLICY

We have noted that cost-effectiveness analyses are primarily used to compare different strategies for preventing or treating a single disease (such as tuberculosis). In addition, they can be used to maximize the quality and quantity of life within a given budget. In this section, we briefly explore how policy decisions are sometimes made using cost-effectiveness analyses, as well as some of the controversies that have arisen as a result of such policy decisions.

Prioritizing Health Interventions

It is possible to use cost-effectiveness analysis to purchase the most health under a fixed budget. If the incremental cost-effectiveness of everything that is done in medicine were known, we would have a sense of the opportunity cost of any health investment we might make (Jamison, Mosley, Measham, and Bobadilla, 1993. It would therefore be possible to list all interventions in a table and then draw a line between what is and is not affordable. When incremental cost-effectiveness ratios for different interventions are listed in a table, it is sometimes called a **league table** (Mauskopf, Rutten, and Schonfeld, 2003).

FOR EXAMPLE

Cost-Effectiveness in Developing Countries

Nowhere else is cost-effectiveness analysis more important than in developing countries. With annual health budgets as low as five dollars per person, efficiency is critical. Recognizing the need for better health purchases, the World Health Organization developed CHOosing Interventions that are Cost-Effective (CHOICE). CHOICE is a program that contains information on costs, mortality, quality-of-life measures, and completed cost-effectiveness analyses for each region of the world (http://www.who.int/choice/en/).

League tables can also be used to place a given intervention in context. For instance, suppose we know that mammography costs $30,000 per QALY gained relative to no mammography. We can't be sure whether this is expensive or cheap relative to other things done in medicine. However, suppose we know that treating an otherwise fatal bacterial pneumonia with a commonly used antibiotic costs $25,000 per QALY gained relative to no treatment. Then we know that $30,000 per QALY gained for mammography is in the ballpark of a treatment that most would agree should not be denied. But if treating bacterial pneumonia were found to cost $300 per QALY gained and heart-lung transplants in active chain smokers were found to cost $15,000 per QALY, then perhaps mammography wouldn't be such a reasonable thing to do.

Let's take a look at how else a league table might be used. Table 1.1 represents a hypothetical league table for a village in Malawi with a total health budget of $58,000. In this table, we rank a number of interventions by their incremental cost-effectiveness ratio relative to not providing the treatment at all. This ratio tells how much it costs to buy one year of perfect health.

TABLE 1.1. Hypothetical League Table for a Village in Malawi with a $58,000 Health Budget

Intervention	Incremental Cost-Effectiveness Ratio[A]	Size of Affected Population	Total Cost per Year
Measles vaccine	$375	5,000	$15,000
Sexually transmitted disease treatment	$420	300	$2,100
Pneumonia treatment	$428	150	$1,800
Mosquito nets	$846	22,000	$44,000
HIV treatment	$3,000	100	$30,000
Totals			$92,900

[A]The reference intervention is to do nothing.

If we know the size of the affected population and the total cost of the intervention, we know how much we will spend per year on any given strategy and the total number of QALYs we'll save. In this case, we only have $58,000, so we can't even provide the first four treatments, which collectively cost nearly $63,000. We might use this table to advocate for more funding or to figure out how we might reassess our interventions. For instance, prioritizing bed nets for children, who have not yet developed immunity to malaria, may be more cost-effective than providing them to family members who are older and less likely to succumb to the disease.

EXERCISES 3 AND 4

3. How many QALYs will $1,000 worth of measles vaccine purchase in this village?
4. A nongovernmental organization geared toward providing mosquito nets comes to a similar village in Malawi to the one represented in Table 1.1. This village has no health budget but wishes to provide $1,000 worth of mosquito nets. How many QALYs will be forgone as a result of spending the money on nets rather than on the measles vaccine?

However tempting it might be to create a list of interventions based on their cost-effectiveness, decisions surrounding the allocation of social resources cannot be made based on numbers alone. For example, HIV medications in Table 1.1 purchase a large amount of health for a small group of people, which might not be seen as fair for the village as a whole. Cost-effectiveness analysis does not provide ethical information; it is just one handy tool policymakers might use when deciding on which interventions they will fund (Gold, Siegel, Russell, and Weinstein, 1996). (Other examples of league tables can be found at: http://www.tufts-nemc.org/cearegistry/. For further discussion, including the limitations of league tables, please see Mauskopf (2003).

FOR EXAMPLE

Chile's Story: How to Succeed by Not Being Cost-Effective

Chile is attempting to create a national health plan, called "Plan Auge," that partly uses a league table to achieve its policy objectives. The idea is to start covering a small number of conditions and then scale up the program as time goes on. Rather than choose the most cost-effective interventions to start with, however, those who designed the plan deliberately chose inefficient but heart-warming treatments, such as chemotherapy for children. The result? An astounding success: the president invited the cured children and other patients for a press conference to tout the success of the program. This single media event defeated the resistance of insurance companies and the national medical association. At the time of printing this book, the list was up to over fifty conditions (A. Infante, personal communication, 2006).

Do Cost-Effectiveness Analyses Actually Change the Way Things Are Done?

Examples of policy decisions that have been influenced by cost-effectiveness analysis include strategies for reducing parasitic infections in immigrant populations (Muennig, Pallin, Sell, and Chan, 1999), conducting cervical cancer screening among low-income elderly women (Fahs, Mandelblatt, Schechter, and Muller, 1992), and adding folate to cereal grains in the United States (Haddix, Teutsch, Shaffer, and Dunet, 1996). These studies appear to have sparked changes in the way that patients received medical care in local health departments, changes in Medicare reimbursement policies, and changes in the rules set by the U.S. Department of Agriculture. Still, although Canada, Australia, and a number of European countries use cost-effectiveness to help decide what should be paid for and what should not, Medicare has not yet officially incorporated cost-effectiveness analysis into its payment policies (Neumann, Rosen, and Weinstein, 2005).

Cost-effectiveness analyses can also lead to policy changes with broader implications than the authors intended. For instance, when supplementing cereal grains was found to be a cost-effective strategy for preventing neural tube defects in the United States, cost-effectiveness analysis not only helped convince the food industry that it was worth the cost, but other countries also considered similar interventions (Schaller and Olson, 1996; Wynn and Wynn, 1998).

Cost-effectiveness analysis has also proven to be a controversial tool when used without taking the broader social implications of health interventions into account. For example, in the state of Oregon in the United States, cost-effectiveness analysis was used to prioritize health interventions paid for by the state government using a league table. Those interventions deemed unaffordable were not paid for, creating a large statewide and national outcry from groups denied treatment on these grounds (Oregon Health Services Commission, 1991; Oregon Office for Health Policy and Research, 2001).

These real-world examples highlight some of the promises and pitfalls of cost-effectiveness analysis for policy. Students embarking on this endeavor may one day find themselves facing tough ethical decisions for which there is no right answer. For instance, you may be working for a government that wishes to base immigration policies on preexisting conditions for applicants. Or you might be working for an insurance company that wishes to deny an effective treatment based on its cost-effectiveness. In such instances, consultation with an ethicist is paramount.