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Maximizing the Benefit: HIV Prevention Planning Based on Cost-Effectiveness

A Practical Tool for Community Planning Groups and Health Departments

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Maximizing the Benefit

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A. Getting Started

Maximizing the Benefit is a tool designed for HIV Prevention Community Planning Groups and health departments to set priorities among different interventions to prevent new HIV infections. The central component of the tool is a spreadsheet designed to help you estimate the relative cost-effectiveness of these different interventions. While estimates of cost-effectiveness are far from precise and cost-effectiveness is not the only criterion to be used in prioritizing interventions, these calculations can be very useful in distinguishing interventions that are very cost-effective from those that are less cost-effective. They also can help people planning and implementing prevention programs to focus these programs on those outcomes that will have the greatest benefit. *Maximizing the Benefit* also contains a priority-setting tool to help you rank different interventions based on a combination of cost-effectiveness and several other important factors (such as feasibility and acceptability of the intervention), including factors that you can choose yourself.

Maximizing the Benefit was designed in Excel 2000 and works within Excel 97 or Excel 2000. To use this tool, you should be familiar with basic use of Excel, including entering data in cells, moving between worksheets, and sorting columns. Although we have tried to include all the formulas needed, it is possible that you will have to type in a couple of basic formulas. If you do not have these skills in Excel, we recommend you work with someone who does.

The Excel file that we have provided to you is designated "read only." The first time you use this file you should do a "Save as…" command and save it with a different file name. Then if you overwrite the default values and later want to restore them, you can refer back to the original file.

To use the tool, open the file in Excel and follow the instructions in section B. *How to Use the Cost-Effectiveness Estimator*. Note that the default values you will see in the *CE Estimator* are taken from many different studies representing many different populations, so they will *not* be relevant for your area; you must replace key values in the spreadsheet with your local values for the results to be of any meaning. As you follow these instructions and determine what interventions to include in your local spreadsheet, you may want to refer to other sections, specifically section C. *HIV Preventive Interventions*. If you want to understand the mathematical formulas on which the *CE Estimator* is based, you can read section E. *How Does the Cost-Effectiveness Estimator Work?* and section F. *Limitations on Cost-Effectiveness Estimations*. References for the articles on the different HIV preventive interventions, on cost-effectiveness, and on default parameters are included in section G.

To use the tool you will need to gather and include data from your local area, such as your best estimates of how many people each intervention can reach (at a certain cost), the cost of implementing the intervention in the population you are targeting, and the HIV prevalence in your target populations. We recommend that you start by trying out the *CE Estimator*; after you are familiar with it, you will understand better the data you need to use it fully.

B. How to Use the *Cost-Effectiveness Estimator*

Step 1. Get Familiar With the Spreadsheet

Maximize is an Excel workbook which contains several worksheets. The primary worksheet you will use is labeled *CE Estimator*. This is the worksheet in which you will estimate the cost-effectiveness of different interventions. After you have completed that step, you can use the *Priority* worksheet and the *Priority Graph* to set priorities among different HIV preventive interventions. An additional option available to you is to estimate the cost-effectiveness of interventions for different specific risk groups, using the *CE Estimator–MSM* worksheet in addition to the *CE Estimator* worksheet.

Start by going to the *CE Estimator* worksheet and familiarizing yourself with the rows and columns:

Rows–Each row represents a different intervention to prevent HIV infection. The names of the interventions are in the column at the far left (column C). The interventions that are included are those for which evaluations have been published suggesting that they reduce HIV infections. The interventions are described in more detail in section D.2.

Some public health organizations conduct interventions that have not been fully evaluated. Although the spreadsheet cannot incorporate all these interventions, there are three rows at the bottom that can be used for special interventions that are conducted locally. These rows can be used only for interventions designed to reduce sexual risk behavior by increasing condom use, reducing the number of sex partners, or reducing the number of sexual encounters.

Columns–

Strength of the Evidence (in gold)–This column is a score indicating the strength of the evidence from the literature of the effectiveness of the intervention. The scoring scheme is described in more detail in section C–5 (page 14). The higher the score, the stronger the evidence that the intervention is effective.

The columns of numbers in white, yellow, green, or blue include parameters used to calculate the cost-effectiveness of each intervention.

Intervention Group–These cells include information on the persons reached by the intervention, including the total number reached, the percentages that are male and female, and the percentage that are men who have sex with men (MSM).

HIV Prevalence–These cells indicate the HIV prevalence in the target population (the population from which the intervention group is drawn). For example, under “Men” a value of 0.2 would indicate that 20% of men in the target population are HIV-infected before the intervention begins. There are separate cells for men in the target population and for these men’s partners (who may be women, men, or both women and men), and likewise there are separate cells for women and the women's partners. For those interventions targeted in large part at men who have sex with men (MSM), there are cells for the HIV prevalence in MSM. Note that for interventions directed at HIV-positive persons (e.g., counseling and testing among HIV+, partner notification for HIV+ partners, STD screening in HIV clinics), the prevalence values for "men" and "women" are 1, meaning that 100% are infected. The important values here are the estimates of the HIV prevalence in their partners.

HIV Incidence–These cells indicate the HIV incidence (rate of new infections per year). The HIV incidence is not known accurately in many populations, but estimates are available for some populations. A small number of interventions require this parameter to estimate cost-effectiveness.

Intervention Effectiveness–These columns include several parameters regarding sexual behavior and needle use that are the focus of most HIV prevention interventions. Sexual risk behavior is measured by condom use (the percentage of sexual acts in which a condom is used), number of sex partners per unit time, and number of sexual encounters per unit time. Needle sharing is measured by the proportion of used needles that are exchanged for sterile needles or replaced by sterile needles through needle sales.

For some interventions the outcome measure for reductions in sexual risk were reductions in rates of non-HIV sexually transmitted diseases. The percent reduction in STD rates for these interventions is included in the column labeled STD reduction.

Time–This column indicates, whenever it was available, the length of time between the initiation of the intervention and the measurement of the outcome. This is a minimum estimate of the duration of the effect of the intervention. Thus an intervention that took place over one week and that was evaluated with behavioral surveys six months later would be classified as a six-month intervention.

Program Cost–These columns are estimates of the cost of implementing the interventions for a specified number of people within a specific target population, either measured per client reached OR measured for the group of persons reached ("per community"). These costs are taken from the perspective of the public health system; they would include the value of items such as volunteer time, but not include costs to clients such as time spent being reached by the interventions.

The columns in pink at the far right are the results of these calculations–the measures of the number of HIV infections prevented and the cost-effectiveness, expressed as the cost per infection prevented. These terms are defined and explained in more detail in section E. *How Does the Cost-Effectiveness Estimator Work?*

Cases Prevented–This column estimates the number of cases of HIV infection that are potentially prevented by the intervention. This number should not be viewed as actual cases prevented, but rather as an index to enable comparisons between interventions.

Cost Effectiveness–This column estimates the cost to prevent one case of HIV infection using each intervention, rounded to two digits.

When you first open the *CE Estimator* spreadsheet, you will find that each cell contains either specific numbers or the letters N/A (for not applicable). The numbers are either taken from studies of these interventions published in the scientific literature or are estimates based on these publications. By putting your mouse over any given cell you can read a comment that indicates how that number was chosen for that cell. The numbers in these cells serve as defaults for you to replace with local data (see Step 3 below). Note that because they come from different studies in different populations, these defaults are not relevant for any single project area. ***The results in the Estimator will only be relevant after you replace the default values with your local values.***

The *Maximize* tool also contains several "internal" worksheets that are not designed specifically for users to alter but that you may view and change if you wish. For more details on these, see section E.4 below.

Step 2. Choose Your Interventions

In your community, you are likely to have several different interventions in place. In this step you should determine which interventions you will include in your final spreadsheet.

The terminology for interventions is not standardized. For some of the interventions implemented in your area you may use the same descriptive terms as the spreadsheet (e.g., HIV Counseling and Testing), but for some others you may use local descriptive terms that you cannot find in the spreadsheet. For those interventions that don't match a label in the spreadsheet, you should first check the definitions of the interventions in section D to see if they match an intervention with a different name. If so, you should use that row to calculate the cost-effectiveness of this intervention. If you use interventions that do not match any of the interventions in the spreadsheet, and if your interventions are designed to reduce sexual risk behavior (by increasing condom use, reducing the number of sex partners, or reducing the number of sexual encounters), you can put your intervention into "Sex risk reduction #1" or #2 or #3 and use these rows to calculate their cost-effectiveness.

You should first concentrate on these rows to compare the interventions that are already implemented in your project area. Then you should look at the other rows and put in "best guess" data to estimate the cost-effectiveness of interventions that are not currently being carried out, but that you might want to consider implementing.

Step 3. Put in Your Local Data and Estimate Cost-Effectiveness

The numbers in the spreadsheet are not necessarily reflective of your local community. For the cost-effectiveness *CE Estimator* to be useful, you must replace certain numbers with your local data. The numbers you must replace ("Required inputs") are in yellow, the numbers that we recommend you replace ("Recommended inputs") are in green, and the numbers you should consider replacing if you have the available data ("Optional inputs") are in blue:

Required inputs – Yellow

For the *CE Estimator* to be relevant to your local area, you must put in the following numbers for each intervention:

Number of people reached–The number of persons you believe are reached or can be reached by your intervention at the cost you indicate below over its planned time period (usually one year). For example, this may be the number of persons counseled, the number of people visiting a needle exchange program, or the number of people reached by a mass media campaign.

Demographic distribution of people reached–The percentage of the population reached that is male and the percentage that is female, and if it is not indicated as N/A, the percentage that are MSM. Percentages should add to 100%, so MSM should not also be included in the Male column. Not all combinations of demographics are allowed, because the studies in the literature often did not provide enough information to make calculations based on these breakdowns. *If a cell contains the entry N/A do not replace it with a number*.

Notes for specific interventions:

- For some interventions your only entry should be the percentage MSM, and the *CE Estimator* will calculate the number of heterosexuals by subtraction.
- *HIV Partner Notification* uses two rows in the spreadsheet, but should be viewed as one intervention. When assigning the percentage of the population in the cells, you should break down the number of *partners* reached into four categories: males who are HIV+, females who are HIV+, males who are HIV-, and females who are HIV-.
- For *Mass Media campaigns* estimate the proportion of the targeted population that is age 17-30 and the proportion that is 31-45 years of age.

