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Technical Guide for VPCCostEffectiveness.xls*

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Introduction

The vaccine calculations spreadsheet (VPCCostEffectiveness.xls) can be used to estimate the cost effectiveness of a commitment to purchase vaccines with specified characteristics.

The spreadsheet's many input parameters and specifications—which any user may change—enhance the flexibility of the analysis. For example, the user may vary general parameters (e.g. the discount rate and the cost effectiveness threshold for a DALY[1]), and parameters that define vaccine efficacy and the number of required doses. Also, the user may change the level of co-payments from countries that are covered under the program and the GNP per capita cutoff that determines program eligibility.

This Technical Guide explains the calculations in detail in the order that the worksheets appear in the Microsoft Excel file, VPCCostEffectiveness.xls. Please refer to the Table of Contents to find the description that corresponds with each worksheet in the Excel file. A companion document, "A Vaccine Purchase Commitment: Preliminary Cost-Effectiveness Estimates and Pricing Guidelines," discusses both the general results of the spreadsheet analysis and sensitivity checks. The accompanying documents "Creating Markets for New Vaccines: Rationale" and "Creating Markets for New Vaccines: Design Issues" discuss the economic justification for a purchase commitment and guidelines for its design. Due to the inclusion of updated data and modification of several model parameters, these two papers may report slightly different results than the spreadsheet.

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[1] DALYs, disability-adjusted life years, are a standard measure of the burden of disease and are defined as the

Quick Guide

Users who are not interested in a detailed description of how the spreadsheet works but simply in the results of the analysis can focus on the *summary* and *options* worksheets. The most important results of the analysis (number of vaccinations, DALYs saved, purchase price, and total cost per DALY saved) are displayed on the *summary* worksheet. Not only are these statistics reported for countries that participate in the purchase program, but also for those that purchase the vaccine on their own once the program has spurred vaccine development. More detailed breakdowns of the number of vaccinations and DALYs saved are on the *vaccinations* and *dalys saved* worksheets, respectively.

The *options* worksheet can be used to examine questions of the following type:

- How many more vaccinations would there be if the GNP per capita program eligibility cutoff were increased by $1000?
- How much would donor contributions need to increase if the level of participating country co-payments were cut by 10%?
- What is the cost effectiveness of a commitment to purchase a vaccine that is not effective against HIV subtype C, which predominates in Africa?

To investigate the answers to many of these questions (and more), the user is directed to the *options* worksheet, which contains all of the assumptions about the model and the vaccine

number of healthy years of life lost due to premature death and disability. Refer to Murray and Lopez (1996) for more details characteristics that the user can change. The *options* worksheet is the tenth worksheet in the Excel file. Simply, enter a different value for one or more of the parameters and view the new results.

In addition, the *co-payments*, *costs*, *cost per daly saved*, and *program* worksheets offer an in-depth look at the characteristics of the purchase program. The *hiv-aids new cohorts*, *malaria new cohorts*, and *tb new cohorts* worksheets have estimates of the burden of disease (in DALYs) for every country in the analysis.

It is helpful to remember the terminology that is used throughout the spreadsheet and the Technical Guide. The age groups are defined as follows: "new cohorts" are newborns. Each year a new group has to be vaccinated. There is also a group of existing cohorts. Two groups are defined. First, "children" are one to ten years olds for the HIV/AIDS and tuberculosis vaccines and one to five year olds for the malaria vaccine. Second, "old cohorts" are ten to thirty-five year olds for the HIV/AIDS and tuberculosis vaccines and women pregnant with their first child for the malaria vaccine. For convenience, this document will, at times, refer to both children and old cohorts as "existing cohorts."

The pages that follow describe the worksheets in the order that they appear in the Excel file.

1. Summary

This worksheet summarizes the main findings of the vaccine calculations spreadsheet.

Rows 4-21 list the base case assumptions that appear on the *options* worksheet.

1.1 COVERED COUNTRIES

1.1.1 FOR THE FIRST TEN YEARS

Row 28. The number of people vaccinated for HIV/AIDS, malaria, and tuberculosis respectively, in millions. This comes from the *vaccinations* worksheet. The total number of people vaccinated for the three diseases combined is also listed.

Row 29. The price to developer per person vaccinated from the *commitment* worksheet. This is the size of the Commitment for ten years divided by the total number of people vaccinated in covered countries.

Row 30. The average co-payment per vaccination comes from the *co-payments* worksheet. This is total co-payments received divided by the total number of people vaccinated in covered countries.

Row 31. Donor contributions needed per year is the total commitment size minus total co-payments received.

Row 32. Total discounted DALYs saved (in millions) comes from the *dalys saved* worksheet.

Row 33. Net Present Value cost per discounted DALY saved is the discounted costs plus discounted co-payments divided by the total number of DALYs saved in covered countries. NPV cost = (discounted costs for ten years + discounted co-payments for ten years)/ DALYs saved for ten years.

1.1.2 TOTAL

Row 36. Total discounted DALYs saved comes from the *dalys saved* worksheet.

Row 33. Total discounted cost per discounted DALY saved is the discounted costs plus discounted co-payments divided by the total number of DALYs saved in covered countries. NPV cost = (total discounted costs + total discounted co-payments)/ DALYs saved.

1.2 NON-COVERED COUNTRIES

1.2.1 FOR THE FIRST TEN YEARS

Row 43. The number of people vaccinated for HIV/AIDS, malaria, tuberculosis, respectively, in millions. Also, the total number of vaccination for the three diseases combined is listed.

