Cost-Effectiveness Analysis

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Cost-effectiveness analysis (CEA) is a commonly used tool to evaluate health care interventions. This chapter will introduce CEA, define it, and describe its limitations and its importance for analyzing behavioral interventions in HIV and STD prevention. The procedures used in conducting CEA and several examples follow.

Rationale for CEA of Behavioral Interventions

This section will define the reasons that CEAs are conducted for health care interventions generally; describe the limitations of CEAs; and briefly describe other economic analysis tools for health care interventions (cost analyses and cost-benefit analyses).

CEA Defined

CEA is a tool that has seen increasing use in recent decades as decision makers at all levels of health care provision seek to value alternative interventions (or programs, tests, or treatments). Although CEAs can be complex, and are often described using somewhat arcane terminology, the concept at the core of any CEA is fairly simple: to combine the net cost of a given intervention and its outcomes with its effectiveness, then use the resulting cost-effectiveness ratio to compare that intervention to alternative interventions that are aimed at accomplishing the same goal (be it changes in behavior, increases in good health outcomes, or decreases in bad ones). Cost-effectiveness ratios can be calculated differently depending on whether the given intervention must be chosen instead of the alternatives, or whether it can be combined with some of the alternatives. An example of the former approach is choosing an optimal interval for repeat testing of women diagnosed with Chlamydia trachomatis infection. An example of the latter approach is deciding whether to combine repeat testing for C. trachomatis with a behavioral intervention designed to reduce risk behavior subsequent to receipt of a positive test, in which case the behavioral intervention could be combined with any of the potential repeat testing intervals, or could even be done instead of repeat testing). Because CEA provides explicit quantitative ratios showing the tradeoffs made when
considering alternative interventions, it can aid in decision making about efficient allocation of resources.

**CEA Limitations**

There are some questions that CEA cannot answer, or that can be better answered by other forms of analysis. For example, CEA expresses intervention costs per unit of outcome. Typically, the outcomes chosen represent the final endpoints of the intervention under consideration, and are fairly straightforward. For STD-associated interventions, the outcomes of choice are usually the number of STD cases detected or prevented, or some other measure related to the sequela of STDs (such as pelvic inflammatory disease [PID] in women following infection with *C. trachomatis* or *Neisseria gonorrhoeae*). Selecting appropriate outcomes for CEAs that incorporate behavioral interventions is more complex, as discussed in the next section. For any CEA in this area, an added complication is that programs with responsibilities for STD-related activities will often need to allocate resources among activities that address different STDs, including HIV. For example, assume that a program can choose between one of the following interventions: an HIV risk reduction intervention that has a net societal cost of $1.3 million per case of HIV averted (1996 U.S. dollars) (1), and a behavioral intervention based on motivational interviewing to encourage STD clinic attendees to return for repeat diagnostic testing, at a net societal cost of $345 per case of *C. trachomatis* or *N. gonorrhoeae* infection treated (2). Which activity represents a better use of resources? By themselves, these ratios do not provide the answer.

To address these questions, a variant of CEA, cost-utility analysis (CUA), has been developed. This approach uses derived outcome measures that are common across different interventions—usually quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs) (3,4). QALY and DALY measures are generated using health-related quality of life weights that apply to health states with a referent of “perfect health” rather than to particular diseases. Therefore, two diseases that cause the same physical condition (and therefore the same reduction in perfect health) would have the same QALY or DALY impact when that condition occurs. For example, an ectopic pregnancy imposes the same level of disability, regardless of whether it results from a chlamydial or gonococcal infection. QALYs and DALYs have been estimated for outcomes related to STD and HIV infection and have been used in several studies (1,5–7).

All CEAs and CUAs, however, are subject to limitations. The analyses are often limited in scope and do not evaluate all potential options, even within a given program. For example, a behavioral intervention aimed at STD-related risk reduction that is not cost-effective if conducted with women aged 18–40 years might be cost-effective if restricted to women aged 18–24 years, if the latter group evidenced more frequent or serious risk behavior, or to such “high-risk” women within any given age group. Studies may not explore these options, either because of data limitations or other considerations, and thus fail to provide information on them. Other studies may not fully consider all of the potential alternative uses of resources used to conduct programs. For example, staff hired for the express purpose of delivering small-group behavioral sessions might alternatively also appropriately (within the limit of their roles)
spend time offering STD/HIV screening in non-clinic-based outreach venues. Most CEAs of interventions (both behavioral and screening) fail to consider the complete set of alternatives available to programs, often limiting the focus to the intervention under study in relative isolation. Data to support more integrated CEAs that accounted for more complex interactions between interventions may be limited. However, even when such data are available, there are practical limits to what any one CEA can accomplish without becoming unreasonably large and complex.