STD rates–Selected interventions use rates of STDs to estimate effectiveness and cost-effectiveness.

Notes for specific interventions:

- For the intervention *STD Screening in HIV clinics*, you should enter your estimate of the prevalence on screening tests of gonorrhea and chlamydia in your local clinic. If you do not have this value, you may leave the default values, which are from the New Orleans HIV clinic.
- For *STD Screening in the General Population*, you should enter your estimate of the prevalence of gonorrhea and chlamydia of a population that you might screen, e.g., in emergency departments, CBO sites, or community sites.
- For *Alcohol Taxes* we have entered the reported gonorrhea *incidence* rate for Los Angeles county. To estimate the benefit of alcohol taxes in a community with a gonorrhea rate similar to that of Los Angeles, you do not need to change this cell; it is related to the population size and will change automatically when you put in your population size. If your rates differ substantially, you should replace this with the number of reported gonorrhea cases in your project area over one year.

Cost (per client or per community)–Your best estimate of the cost to reach the number of people you indicated above with your intervention for the selected time period, from the perspective of the public health system. This cost estimate should include program expenditures other than those covered by categorical federal or state HIV prevention funds (such as costs covered by CBO fundraising) and the value of volunteer time, but should not include costs to clients such as time spent being reached by the interventions.

Costs can be shown in one of two ways: 1) as "per client" costs, with the community costs calculated as the "per client" cost multiplied by the number of persons reached or 2) as "total intervention group" costs, with the "per client" costs calculated as the "total intervention group" costs divided by the number of persons reached. Note that this should include the entire cost of the intervention, not just the marginal costs of adding this intervention to an existing program (such marginal costs are sometimes used in published studies).

You are not likely to know the exact costs of many interventions, but you should be able to estimate these costs accurately enough to be consistent with the precision of the *CE Estimator*. Here are two examples:

Example 1: Suppose a CBO has an annual budget of $250,000 to conduct two interventions: HIV Counseling & Testing and Street Outreach. The CBO has 10 staff, including some part-time and some full-time staff, but adding to 8 full-time equivalent positions. No work is done by volunteers. Of the paid staff, 7 are devoted to Street Outreach and 3 are devoted to Counseling and Testing. From this you can estimate that the Street Outreach costs $175,000 per community (7/10 x $250,000). If you estimate that this activity reaches 10,000 people per year, then it costs $17.50 per client.

Example 2: Health department staff in one region of the state conducts partner notification for persons with HIV infection. In a year, these staff interview 150 persons with HIV infection and notify 200 partners. The staff includes two field workers, one supervisor, and one clerk. The field workers estimate that 20% of their time is devoted to partner notification for HIV infection. If the salaries & fringe benefits for this unit total $140,000, and you estimate the overhead rate for the unit (to cover office space, equipment and supplies) is 25%, then the cost per community for this intervention is
20% x $140,000 x 1.25 = $17,500 and the cost per client is $17,500 / 200 = $175.

Recommended inputs–Green

The number of HIV infections prevented by an intervention depends on how many people have HIV infection already and how many are acquiring HIV infection each year. In general, the higher the HIV prevalence and the higher the HIV incidence of the population reached, the more cases of HIV infection you will prevent. The HIV prevalence and HIV incidence vary widely in different areas of the U.S. and in different subgroups of the population in a given area. The HIV prevalence and HIV incidence defaults in the spreadsheet are based on populations for which these interventions were evaluated, so they vary. You should change these to your local values:

HIV prevalence–Put in your best estimate of the proportion of men, men's partners, women, women's partners, and MSM in your target population who are currently HIV-infected. These values refer to the population reached by the intervention, which may have a higher or lower prevalence than a larger population in your area. This HIV prevalence can be taken from blinded serosurveys (best choice), HIV counseling and testing data, or national estimates of HIV prevalence in different metropolitan areas (see Holmberg 1996, reference in Bibliography). Note that these are expressed as fractions, not percents, so an HIV prevalence of 1.5% would be entered into the spreadsheet as 0.015. You will find that the cost-effectiveness of different interventions is highly dependent on this estimate of the HIV prevalence, therefore it is important that your estimate be as accurate as possible, and even more important that you use the same prevalence estimates for different interventions if the target population is the same.

HIV incidence–If you are considering an intervention that requires an estimate of HIV incidence, put in your best estimate of the target population's HIV incidence per year. HIV incidence is rarely measured, but estimates are available for many different metropolitan areas from Holmberg 1996, reference in Bibliography.

Optional inputs–Blue

These columns contain information about the effect of the intervention strategy on risk behavior and related factors. The numbers come from the original publications that evaluated these strategies. You can just leave these numbers in to estimate the cost-effectiveness of the interventions in your population. However, if you have information from behavioral surveys or other sources that is a more direct measure in your target population, you can replace the default values with your values. Over the long term, the *CE Estimator* will be more valuable if you can use your own numbers, so you should consider recommending that data be collected on your interventions for you to use in future years. The parameters that you can replace are:

Condom use before and after–This is the percentage of sexual acts in which a condom is used, on average across your target population. It is best measured by surveys with the question, "Did you or your partner use a condom the last time you had sex?" In this case, if 55% of respondents answer yes, the value of condom use is 55%. Note that the question, "How often do you use a condom when you have sex?" is not an accurate measure of this parameter because people have trouble estimating the percentage of all encounters in which condoms are used. The "before" column refers to condom use before the intervention began or in a comparison group, and the "after" column refers to condom use after the intervention was implemented in the intervention group.

Notes on specific interventions:

- *Circumcision* uses this column in a slightly different way. For this intervention, the condom use column is actually the proportion of males who are circumcised.

Number of sex partners before and after–This is the average number of different persons with whom a person has sex over the time span of the intervention. For example, if half of the intervention group reports only one partner and half of the intervention group reports two partners, then this value is 1.5. As above, "before" refers to the population before the intervention or in a comparison group, and "after" refers to the intervention group after the intervention is implemented.

Number of sexual encounters before and after--The risk of HIV transmission depends in part on the number of times people have sex in a given time span, even for people who have only one sex partner (because some HIV-negative monogamous people will have HIV-positive partners). The measure of the average number of times persons have sex in a week, month, or 3-month period (with any partners) is therefore important to estimating the number of new HIV infections in a population and the number of HIV infections prevented by an intervention. Unfortunately, this number is rarely measured in simple behavioral surveys. A national survey by Laumann, et al., (1994) suggested that the average number of sexual encounters for persons age 18-44 is approximately 81 per year (or 20.25 per 3-month period), and that this does not vary much in different population subgroups or even in persons with varying numbers of partners. If you do not have data on this measure, you should leave these values as defaults.

STD reduction–This column represents the proportional reduction in STD rates from the intervention, as determined by the study evaluating the intervention. It is used for just three interventions that used this outcome to estimate effectiveness. Unless you have very valid data that suggests a different number, we strongly recommend you leave these default values.

Calculating and Interpreting Estimates of Cost-Effectiveness

As soon as you enter numbers from your local area for the Required and Recommended Inputs, the values in the pink columns will change to numbers indicating the number of HIV infections each intervention prevents in your community and the cost per case of HIV infection prevented.

Cases Prevented–This column estimates the number of cases of HIV infection that are potentially prevented by the intervention. The *CE Estimator* does not round off the Case Prevented number, so it may show that interventions prevent a fraction of a case of HIV infection (e.g., preventing 0.86 cases); this can be interpreted as the probability that a single case will be prevented (e.g., 86% chance of preventing one case). Note the number of cases prevented is based on the number of people reached and the time span of the intervention. If the number of persons reached increases, the number of cases prevented will increase proportionally.

Cost per Case Prevented–This column estimates the cost to prevent one case of HIV infection using each intervention, rounded to two digits. In general, the lower the cost per case prevented, the more cost-effective the intervention is. Remember, though, that the basic mathematical model is just that, a mathematical model, so this estimate of the cost-effectiveness is not really an amount of money, it is just an index to compare different interventions. Furthermore, ***because many of the parameters in the models represent rough estimates, even when used only for comparison purposes, these cost-effectiveness estimates are accurate only within an order of magnitude***, that is, an intervention that costs $26,000 per case prevented is--within the precision of the spreadsheet--equivalent to an intervention that costs $37,000 per case prevented. However, an intervention that costs $37,000 per case prevented is more cost-effective than an intervention that costs $190,000 per case prevented.

Also, remember that the value of comparing cost-effectiveness estimates across interventions is only as good as the consistency of the parameters you put in. If you were not consistent in how you selected your parameters for the *CE Estimator*, the cost-effectiveness ratios will be inconsistently calculated and not comparable.

Optional step: Risk-group specific calculations:

Some community planning groups set priorities for interventions within specific risk groups, e.g., MSM, injection drug users, high-risk heterosexuals, etc. It was not possible to develop a tool to accommodate all of the different possibilities of risk groups and interventions. Furthermore, very few interventions have been evaluated in more than one specific risk group. However, *Maximizing the Benefit* does include a sheet specifically to rank interventions for men who have sex with men (labeled *CE Estimator-MSM*), and the main worksheet (*CE Estimator*) can be used strictly for injection drug users or for high-risk heterosexuals:

MSM worksheet: This sheet is designed like the *CE Estimator* worksheet, with a column for interventions and additional columns for Number Reached, HIV Prevalence, HIV Incidence, Intervention Effectiveness, the Time period of the intervention, the Program Cost and the results expressed as cases of HIV infection prevented and cost per case prevented. It does not include a column on the demographics of the persons reached because it assumes that all persons reached are MSM. *Note that the interventions listed are interventions that **could be** applied to MSM; this does not mean that they have been evaluated and found effective in MSM.* In fact, evaluation data specific to MSM is lacking for many of these interventions. For this reason, default values are not included in most cells.

The cells of this spreadsheet should be completed in the same way that the cells in the *CE Estimator* worksheet were completed, except that because there are often no default values, you must estimate many parameters. As in the main spreadsheet, when you have entered in the appropriate parameters, the results will appear automatically in the column on the right.

Injection Drug Users and High-Risk Heterosexuals: The cost-effectiveness of different interventions to prevent HIV infection in injection drug users can be assessed using the *CE Estimator* worksheet simply by looking only at interventions specific to IDU, that is, Needle Exchange, Needle Deregulation, and Drug Treatment. While other interventions such as street outreach may reduce the risk of transmission through injection use, they have not been adequately evaluated in this way.

