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CHAPTER

Economic Studies in Biosurveillance

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1. INTRODUCTION

Economic considerations often influence the selection, use, and even success of biosurveillance systems. Organizations, when acquiring or planning biosurveillance systems, take into account the considerable financial resources required to develop, use, and maintain such systems, as well as the feasibility and costs of recruiting and retaining capable personnel. Organizations consider the effects of false alarms, which result in the unnecessary mobilization of multiple resources. False alarms can be expensive and in the extreme case may lead to a boy-who-cried-wolf effect in which users of a system begin to ignore a system either partially or completely. Without a proper understanding of the tradeoffs between action and inaction discussed in the previous two chapters, users of a biosurveillance system may also under-react or delay response to early warning signs of an outbreak, potentially resulting in higher levels of injury, loss of life, and damage to the psychology, operations, and infrastructure of the affected region.

Economic studies can contribute to the rational selection, optimal use, and success of biosurveillance systems. An economic study is a formal scientific analysis of different choices that individuals, organizations, or societies have to make when resources are scarce. Economic studies can assist an organization in all phases of biosurveillance system operation: from acquisition to setting of alarm thresholds, to decision making in novel situations. In particular, economic studies of such decisions make explicit the choices available in each situation and the potential costs and rewards of each choice. Economic studies can provide guidance to organizations about how much and where to invest in biosurveillance and what level and type of biosurveillance to develop and maintain. They can provide guidance about whether to develop and configure a biosurveillance system that can catch subtle early warning signs but potentially generate many false alarms, or one that only looks for very suspicious warning signs but may miss insidious cases.

Although the field of economics is mature with many well-established techniques for conducting economic studies, researchers have only rarely applied these techniques to problems in biosurveillance. The economic subfield of biosurveillance is still in its infancy and is relatively uncharted territory. We expect this subfield to grow. For this reason, this chapter will review the strengths and limitations of existing economic techniques and provide examples of these techniques applied to the analysis of decision problems in biosurveillance and, in particular, the modeling of the consequences of outbreaks and bioterrorism. It will also discuss the challenges faced in applying economics in biosurveillance as well as potential future directions.

2. DEFINITIONS AND BASIC CONCEPTS

Economic studies come in a variety of forms, and economists have applied them to almost every sphere of human activity. An economic study can range in complexity from a simple "back-of-the envelope" calculation to a sophisticated model that requires substantial computer power for its evaluation. An economic study may focus on a single possibility or compare multiple alternatives. Despite the diversity of technique and domains found in the published economic literature, economic studies share several basic attributes.

2.1. Perspective

One of the most important attributes of an economic study is its *perspective,* which is the person or organization whose point of view or interests determine the costs and benefits considered in the study. For example, a publicly traded company may be primarily interested in protecting shareholder value, and therefore, an economic study commissioned by the company about the impact of a bioterrorist event might include only elements directly relevant to shareholder value and exclude costs of treating sick individuals other than those employed by the company.

The perspective of an economic study is important because available choices, costs, and benefits vary significantly depending on whom and where you are. For example, people in densely populated areas that are vulnerable to bioterrorist attacks may benefit more from biosurveillance than would people in remote rural areas who are less likely to experience such attacks. If the residents in both areas have to pay the same

amount of taxes (i.e., shoulder equal burdens of paying for the biosurveillance system), the rural residents may be less interested in such a system.

Every economic study should state clearly its perspective: whether it is taking the perspective of an individual, a particular institution or organization, a government body, or society in general. As you might imagine, changing the perspective of a study can drastically alter its composition and results. For any given decision situation, the optimal decision for one individual or organization may differ from that for another individual or organization. The perspective of the economic study should match that of the decision maker.

2.2. Retrospective, Prospective, and Model-Based Analyses

An organization or individual can perform an economic study of an event that has already transpired (retrospective analysis), will soon occur (prospective analysis), or could occur in the future (theoretical or predictive analysis). Each type of study has strengths and limitations and differs in feasibility. Retrospective studies are useful, because the past often repeats itself or helps predict the future. However, current and future situations may not mirror the past, and reconstructing past events can be difficult, especially without accurate and comprehensive data. Prospective studies, which involve collecting data while natural or created situations occur, give an analyst much more control over the situations and the information collected. However, prospective studies can be difficult and expensive to perform and only generate results representing specific situations. In the case of outbreaks, prospective studies may be nearly impossible, because the onset and timing of events are unpredictable and creating such an event would be unethical (and quite damaging to one's career). A limitation shared by both retrospective and prospective studies is that the studies are only feasible if the event has occurred or is likely to occur. Predictive studies overcome this limitation because the analyst builds a mathematical model or computer simulation of hypothetical situations. Because most outbreaks are uncommon and many types have never occurred, many biosurveillance-related economic analyses are at least partially predictive. A predictive analysis is always feasible. Moreover, it provides the analyst more flexibility in manipulating the situation that is being modeled to produce insights about a range of potential situations. The key limitation of a predictive study is that it rests on many modeling assumptions.

Often, answering a question requires a series of economic studies or an economic study that involves retrospective, prospective, and predictive elements. For example, in deciding whether to administer a certain vaccine, retrospective study of previous outbreaks and experience with vaccination programs can provide important quantitative data for a predictive economic model. Performing a prospective study, such as vaccinating a small representative sample of the population and tracking the ensuing costs and rewards, can provide additional estimates that facilitate projections about what would happen if a strategy was applied on a larger scale (e.g., the entire population). Retrospective and prospective analyses often provide data for a predictive analysis, such as a computer model of different potential outbreaks and the effects of vaccination programs.

2.3. Time Horizon

When conducting an economic study, an analyst should choose an appropriate time horizon or period that adequately captures the immediate and longer-term consequences of a decision or action, but does not make the study unrealistic to perform. For example, a study that only measures costs up to one month after a bioterrorist attack may seriously underestimate the impact of that attack because diseases and injuries can have long-term effects. Conversely, if the study attempted to measure the economic impact of that event 300 years into the future, it would clearly run aground on the banks of infeasibility, owing to the many uncertainties whose cumulative effect would be impossible to model. Analysts frequently face a tension between the benefit of increased fidelity from extending the time horizon of an economic study and the difficulty in constructing the model. The ideal balance between the two is often obvious from the specifics of the problem being modeled; nevertheless, it is the rule rather than the exception that economic modelers revise the time horizon as they develop a study.