Row 44. Total discounted DALYs saved (in millions) comes from the *dalys saved* worksheet.

Row 45. Net Present Value cost per discounted DALY saved is the discounted costs divided by the total number of DALYs saved in non-covered countries.

1.2.2 TOTAL

Row 48. Total discounted DALYs saved (in millions) comes from the *dalys saved* worksheet.

Row 49. Net Present Value cost per discounted DALY saved is the discounted costs divided by the total number of DALYs saved in non-covered countries.

1.3 ALL COUNTRIES

1.3.1 FOR THE FIRST TEN YEARS

Row 55. The number of people vaccinated for HIV/AIDS, malaria, and tuberculosis respectively, in millions, comes from the *vaccinations* worksheet. Also, the total number of vaccinations for the three diseases combined is displayed.

Row 56. Total discounted DALYs saved (in millions) comes from the *dalys saved* worksheet.

Row 57. Net Present Value cost per discounted DALY saved is the discounted costs divided by the total number of DALYs saved for all countries.

1.3.2 TOTAL

Row 60. Total discounted DALYs saved comes from the *dalys saved* worksheet.

Row 61. Net Present Value cost per discounted DALY saved is the total discounted costs divided by the total number of DALYs saved in all countries.

2. Basic Data

This worksheet contains much of the basic data upon which the vaccine calculations are based. For the purpose of the calculations, the population, annual births, GNP per capita, and life expectancy of each country are assumed to be constant over time. Further refinement of the spreadsheet analysis can include variation in these numbers over time.

2.1 COUNTRIES AND CODES

The **countries** included in the analysis are World Health Organization member states, which are virtually all countries in the world (WHO 1999, WHO 2000). They are the following:

Afghanistan, Albania, Algeria, Angola, Armenia, Azerbaijan, Bangladesh, Belarus, Belize, Benin, Bhutan, Bolivia, Bosnia & Herzegovina, Bulgaria, Burkina Faso, Burundi, Central African Republic, Cambodia, Cameroon, Cape Verde, Chad, China, Colombia, Comoros, Congo, Congo DR, Costa Rica, Cote d'Ivoire, Cuba, Djibouti, Dominica, Dominican Republic, Ecuador, Egypt, El Salvador, Equatorial Guinea, Eritrea, Ethiopia, Fiji, Gambia, Georgia, Ghana, Guatemala, Guinea, Guinea-Bissau, Guyana, Haiti, Honduras, India, Indonesia, Iran, Iraq, Jamaica, Jordan, Kazakhstan, Kenya, Kiribati, Kyrgyzstan, Lao, Latvia, Lesotho, Liberia, Lithuania, Macedonia, Madagascar, Malawi, Maldives, Mali, Mauritania, Micronesia, Mongolia, Morocco, Mozambique, Myanmar, Namibia, Nepal, Nicaragua, Niger, Nigeria, North Korea, Pakistan, Panama, Papua New Guinea, Paraguay, Peru, Philippines, Republic of Moldova, Romania, Russian Federation, Rwanda, Samoa, Sao Tome & Principe, Senegal, Sierra Leone, Solomon Islands, Somalia, Sri Lanka, St. Vincent & Grenadines, Sudan, Suriname, Swaziland, Syrian Arab Republic, Tajikistan, Tanzania, Thailand, Togo, Tonga, Tunisia, Turkmenistan, Uganda, Ukraine, Uzbekistan, Vanuatu, Vietnam, Yemen, Yugoslavia, Zambia, Zimbabwe, Antigua and Barbuda, Argentina, Bahrain, Barbados, Botswana, Brazil, Chile, Croatia, Czech Republic, Estonia, Gabon, Grenada, Hungary, Lebanon, Libya, Malaysia, Malta, Mauritius, Mexico, Oman, Palau, Poland, Saudi Arabia, Seychelles, Slovakia, South Africa, St. Kitts and Nevis, St. Lucia, Trinidad and Tobago, Turkey, Uruguay, Venezuela, Andorra, Australia, Austria, Bahamas, Belgium, Brunei Darussalam, Canada, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Japan, Kuwait, Luxembourg, Monaco, Netherlands, New Zealand, Norway, Portugal, Qatar, Republic of Korea (South Korea), Singapore, Slovenia, Spain, Sweden, Switzerland, United Arab Emirates, United Kingdom, and USA.

The **color scheme** corresponds with the World Health Organization's regional categories, where:
African Region = AFR = brown
Americas Region = AMR = light blue
Eastern Mediterranean Region = EMR = dark blue
European Region = EUR = orange
South-East Asia Region = SEAR = yellow
Western Pacific Region = WPR = purple

Please see the Appendix A to this document for the World Health Organization List of Member States by Region and Mortality Stratum (WHO 2000, pages 204-5).

Murray and Lopez region codes. Murray and Lopez (1996a) provide data on regional DALY burden by sex and age group. This data is used later in the *hiv-aids new cohorts*, *malaria new cohorts*, and *tb new cohorts* worksheets. Their regional categories are:

chn: China
eme: Established Market Economies
fse: Formerly Socialist Economies of Europe
ind: India
lac: Latin America and the Caribbean
mec: Middle Eastern Crescent
oai: Other Asia and Islands
ssa: Sub-saharan Africa

Please see Appendix B for a list of the countries included in Murray and Lopez regions.