Similarly, the cost-effectiveness of different interventions to prevent HIV infection in high-risk heterosexuals can be assessed using the *CE Estimator* worksheet by looking at interventions that are *not* specifically for injection drug users, changing the "percent MSM" in the Intervention Group column to 0%, and entering the appropriate percent female and male in these columns (to add to 100%).

Step 4. Do "What If" Calculations

Many of the values you put in to the spreadsheet will be estimates, and these estimates may depend on decisions to be made in the future about how interventions are implemented. Before making a judgment regarding the cost-effectiveness of an intervention, you should think about how you might change these programs to make them more cost-effective and then test out these changes by doing “What If” calculations. These sorts of calculations should give you an intuitive feel for whether under any scenario the intervention can be made significantly more cost-effective. They may also direct you toward those changes that will have the largest impact on cost-effectiveness. There are many sorts of “What If” calculations that you can do. A few examples are:

Change the Cost of Intervention–Your estimate of the cost of the program is likely to be uncertain, and it may be possible to make programs more efficient. To test out the effect of increasing the efficiency of the intervention, you can vary the cost (per community or per person reached). The effect of this change on cost-effectiveness is proportional–that is, if you cut your cost per community in half, you should reduce by half the cost per HIV infection prevented.

Make the Intervention More or Less Targeted–All else being equal, interventions are more cost-effective if they are targeted at persons at high risk, i.e., persons in populations with high HIV prevalence. You can test the value of better targeting of your interventions by increasing the HIV prevalence of the target population. When you do this, though, remember that better targeting will probably involve reaching fewer persons at a greater cost per person reached (because it will take more effort to find these persons at high risk), so you may want to reduce the “people reached” and increase the cost per client. Alternatively, you can make your intervention less targeted, by lowering the HIV prevalence, increasing the number of people reached and decreasing the cost per client reached. Under some scenarios in which you greatly reduce the cost per client reached, this may make your intervention more cost-effective.

Change the Effectiveness of Intervention–The effect of the intervention on sexual behavior or needle use is hard to predict. The default values in the spreadsheet are taken from scientific publications; you may have replaced these with values from your own surveys. However, you may feel that if the intervention is improved you can do better than these values. If so, you can change the values in the Intervention Effect columns (blue columns) to reflect what you think your intervention might achieve, and see how much this changes the cost-effectiveness. For example, increase the “after” condom use to 75%, or decrease the number of sex partners to 1.1. Remember, however, that you may not be able to actually increase the effectiveness of an intervention, so if you modify the effectiveness in the *CE Estimator*, you should be able to justify to yourself that your parameters are reasonable and you should measure the actual effect.

The cost per case prevented is an important value to use in prioritizing interventions. However, before ranking your interventions, there are other issues that you should consider. *Maximizing the Benefit* has a separate module to help you through the step of setting these priorities, as explained in the next section.

C. How to Use the Priority-Setting Tool

After you have estimated the cost-effectiveness of the different interventions, you can use the worksheet labeled **Priority-Setting** to help you set priorities among these interventions. This tool operates independently of the *CE Estimator*, so you can use it even if you used a different tool or process to estimate the cost-effectiveness of different interventions. This tool is based on the idea that other factors besides cost-effectiveness should be considered in determining which interventions should be given high priority for funding. This sheet currently has three different factors for you to include in your priority-setting: *Cost-effectiveness*, *Strength of the Evidence* of effectiveness*, Feasibility and Acceptability of the Intervention* in your community. However, you can change any of these factors to suit your needs; in addition, there are also three other columns that you can use to include additional factors.

To use this tool:

1. List your interventions in the left column. The default list of interventions is there now, but you can replace these with your own list.

2. Select the factors to include. Decide what factors (besides cost-effectiveness) you would like to include in your prioritization scheme. The factors are listed in the green cells (C5 to H5). As needed, change the factors included in the spreadsheet as a default and/or add other factors by changing the labels for these factors. For example, depending on how confident you are of the parameters you entered, you may want to add a factor for "confidence of the estimates." Also, some interventions are naturally complementary to others (for example, HIV counseling to HIV-positive persons and HIV partner notification), so you may wish to include a factor on the degree to which this intervention helps strengthen other interventions that you are likely to use.

3. Decide how much weight to assign to each of the factors you have chosen. The greater the weight assigned to each factor, the more that factor will influence the final rating of interventions. We have included default weightings in cells shaded light green just under each factor, but you can change these in any way you want. The default weightings add to 100 total points, but they can add to any number and the *CE Estimator* will still work correctly.

3. Choose cost-effectiveness score for each intervention based on cost per case prevented. The cost-effectiveness should be scored on a scale of 0 to 6, with 0 being the least cost-effective and 6 being the most cost-effective (see Step 3. above). We recommend the following scoring scheme:

Cost per HIV infection prevented	Score
Less than $10,000	6
$10,000 - $49,999	5
$50,000 - $99,999	4
$100,000 - $149,999	3
$150,000 - $199,999	2
$200,000 - $1,000,000	1
Greater than $1,000,000	0

However, the users may change the scheme to reflect their preferences. To do this, please unhide the worksheet *CE Score Ranges* and change the ranges.

4. Choose scores for other factors. Decide how you will determine scores for the other factors and score each intervention for each factor. **The higher the score, the higher priority that intervention will get in the final weighted rating.**

For example, under *Strength of the Evidence* you may score an intervention as follows:

Strength of Evidence	Score
Controlled trials, HIV incidence or STD incidence as outcome	5
Controlled trials, self-reported behavior as outcome OR Uncontrolled trials, HIV incidence or STD incidence as outcome	4
Multiple uncontrolled trials, self-reported behavior as outcome	3
Small number of uncontrolled trials, self-reported behavior as outcome	2
Weak study designs or flaws in study designs	1

Feasibility and Acceptability is meant to be a measure of how easy or difficult it would be to implement this intervention in your local area and for your target group. This measure should take into account the legality of the intervention (for example, with needle exchange programs), political barriers to implementation, acceptability of the intervention in the target population, and the intervention's sustainability (for example, whether you can continue to get people to participate over time). These factors are difficult to assess quantitatively but are nonetheless important to consider when setting priorities for interventions. The higher the score, the more feasible and acceptable the intervention is. An example of a scoring system for *Feasibility and Acceptability* would be as follows:

Feasibility and Acceptability	Score
No legal or political barriers, community acceptability high	5
No legal or political barriers, community acceptability moderate	4
No legal or political barriers, community acceptability low OR Some political barriers present	3
Some legal or political barriers present AND community acceptability low	2
Substantial legal and/or political barriers to implementation	1

Similar explicit, written schemes should be developed for other factors that you choose to include.

5. Determine overall priority ratings based on weighted scores. The tool will automatically calculate weighted priority ratings based on the scores and weightings you entered. These results will appear in the pink column at the far right. To better compare these interventions when you are finishing entering the scores, highlight the block of cells that contain the intervention numbers, the intervention names, the individual scores, and the weighted ratings (columns A through I), and then sort them (descending) by the weighted ratings (column I). The highest priority interventions will appear at the top and the lowest priority interventions will appear at the bottom. These results will be displayed graphically in the sheet labeled **Priority Graph**. If you want to "un-sort" the interventions to return them to the order on the *CE Estimator* worksheet, just highlight the same block of cells and sort them in order of the intervention number.

D. HIV Preventive Interventions

1. Mechanisms of Effect

In the United States, nearly all HIV infections are spread either through sexual contact or reuse of needles and/or syringes associated with illicit drug use. Interventions to prevent HIV infection therefore focus on preventing sexual contact or preventing either drug use or reuse of needles and syringes among drug users. Abstinence from sex and drug use is the most effective method to prevent acquisition of HIV infection. For the large number of persons who will not remain abstinent, there are alternative measures that can significantly reduce the likelihood of HIV transmission. The alternatives that are most frequently the targets of HIV prevention interventions are:*

1) Reducing the number of sex partners.

* Other potential risk-reduction approaches exist, such as changing specific sexual practices (e.g., oral sex versus anal/vaginal sex) or selecting partners that are at lower risk of HIV infection and thus likely to have a lower HIV prevalence. Although many individuals may try to reduce their risk though changes such as these, they are not reliable enough for most public health officials to base prevention programs on. The mathematical model used in the cost-effectiveness estimator cannot incorporate changes in sexual behavior such as these in its calculations.

2) Reducing the frequency of sexual intercourse.

3) Increasing the proportion of sexual encounters in which a condom is used.

4) Reducing the frequency of drug injection.

5) Reducing the proportion of drug injections in which a previously-used syringe is used.

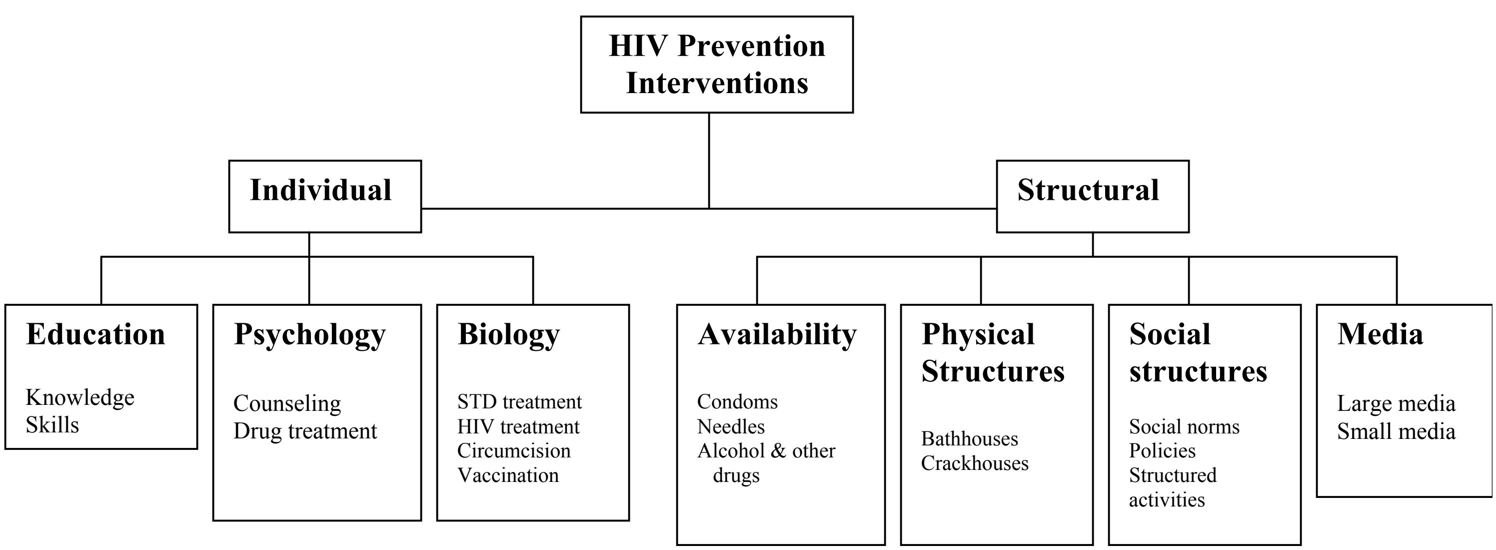
6) Reducing the transmissibility of HIV or susceptibility to HIV through biologic interventions.