2.4. Costs

One of the two major data inputs for an economic study is costs, which can be complicated to measure and very difficult to obtain. A cost is the cash value of money, time, and labor spent for goods or services. Although some costs (e.g., purchasing a stretcher) are relatively straightforward, others (e.g., the cost of caring for a tularemia patient) can include many component costs, such as nursing and physician time, diagnostic testing, medications, and emergency and hospital room occupancy. Each of these "subcosts" may be difficult to quantify and subject to error or variability.

2.4.1. Direct and Indirect Costs

Costs can be subtle or hidden. Even seemingly small events can have immediate and long-term effects on many different people and organizations. People do not even have to be present at the time and place of an event for it to affect them. For instance, a death or severe injury may influence the victim's family, friends, and workplace. Therefore, you must carefully account for every person and organization that may be reasonably involved and affected by an event. For example, a single successful small-scale bioterrorist contamination of a commercial building can lead to many direct costs, including the cost of diagnosing and treating the victims and the cost of decontaminating the building. However, it can also entail indirect costs to the company or companies occupying the building, including lost worker

productivity, the cost of finding replacement employees, and damage to the company's reputation and worker morale. When summed, these "hidden costs" can be considerable and even outweigh the more obvious direct costs.

2.4.2. Methods of Estimating Costs

Once you have identified the causes and sources of the costs, you must quantify them, which can be challenging. Rarely do items and services have clear price tags. Often, you must do a fair amount of sleuthing to determine what an item or service actually costs. There are many methods of gathering or estimating costs, each with its relative advantages and disadvantages:

Charges. In some cases, the *charges* for a service or visit found on hospital, clinic, and insurance bills can serve as reasonable proxies for costs. Of course, these charges usually exceed the actual costs; therefore, an economic modeler will convert them to costs by using established cost-to-charge ratios or conversion factors. Moreover, bills may not break down the charges to the level of detail needed. For example, an emergency department visit charge may aggregate many components (e.g., placing an intravenous line, transporting the patient to different locations) of the visit but not identify what fraction of the charge is associated with each component. Finally, charges often do not always accurately reflect the resources consumed or services provided, as some items and services are not billable and some items on a bill may not have been consumed.

Microcosting. *Microcosting* is typically more accurate than is using charge information, but microcosting is usually expensive and time-consuming to perform. Microcosting identifies every resource used during an event and then assigns a cost to each resource. Time-and-motion studies frequently help microcost. A time-and-motion study may involve following a patient (e.g., tularemia patient) during a given event (e.g., stay in the emergency department) and counting every item used (e.g., medications, catheters, saline, gauze, radiology film) and every service performed (e.g., 30 minutes of a nurse's time, 10 minutes of a patient transporter's time). An analyst would then assign a cost to each item and each fraction of personnel time and sum the costs to compute an overall cost. The use of microcosting tends to be limited to simple and well-defined events.

Resource-Unit Use. Another approach, *resource-unit use* or *health-service-resource use,* involves measuring resources that are more readily measured (e.g., number of hospitalizations, length of hospital stay, number of radiology procedures) and assigning unit costs (e.g., cost per hospitalization, cost per hospital day, cost per radiology procedure) to each resource. For example, if an anthrax attack resulted in a patient staying 30 days in the hospital, then multiplying the cost of a hospital day by 30 could estimate the per-hospitalized-patient cost of the attack. Of course, the resource-unit use method provides gross estimates, may not account for significant variability (e.g., fluctuation in cost of a day in the hospital), and assumes that the resource unit accurately reflects everything that is being done.

Other Resources for Costing. An analyst may obtain costs from the medical literature, insurance reports, or other publications. Before using these numbers in an economic study, one should ascertain whether the source is credible and the source's circumstances are comparable to the study at hand. For example, the cost of hospitalizing a patient for a simple uncomplicated case of diarrhea may not be applicable to a case of bioterrorist agent-induced diarrhea. If there is more than one source for a particular cost and the numbers vary significantly among the sources, the analyst may use either a simple or a weighted average of the costs.

2.5. Benefits

The other major data inputs for an economic study are the benefits of a successful medical, public health, or policy intervention, such as money saved, lives saved, quality-of-life improvements, productivity increases, suffering prevented, or adverse events avoided. An economic study should include benefits relevant to the interventions or actions under study. For example, measuring the number of lives saved by an acne cream would not be a useful measure of benefit, whereas improvement in quality of life (or number of dates saved) would.

Over the years, analysts have developed many measures of benefits, and new measures will emerge to fit the needs of different kinds of studies. The earliest economic studies expressed all benefit in purely monetary terms, converting all potential benefits of an intervention into dollars, pounds, yen, francs, etc. However, researchers soon found that they could not easily express all benefits in monetary terms. For example, they could not use monetary terms to capture completely the value of saving a life (e.g., a person contributes to society in many nonmonetary ways, such as providing emotional and psychological support to friends and families), so researchers began using "life-years saved" as a reward for some interventions. However, life-years saved could not adequately represent the benefits of some quality-of-life-improving interventions (e.g., pain medications, walking devices) that do not save lives or the suffering caused by non-life-threatening diseases. As a result, researchers developed quality-adjusted life years (QALYs) as a health status measure, with one QALY representing a year of perfect health and less than one QALY representing a year of impaired health. Researchers also have developed and used many other reward measures specific to particular classes of interventions, such as the number of bypass operations prevented to measure the success of cardiac medications.

2.6. Discounting

If the time horizon of an analysis is longer than a year, an analyst will discount future costs and benefits. The practice of

discounting recognizes that inflation and opportunity costs (i.e., the value of the next best alternative that you must forego when you make a choice) make a dollar (or any other cost or reward) in the future worth less than a dollar today. An analyst uses discount rates to adjust future costs and rewards to present day values. A discount rate, denoted typically by r, is the rate used to convert future costs or benefits to their present value.