Accurately determining the cost of an intervention can also be difficult. Programs often lack line-item cost data for factors such as building space, and other costs can be difficult to determine (e.g., the amount of administrative staff effort that should be apportioned to a given intervention). For some CEAs, patient costs are important, including lost productivity or transportation costs. These can also be challenging to determine, because preparing good estimates may require collecting data directly from patients.

Another limitation of CEA is that it can be difficult to completely incorporate all of the outcomes associated with an intervention, whether they are beneficial or harmful. It can be difficult to even determine what all such outcomes may be. For example, a behavioral intervention designed to promote healthcare seeking may increase annual wellness visits to health care providers. At these visits, a number of beneficial counseling messages might be delivered, and preventive screening procedures may occur. One of these interventions could be C. trachomatis screening (8), which would result in an increase in C. trachomatis detection and, ideally, treatment. However, a CEA that expresses the cost of the intervention as a cost per case of C. trachomatis treated will not account for the other potential benefits. Alternatively, interventions may produce harmful outcomes that may not be considered in the CEA, or there may be harmful outcomes that are otherwise not incorporated. As an example, azithromycin has been used in some settings to treat patients and distributed as patient-delivered partner therapy for incubating syphilis (9,10). In 2003, several cases of azithromycin treatment failure were noted in areas where azithromycin therapy was in use, and macrolide resistance was subsequently documented (10,11). CEAs of azithromycin for treatment of syphilis are incomplete if they do not account for possible treatment failure or the potential for increasing Treponema pallidum resistance (12).

Other Economic Tools

CEA is not the only economic tool used in health care evaluation. Cost analysis, which includes the cost of an intervention but does not explicitly consider the outcomes achieved by the intervention or their costs, is less complicated. Depending on the costs associated with the outcomes and the perspective of the analysis, the cost derived using this procedure may be close to or substantially different from the net cost calculated in a CEA. Cost analysis is easier to perform, but may produce misleading results because of its limited scope, since it only considers intervention costs and not outcomes. For example, a study of interventions to encourage patients diagnosed with C. trachomatis or N. gonorrhoeae infection to return for repeat testing found that the cost of a brief recommendation to return was $15.13 per patient (2001 U.S. dollars), while a motivational interview plus a phone reminder was $24.42. A cost
Cost-benefit analysis would show that the motivational interview and reminder cost 61% more per patient. However, because the motivational interview and reminder was more successful in bringing patients back, it increased *C. trachomatis* and *N. gonorrhoeae* case detection and treatment by 204% over the brief recommendation (2).

Cost-benefit analysis (CBA) is another approach. To conduct a CBA, the costs and outcomes associated with an intervention are rendered in dollar terms to derive a cost-benefit ratio. These calculations include dollar values of welfare changes attributable to the intervention, such as a reduction in pain and suffering realized through a reduction in disease incidence, duration, or severity. Because all aspects of the intervention are expressed in dollars, it is possible to compare the findings across different interventions with different outcomes. While this feature gives CBA a theoretical edge over CEA and cost analysis, it can be difficult to determine appropriate dollar values for all outcomes, many of which are not commonly expressed in monetary terms. Therefore, CBA is used less frequently than CEA or cost analysis.

These different analyses are summarized in Table 1.

### Importance of CEA for Understanding and Improving Behavioral Interventions

Even considering these limitations, CEA offers advantages when used to analyze behavioral interventions by enabling a discussion of their value and enabling comparisons between interventions and populations.

### Understanding the Impact of Behavioral Interventions

CEA clarifies and quantifies the impact of interventions in different populations, both in terms of cost and cost per unit of outcome achieved. Numerous factors (prevalence, populations, access, cost) can differ among various STD prevention programs, making comparisons of programs in the absence of a

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**Table 1** Types of cost and prevention effectiveness analysis.

<table>
<thead>
<tr>
<th>Analysis type</th>
<th>Strengths</th>
<th>Weaknesses</th>
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<tbody>
<tr>
<td>Cost analysis</td>
<td>• Relatively easy to perform</td>
<td>• Does not explicitly account for program effectiveness</td>
</tr>
<tr>
<td>Cost-effectiveness</td>
<td>• Expressed as cost per natural unit of outcome</td>
<td>• Does not readily allow for comparison between interventions producing different outcomes</td>
</tr>
<tr>
<td>analysis</td>
<td>• Allows for comparison of interventions achieving the same outcome</td>
<td></td>
</tr>
<tr>
<td>Cost-utility analysis</td>
<td>• Expressed as cost per unit of health-related quality of life</td>
<td>• Quality of life measures may not be well-defined for some conditions</td>
</tr>
<tr>
<td></td>
<td>• Allows for comparison of interventions achieving different natural outcomes</td>
<td></td>
</tr>
<tr>
<td>Cost-benefit analysis</td>
<td>• All costs and outcomes expressed in monetary terms</td>
<td>• Requires expression of welfare effects in monetary terms, which can be difficult and may not be widely accepted</td>
</tr>
<tr>
<td></td>
<td>• Allows for comparison of very different interventions</td>
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CEA very difficult. For example, there are numerous behavioral and non-behavioral interventions that are designed to reduce HIV transmission (13,14). These interventions have different costs; the targeted populations differ and have different HIV prevalences; and the interventions’ effects differ. Cost-effectiveness ratios can provide information that dramatically eases the comparison of the relative efficiency of each intervention. As noted above, CEA does not provide a direct comparison when prioritizing disease prevention interventions aimed at different conditions, unless all CEAs are rendered in a common denominator. However, the information that results—namely, quantification of the cost per unit of outcome achieved by each intervention—can still provide information that is useful to decision makers.