These measures can be achieved by various interventions applied at different levels. Many interventions (if successful) will have more than one of these effects. The effectiveness of any given intervention is directly related to how successful it is in bringing about these changes.

2. A Taxonomy

Several different organizational schemes have been proposed to classify different interventions to prevent HIV infection. The organizational scheme, or taxonomy, we use in this tool categorizes interventions first based on the general mechanism of action (either *individual* or *structural*) and second on the specific intervention targets that the intervention influences. The taxonomy is illustrated in Figure 1. below:

Figure 1. Organizational scheme for interventions to prevent HIV transmission



While health interventions can be applied at many levels, such as the individual, the family, the neighborhood, the worksite, the organization, the community, or the state, there are essentially two basic targets of health interventions—factors within the control of the individual or factors external to the control of the individual. Examples of interventions that use an individual-level approach to change behavior include counseling or education, either one-on-one or in small groups. These interventions influence knowledge, attitudes, skills, beliefs and cognitions.

Interventions that change conditions beyond individual control such as the social and physical environments are structural interventions (also called ecologic or environmental interventions). The levels at which these interventions are applied are generally at the neighborhood, worksite, or community, which correspond to the environments that various populations occupy. However, just because an intervention may be applied for a large number of people does not mean that the intervention is structural. For example, community interventions can target either structural factors or individual factors. A community-level program is in fact an individual intervention if the approach leaves it up to individuals to change their behavior, e.g., large-scale education to reduce sexual risk-taking. On the other hand, if the community-level intervention increases the availability of condoms, then it is primarily a structural type of intervention, as it targets conditions outside the control of single individual.

In general, individual interventions have the advantage that they can be applied to persons at the highest risk--indeed because they are often costly on a per-person basis, they are generally reserved for persons at high risk. They have the disadvantage that they may not prevent HIV transmission among persons at average risk or among persons who are not identifiable as being at high risk. Structural interventions, on the other hand, are usually applied to large populations. They have the advantage that they are generally inexpensive on a per-person basis but the disadvantage that they may have a small impact on individual persons, including persons at the highest risk. Cost-effectiveness analysis provides one tool to weigh the advantages and disadvantages of these two types of interventions.

This taxonomy of HIV prevention interventions is broader than some, and it includes several interventions that health departments and community planning groups are not undertaking to prevent HIV transmission (e.g., alcohol taxes, circumcision). These interventions are included to expand the list of possible HIV prevention programs that community plannning groups and health departments may want to consider, and to try to allow comparison of the cost-effectiveness across very different types of interventions.

Below is a summary of different interventions that are included in *Maximizing the Benefit* or are commonly used in the United States, classified according to the above taxonomy. For each intervention, we include references of descriptions or evaluations of the intervention, as well as the expected proximate outcomes of these interventions. Other reviews of HIV prevention interventions also available (see Johnson, 2002; Neumann, 2002; Rotheram-Borus, 2000; Semaan, 2002 and **http://www.cdc.gov/hiv/pubs/hivcompendium/toc.htm**).

Individual Interventions

Educational and Psychological Interventions:

Several different interventions that use educational or psychological approaches are used commonly and/or have been evaluated and found successful. These interventions generally attempt to increase knowledge about HIV, provide skills (e.g., how to use a condom, how to negotiate condom use) or use counseling to motivate and persuade persons to change their risky behavior, especially their risky sexual behavior.

- *School-based HIV education programs:* These programs usually provide information about HIV, transmission, prevention, and consequences. Many states regulate the content of what can be included in public school HIV curricula. They usually stress abstinence, and in some states may restrict discussion about other methods of prevention. ***References:*** (Coyle, 1999; Wang, 2000) ***Expected proximate outcomes***: *Reduction in the number of sex partners, reduction in frequency of sexual intercourse, increase in proportion of sexual encounters in which a condom is used*

- *Individual counseling with HIV testing:* This is probably the most commonly used intervention to prevent HIV. The key element is to increase one's awareness of risk, to impart more knowledge about HIV transmission and to motivate individuals to reduce their high-risk behaviors. Usually, testing and counseling is done in two sessions: one in which the decision is made to get the test, the next session is to discuss the results of the test. At posttest, emphasis is on reduction of risky behaviors to prevent infection in the future. For those who test positive, there is emphasis on getting health care services and treatment to prevent disease progression. Studies have found that counseling that is tailored to the current attitudes and behaviors of those seeking testing (i.e., client-centered counseling) appears to be more effective than counseling that covers more standardized protocols. Other studies suggest that the intervention may have a different effect on the behavior of HIV-positive versus HIV-negative persons; furthermore, behavior change in HIV-positive persons will have a different population-level effect on HIV transmission than the same behavior change in HIV-negative persons. ***References:*** (Weinhardt, et al., 1999) ***Expected proximate outcomes***: *Reduction in the number of sex partners, increase in proportion of sexual encounters in which a condom is used*

- *Individual counseling without HIV testing:* This approach also usually increases one's awareness of risk, imparts knowledge about HIV transmission and motivates individuals to reduce their high-risk behaviors. No HIV testing is provided. ***References:*** (Weinhardt, et al., 1999) ***Expected proximate outcomes***: *Reduction in the number of sex partners, increase in proportion of sexual encounters in which a condom is used*

- *Prevention Case Management:* Prevention case management (PCM) for HIV is an intervention that combines individual HIV risk-reduction counseling and case management, which assists individuals in obtaining a variety of services, such as housing, health care, and transportation. ***Expected proximate outcomes***: *Reduction in the number of sex partners, increase in proportion of sexual encounters in which a condom is used*

- *Video sessions in clinic waiting rooms:* This approach essentially takes advantage of the time people are waiting to be seen in an STD clinic. A videotape is shown that provides information about STDs and HIV. The format can be dramatic, in a soap-opera style, and may personalize the issue of HIV prevention. Studies using this method have shown that patients watching the videotape have fewer return visits for new STDs than patients who did not watch the videotape. ***References:*** (Cohen, et al., 1992; O'Donnell, et al., 1998) ***Expected proximate outcomes****: Reduction in the number of sex partners, increase in proportion of sexual encounters in which a condom is used.*

- *Discordant couple counseling*: This intervention involves counseling of a couple in which one person is HIV-positive and one is HIV-negative. This counseling is done jointly, usually over repeated sessions, and allows the couple to make decisions together about how to protect the HIV negative partner. ***References:*** (Weinhardt, et al., 1999) ***Expected proximate outcomes****: Increase in proportion of sexual encounters in which a condom is used*

- *Small group sessions*: This refers to any intervention in which a group of people is counseled or trained in risk reduction techniques at the same time and place. Usually, only persons at high risk are targeted. Not only can people learn skills and get information, but also there is an opportunity to learn from each other and obtain social support for behavior change, and for people to adjust their social norms. Usually these sessions are scheduled several times over the course of several weeks. ***References:*** (Holtgrave and Kelly, 1996; Kelly, et al., 1994; Pinkerton, Holtgrave and Valdiserri, 1997; Valdiserri, et al., 1989) ***Expected proximate outcomes****: Reduction in the number of sex partners, increase in proportion of sexual encounters in which a condom is used*

- *Partner notification*: This is typically an intervention performed by trained health department personnel (Disease Intervention Specialists or DIS) who locate persons with HIV infection, ask them to name their sex and needle-sharing partners and attempt to locate these partners. The DIS advise the partners (while maintaining the confidentiality of the index person) they may have been exposed to HIV, encourage them to be tested for HIV infection, and encourage them to reduce their risky sexual behavior. Many DIS will also provide the testing onsite using saliva samples or if they are trained in phlebotomy, will be able to draw blood in the field. In this case, the DIS will also offer individualized HIV C & T. The effect of this intervention on risk behavior may be different in HIV negative vs. HIV positive partners. ***References:*** (Toomey, et al., 1998; Wykoff, et al., 1991). ***Expected proximate outcomes****: Reduction in the number of sex partners, increase in proportion of sexual encounters in which a condom is used*

Biological Interventions:

There are three types of biological interventions known or believed to have an effect on HIV transmission: STD treatment, HIV treatment, and circumcision. HIV preventive vaccines are potentially another biological intervention but have not currently been shown to be effective. The distinguishing feature of these interventions are that they change something biological within a person that can reduce the likelihood of HIV transmission even if that person's behavior does not change.