For example, if C_n represents a cost n years from now and r is the discount rate, C_0 (i.e., the current or net present value of C_n) is $C_n/(1 + r)^n$. Although typically researchers use a discount rate between 3% to 5%, there is still considerable debate over the exact appropriate rate (van Hout, 1998; Gravelle and Smith, 2001; Brouwer and van Exel, 2004). By using a 3% discount rate in the above formula, an intervention that earns a $100 ten years from now will be worth $\$100/(1 + 0.03)^{10} = \$74.41$ in today's dollars.

3. TYPES OF ECONOMIC ANALYSES

Economic studies relevant to biosurveillance can be of several types, which we summarize in Table 31.1 and discuss in this section.

The question often dictates the appropriate method. For example, do we want to know the magnitude of a problem to help decide the course of action? Are we unsure about how much money to invest in a given strategy? If a strategy has different "settings" or "calibrations," how should they be set? An analyst selects the appropriate method for a study after first defining the question. In many cases, one analytic method will not be enough, and only a progression of different methods will answer a question.

3.1. Cost-of-Illness

A *cost-of-illness* study can quantify the magnitude of a problem. It can quantify a disease's total monetary effect, including all the resulting medical costs and, if necessary, loss of productivity. A well-performed cost-of-illness study will estimate not only the total cost but also different categories of cost, such as the amount spent on medications, hospitalizations, emergency care, and days off from work, allowing one to target the areas of greatest economic burden. Often, the first step in tackling a new and unfamiliar problem is a cost-of-illness study to "map out" the problem.

3.2. Cost-of-Intervention or Treatment

After quantifying the magnitude of a problem (sometimes referred to as *profiling* the problem), a *cost-of-intervention* or *cost-of-treatment* analysis can estimate the cost of possible solutions. These studies calculate all the monetary costs associated with executing a solution. Such studies should include and clearly identify every important fixed and variable cost. Running multiple scenarios may show how variable costs change with different situations. Such studies can help decision makers allocate an appropriate level of funds and identify particularly costly aspects of the solution that may be targets of cost reduction.

3.3. Cost-Minimization Analysis

After one profiles the possible solutions, a *cost-minimization analysis (CMA), cost-benefit analysis (CBA), cost-effective analysis (CEA)* or *cost-utility analysis (CUA)* can help choose among multiple alternative solutions. The type of problem guides the choice of analysis.

If all alternatives yield identical rewards, a CMA, which focuses only on costs, can help choose the least costly possibility. For example, if medication A and medication B have the same success rate in treating a disease, a CMA might find that medication A should be used because it costs $200 less. This type of analysis seems to apply to only a small number of not-too-difficult decisions in biosurveillance, such as which of two identical surveillance systems to purchase. We note that formally asking and conducting such a study will have the benefit of requiring clarity about whether two systems are equally effective.

3.4. Cost-Benefit Analysis

A CBA is suitable when the potential benefits are different but easily translate to monetary terms (e.g., dollars, yen, pounds).

TABLE 31.1 Types of Economic Studies Relevant To Biosurveillance

Type of Study	Typical Cost Units	Typical Benefit Units	Types of Biosurveillance Decision That Can Be Analyzed
Cost-of-illness	Dollars	N/A	Quantify a disease or outbreak's total monetary effect
Cost-of-intervention/treatment	Dollars	N/A	Profile the costs of interventions and treatments
Cost-minimization analysis	Dollars	Benefits must be identical	Choose between alternatives (systems, response strategies) that have the same benefits but different costs
Cost-benefit analysis	Dollars	Dollars	Choose between alternatives in which all the costs and benefits can be expressed in monetary terms
Cost-effectiveness analysis	Dollars	Clinical measures such as *life years saved* or *deaths averted*	Choose between alternatives in which benefits are expressed in clinical measures
Cost-utility analysis	Dollars	Health status measure such as *quality-adjusted life years* (QALYs)	Choose between alternatives in which benefits are expressed in health status measures

So, for instance, a CBA may compare building a $20 million wall with building a $10 million wall to protect a $100 million building. Let us assume that the $20 million wall would save the entire building during an explosion while the $10 million wall would only save half of the building, or $50 million. Then, a CBA would find the $20 million wall (which would provide a net benefit of $80 million = $100 million – $20 million) to be more favorable than the $10 million wall (which would offer only a net benefit of $40 million). The analysis in Chapter 29 is a CBA.

3.5. CEA and CUA

However, if all the potential rewards do not translate easily into pure monetary terms, a CEA (which measures rewards in simple clinical units such as life years saved, deaths avoided, or operations avoided) or a CUA (which measures rewards in health status measures such as QALYs or utilities) is more useful. Because it can be difficult to quantify the economic value of saving a single life or avoiding a medical procedure, a CEA and CUA will measure the costs and benefits of each alternative separately and compare the alternatives by using incremental cost-effectiveness (or cost-utility) ratios, described in the next section.

3.6. Marginal and Incremental Analyses

Incremental analyses quantify the resulting differences in choosing one alternative over others. An incremental analysis can tell you whether strategy A is more preferable than B, but will not tell you in absolute terms whether either strategy is better than doing nothing.

In CBAs, the *incremental cost* indicates the change in cost when moving from one alternative to another. For example, if cb_x and cb_y are the net costs and rewards of strategies X and Y, respectively, then the incremental cost of using strategy Y instead of X is $cb_y - cb_x$. A negative incremental cost suggests that strategy Y is preferable over X, whereas a positive one favors X.

Similarly in CEAs, an *incremental cost-effectiveness ratio (ICER)* is the change in cost per change in effectiveness when shifting from one alternative to another, and in CUAs, an *incremental cost-utility ratio* is the change in cost per change in health status when shifting from one alternative to another. For example, if C_A and C_B are the costs of strategies A and B, respectively, and E_A and E_B are the resulting effectiveness (benefit) of A and B, respectively, then the ICER is $(C_B - C_A)/(E_B - E_A)$. Interpreting this ratio is somewhat more complicated than is interpreting an incremental cost. If the ICER is negative, then strategy B is favorable or dominant to strategy A. If the ICER is positive, then the magnitude of the ICER matters. If for instance, the ICER is $10 per life year saved, then choosing strategy B requires only $10 more for each life year saved. Most, except for the most penurious, would view this as a worthwhile investment and choose B. However, if the ICER were $100,000 per life year saved, then decision makers would have to debate over whether this reward is worth the investment. There is extensive literature debating the appropriate threshold dollar value per life year (Gold et al., 1996; Neumann et al., 2000; Hershey et al., 2003; Ubel et al., 2003).