World Bank Code. The World Bank makes the following income classifications (World Bank 2000a):

1 = low-income: GNP per capita is $760 or less

2 = lower-middle income: GNP per capita is $761 to $3030

3 = upper-middle income: GNP per capita is $3031 to 9360

4 = high income: GNP per capita is $9361 or more

World Health Organization (WHO) region and sub-region codes. WHO (2000) provides regional DALY burden numbers for HIV, malaria, and tuberculosis. Their publication *World Health Report 2000* establishes categories and sub-categories based on region and mortality stratum in the following way. For further information, please see this reference, pages 204 and 205.

AFR1	high child, high adult
AFR2	high child, very high adult
AMR1	very low child, very low adult
AMR2	low child, low adult
AMR3	high child, high adult
EMR1	low child, low adult
EMR2	high child, high adult
EUR1	very low child, very low adult
EUR2	low child, low adult
EUR3	low child, high adult
SEAR1	low child, low adult
SEAR2	high child, high adult
WPR1	very low child, very low adult
WPR2	low child, low adult

2.2 GENERAL COUNTRY DATA

Births. This equals the crude birth rate per thousand for 1998 multiplied by the 1998 country population then divided by 1,000. Both the crude birth rate and population come from the World Bank's *World Development Indicators 2000.*

Population. This is an indicator for 1998 that comes from the World Bank's *World Development Indicators 2000*.

GNP per capita. This is 1998 GNP per capita in US current dollars, calculated using the World Bank Atlas method. The source is *World Development Indicators 2000*. Please refer to the World Bank per capita income classification described above.

Life expectancy. This is a 1998 figure from *World Development Indicators 2000*.

2.3 ADJUSTMENT OF DALY FOR COUNTRIES

Ratio of DALY burden averted by preventing disease to DALY burden of disease. The WHO provides information on the DALY burden of disease, which is calculated under the assumption that people would face a very favorable (Japanese female) life expectancy in the absence of the disease. The DALY burden will, in general, be greater than the number of DALYs saved by eliminating the diseases, because the diseases affect countries where people face many other competing risks. DALYs saved in countries with relatively low life expectancies would be overestimated without the ratio of DALY burden adjustment. The ratio equals the present value of one dollar each year of the life expectancy of a country at the real interest rate divided by the present value of one dollar each year for 81.25 years (the life expectancy of a Japanese woman) at the real interest rate.

2.4 COUNTRY ELIGIBILITY

IDA eligibility/coding. If a country is eligible for World Bank International Development Association (IDA) loans, then the cell equals one, and zero otherwise. IDA eligibility is based on (1) relative poverty, (2) weak creditworthiness, and (3) good economic and social policy performance. Refer to http://www.worldbank.org/ida/ for more information. Although this variable does not enter into any of the calculations, it is provided here for the user's reference.

Commitment eligibility. If a country is eligible to participate in at least one purchase program, then the cell equals one; if the country is ineligible to participate, then the cell equals zero. Eligibility is determined by comparing the countries GNP per capita with a cutoff point, which can be adjusted by the user on the *options* worksheet.

3. Age Distribution

This worksheet contains the age distribution for each country in five-year intervals for the year 2000.

The interpretation of this data is straightforward. For example, about 8% of China's population is under the age of 5, and about 10% are between the ages of 30 and 35. This is calculated from *World Population Projections,* International Bank for Reconstruction and Development / World Bank Group, 2000, which is reported in *World Development Indicators 2000*. For the purpose of the calculations, the age distribution in each country is assumed to be constant over time. Further refinement of the spreadsheet analysis can include change in the population distribution in a country over time.

4. Fertility

This worksheet displays the distribution of births to women ages 15-50 in each country for the year 2000.

The interpretation of this data is straightforward. For example, about 36% of China's births were to women between the ages of 25 and 29, and about 15% of births were to women between the ages of 35 and 39. These are 2000 figures calculated from U.S. Bureau of the Census, International Data Base, Table 028: "Age-Specific Fertility Rates and Selected Derived Measures." The data can be found on the internet at http://www.census.gov/ipc/www/idbnew.html

For the purpose of the calculations, the fertility distribution in each country is assumed to be constant over time. Further refinement of the spreadsheet analysis in the future can include change in the fertility distribution in a country over time.

5. HIV-AIDS Cases

This worksheet estimates the *distribution* of HIV-AIDS burden among countries *within* the same WHO region.

5.1 ESTIMATING DISTRIBUTION OF DISEASE BURDEN

WHO does not report country-level data for burden of disease, but only regional data. To calculate cost effectiveness of a country-based vaccine purchase commitment, however, it is necessary to calculate country-level burdens. Therefore, regional burden is divided according to the distribution of burden among countries within each region based on USAIDS data of HIV seroprevalence. The data comes from the Epidemiological Fact Sheets by Country (June 2000), which report the estimated number of HIV positive 0 to 49 year olds at the end of 1999. See http://www.unaids.org/hivaidsinfo/statistics/june00/fact_sheets/

UNAIDS data on HIV seroprevalence in a country are in column E. First, the number of HIV positive people for all countries in a particular region are aggregated. The fourteen regional totals appear at the bottom of the worksheet. Then the country number is divided by the regional total to obtain the country's proportion of seroprevalence in its region. As the DALY burden is not perfectly correlated with the rate of HIV seroprevalence, there will be a degree of error in using these shares to distribute the WHO regional burden data among countries within a particular region.