Use of Cost-Effectiveness Analyses to Guide Resource Allocation

Although allocation of resources for HIV-related care expanded rapidly throughout the 1990s, resources for non-HIV, STD-related services have in many cases become either increasingly scarce or have remained static in the face of a sustained burden of STD in the U.S. population. Thus, a major role for CEA has evolved with the purpose of informing decisions about optimal allocation of scant resources. Numerous examples exist for the clinical realm, including the choice of diagnostic test for C. trachomatis screening programs and of optimal screening and management algorithms for cervical neoplasia. Fewer studies have been published in the behavioral realm, in part because such analyses need to systematically and carefully account for the staff and facility time involved in developing and implementing behavioral interventions in diverse clinical settings. Such studies have inherent limitations. Many have estimated costs using a retrospective approach, rather than prospectively collecting them as the study progressed. Some rely on estimates of the number of future STDs or HIV averted, rather than using prospective biomedical measurement of actual STD/HIV incidence over the course of the study. Importantly, many do not consider the costs of starting up new programs, and assume that the infrastructure to get these intervention programs off the ground already exists.

CEA can provide additional insight into the reality of implementing behavioral interventions through several ways. First, CEA can help to address the question of how best to optimize types of staff involved in the delivery of behavioral interventions. For example, is it cost-effective to train a smaller number of dedicated prevention counselors to deliver a relatively complex intervention to a select group of high-risk patients, or would a less complex intervention delivered by less specialized staff (e.g., primary care providers) to all patients be preferable? One study addressed this issue using the framework and data from Project RESPECT, which studied the effect of three strategies for prevention counseling: “usual” counseling considered typical of clinical practice, a two-session risk-reduction counseling model delivered at a single time by trained prevention counselors, and enhanced (four-session) behavior theory-based intervention also delivered by trained counselors (15). Because both two- and four-session models were associated with reduced risk of future STD acquisition, programs were eager to understand whether CEA could help define how they might prioritize the integration of this approach. Varghese and colleagues (16) attempted to address this question by performing a CEA of
Project RESPECT’s approaches. These investigators collected time and wages for counseling and administration, included patient and treatment costs for STD, and estimated effectiveness for STD and HIV prevented over a 12-month period. Calculated costs (1999 U.S. dollars) of counseling per person for the provider (society) were $22 ($260) for usual care, $33 ($249) for the two-session model, and $128 ($410) for the four-session model. Overall and incremental costs, as well as incremental number of cases prevented (in parentheses) were summarized as detailed in Table 2.

The investigators concluded that while both the two- and four-session models were effective in preventing STD and HIV, the two-session model was considerably less costly, and overall was very cost-effective.

Second, CEA can help to inform program priorities as new research indicates where prevention dollars might be best spent. A good example is the role of repeat testing of persons with chlamydia and gonorrhea. Numerous studies have now shown that persons who acquire these STDs are at high risk for reinfection during the months immediately following their initial diagnosis, most often from untreated sex partners with whom they resume sex. Studies have estimated rates of recurrence within seven months to be between 10% and 73% (17–19), a prevalence far higher than the typical threshold prevalence (3–5%) typically used to define cost-effectiveness of chlamydia screening programs. However, given that chlamydia screening is performed substantially less frequently than national guidelines recommend (20,21), should programs be “diverting” resources from the promotion of routine baseline screening in all women of appropriate age to the new focus of repeat testing?

A major challenge, as discussed above under “CEA Limitations,” is defining what the desired outcomes for CEA performed on behavioral interventions are. For example, should the goal of STD programs be to maximize the desired outcome related to disease occurrence or risk behavior (e.g., reduction in frequency of reported risk behaviors or in future STD acquisition)? Or should the goal be to maximize program efficiency (e.g., using the fewest number of staff to effect the minimum acceptable level of the desired outcome)? Ideally, the

Table 2 Incremental cost-effectiveness of three counseling models in preventing STD and HIV, as assessed in project RESPECT (costs and outcomes shown are for 10,000 patients receiving counseling or usual care).