Marginal cost and marginal cost-effectiveness studies can help reveal the implications of changing a certain parameter (e.g., number of medications given, dollars invested, items used, people employed) by a single unit. For example, in a CBA, to measure the added cost of giving every patient an extra day of a medication, if C_N represents the net monetary value of giving a medication for N days and C_{N+1} is the net monetary value for giving it $N + 1$ days, then the marginal cost would be $C_{N+1} - C_N$. In a CEA, if C_N and E_N represents the cost and effectiveness, respectively, of giving a medication N days and C_{N+1} and E_{N+1} represent the cost and effectiveness, respectively, of giving the medication $N + 1$ days, the marginal cost-effectiveness of an additional day of medication is $(C_{N+1} - C_N)/(E_{N+1} - E_N)$. A similar calculation would yield a marginal cost-utility in a CUA.

3.7. Decision Analysis and CEA and CUA

The procedure to perform a CEA or CUA is similar to procedure described in Chapter 29, except that each branch in the decision tree has two sets of outcomes (i.e., costs and effectiveness measures or costs and utility measures) instead of just one (i.e., the net costs and benefits denominated in dollars). Therefore, you will need to fold back costs separately and then effectiveness or utilities separately before combining them in ICERs. By using the example in Chapter 29, Figure 31.1 shows the same decision tree structure as Figure 29.3 with one difference: each branch has a cost outcome (C_1,C_2,C_3,C_4) and an effectiveness outcome (E_1,E_2,E_3,E_4). So if C_1 was equal to cb_1 or –$89,315,780.49, C_2 was equal to cb_2 or –$8,025,000, C_3 was equal to cb_3 or –$115,454,219.50, and C_4 was equal to cb_4 or –$115,454,219.50, then folding back the costs would yield an expected cost value of *act now* of –$11,357,922 and an expected cost value of *wait* of –$4,733,623. Now, if both E_1 was equal to 10,000 life years saved, E_3 was equal to 10 life years saved, and both E_2 and E_3 were equal to 0 life years saved, then the expected life years saved for *act now* would be $p \cdot E_1 + (1 - p) \cdot E_1 = 0.041 \times 10{,}000$ life years saved + 0.959×0 life years saved = 4.1 life years saved. The expected value of *wait* is $p \cdot E_3 + (1 - p) \cdot E_4 = 0.041 \times 10$ life years saved + 0.959×0 life years saved = 0.41 life years saved. The ICER of *act now* would then be [Expected $\text{Costs}_{\text{actnow}}$ – Expected $\text{Costs}_{\text{wait}}$]/[Expected $\text{Effectiveness}_{\text{actnow}}$ – Expected $\text{Effectiveness}_{\text{wait}}$] or [–$11,357,922 – (–$4,733,623)]/[10,000 – 10] = $16,173 per life year saved.

4. SENSITIVITY ANALYSES

Because it is impossible to collect perfect data, an analyst frequently has to make a series of assumptions based on findings from prior studies, expert opinion, educated guesses from

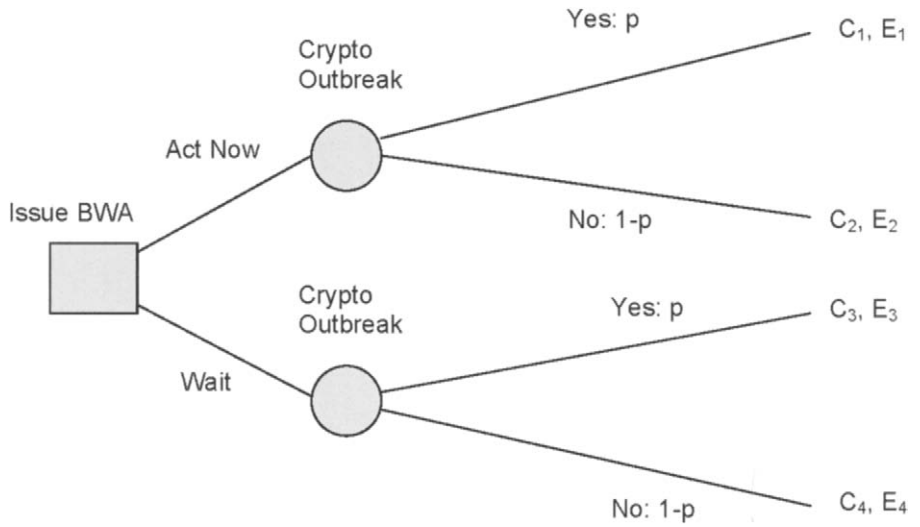

FIGURE 31.1 Decision tree for a cost-effectiveness analysis. This tree is identical to that for the cost-benefit analysis in Chapter 29 (Figure 29.3), except the leafs of the tree are pairs of numbers corresponding to dollar costs *(C)* and a measure of effectiveness *(E)* instead of a single number representing net benefit in dollars (*cb* in Figure 29.3).

personal experience, or, in some cases, truly random guesses. The study assumes that available information about costs and other model parameters is accurate, and make estimates for model parameters for which published data are not available. As a result, an economic study is only as strong as the information on which it rests, including its assumptions. For this reason, an organization or other consumer of an economic study must be aware of all assumptions and their accompanying reasons. Although some assumptions may be minor and have little bearing on the study results, others may be very controversial and dramatically influence study conclusions. Sensitivity analyses can help ascertain the impact of these assumptions.