5.2 ADJUSTING FOR MISSING VALUES

The following countries have no data on HIV seroprevalence and are indicated by an asterisk in column F:

> Andorra, Antigua and Barbuda, Cape Verde, Dominica, Grenada, Kiribati, Micronesia, Monaco, Palau, Samoa, Sao Tome and Principe, Seychelles, Solomon Islands, St. Kitts and Nevis, St. Lucia, St. Vincent and Grenadines, Tonga, Vanuatu, Somalia.

To fill in these values in column E, the average percent of population that is HIV positive for the country's WHO subregion is multiplied by the country's population. Adjusting for missing data in this way has no important impact on the results, as these countries have only a small fraction of the worldwide HIV/AIDS burden.

6. Malaria Cases

This worksheet estimates the *distribution* of malaria burden among countries *within* the same WHO region.

6.1 ESTIMATING DISTRIBUTION OF DISEASE BURDEN

Since country-by-country figures on malaria burden are unavailable, a proxy for burden is used to estimate the distribution of DALYs within regions. For this purpose, numbers on high and low probability of getting malaria in a country are used. This data comes from the WHO's "World Malaria Situation in 1994, Part I" (WHO 1997c).

Column G. To obtain the malaria "burden" in a country, the country's 1998 population is multiplied by a linear combination of low and high probabilities. A parameter in the *options* worksheet allows the user to change the linear combination of low and high probabilities as desired. For example, if 20 percent of the people in a country (with population 1000) live in low-risk areas, 50 percent live in high-risk areas, and 30 percent live in areas without malaria, the estimated "burden" for the country is (1 x 0.2 x 1000) + (10 x 0.5 x 1000). Of course, the malaria cases parameter can change the weighting of the high and low risk variables, as the user desires. Please note that the distribution of burden that is ultimately obtained (column I) is not very sensitive to the particular value for this parameter.

Column H. The country "burden" numbers are aggregated according to the fourteen WHO categories.

Column I. The country "burden" is divided by the total regional "burden" to get that country's share of malaria burden of its region.

7. TB Cases

This worksheet estimates the *distribution* of tuberculosis burden among countries *within* the same WHO region.

7.1 ESTIMATING DISTRIBUTION OF DISEASE BURDEN

WHO does not report country-level data for burden of disease, but only regional data. It is, nevertheless necessary to have country-level estimates. Therefore, regional burden is divided according to the distribution of burden within the region.

The data on the estimated incidence of tuberculosis in 1998 is listed in column D. The data come from WHO's *Global Tuberculosis Control 2000* (WHO 2000b).
Please see: http://www.who.int/gtb/publications/globrep00/download.html

Then the number of cases for each WHO region are aggregated (column E).

Finally in column F, the country cases are divided by the region cases to get a country's proportion of cases in its region. This is used as the estimate for the distribution of tuberculosis burden (in DALYs) within regions.

8. Disease Types

This worksheet describes which disease types are prevalent in each country given the vaccine is effective against those types.

It is possible that a vaccine developed for HIV/AIDS (or malaria) will not be effective against all HIV-1 subtypes (or malaria species). As these subtypes follow a distinct geographical distribution, this vaccine characteristic may have an extremely significant effect on the number of DALYs saved. Therefore, the *options* worksheet lets the user specify which malaria species and HIV-1 subtypes the vaccine will be effective against. To operationalize this set of parameters, the spreadsheet includes information on which disease types are prevalent in each country.

8.1 HIV/AIDS SUBTYPES

Columns G through O show HIV-1 subtypes by country. A value of 1 means that the HIV subtype is prevalent in the country AND the HIV/AIDS vaccine is effective against the subtype (see *options* for this set of parameters). A value of 0 means otherwise (EITHER the vaccine is effective against the subtype, but the subtype is not prevalent in the country; OR the subtype is prevalent, but the HIV vaccine does not work against it).

Column P shows which countries have *any* prevalent subtype against which the HIV vaccine is effective. **Warning:** If two subtypes are prevalent in a country and the vaccine is only effective against one of the subtypes, the spreadsheet currently assumes the vaccine will still be able to avert the same amount of burden *as if* the vaccine were effective against both subtypes in the country. Therefore, this analysis will produce an overoptimistic picture of the effects of vaccines effective against only some subtypes. Further work will refine the treatment of multiple subtypes prevalent in a particular country.

As listed in the *options* documentation, the geographic distribution of HIV is:

A Central and East Africa
B Americas/ Europe/ Japan/ Australia/ Asia
C Sub-Saharan Africa/ India/ Brazil
D Central and East Africa
E C. African Rep/ Thailand
F Brazil/ Romania
G Russia/ Gabon
H Zaire/ Cameroon
O Cameroon/ Gabon

For more information please refer to **http://www.unaids.org** and Osmanov, Heyward, and Esparza (1996).

8.2 MALARIA SPECIES

Columns W through Y show malaria species by country. A value of 1 means that that malaria species is prevalent in the country AND the malaria vaccine is effective against the species (see *options* for this parameter). A value of 0 means otherwise (EITHER the vaccine is effective against the species, but the species is not prevalent in the country; OR the species is prevalent, but the malaria vaccine does not work against it).

Column Z shows which countries have *any* prevalent species against which the malaria vaccine is effective. **Warning:** If two malaria species are prevalent in a country and the vaccine is only effective against one of the species, the spreadsheet currently assumes the vaccine will still be able to avert the same amount of burden *as if* the vaccine were effective against both species in the country. Therefore, this analysis will produce an overoptimistic picture of the effects of vaccines effective against only some species. Further work will refine the treatment of multiple species prevalent in a particular country.