<table>
<thead>
<tr>
<th>Description</th>
<th>Usual care</th>
<th>Two-session</th>
<th>Four-session</th>
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<tr>
<td>STD cases during follow-up [cases prevented compared to usual care]</td>
<td>2607 (referent)</td>
<td>2183 [424]</td>
<td>2085 [522]</td>
</tr>
<tr>
<td>Costs of intervention to provider*</td>
<td>$201,404</td>
<td>$305,623</td>
<td>$959,403</td>
</tr>
<tr>
<td>Incremental cost to society per STD case prevented*</td>
<td>Referent</td>
<td>$70</td>
<td>$2,232</td>
</tr>
<tr>
<td>HIV cases [cases prevented compared to usual care]†</td>
<td>30 (referent)</td>
<td>25 [5]</td>
<td>24 [6]</td>
</tr>
<tr>
<td>Incremental cost (savings) to society per HIV prevented*</td>
<td>Referent</td>
<td>$(157,959)</td>
<td>$34,580</td>
</tr>
</tbody>
</table>

*All costs are in 1999 U.S. dollars.
†The HIV cases in each counseling group were estimated based on the observed STD cases during the follow-up period of 12 months (15,16).
most effective intervention would also be the most efficient, and a tradeoff between these two parameters need not be incurred; in reality, however, these two goals are often in conflict.

Conducting CEA of Behavioral Interventions

This short chapter cannot fully describe all of the steps and considerations in performing a CEA. There are several useful guides on the subject that devote entire chapters to topics that can only be touched on here (3,22–24). However, a brief explanation of the process involved and some examples can be of use for programs considering conducting CEAs of their own behavioral interventions or modifying existing CEAs to fit their needs. Topics that are largely beyond the scope of this chapter are the mechanics of decision analysis, Markov processes, and the differences between static and dynamic analysis. Decision analysis is simply a process of quantifying programmatic alternatives for systematic analysis. A Markov chain is a multi-step analysis in which the likelihood of a particular event (such as re-infection) may vary depending upon the preceding event (such as initial infection). A dynamic analysis is also multi-step, and preceding events usually impact the likelihood of subsequent events. For example, a disease with a high transmission rate may become more prevalent with each subsequent time period up to a certain point; this will be reflected in a higher prevalence of the disease as time goes on. A static analysis generally does not incorporate effects such as this.

Preliminary Considerations

Certain steps are common to all CEAs. The first step is to position the problem within a frame of reference that consists of determining a baseline to which the alternative intervention or interventions can be compared. Most CEA texts note that the baseline should usually be the current program, if one exists. A baseline of no program can also be used (3,22). An appropriate outcome must be selected, which can be challenging for CEAs assessing behavioral interventions relative to those that compare different screening strategies or pharmacologic treatments. For the latter, immediate outcomes are often obvious, consisting of cases of disease detected and cases of infection successfully treated. The examples below demonstrate some outcomes that have been used in CEAs of behavioral interventions. Observable changes in behavior, such as the percentage of sexual encounters in which condoms are used are often used to estimate changes in rates of disease acquisition, particularly in HIV evaluations.

A critical step in planning the analysis is to determine the cost perspective. The perspective determines which costs will be included, and which costs (if any) will be attributed to the outcomes. The Panel on Cost-Effectiveness in Health and Medicine recommends that CEAs should be conducted from a societal perspective (3). In a societal-perspective analysis, all costs, regardless of who incurs them, are included. The societal perspective gives the best indication of the overall cost-effectiveness of any intervention and is therefore most useful for resource allocation. However, it is sometimes of limited use to local programs, because much of the societal-level impact of an intervention may come through averted health care costs for cases of disease prevented.
Often, these averted costs are for sequelae of disease that would not be treated in public clinics; therefore, individual programs realize no savings through these averted costs. An example of this was demonstrated by Haddix and colleagues (25), who conducted a CEA comparing azithromycin with doxycycline for treating C. trachomatis infection in women. At the then-current price of $24–39 per course (1993 U.S. dollars) for azithromycin, they showed it was cost-saving (i.e., less expensive and more effective) from a health care system perspective compared to doxycycline, but that from the perspective of an individual clinic, it was more costly. This helped to explain why an apparently more cost-effective drug had not been adopted more widely by the programs purchasing medications for STD clinics. This is not to suggest that a narrow program perspective, in which only costs and averted costs borne by the program are considered, is necessarily preferable. An intervention that is less costly to a local program but expensive to participants may not be optimal. An example of this might be a less costly intervention that results in a higher rate of return visits. A CEA of laboratory-based versus rapid, on-site HIV testing nicely illustrates this difference (26). In this study, the cost of anonymous testing from the perspective of the clinic was $101 for the laboratory-based test versus $103 for the rapid, on-site test (1993 U.S. dollars), primarily because the rapid test required additional staff time to process over simply preparing specimens for transport to the lab. The societal-perspective costs, which included patient transportation and lost productivity costs for return trips to obtain the results of testing, were $141 for the lab-based test and $130 for the rapid test. Because more patients received their test results with the rapid test, it was cost-saving from the societal perspective. Presenting both sets of results showed programs that were interested in adopting the rapid test that its use would actually help more clients learn their results relative to using laboratory-based testing and would be cost-saving to society, but that it would also cost clinics more than laboratory-based testing.