Sensitivity analyses involves changing important variables along a range of different values and measuring the consequent effects on the results. For example, what would happen to the results if the discount rate varied from 2% to 6%, the cost of a specific medication ranged from $100 to $500, the percentage of people receiving a certain test changed from 40% to 60%, or the study excluded certain costs that were previously included? Running these different scenarios will not only identify the variables that have an important impact on the results but also demonstrate the credibility of the economic study. An economic study that does not change significantly is considered "robust"; i.e., most analysts would consider its results definitive. However, an economic study with results that fluctuate significantly during sensitivity analyses is not necessarily useless. The sensitivity analyses can help target the items and issues that are most responsible for the costs and rewards of a situation. If, for example, if the results of a study depend heavily on medication costs, then one may make extra efforts to either reduce the cost of medications or find alternative treatments.

5. EXAMPLES OF ECONOMIC ANALYSES IN BIOSURVEILLANCE

The following examples demonstrate how economic studies can address many issues important to biosurveillance. In each case, understanding of the above principles of economic analysis will help a reader (a consumer of these published studies) to catch more subtle implications from the study. Rather than accept or reject a final conclusion, one should fully discern the set of steps that led to that conclusion. Even if the results are not applicable to a decision maker's specific situation, components of the analysis may be. In fact, many times the greatest value of a study is not in the answers it provides, but instead in the questions that it raises. A study such as the boil-water CBA in Chapter 29 may focus decision makers on the key parameters or the crux of the matter. Economic studies may identify the need for additional future studies. In addition, there may be multiple approaches in dealing with a given decision or problem. Therefore, for each issue, although the selected examples offer important teaching points, they are not necessarily the best or most definitive studies.

5.1. How Significant Is the Threat?

Corso et al. (2003) conducted a retrospective cost-of-illness study of the 1993 Milwaukee *Cryptosporidium* outbreak. This study is a good example of a study that used multiple disparate sources to profile the economic impact of an outbreak. The analysts conducted a telephone survey of a random sample of

Milwaukee residents to estimate the total number of people affected by the outbreak, the percentages who sought different levels of medical care, the length of illness for those who did not seek medical care, and the total number of work days missed. The investigators also selected a representative sample of patients who sought medical care and reviewed each patient's medical chart to determine the medical resources (e.g., medications, diagnostic tests, emergency medical services) each patient consumed. They then used billing records to obtain the associated hospital charges. They used the Wisconsin 1993 average urban hospital and emergency department cost-to-charge ratios (0.70 and 0.67, respectively) to convert charges to costs.

As with most economic studies, the investigators made assumptions about information that was not readily available and used standard industry and government sources to estimate some costs. For example, they assumed patients with mild illness would self-medicate themselves with either loperamide or oral rehydration solution for 50% of the duration of illness. They used 1993 retail drug prices to estimate the unit cost of each medication. The City of Milwaukee Health Department provided data on the average cost of a single outpatient physician visit.

The study demonstrated not only that the outbreak had a substantial economic impact (in Milwaukee, $96.2 million) but that decreased worker productivity represented the largest economic consequence of the outbreak ($64.6 million), a finding confirmed by studies of outbreaks of other diseases such as severe acute respiratory syndrome (SARS) (Achonu et al., 2005) and hepatitis A (Sansom et al., 2003). One implication of these studies for biosurveillance economic analyses is that any cost-of-illness study that fails to include productivity losses may seriously underestimate the potential impact of an outbreak. Outbreaks can be devastating to not only the health care system and directly affected individuals but also many businesses and the economy. This result, if further developed, may perhaps persuade individuals and organizations initially uninterested in biosurveillance to reconsider their stance. In fact, the Milwaukee study actually underestimated productivity costs by not accounting for the lost lifetime productivity of those who died from the outbreak, the degree to which the outbreak diverted companies and the government from daily normal operations, and the damage the outbreak had on consumer and public confidence.

5.2. What Investigation and Response Options Are Available?

Cost-of-investigation/response studies can identify which potential investigation and response options are economically feasible. No matter how effective, a prohibitively expensive response option may not be possible. In addition, this type of analysis can guide the structure of more detailed analyses. An analyst may exclude relatively expensive investigation and response options such as mobilizing the Strategic National Stockpile from a study of the appropriate initial actions for a low probability alert.

Costs-of-investigations/responses have not been well studied; in some cases, cost-of-investigation/response analyses are included almost as afterthoughts in overall cost estimates that focus mainly on cost of illness. In some of these studies, the cost-of-investigation appeared to be relatively small compared with the overall economic burden of an outbreak, accounting for less than 5% of the total costs in a *Salmonella* outbreak (Cohen et al., 1978) and less than 3% in a New Mexico botulism outbreak (Mann et al., 1983). In other studies, such as Zhorabian et al. (2004) study of the 2002 Louisiana West Nile virus outbreak, the cost-of-response is a sizable percentage of the overall costs ($9.2 million of the $20.1 million total in the West Nile virus study). However, depending on retrospective cost-of-illness studies to determine costs-of-investigation is fraught with problems. The type and degree of response depend on the severity, nature, and location of the problem. Moreover, there is considerable regional and potentially temporal (e.g., varying by time of day, day of week, and month of year) variation in response mechanisms. In addition, some locations have antiquated accounting systems (Roberts et al., 1989; Bownds et al., 2003), making it difficult to accurately capture all costs. Therefore, there is a need for predictive studies.