As listed in the *options* documentation, the geographic distribution of malaria is:

Plasmodium falciparum	Africa, Haiti, Dominican Rep, EMR2, SEAR1, SEAR2, WPR2
Plasmodium vivax	Asia, Middle East, Oceania, Americas, Europe
Plasmodium malariae	Cambodia, Myanmar, Laos, Thailand

For more information please refer to **http://www.malaria.org** and **http://mosquito.who.int/**

9. Options

This worksheet describes the parameters in the model that the user may vary. In the spreadsheet there are a few numbers that are highlighted in color. These should *not* be changed by the user. The user may change all of the numbers that are not highlighted in color.

ASSUMPTIONS OF THE MODEL

9.1 GENERAL PARAMETERS

Size of purchase commitment per year. The total annual size of the Vaccine Purchase Commitment for each disease in nominal dollars. The life of the Commitment is ten years. The Commitment consists of both the co-payments received from participating countries and donor contributions. A respected pharmaceutical consulting firm, Mercer Management Consulting, estimates that a $250 million annual market is needed to motivate pharmaceutical firms (Whitehead, 1999). A ten-year purchase commitment would likely be sufficient to motivate research, given that potential vaccine developers are likely to heavily discount sales after this period, and that competing vaccines are likely to emerge after ten years in any case, and drive down prices to the point at which they could be more broadly affordable. However, the larger the commitment size, the faster a vaccine will be developed. In the default case, the annual commitment size is $336 million dollars.

Inflation rate. The default inflation rate is assumed to be 2%.

Real discount rate. The real discount rate is used to discount future costs and benefits, such as lives saved, which are presented in real terms. The default real discount rate is 3%, which is selected for comparability with other cost effectiveness studies in health. Note that if the discount rate is increased for comparability with non-health investments, the implicit DALY cost effectiveness threshold should be raised as well, since the cost effectiveness threshold is based in large part on looking at other potential health investments.

Nominal discount rate. The nominal discount rate is used to discount future nominal cash payments. Cash payments include co-payments (on the *co-payments* worksheet) and donor contributions ("purchase costs" on the *costs* worksheet). As inflation is assumed to be 2% and the real discount rate is assumed to by 3%, the default nominal rate is 5%. To change the nominal discount rate, the user should adjust the real discount rate and/or the inflation rate.

Dollars per DALY Cost-effectiveness Threshold. Vaccines would only be administered on a wide scale where a mass vaccination program would be cost effective. This number determines the cutoff for what is considered cost effective in terms of dollars per DALY saved. The base case is $25/per DALY. In the 1993 *World Development Report*, the World Bank refers to several health interventions in developing countries, which cost in the range of $25 to $150 per DALY. In these instances, it is implied that these interventions are considered "highly cost effective" (World Bank 1993, pages 8, 64, and 68). Health interventions are considered cost-effective in the U.S. at $50,000-$100,000 per year of life saved (Neumann et al., 2000). The implied ratio of

U.S. to developing country DALY thresholds far exceeds the corresponding ratio of GDP. Thus, the DALY threshold may be considered conservative. This threshold is used to determine which countries undertake mass vaccination programs and for what age groups.

GNP per capita program eligibility cutoff. If a country has per capita GNP lower than this number, then the country may participate in the vaccine purchase commitment; the country is considered "covered." Note that not all countries that are eligible for program participation may receive vaccinations, as vaccination in an eligible country must be cost effective for that country to participate in the program. The default value is $2,990 GNP per capita, which is the World Bank average for a "middle income" country in 1998 (World Bank 2000).

9.2 BASIC VACCINE COVERAGE

% of new cohorts vaccinated. The percent of new cohorts that will receive a particular vaccination if a single dose is required. The default coverage rate is 75%—roughly the same coverage for new cohorts as in the Expanded Program on Immunization (EPI). This coverage rate encompasses both decisions of whether to participate in the program and decisions of individuals whether to participate given that their country participates.

% of children vaccinated. The percent of children (1-10 year olds for HIV/AIDS and TB and 1-5 year olds for malaria) that will receive a particular vaccination if no extra doses are required. The default coverage rate for children is 30%. This coverage rate encompasses both decisions of whether to participate in the program and decisions of individuals whether to participate given that their country participates.

% of old cohorts vaccinated. The percent of adults (for AIDS and tuberculosis) or women pregnant with their first child (for malaria) who will receive a particular vaccination if no extra doses are required. The coverage rate for HIV/AIDS and tuberculosis is 30% and 50% for malaria. Since pregnant women in many developing countries receive medical services at clinics, coverage for this cohort will likely be higher than that for other adult cohorts.

9.3 COVERAGE WHEN MORE THAN ONE DOSE IS NECESSARY

It is likely that vaccine coverage will be further reduced if extra doses are necessary. The following set of parameters affects vaccine coverage for the three cohorts when a vaccine requires several doses to remain effective.

% of new cohorts/ children/ old cohorts who receive each additional dose. The percent of new cohorts, children, and old cohorts, respectively, that receives each additional dose. The base case assumption is 80%.

Then, the overall coverage (% of total cohort that are vaccinated) may expressed in the following way: Let C = percent basic coverage of cohort, D = number of *additional* doses, Y = fraction of cohort that receives each additional dose. The total coverage (% of total cohort actually vaccinated) would equal C * Y ^ D, if D>0 and would equal C, if D=0.