Another step in conducting a CEA is determining the time frame and analytic horizon. The time frame represents the amount of time over which the analysis is projected. A common time frame is one year, which allows for a full budget cycle in most programs. The analytic horizon defines the time in which outcomes and costs are considered. Costs for HIV cases are usually defined as discounted lifetime costs; therefore, the analytic horizon is the patients’ lifespans. Often the analytic horizon will be most relevant for societal-perspective analyses and less so for those conducted from a more limited perspective, because deferred costs will not be considered.

Cost Measurement

The cost of a resource can be valued differently, depending on whether its economic or financial cost is being considered. Financial costs typically include the prices paid for resources, while economic costs are the value of the best foregone use of the resources. These two values may or may not be equivalent. An example of how the two may differ is in valuing the cost of volunteer time. There is usually no financial cost associated with a volunteer’s time, but there is an economic cost, because the volunteer could be doing something else during the time spent in the volunteer activity: the economic cost is generally considered to either be a function of the volunteer’s wages or the equivalent wages
someone would earn if being paid to do the volunteer’s task (22). A CEA performed from the program perspective may legitimately value volunteer time at zero cost, but a societal-perspective CEA should not.

Another consideration in performing CEA is that costs that are incurred or averted in the future should be discounted. A common misconception is that this technique adjusts for inflation. Rather, it is used to reflect time preference. A dollar saved today is preferable to a dollar saved in the future; therefore, a dollar saved one year from now should be discounted. Likewise, a dollar that must be paid a year from now does not have the same impact as a dollar that must be paid today; therefore, the future dollar should be discounted. The most commonly used discount rate in studies conducted in the U.S. is 3%, indicating that a dollar one year in the future is equivalent to $0.9709 now (3,22).

Cost data can come from many sources. The most obvious source is from a program itself. Staff time associated with delivering an intervention can be measured directly, via time diaries or third-party observation, sometimes referred to as time-motion analysis (22). Supplies, test kits, and other materials can usually be directly determined. Participant surveys can help define participants’ time commitment and identify travel costs. Costs for facilities used in the intervention, or by staff while they are performing intervention-related duties, including rent, utilities, janitorial service, and maintenance, may or may not be directly available from financial records. Commercial lease and utilities rates are often used if primary data are unavailable. Other cost data sources include insurance claims for direct medical costs. The U.S. Center for Medicare and Medicaid Services publishes lists of allowable charges for medical services and procedures (27). Some states publish hospital discharge data that include gross charges, but because charges are often inflated and then are discounted, they do not represent a reliable source of cost data. The medical literature is another source of cost data, but care must be taken when consulting literature sources. Often cost details, including the perspective used for the CEA, are only briefly described or are not described at all, so it can be difficult to determine how cost figures were determined.

Outcome Measurement

Outcome data can come from many sources as well. A behavioral study will often provide some type of outcome measure that can be directly observed, typically by direct study measures, such as incident cases of a specific disease in an intervention group compared to a control group over a given follow-up period. These may not be sufficient to define efficacy of the intervention at a larger program level, but can be used to derive CEA outcomes. In many instances, the outcome data collected in the time frame of a CEA can be used to estimate another outcome via modeling, often using literature estimates regarding parameter values that are not observable directly. For example, a CEA of a small-group intervention designed to increase condom usage also had data available on the percentage of sexual encounters in which condoms were used after vs. without the intervention (1,28). From published literature, the authors then derived the annual likelihood of HIV infection without the intervention, the effectiveness of condoms in preventing HIV infection, the societal cost per HIV infection, and the number of QALYs gained per HIV infection averted to determine a societal-perspective cost per QALY gained by the intervention.
Outcomes realized in the future should also be discounted in a manner similar to costs. This process may seem counterintuitive, but the principle is the same as with costs. A good outcome that can be realized today is preferred to one that is only realized in the future, and a bad outcome which is incurred in the future is not as bad as one which is incurred today.