- *STD treatment:* Sexually transmitted diseases have been shown to act as co-factors for HIV transmission, that is, they increase either the infectivity of an HIV-positive person or the susceptibility of an HIV-negative person. Treatment of curable STDs is the only intervention that has been proven effective in reducing HIV incidence in a prospective randomized controlled trial. The degree to which STDs increase HIV transmission varies with the type of STD, but both ulcerative (e.g., syphilis) and inflammatory (e.g., gonorrhea) STDs appear to have this effect. STD treatment is usually given only to persons with proven disease or symptoms, so STD treatment is usually combined with STD screening. This screening and treatment can take place in the general population or in HIV clinics. The screening in HIV clinics is likely to have a greater population-level effect because all persons identified with STDs are HIV positive. ***References:*** (Chesson and Pinkerton, 2000; Chesson, et al., 1999; Grosskurth, et al., 2000; Grosskurth, et al., 1995) ***Expected proximate outcomes***: *Reduction in the prevalence of cofactors (STDs)*

- *HIV treatment*: Treatment with HAART (Highly Active Antiretroviral Therapy) is effective in reducing viral load in blood. The body fluids that transit HIV are blood, seminal fluid, and vaginal fluid. Although these seminal and vaginal fluids are sometimes independent of blood, there is some evidence that a lower viral load in the blood will translate to a lower viral load in vaginal fluid and semen, which would decrease the likelihood of sexual transmission. ***References:*** (Lepri, et al., 2001) ***Expected proximate outcomes***: *Reduction in viral load in HIV-infected persons*

- *Circumcision*: Circumcision has been found in epidemiologic studies to be strongly associated with a decreased risk of HIV transmission. The mechanism is believed to be a toughened skin surface of the glans in circumcised persons providing a greater barrier to the virus. ***References:*** (Gray, et al., 2000; Weiss, Quigley and Hayes, 2000). ***Expected proximate outcomes***: *Increase in the proportion of men who are circumcised*

Comment:

The use of these three biologic interventions are currently widespread, however, they are rarely used for the expressed purpose of preventing HIV transmission. Nonetheless the evidence that they reduce the spread of HIV infection is at least as strong as that for educational and psychological interventions, so they should be considered in the range of options when planning HIV prevention strategies.

While STD treatment is widely used in the U.S., there are many ways in which this strategy can be enhanced to reduce HIV transmission, such as providing patient-delivered therapy for partners of persons with STDs, providing empiric treatment for STDs in clinics other than public STD clinics (which already provide empiric treatment), and expanding STD screening programs in settings where HIV prevalence is high, such as jails and public hospital emergency departments.

The main advantage of biological approaches is that they can work even when persons do not reduce their risky sexual behavior. Circumcision offers the additional benefit in that its effects are permanent. These interventions can be used to complement behavioral interventions.

Other individual level approaches to HIV prevention:

- *Drug treatment*: Treatment for drug addiction is an intervention that could be described as educational or psychological. This intervention has two effects: 1) by reducing drug use, it reduces the frequency of drug injection and thus the frequency of reuse of infected needles and syringe, and 2) by reducing drug use, it also reduces the likelihood of persons' trading sex for drugs or taking sexual risks while under the influence of drugs. ***References:*** (Lampinen, 1991; Prendergast, Urada and Podus, 2001; Woods, et al., 1999). ***Expected proximate outcomes****: Reduction in frequency of drug injection, reduction in number of sex partners, increase in proportion of sexual encounters in which a condom is used*

Structural Interventions

Availability

- *Condom availability*: Condom availability simply provides access to condoms and does not necessarily require overt motivational or educational messages. The rationale for these programs is that by simply increasing the number of condoms available and accessibility of them, condom use will increase. Usually, however, condom availability is coupled with some motivational or marketing message, to increase awareness and to make condoms appear to be socially acceptable and desirable. Globally, condom social marketing, condom subsidies and condom availability have been the cornerstones of HIV prevention campaigns. In the United States, condom availability has been an explicit component of 1) condom social marketing programs, 2) school-based condom availability programs and 3) clinic and community-based condom availability programs. In contrast, condom availability is often an unacknowledged component in 1) group, peer and street outreach interventions and 2) individual and group counseling, with or without HIV testing. ***References:*** (Arnold and Cogswell, 1971; Bedimo, et al., 2002; Calsyn, et al., 1992; Cohen, et al., 1999; Hanenberg, et al., 1994; Robinson, et al., 1996; Rojanapithayakorn and Hanenberg, 1996) ***Expected proximate outcomes****: Increase in proportion of sexual encounters in which a condom is used*

- *Needle exchange programs****:*** Needle/syringe exchange programs provide sterile needles to individuals who return used needles in exchange, thereby reducing the likelihood of reuse of an infected needle. These programs have the added advantage that they may reduce the number of discarded needles and syringes on streets. Needle exchange programs are in operation in many states and cities in the U.S. They operate through fixed or mobile sites and can include van stops, scheduled street exchange sites, or even provide delivery services. Almost all U.S. needle exchange programs provide only one syringe for each syringe brought in to the NEP; but many provide small numbers of syringes to IDUs making their first visit to the NEP. ***References:*** (Heimer, et al., 1998; Jacobs, et al., 1999; Kaplan, 1995; Kaplan and Heimer, 1992) ***Expected proximate outcomes****: Reduction in proportion of drug injections in which a previously-used syringe is used*

- *Needle deregulation:* In many states there are laws and regulations that inhibit availability of sterile needles and syringes to IDU. These include laws requiring prescriptions for needles/syringes and laws banning the possession of needles/syringes as "drug paraphernalia." These laws are not present or are not enforced in many states, and some states have passed laws that make explicit exemptions in them to increase the availability of sterile needles/syringes to IDU. By allowing IDU to purchase their own sterile needles/syringes, needle deregulation efforts should reduce the likelihood that IDU will reuse infected needles/syringes from others. ***References:*** (Anonymous, 1993; Calsyn, et al., 1991; Cotten-Oldenburg, et al., 2001; Groseclose, et al., 1995; Holtgrave, et al., 1998) ***Expected proximate outcomes****: Reduction in the proportion of drug injections in which a previously-used syringe is used*

- *Alcohol taxes*: Alcohol use has been associated with high-risk behaviors in many studies, including high-risk sexual behavior. While reducing alcohol availability is not usually considered as an HIV prevention strategy for individuals, it may be a useful tool to reducing HIV transmission in populations. Alcohol availability is determined by a variety of factors including the strictness and strength of enforcement of alcohol beverage control laws, the price of alcohol (often associated with alcohol taxes), the number and type of outlets where alcohol can be purchased, and the places where alcohol consumption is permitted (e.g., in public settings, cars, or clubs). Raises in alcohol taxes have specifically been followed by reductions in STDs. ***References:*** (Chesson, Harrison, and Kassler, 2000; Scribner, Cohen, and Farley, 1998) ***Expected proximate outcomes****: Reduction in number of sex partners*

Social Structures

- *Community mobilization and street outreach programs*: Outreach to persons at risk can be conducted in a variety of ways and for various purposes, including as a mechanism to bring people in to receive other interventions. In this context, however, we use the term Street Outreach to describe a community-based strategy in which the risk-reduction intervention is delivered in community settings, usually outdoors in high-incidence neighborhoods. The goal of the intervention is to reduce the spread of HIV and STDs by increasing condom use and reducing the sharing of needles. Street outreach is usually conducted by peers from the community in which it is undertaken and involves a face-to-face personal interaction with high-risk persons. Community mobilization campaigns, on the other hand, also involve street contacts by peer educators, but the aim is to change the norms of risky behavior for an entire community. However, the two programs in practice may be similar, because people with whom outreach workers have contact may continue to spread risk reduction messages; thus, individuals in the target communities who have not been personally reached by outreach workers still get messages about safer sex and drug use through others. ***References:*** (Kahn, et al., 2001; Kegeles, Hays, and Coates, 1996) ***Expected proximate outcomes****: Reduction in the number of sex partners, increase in proportion of sexual encounters in which a condom is used, reduction in the proportion of drug injections in which a previously-used needle is used*

- *Opinion leader programs*: These programs identify, train, and enlist the help of key opinion leaders to change risky sexual norms and behaviors; they have only been well evaluated as they have been applied to men who have sex with men (MSM). The program is based on diffusion of innovation/social influence principles, which states that trends and innovations are often initiated by a relatively small segment of opinion leaders in the population. Once innovations are visibly modeled and accepted, they then diffuse throughout a population, influencing others. Their ultimate goal is reduction of sexual risk behavior in MSM. ***References:*** (Kelly, et al., 1992; Kelly, et al., 1991; Pinkerton, et al., 1998). ***Expected proximate outcomes****: Reduction in the number of sex partners, increase in proportion of sexual encounters in which a condom is used*

- *Supervised activities for youth*: If youth are supervised, in theory they have less time to engage in high-risk behaviors. There are many types of programs that involve youth in supervised activities. Very few studies have evaluated the impact of supervised activities on HIV risk behaviors. However, one program that placed youth in community service activities showed a reduction in unprotected sex. ***References:*** (O'Donnell, et al., 1999). ***Expected proximate outcomes****: Reduction in the number of sex partners, reduction in the frequency of sexual intercourse*

Physical structures

- *Bathhouse regulations/closure*: Bathhouses are establishments for men to have sex (usually anonymously) with other men. Many establishments have rules that require condoms be used during sex, but these policies may not be enforced. The enhanced opportunities for sex with many individuals increase the risk of disease transmission. Recently, syphilis outbreaks have been traced to gay bathhouses. Bathhouses can be further regulated to enforce condom use or be closed if condom use is not routine. This intervention was used in some cities in the 1980s, but it has not been evaluated. ***Expected proximate outcomes****: Reduction in the number of sex partners, increase in proportion of sexual encounters in which a condom is used*

- *Crackhouse or shooting gallery regulation or closure:* Crackhouses and shooting galleries serve as places for people to engage in sex, non-injection drug use, injection drug use, or all of these. These establishments exist outside of the law, but in theory may be identifiable and subject to regulation or closure. This intervention has not been evaluated. ***Expected proximate outcomes****: Reduction in the number of sex partners,* *increase in proportion of sexual encounters in which a condom is used, reduction in the proportion of drug injections in which a previously-used syringe is used*

Media

- *Media campaigns*: These interventions are efforts to use both small and large media to either promote products or behaviors related to HIV prevention. Media campaigns promoting condom use have been very successful in Europe and in developing countries. Large-scale media campaigns have not been used for condom promotion in the United States to date. Because HIV and the behaviors associated with transmission are stigmatized in the U.S, large-scale campaigns have been very general, information-based or fear-based and have not been found effective. Campaigns using small media have been much more commonly employed, and these include the distribution of novellas, posters, flyers, and other promotional items. These smaller campaigns can be less visible to the general public and more targeted at a variety of subgroups. However, intervention effectiveness has not been well documented. ***References:*** (Dubois-Arber, et al., 1997; Lehmann, et al., 1987) ***Expected proximate outcomes****: Reduction in the number of sex partners, increase in proportion of sexual encounters in which a condom is used*

Comment:
While we have included data from studies that evaluated each intervention independently of other interventions that may have been taking place in the same geographic areas, it is possible that interventions may potentially enhance or detract from the effectiveness of each other. However, no data are available to tell us how well different HIV prevention interventions complement each other.