Total vaccination coverage. The total vaccine coverage of new cohorts, children, and old cohorts taking into consideration the values for the basic coverage, number of extra doses, and fraction of cohort that receive each additional dose. The user does not change these values; total vaccination coverage is listed at the end of the *options* worksheet.

9.4 PARAMETERS RELATED TO CO-PAYMENTS

% of GNP per capita for co-payment per vaccination. Under a vaccine purchase commitment, participating covered countries could be required to pay a certain co-payment for each vaccination. A modest co-payment will help ensure that the countries feel that the vaccine are useful given the conditions in the countries, and also ensures that the participating countries' are committed to the program. Setting co-payments from countries receiving vaccines just below their estimated willingness to pay for vaccines will maximize incentives for vaccine development while not reducing consumption of vaccines below the optimal level. Since richer countries are likely to be willing to pay more for vaccines than poorer countries, this implies that co-payments should rise with per capita income. Therefore, the co-payment is a function of each country's respective GNP per capita. The co-payment percentages are chosen to be proportional to the each vaccine's DALY benefits per person immunized, as willingness to pay presumably increases with DALY benefits per person vaccinated. Willingness to pay is also likely to be higher for countries with a greater burden of disease; though, requiring a greater co-payment from countries with a greater burden of disease seems inequitable and is likely to be politically infeasible.

Operationally, the malaria and tuberculosis co-payment levels are set relative to the HIV/AIDS co-payment level according to the DALY benefits per person immunized. In order to make sure that no covered country will have a co-payment that is greater than the vaccine purchase price, the HIV/AIDS co-payment level is set such that the highest possible co-payment for a country at the GNP per capita cutoff is 80% of the HIV/AIDS purchase price.

Co-payment inflator. This parameter controls the level of co-payments with respect to the default level. To increase the co-payments by 15 percent relative to the default, set the parameter at 115%. Note that, regardless of the co-payment level, the percent of per capita GNP for the three vaccines will remain proportional to their relative per person DALY benefits.

9.5 PARAMETERS RELATED TO COSTS

9.5.1 STANDARD DELIVERY COSTS

New cohorts. The per dose vaccine delivery cost for a new cohort is assumed to be $0.40. The base case is that of a vaccine requiring a single dose which could be added to the standard package of vaccines that are delivered under the Expanded Program on Immunization (EPI) package. This package currently makes three contacts with each child costing about $15.00. (World Bank 1993b, page 168). This is roughly $5.00 per contact. The addition of both the hepatitis B and the yellow fever vaccines (which are relatively expensive) to the EPI increased the $15 cost of the program by 15%, or $2.25, including both manufacturing and distribution costs. If adding one vaccine costs about $1.12 and half of the cost was attributed to manufacturing, then the additional delivery cost of adding one additional dose of a vaccine to the package is assumed not to exceed $0.40.

Children. The vaccine delivery cost for a child is assumed to be $2.00.

Old cohorts. The vaccine delivery cost for an old cohort vaccination for HIV and tuberculosis is assumed to be $3.33. The delivery cost of a malaria vaccine for pregnant woman is assumed to be $2.00, as many women receive medical services at clinics, where deliver will likely be less costly.

9.5.2 TOTAL DELIVERY COSTS

Delivery cost per vaccine. This is not a parameter that the user may change. It simply displays the sum of the delivery costs per cohort based on the specified values for the parameters standard delivery costs and additional clinical costs. The user does not change these values; total delivery costs is listed at the bottom of the *options* worksheet.

9.5.3 MANUFACTURING COSTS

Marginal manufacturing cost of one additional dose given a very high manufacturing volume. This variable does not include R&D costs for the vaccine or costs for developing bulk manufacturing systems. It is the cost of producing enough additional vaccine to immunize one additional person, given that large-scale production is already taking place. The package of five vaccines in the EPI program sells for $0.50 and vaccines would be purchased in bulk under the program (Robbins and Freeman, 1988). However, since conjugate vaccines may be particularly expensive, the default marginal manufacturing cost for each vaccine is assumed to be $0.50.

9.5.4 MARGINAL COST

Marginal cost for vaccination. The marginal cost, expressed in DALYs, is the sum of the total marginal manufacturing cost and the total delivery cost, all divided by cost-effectiveness threshold per DALY. In other words, this is the marginal cost of vaccinating one additional person divided by the DALY threshold. Later in the spreadsheet, this is compared to the lifetime burden of disease (or marginal benefit per person) to identity which people it is cost effective to vaccinate. See the hidden rows after marginal manufacturing cost for the values of the marginal cost for vaccination.

9.6 OTHER PARAMETERS

Malaria cases parameter. On the *malaria cases* worksheet, the formula in column H involves a linear combination of the "low probability of getting malaria" and "high probability of getting malaria" to obtain a measure of malaria burden in each country. The overall purpose of this worksheet is to estimate the *distribution* of malaria burden among countries within regions. In order to increase the flexibility of this formula, which combines low and high probabilities to yield a proxy for country burden, the malaria cases parameter allows the user to adjust the relative weights in the algorithm. In more formal terms, let country population equal *P*, the proportion of the population in low malaria burden areas equal *A*, the proportion of the population in high malaria burden areas equal *Z*, and the malaria cases parameter equal *M*. Therefore, the formula in column H equals P*(1*A + M*Z).