An example of a predictive study is the evaluation by Gupta et al. (2005) of whether mass quarantine during a SARS epidemic would be cost saving, life saving, or both. They estimated the direct costs of SARS by the following formula:

Direct Cost of SARS/person =
[(probability of hospitalization) ×
(Average Hospital Length of Stay) ×
(Cost per hospital day)]
+
[(probability of an intensive care unit stay) ×
(Average ICU Length of Stay) ×
(Cost per ICU day)]

They calculated the indirect costs or the lost productivity using the following:

Indirect Cost of SARS/person =
[(Average Hospital Length of Stay) ×
(Average Daily Wage)]
+
[(Probability of Death) ×
(Years of Potential Life Lost) ×
(Annual Salary)]

In the second formula (and in many economic studies), the cost of a death is equivalent to the total value of the victim's potential future earnings. (This means that people are only worth as much as they can potentially earn in their lifetimes. Of course, some may take issue with this contention, but that is a discussion best left for another time.) The following formula generated the cost of quarantine:

Total Cost of Quarantine =
[(Number of People Coming into Contact with SARS) × (Incubation period of SARS) × (Average Daily Wage)]
+
Fixed Administrative Costs

As can be seen, lost worker productivity is one component cost associated with quarantine. In the 2003 Toronto outbreak, the fixed administrative costs associated with quarantine were around $12 million. The component owing to lost productivity was $1140 per person quarantined, for a total of $0.2 million for the primary wave, $1 million for the second wave, and $5 million for the tertiary wave of the Toronto outbreak. The following equation yielded the net savings from quarantine:

Net Savings =
[(Total Cost of SARS/person) × (Total Number of Infections-number infected before Quarantine)]
−
Total Cost of Quarantine

In other words, the net savings is the difference between the number of SARS cases prevented times the total cost of SARS per person and the total cost of quarantine. The investigators found that mass quarantine would not only save lives but also costs: $279 million during the primary wave of a SARS epidemic, $274 million during a secondary wave, and $232 million during a tertiary wave.

5.3. What is the Value of Rapid Response?

As is often said, time is money, especially in biosurveillance, in which delays in response can have significant consequences. Early action can lead to effective containment of a threat, and prompt measures can minimize disruptions in government and business operations. Many treatment options are only effective very early in an outbreak. Because biological agents used by terrorists would be expected to kill quickly, a tardy response can result in substantial morbidity and mortality. A predictive CBA, such as Kaufmann, Meltzer and Schmid's simulation of three types of bioterrorist attacks (with *Bacillus anthracis, Brucella melitensis,* and *Francisella tularensis*) over a major city suburb of 100,000 people, can help quantify the cost of such delays.

Because outbreaks of *B. anthracis, B. melitensis,* and *F. tularensis* have been rare, the investigators in this study had to make a number of assumptions to create an economic model involving extrapolations from available data. First, the investigators assumed that the spread (e.g., weather conditions would be ideal and the agents would travel with prevailing winds), physical and biologic decay (minimal decay), and infectivity of the agents (ID_{50} = infectious dose 50% = the number of infectious particles (spores, viral particles, bacteria, etc.) needed to cause disease in 50% of the people who are exposed of 20,000 spores of *B. anthracis* or 1,000 cells of *B. melitensis* or *F. tularensis*) would be uncomplicated. Then, data from the few previous outbreaks of these agents helped forecast how soon patients would develop symptoms and die after exposure. Next, extrapolations from published laboratory and clinical experimental data supplied the clinical efficacy of administering different antibiotic interventions to the exposed population. The investigators also postulated that 90% of the exposed population would participate in the treatments.

The analysts obtained cost estimates from several different sources and used the following formula to calculate the potential economic benefit of each antibiotic intervention program:

Net savings =
Number of Deaths Averted × Present Value of Expected Future Earnings
+
(Number of Days of Hospitalization Averted) × (Cost of Hospitalization)
+
(Number of Outpatient Visits Averted × Cost of Outpatient Visits)
−
Cost of Intervention

Once again, the cost of a death was equivalent to the present value of the victim's potential future earnings. The investigators derived age- and sex-specific salary data from the U.S. census and adjusted these numbers to match the age and sex distribution of their theoretical suburban population. They used discount rates of 3% (in one set of scenarios) and 5% (in another set) to express all future earnings in current dollars. The cost per day of hospitalization came from multiplying an average single hospital day charge ($875 in 1993 from the National Center for Health Statistics) by the April 1994 New York State cost-to-charge ratio (0.635) and adding a cost of $65 per day for missing work (lost productivity to society), a figure frequently used by health economists. To tabulate outpatient costs, they surmised the number of outpatient visits that victims would require and then used Medicare average allowance data to derive the cost per outpatient visit. The 1996 *Drug Topics*

Redbook provided prices to calculate the costs of the antibiotic interventions.

The study included multiple scenarios that varied in the period between the initial release of biological agent and antibiotic intervention, and found that a rapid response was the single most important means of preventing significant mortality, morbidity, and accompanying costs. In the absence of any intervention (antibiotic or vaccine), *B. anthracis* was most costly to society (ranging from $18 billion to more than $26 billion), followed by *F. tularensis* ($3.8 billion to more than $5.4 billion) and a *B. melitensis* ($477 million to more than $579 million). The potential cost savings of antibiotic interventions may be huge if initiated during the first day after the attack, but savings exponentially shrink with each passing day. For example, for an anthrax attack, antibiotic prophylaxis could save somewhere between $14 billion and $22 billion if administered on the day of the attack, $12 billion to $20 billion when administered the day after the attack, but only $5 billion to $8 billion when administered three days after the attack.

5.4. How Much Should One Pay for "Insurance" against an Attack or Outbreak?

Investing in biosurveillance (and other types of emergency preparedness) is analogous to taking out an insurance policy for protection against accidents, disability, death, or natural disasters. Similar to an accident, an outbreak or attack may occur at any moment or location. Although on most days, carrying an "insurance policy" may feel like paying a cost without obvious rewards, it is actually protection against that uncommon but potentially catastrophic occurrence. Therefore, to realize what "premium" is fair to pay for such "insurance," one must factor in the risk and the cost of the occurrence as well as the risk reduction that the "insurance policy" provides. CBAs, such as the analysis of Meltzer et al. (1999) of vaccination responses to a simulated U.S. influenza epidemic, can help ascertain the fair premium for such insurance.

In this economic study, investigators used prior clinical studies, charge data, and salary information to evaluate the economic benefit of employing different mass vaccination strategies to curtail a theoretical influenza pandemic. The analysts identified the diagnosis codes (International Classification of Diseases, Ninth Edition [ICD-9]) associated with each possible clinical sequela of influenza, such as pneumonia, bronchitis, and exacerbations of pre-existing conditions (e.g., heart disease), and searched health insurance claims data to calculate the average charges associated with each code. Previous clinical studies furnished the risk of each outcome for each age and risk category (high risk versus not high risk for contracting influenza). Age- and sex-weighted average wage data helped estimate lost productivity for each outcome. As before, the economic cost of a death was equal to the present value of how much the victim would have earned in his or her remaining lifetime. By use of this procedure, the investigators estimated that without large-scale immunization, an influenza epidemic would cost somewhere between $71.3 billion and $166.5 billion. The majority of these costs would come from deaths, suggesting that vaccine strategies should target those patients most likely to die from influenza.