3. Evaluating Effectiveness

a. Basic approaches to evaluating HIV preventive interventions

We have tried to include in *Maximizing the Benefit* examples of a wide variety of HIV preventive interventions that have been shown effective or are commonly used in the U.S. Our list is not exhaustive and it may be useful to consult other lists or literature reviews for other interventions (see Johnson, 2002; Neumann, 2002; Rotheram-Borus, 2000; Semaan, 2002; and **http://www.cdc.gov/hiv/pubs/hivcompendium/toc.htm**). Not all interventions described in the literature or commonly used have been evaluated with rigorous designs, and few have been replicated and have repeatedly been shown to be effective when implemented in other settings. Therefore, the strength of the evidence that the interventions are in fact effective varies. It makes sense to set a higher priority on interventions for which the evidence of effectiveness is stronger. More detail on how we suggest you use strength of the evidence in priority-setting is included in section C. *How to Use the Priority-Setting Tool.* This section provides more background on the different types of studies that are used to evaluate effectiveness.

There are many types of evaluation methods employed to determine whether prevention programs work or not, including the most definitive designs (randomized controlled trials), and less definitive designs. Some HIV preventive interventions have been found effective in randomized controlled trials and some have been evaluated only with the less definitive designs.

Randomized controlled trials--In these studies, target groups are chosen and then randomly assigned to receive either the intervention to be evaluated or not (the "control" or comparison condition); control or comparison groups either receive a usual intervention or no intervention at all. Surveys and measures are taken in both groups before the intervention is implemented and then again when it is complete. Then the results of the surveys are compared. At baseline, the two groups should be the same; however, if the intervention is successful, at the end of the intervention the group that received this intervention should have better results than the group that did not.

Quasi-experimental designs--This term refers to nearly any evaluation approach that does not meet all the criteria of a randomized controlled trial. This may include a lack of random assignment, lack of measures on the two groups before the intervention, or two groups that are not equivalent before the intervention. When these deficits exist, one cannot be sure whether any observed differences are due to some pre-existing differences or some other bias in the group chosen. However, if an improvement in the outcome takes place in the intervention group without a similar improvement in the comparison group, one might have more confidence in the program's effectiveness.

Longitudinal studies with no comparison group--For many interventions, particularly those that are large or offer services that require a response (such as STD treatment) is it difficult or unethical to have a comparison group that does not receive the intervention. For example, the 100% Condom Program in Thailand and the STOP AIDS mass media campaign in Switzerland were implemented across entire countries, without comparison countries included in the evaluations. Evaluations of these programs are dependent on comparing behavior and/or HIV/STD incidence before and after the programs were implemented. Any improvement suggests that the change is due to the intervention, but it is also possible that the results might have been the same without the intervention. Perhaps the disease is going away on its own, or people are changing their behaviors on their own. While non-controlled studies are considered scientifically weak designs, they have more credibility if there are several points of measurement before the intervention that do not show any change in the outcome of interest (or a change in the wrong direction), and there are several points after the interventions where there has been a big change in the desired direction. If these changes are timed to coincide with the intervention, and there is little reason to think that the situation would have changed on its own, one might have greater confidence in the intervention's effectiveness. For example, in the case of the 100% Condom Program in Thailand, STD and HIV had been increasing prior to the intervention and the declines in STD and HIV occurred just after the program began, suggesting the effectiveness of the program. Because certain types of interventions (e.g., mass media campaigns) may never be evaluated with randomized controlled designs, it is important to consider these interventions, even if the studies on them used uncontrolled designs.

Note: Even when a well-designed study has demonstrated that an intervention is effective, you should not assume that this intervention could be implemented successfully elsewhere. Something that works for gay men in New York may not be feasible in a more politically conservative city. And the ease of replicating a study is directly proportional to how complicated the intervention and protocols are. The more complicated, the higher the level of talent needed to implement it and the higher the expense, the more difficult it will be. All interventions should be evaluated with outcome measures on a regular or continuous basis to try to assess their effectiveness when implemented locally.

b. Limitations in evaluations of HIV preventive interventions

When assessing the relative value of different HIV preventive interventions, it is important not only to determine whether they have been formally evaluated and found effective, but also to understand the limitations on these evaluations. Some of these limitations are discussed below:

- **Many interventions have never been carefully evaluated.** Several interventions that are routine components of many HIV program have not been evaluated for their effectiveness. These include prevention case management and public information programs, such as AIDS hotlines. Because they have not been evaluated we do not know whether these interventions are or are not effective in reducing HIV transmission, or if they are effective, the degree to which they are effective. Without data on effectiveness, this tool cannot provide guidance on their cost-effectiveness. [However, you can include these interventions in "sexual risk reduction #x" rows of the *CE Estimator* and by performing "What If" calculations, estimate how effective they would have to be to make them cost-effective relative to your other interventions.]

- **Weakness of evaluations.** The various interventions that we included in our spreadsheet were not all evaluated using randomized controlled study designs with adequate blinding procedures and objective measures as the outcome. In some studies, the evaluation consisted of measurements before vs. after the intervention was conducted, and in other studies, intervention and comparison groups were assigned as a matter of convenience. In these study designs, the benefits of the intervention are often overstated.

- **Scalability and replicability.** Interventions are evaluated in a group of a given size, and it may not be easy to achieve the same effect in groups of different sizes. For example, if an intervention was found to be effective using 100 subjects, it may not be the case that it will be effective using 1,000, 10,000, or even 20 subjects. The logistics of the interventions change with number of people in the target group. As such, the actual dynamics of the intervention may change and it may no longer be effective. Programs found to be cost-effective in controlled intervention trials often prove to be less effective when replicated on a larger scale or targeted to a different audience.[6, 7]

  Usually, the initial trial conducted as a research study has a relatively generous budget, and a great deal of attention is paid to the details of implementation. Special efforts are made to encourage compliance and attendance, including the provision of incentives for participants. These interventions may be hard to replicate due to their complexity, need for multiple sessions, and highly skilled staff. A notable example, DARE, a drug-use prevention program that uses police as facilitators, was successful as a research protocol but unsuccessful when expanded to reach a larger audience.[7] Another example is Postponing Sexual Involvement, a teen pregnancy prevention program that reduced risk behaviors in initial phases but failed to have any impact when expanded and replicated.[8]

- **Self-report bias.** Studies that rely on the self-reported behavior of subjects are somewhat suspect, especially with "before vs. after" designs, because people tend to report behaviors that they think the researchers want to hear. This "social desirability bias" is worse with sensitive behaviors, such as condom use or sex in general. Objective measures such as presence of STDs or HIV may be more easily believable, as they rely on laboratory diagnosis.

- **Complementary interventions.** Some interventions may be more effective (or only effective) if they are combined with other interventions. For example, hotlines may have value only if persons calling the hotlines can be referred to convenient sites for counseling and testing. Likewise, street outreach may only be effective if combined with a program to increase the availability and accessibility of condoms. *Maximizing the Benefit* does not have the ability to quantify how interventions may influence each other. However, you can use the Priority Setting tool to take into account advantages and disadvantages of different combinations of interventions.

- **Duration of intervention effectiveness and timing of evaluation.** Interventions may be implemented over a short period of time, yet in order to determine effectiveness, the participants may be questioned at different intervals after the intervention, sometimes within 3, 6 or even 12 months or longer. If the follow-up evaluation is at 3 months, we will not know whether the effects are longer lasting, although they may well be.

c. Evaluating your interventions

Any group can evaluate its own interventions. While these evaluations may not be of sufficient scientific quality to be publishable in research journals, their results can be extremely valuable to persons planning or implementing these programs. The key to evaluation of an HIV prevention intervention is to determine the proximate outcome that the intervention is designed to change. These outcomes are described in section D.1. above as:

- the number of sex partners
- the frequency of sexual intercourse
- the proportion of sexual encounters in which a condom is used
- the frequency of drug injection
- the proportion of drug injections in which a previously-used syringe is used
- the prevalence of biologic cofactors, such as other STDs.

The outcomes should be measured before the intervention begins and periodically afterwards and the differences examined. If possible, the changes should be compared to changes in a second group that did not get the intervention to determine whether the changes can be attributed to the intervention.

E. How Does the Cost-Effectiveness Estimator Work?

1. Cost-Effectiveness in HIV Prevention Planning

Since the Community Planning process began, the CDC has asked community planning groups and health departments to explicitly consider cost-effectiveness in setting priorities for HIV prevention strategies. This is because there will never be enough money to fully carry out every possible strategy to prevent HIV transmission. The purpose of considering cost-effectiveness in planning HIV prevention programs is to prevent the greatest number of persons from becoming infected with HIV within the funds available.

Some HIV prevention interventions may be costly, but may prevent many cases of HIV infection; others may be inexpensive, but may not prevent many cases. It is not always clear which of these interventions are the best use of limited funds. Cost-effectiveness calculations allow planning groups to compare these different interventions to estimate which should prevent the most cases of HIV infection for the dollars they have available. What follows is a brief introduction to cost-effectiveness. For those who would like to learn more about cost-effectiveness methods in HIV prevention, many excellent sources exist, and some of these were used to inform *Maximizing the Benefit*. (See Weinstein, et al., 1989; Pinkerton, et al., 2001; Creese, et al., 2002 and others in the Bibliography.)

The concept of cost-effectiveness came from economists and financial analysts who wanted to compare the two different approaches to achieving a goal using a common yardstick. In general, cost-effectiveness calculations produce a ratio of the *cost* of implementing a strategy relative to the quantitative *effect* of a strategy (measured in various units). For example, two different advertising strategies could be compared by the advertising costs per new customer recruited.

In the prevention of HIV transmission, the *effect* that we measure is the number of HIV infections prevented, and the *cost* is the cost of implementing a particular strategy. The ratio is the cost per HIV case prevented, or:

$$\frac{\text{Total program cost of an intervention}}{\text{Number of HIV cases prevented}} = \text{Cost per HIV case prevented}$$

This calculation looks at economic costs from the perspective of the public health system. In other words, it counts the total cost to the public health system of the intervention, and the effectiveness is the number of reduced HIV cases as a result of the intervention. It accounts for the cost of all resources (purchased, donated, or volunteered) used to implement the intervention, but excludes any cost incurred by the participants, unless they are reimbursed. Similarly, it excludes the HIV cases prevented beyond primary and secondary transmission from persons reached by the intervention.