Targeting factor for old cohorts. Vaccination programs can be targeted to high-risk groups using criteria other than age and nation of residence. For example, a potential malaria vaccine can be targeted to geographic areas with a particularly high burden of malaria. A tuberculosis vaccine can be targeted to people in prisons and urban slums with high prevalence of the disease. An HIV/AIDS vaccine can be targeted to soldiers and sex workers. It is assumed that there is no effective targeting for new cohorts or children, but that the vaccination of older cohorts is targeted to high-risk people. For example, only women pregnant with their first child receive the malaria vaccine. Murray and Lopez (1996) estimate the burden of malaria for 15-44 year old females is about 25% higher than that for 15-44 year old males. If this is due entirely to the greater burden on first-time mothers, and if 1/20th of these women are first-time mothers, then this implies their malaria burden is about five times higher than the average burden for a 15-44 year old person. Therefore, the default value for targeting first-time pregnant women is five. The user may set the targeting factor to one to simulate no gains to targeting. The default values are two for HIV/AIDS and tuberculosis.

PARAMETERS RELATED TO VACCINE CHARACTERISTICS

The default values for the parameters in this section correspond to the ideal vaccine case. The user can vary these values to create a less-than-ideal vaccine.

9.7 EFFECTIVENESS OF THE VACCINE

Vaccine efficacy. The percentage of vaccinated people who are effectively protected against the disease.

Number of years the vaccine is effective. This controls the number of years a vaccine remains effective. Denote the number of years the vaccine is effective as *T*. This implies, for a particular individual, a vaccine remains effective from the age at which the person receives the vaccination, say age *Y*, to the age *Y+T*. For all practical purposes, a vaccine that is effective for 75 or more years is considered a lifetime vaccine, which is the default setting. **Warning:** the spreadsheet does not yet take into account the fact that a person may receive a second vaccination after the first vaccination becomes ineffective. Therefore, the user is cautioned that the spreadsheet currently severely underestimates the cost effectiveness of vaccines that are only effective for a limited number of years. Further work will rectify this problem.

Scaling factor for benefits ages 0-4. This factor scales down the DALYs saved from protection from the disease in the 0-4 age group. This may be necessary if the vaccine cannot be given to infected people as infants or if the vaccine is not as effective for infants. For example, an HIV vaccine might not prevent transmission from mother to infant or might only protect against transmission through breast milk, but not against transmission during birth. A default value of 100% allows the vaccine to effectively protect the 0-4 age group. A value of 20% would reduce the DALYs saved for the ages 0-4 by 80%.

9.8 ADDITIONAL VACCINE DOSES

Number of extra doses. The number of *extra* doses necessary to maintain vaccine efficacy over the full number of years that the vaccine is effective (see the number of years the vaccine will be effective parameter). The effect the number of doses has on vaccine coverage—the percent of a cohort that actually receive the vaccine—will be discussed below. The base case assumes no extra doses are necessary. In addition, the delivery and manufacturing costs associated with a vaccine are increased by a factor equal to the number of doses required. In other words, if two extra doses are required, then the delivery and manufacturing costs of that vaccine increase by 200%.

9.9 CLINICAL USE AND CONTRA-INDICATED CONDITIONS

Clinical use. If one or more of the target cohorts cannot receive the vaccine for medical reasons, then this parameter equals zero. If, in general, the target group may receive the vaccine, then the parameter equals one. For example, pregnant women cannot receive some vaccines. Generally, the administration of live attenuated vaccines should be avoided in pregnancy and inactivated vaccines should not be given until the second trimester. Certain vaccines, like rubella, are contraindicated in women who are pregnant or may become pregnant within three months following administration. In addition, some vaccines may not be given to new cohorts.

Contra-indicated condition. A certain portion of the population may have allergies that would cause them to have anaphylactic shock if they received the vaccine. For example, an influenza vaccine cannot be given to people with allergies to eggs (Riddiough et al. 1983). Thus, this parameter specifies the percent of a target group that cannot receive the vaccine on account of a certain prevalence of a contra-indicated condition or disease. If there were, in fact, a contra-indicated condition, then it would be necessary to take into account the additional costs of screening for this condition in potential vaccine recipients. Thus, a contra-indicated condition may affect the overall cost-effectiveness of the purchase program. Another parameter described below, additional clinical costs, allows the user to introduce possible testing costs into the calculations.

9.10 OTHER CLINICAL COSTS

Additional clinical costs. This parameter allows the user to account for *any other* clinical costs over and above those the base case considers. In order to add costs, simply set the dichotomous parameter to one and specify the desired percent of "extra costs." Testing for contra-indicated conditions prior to the administration of a vaccine is an example of additional clinical costs that may affect the cost effectiveness of the purchase program.

9.11 VACCINE EFFICACY AGAINST DISEASE TYPES

HIV-1 Subtypes. Not every possible HIV vaccine may be effective against all subtypes of HIV. With this set of parameters, the user may specify against which subtypes (A, B, C, D, E, F, G, H, and O) the vaccine will be effective. A value of one indicates that the vaccine is effective against the particular subtype; a zero indicates the vaccine will not be effective against the subtype.

Warning: If two subtypes are prevalent in a country and the vaccine is only effective against one of the subtypes, the spreadsheet currently assumes the vaccine will still be able to avert the same amount of burden *as if* the vaccine were effective against both subtypes in the country. Therefore, this analysis will produce an overoptimistic picture of the effects of vaccines effective against only some subtypes. Further work will refine the treatment of multiple subtypes prevalent in a particular country.

The geographic distribution of HIV subtypes is listed here but refer to the documentation for the *disease types* worksheet for more information.