Calculating Cost-Effectiveness

Once cost and outcome data are assembled, cost-effectiveness ratios can be calculated. The cost-effectiveness ratio that is of most use will depend on the type of intervention being evaluated. If the intervention is independent, meaning that it can be chosen whether another is chosen or not, the average cost-effectiveness ratio (ACER) is most useful. If the interventions are mutually exclusive, however, the incremental cost-effectiveness ratio (ICER) is more important. The ACER is the net cost of the intervention divided by the outcomes achieved, with both cost and outcomes in comparison to the baseline. Interventions with lower ACERs are relatively more efficient. The ICER is calculated by ordering the interventions from least to most effective in terms of outcomes achieved, then for each intervention dividing the change in cost from the next-least-effective intervention by the change in outcomes achieved. If intervention A costs $10 and produces 10 outcomes, and intervention B costs $40 and produces 20 outcomes, then the ICER is \((40 - 10) / (20 - 10) = 3\) per outcome. Thus, it costs $3 per additional outcome achieved when picking intervention B over intervention A (note that the ACER for B, \(40 / 20 = 2\) per outcome, does not show the true tradeoff when considering B instead of A).

Sensitivity Analyses

Regardless of where the data used in a CEA come from, sensitivity analyses are usually an important part of the overall analysis. A sensitivity analysis is a test of alternative values for selected variables used in the CEA. It can be used to test for the robustness of the results and also to indicate data elements to which the CEA results are particularly sensitive. Sensitivity analyses allow for demonstration of important analysis thresholds, such as where one intervention becomes more expensive or more effective than another. Sensitivity analysis can also be used to extend the findings of the CEA to other settings, such as populations with different rates of risk behavior, disease prevalence, or associated settings’ costs. The sources of data for ranges used in the sensitivity analysis are often in the literature, but data collected as a part of the study can be used as well. A common practice is to use the 95% confidence interval from either the data collected in the study or from previously reported studies as established in previous studies for a given factor (e.g., the prevalence of disease in a population, or the accuracy of a given diagnostic test) to define the sensitivity analysis range. Variables can be tested one at a time (one-way sensitivity analysis), two at a time (two-way sensitivity analysis), or more at a time. It becomes difficult to visualize \(n\)-way sensitivity analyses when the number of variables exceeds three.

Extensions of CEA

CEAs need not be restricted to interventions conducted in the context of a given program or conducted simultaneously. There are many CEAs that have
been conducted by synthesizing the literature, and it is possible to use the literature to generate alternative interventions for comparison purposes that were never conducted locally. This is often a difficult process with behavioral interventions that may have a population- or region-specific effect; in such cases, sensitivity analyses are important.

Examples of CEA of Behavioral Interventions

As detailed under “Use of Cost-Effectiveness Analyses to Guide Resource Allocation”, CEA can be used to assess the most appropriate way to allocate staffing of behavioral interventions. In general, there are surprisingly few examples of published CEA assessing the delivery of behavioral interventions. Those published can be grouped into interventions aimed at groups of people with a specific characteristic (e.g., HIV-infected persons; adolescents), or at the individual (e.g., a person attending a specific clinic, such as a family planning or STD clinic). We have grouped the discussion of the available studies in these two divisions, below.

Group Interventions

In the United States, incidence of new HIV infections has not declined in the last several years. This observation has re-emphasized the need for aggressive incorporation of prevention counseling into the care of populations at increased risk of HIV, and, more recently, among HIV-infected persons themselves (29). The care of HIV-infected persons involves substantial costs—even more than direct medical expenses, such as those for antiretroviral medications, might indicate. Thus, additional resources for behavioral interventions in this population, while clearly a major public health priority, have been an important topic that, interestingly, has not been extensively addressed in the CEA literature. Finally, when one judges the results of CEA focused on HIV prevention, one must ask: what is the economic value (or, acceptable dollar cost) of averting a single case of HIV infection, given the profound human cost this infection has? One review suggested that an HIV prevention intervention should be considered cost-effective if the cost per QALY saved was less than $50,000 (30), but consensus on this value has not been reached.

HIV incidence is currently high among some groups of urban women in the United States. Holtgrave and Kelly (31) performed a CEA of an intervention that was evaluated as part of a randomized controlled trial of a five-session cognitive-behavioral group intervention for women, predominantly African-American, at high risk for HIV infection attending an urban primary health care clinic. The intervention consisted of skills training in condom use and sexual negotiation, problem solving, self-management, and peer support. Relative to the control group, who received nutritional information and skills unrelated to HIV/AIDS, women enrolled in the intervention arm were more likely to report consistent condom use at three-month follow-up. Under base case assumptions, the total societal cost of the intervention was $26,914 (1992 U.S. dollars), or $269 per client, with 0.38 HIV infections averted and a base case cost-utility ratio of $2024 per discounted QALY saved. This cost-utility ratio was considered to be very cost-effective even across a wide range of sensitivity analyses assessed. In another CEA, Chesson and colleagues (1,32)
evaluated the WINGS project, an intervention to prevent HIV/STD among urban women at high risk for HIV acquisition that involved group skills-building in condom use and communication in negotiating condom use. Relative to controls, who underwent a single educational session on nutrition, reported condom use and communication skills among women in the intervention arm increased significantly. In the CEA of this approach, the authors estimated that, under base-case assumptions, the intervention prevented an estimated 0.2195 cases of HIV at a cost of $215,690 (1996 U.S. dollars) per case of HIV averted (1). Excluding indirect costs of HIV from the CEA resulted in a cost-effectiveness ratio of $357,690 per case of HIV averted and $31,851 per QALY saved. Most of the savings could be attributed to the effects of enhanced condom use following the intervention. The authors concluded that this intervention “could” be cost-effective in preventing HIV among women, but that targeting priority groups and reducing the intervention’s cost would be optimal.