2. Estimation of HIV Infections Potentially Prevented

It is not possible to measure the number of persons who were NOT infected with HIV as a result of a prevention program. Therefore cost-effectiveness calculations in HIV prevention planning rely on mathematical estimates. These estimates are based on subtracting an estimate of the number of HIV infections that would have happened if the prevention program had not been in place from an estimate of the number of HIV infections that may have happened even with the program in place. This number should not be viewed as actual cases prevented, but rather as an index to enable comparisons between interventions. The most common mathematical model to estimate the number of new infections in a population is called the Bernoulli-process model (Pinkerton & Abramson, 1998; Pinkerton, Holtgrave, Leviton, et al., 1998; Weinstein, Graham, Siegel, et al., 1989). We used this model as the basic formula to calculate the total number of HIV cases potentially prevented in the Estimator.

The Bernoulli-process model, like all mathematical models, is based on assumptions that we cannot verify, so the *absolute* number of HIV infections prevented in our calculations may not be accurate. However, because we used the same assumptions for all calculations, the comparison between interventions of the *relative* numbers of infections prevented should be accurate within a reasonable range. ***It is important for users to understand that the estimation involved means that the cost-effectiveness ratios should only be viewed as rough approximations, not precise numbers, and that two interventions with roughly similar cost-effectiveness ratios should be considered the same in cost-effectiveness as far as our tool can determine.***

How do the basic mathematical models work?

In the Bernoulli model, each sex act is treated as an independent event with a small, fixed probability that HIV would be transmitted between members of a couple who are discordant in their HIV status (i.e., one is infected while the other is not). From this per-act probability, the model can then estimate the cumulative probability that an uninfected individual with given sexual behaviors (number of partners, frequency of sex acts) would become infected during a specified time period. The number of new HIV cases is determined by the size of the population with given behaviors and their cumulative probability of transmission.

An intervention may modify the risky sex behaviors by increasing condom use, decreasing number of sex partners and/or sex acts. Other interventions may improve the diagnosis and treatment of STDs that facilitate HIV transmission. Both outcomes will result in reduced probability of HIV transmission and translate to HIV cases prevented. A similar formula is used to calculate prevented HIV transmission from IV drug use based on HIV prevalence in HIV drug users, number of injections, and frequency of needle sharing.

3. The internal worksheets

Different interventions prevent HIV transmission in different ways, as described in section D. For example, some prevent HIV transmission by increasing condom use and some by reducing syringe sharing. The spreadsheet includes five different internal worksheets to estimate the number of HIV cases prevented from different intervention outcomes:

- *Sex & Condom* sheet: changing risky sexual behaviors (the most commonly used sheet)
- *STD Scrn & Rx* sheet: changing the screening and treatment of STDs in general population
- *STD Scrn in HIV clinics* sheet: changing the screening and treatment of STDs in HIV clinics

- *Needle* sheet: changing number of injections, and frequency of needle sharing, and
- *STD Reduction* sheet: changing sexual risk behaviors and STD incidence, measured by reductions in STD incidence.

Four additional internal worksheets similar to these (except the Needle sheet) are included to conduct these calculations specifically for men who have sex with men.

The following table lists the corresponding formula worksheet for each intervention listed in the *CE Estimator* worksheet.

Intervention	Formula worksheet
HIV counseling and testing Among HIV-positives Among HIV-negatives	Sex & Condom
Client-centered	STD Reduction
Individual counseling (without testing); single session	Sex & Condom
Discordant couples counseling	Sex & Condom
Videos in STD clinics	STD Reduction
Group counseling, multiple session (Kelly, et al.)	Sex & Condom
Group counseling, multiple session (Shain, et al.)	Sex & Condom
Partner notification for HIV + partners Partner notification for HIV–partners	Sex & Condom
School-based education, multiple session	Sex & Condom
Opinion leader programs	Sex & Condom
Drug treatment programs	Needle
Street outreach (Sikkema, et al.)	Sex & Condom
Street outreach (Wendell, et al.)	Sex & Condom
Community mobilization campaigns	Sex & Condom
Community mobilization (Mpowerment)	Sex & Condom
STD diagnosis and treatment STD screening in HIV clinic	STD Scrn in HIV clinics
STD diagnosis and treatment STD screening in general population	STD Scrn & Rx
HIV antiviral treatment	Sex & Condom
Male circumcision (all males)	Sex & Condom
Male circumcision (high risk populations)	Sex & Condom
Condom availability/accessibility	Sex & Condom
Needle exchange	Needle
Needle deregulation	Needle
Alcohol taxes	STD Reduction
Youth supervision programs	Sex & Condom
Mass media campaigns	Sex & Condom
Sexual Risk Reduction (generic)	Sex & Condom

The internal worksheets are not specifically designed for users to modify, but you can open them and alter them if you wish. The workbook will permit you to change either internal default values or the actual formulas. ***Before you change any cell in them, however, we strongly suggest that you read and fully understand the detailed discussion below, or you risk producing results that are incorrect or inconsistent across interventions.***

To prevent inadvertent changes to the internal worksheets, they are both hidden and "protected" in Excel. You can "unhide" them by using the *Format…Sheet* command and selecting the internal spreadsheet you wish to view. Then you can "unprotect" a worksheet by using the *Tools…Protection…Unprotect sheet* command. No password is needed.

The internal worksheets contain cells with values carried forward from the *CE Estimator* worksheets (highlighted in blue), additional default parameters, and formulas to calculate intermediate values. You should not change the cells highlighted in blue or the tool will not work at all. You may want to change default parameters (e.g., reductions in HIV transmission caused by condom use), but be sure you understand what you are changing before you do this. ***We do not recommend you change the formulas unless you are very experienced in Bernouli-process models for HIV transmission or other relevant mathematical models.***

4. Details on Formulas for Specific Categories of Interventions

Sex and condom use formula

Below briefly displays the mathematical formula used in the Sex & Condom worksheet in estimating the number of HIV infections prevented. Interested readers can find more details in Pinkerton & Abramson (1998), Pinkerton, Holtgrave, Leviton, et al., (1998), and Bedimo, Pinkerton, Cohen, et al., (2002).

The total number of HIV infections prevented by an intervention is:
$A = A_p + A_s$,
where A_p is the total number of *primary* infections prevented by an intervention and A_s is the total number of *secondary* infections prevented (that is, "downstream" infections in partners prevented as a result of prevention of infection in targeted persons).

$A_p = (P_1 – P_2)\ [(1\text{-}\pi)N]$, where
$P_1 = 1\text{-}[(1\text{-}\ \pi^*) + \pi^*(1\text{-}\ \_)^{(1\text{-}f1)n1}(1\text{-}\ \_')^{f1n1}]^{m1}$ = mean pre-intervention risks for uninfected intervention participants to become infected
$P_2 = 1\text{-}[(1\text{-}\ \pi^*) + \pi^*(1\text{-}\ \_)^{(1\text{-}f2)n2}(1\text{-}\ \_')^{f2n2}]^{m2}$ = mean post-intervention risks for uninfected intervention participants to become infected

Similarly,
$A_s = (S_1 – S_2)(\pi N)$, where
$S_1 = (1\text{-}\ \pi^*)m_1[1\text{-}(1\text{-}\ \_)^{(1\text{-}f1)n1}(1\text{-}\ \_')^{f1n1}]$ = mean pre-intervention value for the expected number of secondary infections arising from the sexual behavior of already infected participants
$S_2 = (1\text{-}\ \pi^*)m_2[1\text{-}(1\text{-}\ \_)^{(1\text{-}f2)n2}(1\text{-}\ \_')^{f2n2}]$ = mean post-intervention value for the expected number of secondary infections arising from the sexual behavior of already infected participants

The symbols represent:
π = prevalence of HIV infection in intervention participants
π^*= prevalence of HIV infection in intervention participants' sex partners
_ = probability of HIV transmission, per act of unprotected intercourse
_'= probability of HIV transmission, per act of condom-protected intercourse
f_1 = Proportion of sexual encounters in which a condom was used, pre-intervention
f_2 = Proportion of sexual encounters in which a condom was used, post-intervention
n_1 = Number of acts of intercourse, per partner, pre-intervention
n_2 = Number of acts of intercourse, per partner, post-intervention
m_1 = Number of sex partners, pre-intervention
m_2 = Number of sex partners, post-intervention
N = Number of participants reached by intervention

STD Screening and Treatment Formula

Chesson and Pinkerton (Chesson, 2000) used an extension of the Bernouli model described above to estimate the number of HIV infections that would be prevented by treatment of different sexually-transmitted diseases that act as cofactors for HIV transmission. This extension used the same formula above, except it included a value □ (theta) for the increase in the probability of HIV transmission between partners associated with the presence of a specific STD. In this model, the value of □ for gonorrhea was set to 10, indicating that the per-contact probability of HIV spread would be increased ten-fold in the presence of gonorrhea. The value of □ for chlamydia was set to five. This model also incorporated estimates of the number of days in which persons infected with STDs remain infected and sexually active.

We used the Chesson and Pinkerton model to estimate the prevention benefit of providing screening and treatment for gonorrhea and chlamydia. For the per-act probability of transmission of HIV from males to females in the absence of STDs we used the value of .001, and for the per-act probability of transmission from females to males we used the value of .0006. Chesson and Pinkerton allocated persons with STDs into three groups: those who stop sexual activity and sought treatment immediately (Group 1), those who continue sexual activity but seek treatment quickly (Group 2), and those who are asymptomatic and continue sexual activity (Group 3). A program to screen persons for STDs will identify persons in the second and third groups, who either have some delay in treatment for symptoms or are asymptomatic. Based on the findings of a screening program that we conducted in New Orleans, we estimated that 86% of persons identified with either gonorrhea or chlamydia would be asymptomatic (in Group 3) and 14% would have symptoms for which they were not yet treated (in Group 2).