The investigators then computed the economic value of different vaccination strategies (ranging from vaccinating specific populations to vaccinating the entire population), while varying the influenza attack rates, vaccine effectiveness, the rates of people vaccinated (i.e., compliance), and vaccine costs ($21 and $62). The investigators calculated the net returns of vaccinating each different age and risk category by the following formula:

$$\begin{aligned}\text{Net Returns}_{\text{age, risk group}} = {} & \text{Savings from Outcomes Averted in Population}_{\text{age, risk group}} \\ & - \\ & \text{Cost of Vaccination of Population}_{\text{age, risk group}}\end{aligned}$$

The "Savings from Outcomes Averted" for each age and risk group came from

$$\begin{aligned}\text{Savings from Outcomes Averted}_{\text{age, risk group}} = {} & \text{Number with outcomes before intervention}_{\text{age, risk group}} \times \\ & \text{Compliance} \times \text{Vaccine Effectiveness}_{\text{Outcomes}} \times \\ & \text{Value of Outcome Prevented}\end{aligned}$$

The "Cost of Vaccination of Population" for each age and risk group came from

$$\begin{aligned}\text{Cost of Vaccination of Population}_{\text{age, risk group}} = {} & \text{\$Cost/Vaccine} \times \text{Population}_{\text{age, risk group}} \times \\ & \text{Compliance}_{\text{age, risk group}}\end{aligned}$$

The cost per vaccinated person included the cost of the vaccine, the distribution and administrative costs, patient travel, time lost from work, and side effects, including Guillain-Barre syndrome.

According to the study, the amount of "insurance premium" to spend on maintaining proper influenza preparedness ranges from $48 million to $2,184 million annually. The investigators calculated this premium by using the following formula:

$$\begin{aligned}\text{Annual Insurance Premium} = {} & \text{Net returns from an intervention} \times \\ & \text{Annual probability of a pandemic}\end{aligned}$$

The results of this study suggest that the United States should be willing to spend somewhere between $48 million and $2 billion per year to prevent an influenza pandemic, depending on which assumptions one uses. Moreover, although the influenza attack rate, vaccine effectiveness, and compliance

all affect this premium, the probability of the pandemic was the most important driving factor. This implies that ongoing monitoring and threat assessment is important, as determining the risk of pandemic will help determine the appropriate level of vaccination.

5.5. What Is the Economic Value of an Intervention?

Often, the economic benefits and penalties of an intervention are not necessarily obvious, and economic studies can better elucidate the true value of the intervention. For example, the CUA by Khan et al. (2005) compared different response strategies to a hypothetical SARS outbreak in New York City. Because SARS can be very difficult to distinguish from other illnesses (e.g., caused by influenza, respiratory syncytial virus, *Bordetella pertussis, Legionella pneumophilia*) that cause respiratory symptoms and fever, i.e., febrile respiratory illnesses (FRI), the investigators wanted to see the value of home isolation versus testing (for SARS or other common diseases) of patients with FRI. Their analysis included a variety of costs (such as transportation, laboratory tests, influenza vaccination, antimicrobial agents, hospitalization, public health investigation, and patient time) and used the Health Utilities Index Mark 3 (HUI) to estimate the changes in health-related quality of life from different situations such as home isolation. The study revealed that using a test (multiplex polymerase chain reaction [PCR] assays) to diagnose other common respiratory infections[1] would save $79 million and 8,474 quality-adjusted life-years over home isolation.[1] Adding SARS testing to the multiplex PCR assays would actually cost $87 million more and decrease utility. The explanation for this less-testing-is-better result is that causes of FRIs other than SARS are much more common than is SARS; therefore, SARS testing would generate false positives, resulting in more patients without SARS erroneously isolated. This study is an excellent example of how additional information provided by testing could actually be suboptimal.

5.6. What Factors Affect the Economic Value of an Intervention?

Because the right choice in some situations can be the wrong choice in others, economic studies can help determine what factors affect the relative values of different interventions. An example is a CUA conducted by Fowler et al. (2005) that evaluated the incremental cost-utility of four different postanthrax attack strategies (doing nothing, vaccination, administering antibiotics, and administering both antibiotics and vaccinations) and two preanthrax attack strategies (vaccination versus no vaccination). The investigators created a hypothetical cohort of a large metropolitan population with a similar age and sex distribution to New York City and obtained costs, probabilities, and rewards from a variety of sources, including the published literature, Centers for Medicare and Medicaid Services data, and the 1998 Statistical Abstract of the United States. The analyses showed that administering vaccine and antibiotics offered more utility (21.36 QALYs) and cost less ($46,099) than did the other three postattack strategies. Of the two preattack strategies, no vaccination was less expensive and resulted in higher QALYs gained per person when the annual risk for attack was 1% and during an attack 10% of the population was infected. However, sensitivity analyses revealed an interesting finding: if the probability of an individual being exposed (i.e., the risk for an attack multiplied by the probability of exposure given an attack) is less than one in 200, then the ICER drops below $50,000 per QALY. In health economics, an ICER of $50,000 per QALY is often used as an arbitrary threshold, as researchers consider anything below this threshold cost-effective. These findings imply that probability of exposure is pivotal in deciding whether to mass vaccinate a population preemptively, another important implication for biosurveillance.