Men who have sex with men (MSM) comprise a group at highest risk for HIV acquisition, and several CEA have evaluated group interventions aimed at them. Among these interventions was a 12-session, peer-led, small-group workshop-format, cognitive-behavioral HIV prevention intervention that had been previously shown to have a favorable effect on rates of self-reported condom use at four months (33). Under base-case assumptions, the intervention was shown to be cost-saving, with a cost of $24,000 (1993 U.S. dollars) per delivery. The discounted medical costs averted by preventing HIV infection were equal to $42,000, and the intervention saved 5.5 discounted QALYs (therefore, the intervention averted more health care costs than were incurred in delivering the intervention) (34). This conclusion was generally robust to sensitivity analysis. An analysis by the same group of a similar intervention that used peer leaders in a small southern city to endorse risk reduction of MSM (35) calculated an intervention cost of $17,150 (1996 U.S. dollars), or approximately $65,000 per HIV infection averted, and was viewed as cost-saving even under conservative modeling assumptions (36). Finally, Pinkerton (37) also compared the incremental cost-effectiveness of two other approaches aimed at MSM: a “safer sex” lecture, and the same lecture coupled with a 1.5-hour skills-training session. In an efficacy study, the latter approach was associated with a significant increase in self-reported condom use at 12-month follow-up. In the base-case scenario, the incremental cost of the additional skills training was approximately $13,000 ($40 per person); discounted medical costs averted by incrementally preventing HIV infection with the skills training were over $170,000, and more than 21 discounted QALYs were saved.

Young adolescents in dense urban areas are very much at risk for common STDs, especially chlamydial and gonococcal infections. An intensive, one-day sexual risk reduction intervention aimed at African-American male adolescents in Philadelphia, designed to increase subjects’ knowledge of HIV/AIDS and to undermine problematic attitudes towards risky sexual practices and paired with a control workshop on career opportunities, had high rates of compliance with follow-up at three months. Compared with adolescents in the control group, intervention participants reported engaging in vaginal and anal sex on fewer days, fewer partners, and more frequent condom use (38). A subsequent CEA employed a mathematical model of HIV transmission to translate these observations into an estimate of the number of HIV infections averted (39).
The cost-utility ratio was approximately $57,000 U.S. per QALY saved when training costs were included, and $41,000 U.S. per QALY saved when they were excluded. Factors affecting the cost-utility ratio included whether or not the intervention was restricted to participants who reported being sexually active at baseline, and, importantly, assumptions about prevalence of HIV infection and the duration of the intervention’s protective effect. The authors concluded that the intervention was moderately cost-effective in comparison with other health care programs, and that selective implementation in high–HIV prevalence communities with sexually active youth could enhance cost-effectiveness. Of interest, a similar conclusion regarding targeted delivery to priority groups was reached in a CEA that focused on delivery of a nine-session small-group HIV prevention intervention to adult women with mental illness recruited from community mental health clinics in Milwaukee, Wisconsin (40).

While these analyses provide compelling support for consideration of the behavioral interventions described, their major limitation is that they used self-report of condom use as an outcome to model expected reductions in concurrent HIV acquisition, because the latter was not directly measured. Further, while sensitivity analyses provide some assurance that the conclusions are relatively robust, all models are, not surprisingly, most sensitive to assumptions regarding the per-contact risk of HIV transmission. Since these analyses were conducted, collective understanding of HIV transmission has grown considerably, and it is probably simplistic to assume a single transmission rate that applies equally to all members of a given population, even when this population is defined by a “single” sexual risk behavior, such as anal sex. Many factors impact the likelihood of HIV transmission, including HIV viral load in both serum and genital fluid (41), presence of concurrent STD (especially genital herpes) (42), circumcision status of men (43), and (probably profoundly), stage of HIV infection (44). Recent modeling analyses have suggested that transmission in the period immediately following HIV acquisition (primary infection period) may be responsible for the majority of all HIV transmission, because the primary infection period is characterized by profoundly high viral load and infrequent systemic clinical manifestations that might alert people to the fact that they are highly infectious (44). Future CEA will need to account for more sophisticated understanding of the complexities of HIV transmission dynamics such as these.