For an STD screening intervention, the Estimator has a default value for the prevalence of gonorrhea of 2.3% and for the prevalence of chlamydia of 10.1%. These values were obtained from STD screening in convenience samples of persons from various sites in New Orleans. These values can be changed to the expected prevalence in any other population by "unhiding" the columns with the STD prevalence values (columns L and M).

STD Screening in HIV Clinics Formula

Screening and treatment for STDs in HIV clinics is similar to STD screening in the general population in its potential to transmit HIV infection, with a key exception: all persons screened are HIV-infected, and the benefit to STD screening and treatment is prevention of transmission of HIV to their partners.

The formula for this intervention is a further modification of the Bernouli model used above to calculate the number of HIV infections prevented by STD screening in the general population. It makes the same assumptions with regard to the proportion of persons with STDs who are asymptomatic. It assumes as a default value that 46% of partners of HIV-infected persons are themselves already HIV-infected (from Toomey et al., 1998); this default value can be changed. It assumes as a default value that prevalence of gonorrhea is 1.7% and the prevalence of chlamydia is 2.1%. It assumes that 65% of the gonorrhea cases and 54% of the chlamydia cases identified in the HIV clinic are in males (based on our unpublished data on STD screening in the HIV clinic in New Orleans). It then calculates the number of cases of HIV infection in partners attributable to these STDs that would be prevented by curing these STDs.

Needle Exchange/Needle Sales Formula

This formula is to estimate HIV infections prevented through needle exchange and needle sale programs. It is adapted from the Weinstein et al., (1989) (p. 490) "personal risk of HIV infection."

Let
$\square$ = per-injection probability of virus transmission if the needle was infected
$\square$ = the probability that a randomly selected needle is infected
$\square\square$ = probability of becoming infected by an infected needle during a single injection

If there are *n* exposures with the same infected needle, the risk of infection becomes
$P = 1 - (1- \square\square)^n$

If the uninfected IDU gets a needle randomly from the pool of available needles and $\square$ is the probability that a needle is infected, the cumulative risk of infection then becomes
$P' = \square[1 - (1- \square\square)^n]$

Most IDUs will have more than one needle. If the uninfected IDU has *n* exposures with each of m randomly picked needles, the cumulative risk of infection becomes
$P_D = 1 - [\square(1- \square\square)^n + (1- \square)]^m$

Let *c* = the proportion of previously unsterile injections for which sterile syringes will be available because of expanded pharmacy syringe sales and/or increased syringe exchange program activity.

Then the probability that a randomly selected needle is infected becomes (1-c) $\square$

And the cumulative risk of infection with program becomes
$P_{Dc} = 1 - \{(1\text{-}c)\square[1\text{-} (1\text{-}c)\square\square]^{n} + [1\text{-} (1\text{-}c)\square]\}^{m}$

Thus, the number of infections reduced as a result of a program is
$N * (1\text{-} \square)*(P_{D} \text{-} P_{Dc})$
Where N = number of active IDUs reached by a program, and
$\square$ = HIV prevalence among IDUs

STD Reduction formula

The MMWR (Anonymous, 2000) reported that increases in alcohol taxes were followed by reductions in rates of gonorrhea. Assuming that the mechanism for this is reduction in risky sexual behavior associated with alcohol use, then alcohol taxes should also be followed by similar reductions in HIV incidence. The epidemiology of HIV is different from the epidemiology of gonorrhea, so the reductions in HIV incidence could either be larger or smaller than the reductions in gonorrhea incidence; for the purpose of this cost-effectiveness estimation, we assumed that the reductions in HIV incidence were proportional to the reductions in gonorrhea incidence. The calculations are based on a 20-cent increase in the tax on a six-pack of beer, which was estimated to reduce gonorrhea incidence by 8.9%. This 8.9% reduction was applied to the HIV incidence in the high-risk population (using Los Angeles as an example for the default values) and multiplied by the size of the high-risk population to estimate the total number of HIV infections prevented by reductions in risky sexual behavior by the alcohol tax (in the first year).

The reductions in gonorrhea would have a secondary benefit of reducing HIV transmission through reductions in gonorrhea as a cofactor. This additional benefit was estimated by using the formula of Chesson and Pinkerton (2000) for the HIV incidence attributable to different STDs. The number of cases of gonorrhea was multiplied by the number of HIV cases attributable to each case (.00066). This number of HIV infections was added to the number of HIV cases prevented by reductions in sexual risk behavior to arrive at the total number of HIV infections prevented by the alcohol tax.

The default HIV incidence estimates and the size of the total population reached were taken from Holmberg (1996) for Los Angeles; these should be replaced with local HIV incidence estimates. Likewise the annual number of gonorrhea cases for Los Angeles was used as a default; this can be changed by “unhiding” column L. The estimated 8.9% reduction is in the Alcohol Tax tab. This number can be modified if a different size tax is planned or you wish to change the assumption regarding the size of the HIV transmission reduction from a tax.

5. Default Values Used in Formulas

The default values in the Estimator are based on values reported in the selected intervention trials, with the exception that to maintain the comparability of the cost-effectiveness calculations of various interventions we used standard estimates of HIV transmission probabilities. If values of parameters for sexual behavior were not reported in the intervention trials we used standard default values. You may change the values to meet your local conditions.

Per-act HIV transmission probability:

Male to female vaginal sex - 0.001 (Mastro & Kitayaporn, 1998)
Female to male vaginal sex - 0.0006 (Mastro & Kitayaporn, 1998)
Male to male anal sex – 0.01 (Mastro & Kitayaporn, 1998)
Injection with an infected needle/syringe - 0.0067 (Kaplan & Heimer, 1992)
Infection of a needle used by an HIV-infected person – 0.9 (Pinkerton et al., 2000)
Proportionate reduction in sexual transmission as a result of condom use – 0.9 (Pinkerton & Abramson, 1997)

Sexual activity:

Number of **sex partners** in different time periods:

Heterosexuals - 3 months: 2.3 (Kamb, et al., 1998)
6 months: 2.6 (based on 3 month value)
1 year: 3.0 (based on 3 month value)

MSM - 3 months: 2.5 (Kelly, et al., 1997)
6 months: 2.7 (based on 3 month & 1 year values)
1 year: 3.1 (Laumann, et al., 1994, Table 8.4)

Number of **sex acts** per year:

Heterosexuals - 81 (Laumann, et al., 1994, Table 3.6)

MSM - 54 (Laumann, et al., 1994, Table 8.5)

F. Limitations of Cost-Effectiveness Estimations Using *Maximizing the Benefit*

There are many limitations to these cost-effectiveness analyses. HIV prevention interventions rely on a variety of assumptions including: information on per exposure HIV transmission probability, average risk behaviors, population prevalence of infection, and many other parameters that are not usually measured in an intervention trial. These assumptions are, therefore, somewhat suspect, making the *absolute value* of the cost of interventions per infection prevented questionable. However, when the same assumptions are used across programs, the *relative value* of the costs of different interventions per infection prevented is substantially valid; thus, cost-effectiveness analyses can be extremely helpful in choosing among a variety of effective, competing intervention programs.

The following is a discussion of the variety of limitations of cost-effective analysis using *Maximizing the Benefit*. This long list is not meant to cast so much doubt on the procedure as a whole to scare away those who would like some better guidance as to how to prioritize interventions; rather, it is meant to provide an appreciation of the complexity of the procedure and to emphasize that cost-effectiveness analysis produces only estimates, not exact, hard figures of the true benefits. In spite of these limitations, the procedure provides a means to compare the impact of a wide variety of interventions that communities have to choose among.

The main limitations of cost-effectiveness analysis to evaluate HIV preventive interventions include:

- **Different formulas for different interventions/ condom vs. IDU, vs. STD infection.** *Maximizing the Benefit* uses three different types of formulas to calculate cost effectiveness. The formulas for condom use and IDU had different parameters related to transmission. The STD formula makes a key assumption that the reduction in STD incidence will be proportional to the reduction in HIV incidence. It is possible that this is not exactly the case, and so these estimates might be wrong, even through they are plausible. The different methodologies threaten the validity of comparing some of the interventions.

- **Mixing patterns were not considered**. The Bernouli-process models underlying most of the calculations of the number of HIV infections potentially prevented assume that people choose partners randomly from a population of known HIV prevalence. In fact, people tend to select partners from the population who are similar to them in risk, thus high-risk people tend to choose high-risk partners. This type of mixing pattern changes the short- and long-term HIV transmission rate in populations in ways that are difficult to estimate mathematically. While this limitation biases the estimates of the number of HIV infections prevented for each individual intervention, if the bias is consistent across interventions, the results are still comparable.

- **Infection versus QALYS.** The primary outcome in the calculations of *Maximizing the Benefit* is the number of HIV cases potentially prevented. Other studies of cost-effectiveness have gone beyond this to investigate QALYs—quality adjusted life years that take into account the number of years of additional life that are saved. In general use of QALYs puts a greater value on preventing infection for a young person than for an older person. Because the age range of the subjects for each intervention is not known, QALYs would be extremely difficult to calculate in this tool.

- **The estimates we used for cost were not adjusted for inflation or discounting**. Some of the interventions were conducted in cities with lower or higher cost of living than where other people may live. That is why it is "required" for users of the spreadsheet to put in their own local current cost estimates to determine the potential cost-effectiveness of the intervention in their areas.

- **Public health system perspective vs. societal perspective**. Our analysis took the perspective of the public health system when assigning costs. This means that when we estimated costs, we only included costs relevant to the program implementation and not costs associated with the time spent by the participants, even if that ended up costing something as far as lost wages or travel time and expenses. Other societal costs were also not included. We did this across all interventions, so at least the perspective should be comparable.

- **Duration of intervention effectiveness.** When interventions are evaluated, their effect is usually measured after a single time interval. The duration of the benefit of the intervention after this measurement is unknown. The time periods of the interventions included in *Maximizing the Benefit* vary from a few months to several years. There is no way to take these varying time periods into account in the cost-effectiveness estimates. It may always not be appropriate to compare interventions where effectiveness is measured after different time periods.

In spite of these limitations, this tool does provide standards and means to estimate the relative cost-effectiveness of different interventions. Because the cost-effectiveness estimates are imperfect, we do not advocate that these be the sole criteria for prioritizing interventions. Other factors, such as feasibility, scalability, replicability and acceptability, and others that may be important in your community, should also be considered when finalizing priorities for interventions.

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