6. CURRENT LIMITATIONS AND FUTURE DIRECTIONS

Although the current body of published literature addresses some critical issues and raises important questions, it is still limited in both the range of problems that have been studied and in the technical approaches used in the studies. A lack of funding and interest may partly explain the current state of the art. However, as interest in biosurveillance grows, so will the sophistication and use of economic studies of biosurveillance. Future methods and studies will have to address some of the following technical limitations:

6.1. Current Measures May Not Be Adequate

It remains to be seen whether the traditional cost and reward measures (such as dollars, life years, and QALYs) in their present forms are appropriate or if researchers need to modify current measures or develop new ones to match the unique aspects of bioterrorist attacks and epidemics. After all, many of these current measures originally arose in the context of more well circumscribed medical events, such as individual acute and chronic diseases. Such measures may not capture the complex scientific, economic, and social interactions that occur when the ambient environment is threatened and changed. For example, how does surrounding panic or loss of faith in daily business operations affect quality of life? Will existing measures adequately represent psychological distress? What is the cost of losing or damaging the life of a person, such as a healthcare worker, who is essential to mounting an adequate response to the outbreak? Do potential future earnings fully represent costs from a death? Because different measures may lead to different results and

1 This diagnostic strategy is an example of excluding SARS as a diagnosis by ruling-in another cause for a patient's illness.

different optimal choices, it will be important to use and develop measures germane to decision makers.

6.2. Studies Are Not Capturing All of the Effects

Most existing studies likely underestimate the impact of an outbreak or attack and do not account for all of the short-term and long-term effects. Outbreaks can shake the foundation of businesses, governments, and other organizations. Depending on who becomes ill, an attack can impede or disrupt vital services, such as transportation, health care, law enforcement, and food distribution, further compounding problems. For example, a sudden massive influx of victims into the healthcare system would divert resources and attention from other patients with more "traditional" but still urgent medical conditions, such as heart disease and stroke. Losing healthcare workers to death or quarantine would decrease an already limited response capacity. Setting up areas to place or quarantine victims would disrupt hospital workflow and reduce overall available space.

Existing studies also frequently overlook the psychological consequences of an outbreak, such as fear, hysteria, loss of confidence, and depression, which in sum could be substantial. Studies have shown that stress (Manning et al., 1996; Bejean and Sultan-Taieb, 2005), post-traumatic stress disorder (Frayne et al., 2004), and depression (Greenberg et al., 2003) are extremely costly ailments with insidious long-term consequences. Fear and hysteria can result in injury and bodily harm, as well as hinder response. A decline in consumer confidence could be very detrimental to businesses and the overall economy.

6.3. Studies Should Look at Other Scenarios

Many studies include only a limited number of scenarios, when, in fact, there is tremendous variability in where an outbreak can arise, how an agent may spread, and how a public health response may proceed. Although a number of studies have focused on very large cities such as New York City, attacks and outbreaks can occur almost anywhere. Conclusions from a New York City scenario may not be applicable to other cities and locations. A plethora of factors, including weather and climate conditions, geography, social structure and interactions, and transportation systems, can influence the pattern of spread, detection, and the ensuing response. Many other human and economic factors can alter the response. In addition, the response may not be efficient, especially if the event occurs during the weekends, holidays, or other concomitant crises.

6.4. Studies Should Take Other Perspectives

Most studies take the societal perspective, which is not necessarily the ideal perspective for all decision makers. The societal perspective may seem too abstract and inapplicable to many organizations and businesses that are busy addressing competing concerns that affect their daily operations. As a result, they may not make the time or effort to draw the link between the impact on society and the impact on their own situations. Therefore, taking other perspectives to show specifically how outbreak and bioterrorist attacks will harm their own interests may be helpful for planning, lobbying, and funding purposes.

6.5. Costs and Rewards Are Not Necessarily Linear

Many of the studies assume that costs and rewards change linearly, which is not always the case in real life. For example, in many analyses, doubling the number of people killed by an attack will double the productivity losses. However, in reality, the cost of losing two million people presumably will not be exactly twice the cost of losing one million people. Similarly, doubling the death toll from seven to 14 is not the same as doubling it from 700,000 to 1.4 million. The relationship between costs and deaths is probably much more complicated and shifts at different thresholds.

6.6. There Is a Need for More Data

Because the current poverty of data forces researchers to make many assumptions, future studies should further assess the validity of these assumptions and acquire more data to improve existing and future economic studies. Multidimensional sensitivity analyses, i.e., sensitivity analyses that vary more than one variable at a time, can test these assumptions. Complex simulation studies can measure how these assumptions may behave in a variety of conditions. Researchers can see how these assumptions fare when applied to other better-characterized diseases and problems. At the same time, organizational and policy changes can help data collection. Collecting and generating necessary data requires adequate accounting systems, cooperation from correspondent authorities, alleviation of administrative barriers, appropriately trained personnel, and, in some cases, innovative research methods.

6.7. Current Analytic Methods, Benchmarks, and Resources May Not Be Enough

Because the nature, scale, and impact of bioterrorist attacks and outbreaks are so different from many other medical and health problems, established health economic analytic methods, benchmarks (such as $50,000 QALY) and resources (such as the HUI) may not be applicable or enough to tackle important biosurveillance questions. For instance, is it appropriate to label a biosurveillance measure as not cost-effective if its cost-utility exceeds $50,000 QALY? Is it reasonable to rely on quality-of-life data derived from people who were not in the midst of an epidemic or attack? Can researchers use other more advanced economic methods from other industries? These are just some of the questions researchers and decision makers will struggle with in the near future.

7. SUMMARY

Economics has and will continue to play a significant role in biosurveillance. Economic studies can provide insight about some of the most challenging decisions related to biosurveillance,

including what level of investment is justified by the threat, how best to invest available resources, and how to react to anomalies in surveillance data. The available methods of economic study include cost-of-illness, cost-of-intervention, and a set of techniques, such as CBA, that allow decision makers to explore the ever present tradeoff between cost and benefit in a world in which resources are finite. Although the field of economics is well developed in many areas, the economic study of biosurveillance is still in its early stages. Analysts have applied the existing set of techniques to but a handful of important problems. It is likely that this domain, as have many domains to which economics has been applied, will require the development of additional methods. There remain a large number of pressing problems, especially in the area of bioterrorism preparedness, still to be explored.

ADDITIONAL RESOURCES

Harvard CEA Registry (*www.hsph.harvard.edu/cearegistry*). Provides electronic access to a database of cost-effectiveness ratios in the published literature.

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