Relatively few effectiveness studies and, concomitantly, CEA, have evaluated group interventions focused on non-HIV STD acquisition. One effectiveness study assessed a three-session intervention (part of the Gonorrhea Community Action Project) to enhance preventive health care seeking among adolescents, measured at three months after completion (8). Relative to a control group, female (but not male) participants were more likely to have scheduled a health care appointment, undergone a checkup, and discussed with friends or family members the importance of undergoing a checkup. Importantly, although these adolescents were at high risk for STDs, STD screening or diagnosis were not included as outcome measures of the study, and the relative cost of delivering the intervention has not yet been assessed.

Individual-Level Interventions

Relative to group interventions, interventions aimed at the individual offer different trade-offs in terms of costs and benefits. While the advantages of
individual-level interventions include flexibility in tailoring to the individual’s situation, a major disadvantage can be the need for appropriately trained staff to deliver them in priority settings. Thus, CEA of these interventions can provide critically needed insight into prioritizing program implementation. Several of these CEA in this area have again focused on HIV prevention interventions. One of these assessed cost-effectiveness of an intensive, statewide HIV prevention intervention for gay and bisexual male adolescents in Minnesota. The intervention included individual risk assessment and risk reduction counseling, peer education, optional HIV antibody testing and counseling, referral to medical and psychosocial services as needed, and longitudinal follow-up, and in analysis using a pretest and posttest design (not a randomized controlled trial) was associated with reported reductions in the number of sex partners and the frequency of unprotected anal intercourse among participants (45). For the CEA of this intervention, the investigators modeled HIV seroincidence over a 10-year period using self-reported number of partners for unprotected anal sex as the principal input. The projected total costs of the intervention, including medical treatment costs saved, were $1,100,000 for the 10-year period. The number of HIV infections averted and QALYs saved were projected at 13 and 180, respectively, with a projected incremental cost-effectiveness ratio of $6180 per QALY saved, which indicated cost-effectiveness from the societal perspective. HIV prevalence in the target population was projected to be 6.1% without and 5.6% with intervention by the end of the 10-year period (46).

Because persons with chlamydia or gonorrhea are at increased risk for reinfection with these STDs soon after their initial diagnosis, Gift and colleagues (2) performed a CEA of five separate interventions designed to promote rescreening for these STD three months after initial treatment in public STD clinic settings. The cost per patient counseled with a brief recommendation to return, followed by a telephone reminder after three months, was higher than two interventions: a brief recommendation to return with no reminder and a $20 incentive, received on return. However, the brief recommendation with a telephone reminder yielded the highest return rate (33%) and was the least costly in terms of cost per infection treated ($622 program, $813 societal in 2001 U.S. dollars). In-depth motivational counseling that helped clients identify risk factors and provided reasons for returning was more costly than a phone reminder alone and was not more effective. The authors concluded that in this setting, phone reminders were more cost-effective than motivational counseling, and could improve return rates for rescreening relative to those obtained with a brief recommendation given at the time of initial treatment.

A critical area of STD control is management of sex partners of persons with STD. Partner management in the United States is performed infrequently, and there is considerable confusion about the legal status of expedited partner management (EPT, which includes partner-delivered therapy) among providers, pharmacists, and program staff (47). CEAs on this important topic are emerging, but one of the earliest was published by Howell and colleagues in 1997 (48). These investigators studied the cost-effectiveness of two strategies of partner management to prevent PID in women by comparing early diagnosis and treatment of female sex partners of men diagnosed with chlamydia (strategy 1) to preventing reinfection in women through diagnosis and treatment of their male sex partners (strategy 2). Main outcome measures among a
hypothesized cohort of 1000 male and 1000 female index patients were cases of PID prevented and net costs from the health care system perspective. In this framework, strategy 1 prevented 64 cases of PID, saving $247,000 (1994 U.S. dollars) over no partner management, while strategy 2 prevented 20 cases of PID and saved $33,000 over no partner management. Strategy 1 remained cost-effective over a wide range of sensitivity analyses, while the cost-effectiveness of strategy 2 was more sensitive to assumptions (though favorable in the base-case scenario). While the authors concluded that both strategies were clearly important for controlling chlamydial disease and improving patients’ health, and that implementation of both should be prioritized, the analysis was, interestingly, still able to demonstrate a differential effect of male vs. female-focused partner management efforts in reducing the probable future outcome of upper genital tract disease in women.

Resources for More In-Depth Discussion of Methodology

The following sources provide more detailed discussion of CEA in general and of methodology given short treatment here, such as discounting, generation of health-related quality of life measures, and cost estimation:


References