Subtype	**Regions**
A	Central and East Africa
B	Americas/ Europe/ Japan/ Australia/ Asia
C	Sub-Saharan Africa/ India/ Brazil
D	Central and East Africa
E	C. African Rep/ Thailand
F	Brazil/ Romania
G	Russia/ Gabon
H	Zaire/ Cameroon
O	Cameroon/ Gabon

Malaria Species. Analogously, not every malaria vaccine may be effective against all species of malaria. Here the user may specify which species (*Plasmodium falciparum, P. vivax, P. malariae*) the vaccine will be effective against. 1 indicates that the vaccine is effective against the particular species; 0 indicates the vaccine will not be effective against the species.

Warning: If two malaria species are prevalent in a country and the vaccine is only effective against one of the species, the spreadsheet currently assumes the vaccine will still be able to avert the same amount of burden *as if* the vaccine were effective against both species in the country. Therefore, this analysis will produce an overoptimistic picture of the effects of vaccines effective against only some species. Further work will refine the treatment of multiple species prevalent in a particular country.

The geographic distribution of malaria is listed here but refer to the documentation for the *disease types* worksheet for more information.

Species	**Regions**
Plasmodium falciparum	Africa, Haiti, Dominican Republic, Eastern Mediterranean Region (low child, low adult), South East Asian Region, and Western Pacific Region (low child, low adult)
Plasmodium vivax	Asia, Middle East, Oceania, Americas, Europe
Plasmodium malariae	Cambodia, Myanmar, Laos, Thailand

At the bottom of the *options* worksheet, the total NPV/DALY saved is displayed to allow the user to immediately view the effect of changing a parameter on the cost effectiveness of the purchase program.

10. Vaccinations

This worksheet calculates the number of vaccinations for each disease for the ten years of the Vaccine Purchase Commitment period by status of program participation (covered, non-covered countries, and all countries).

10.1 NEW COHORT VACCINATIONS

Row 4. This lists the number of annual births in all covered countries where vaccination is cost effective. These numbers come from the *hiv-aids, malaria*, and *tb* worksheets.

Row 5. This calculates the number of new cohorts actually vaccinated each year by multiplying the value in Row 4 by the vaccine coverage rate. Note that the default coverage rate for new cohorts is 75%. Please see the documentation for the *options* worksheet for a more detailed description of the coverage rates.

Row 6. This multiplies the actual number of new cohorts vaccinated each year (Row 5) by ten. This is because new cohorts are vaccinated in a country for each year of the purchase program (ten years in all).

10.2 CHILDREN VACCINATIONS

Row 7. This lists the number of children ages one to ten in all covered countries where vaccination is cost effective. These numbers come from the *hiv-aids*, *malaria*, and *tb* worksheets.

Row 8. This calculates the number of children actually vaccinated by multiplying the value in Row 7 by the actual vaccine coverage rate, which is given in cells B26, C26, and D26 respectively. Note that the default coverage rate for children is 30%. Please see the documentation for the *options* worksheet for a more detailed description of the coverage rates.

Row 9. This multiplies the actual number of children vaccinated (Row 8) by one. This is because children in a country are vaccinated only once (during the first year of the purchase program).

10.3 OLD COHORT VACCINATIONS

Row 10. This lists the number of people ages 10 to 35 (for HIV/AIDS and TB) and the number of first-time mothers (for malaria) for both covered and non-covered countries. These numbers come from the *hiv-aids*, *malaria*, and *tb* worksheets.

Row 11. This calculates the number of old cohort vaccinations by multiplying Row 10 by the actual vaccine coverage rate, which is given in cells B27, C27, and D27 respectively. Note that the default coverage rate for old cohorts is 30% for HIV and TB and 50% for malaria. Please see the documentation for the *options* worksheet for a more detailed description of the coverage rates.

Row 12. The number in Row 11 is multiplied by one for HIV and TB vaccines; the number in Row 11 is multiplied by ten for the malaria vaccine. This is because old cohorts in a country are only vaccinated during the first year of the purchase program for HIV and tuberculosis, whereas women pregnant with their first child are vaccinated for malaria during all ten years of the purchase program.

10.4 VACCINATIONS FOR THE FIRST TEN YEARS

Row 13. This adds up the number of people (in any cohort) receiving vaccinations for the ten years of the purchase program.

10.5 NUMBER OF COUNTRIES THAT RECEIVE VACCINATIONS

Rows 15 through 18. Lists the number of countries getting new cohort, children, old cohort, and any vaccinations, respectively.

Row 20. This row shows the fraction of countries that receive vaccinations that are IDA eligible. Please see the notes on IDA eligibility in the documentation for *basic data*.

11. DALYS SAVED

This worksheet calculates the total discounted DALYs saved by each vaccine and the discounted DALYs saved for the first ten years of the program. The results for covered countries, non-covered countries, and all countries are displayed. DALYs, disability-adjusted life years, are defined as the number of healthy years of life lost due to premature death and disability.

11.1. COVERED COUNTRIES

11.1.1. DISCOUNTED DALYS FOR THE FIRST TEN YEARS

Row 7. This is the annual number of people born in all covered countries where vaccination is cost effective.

Row 8. The total new cohorts vaccinated at the coverage rate. The default coverage rate for new cohorts is 75%.

Row 9. The total new cohorts vaccinated in the first ten years at the coverage rate. Row 8 is multiplied by ten because new cohorts are vaccinated for each of the ten years of the purchase program.

Row 10. The new cohort DALYs saved for each of the three vaccines comes from the *hiv-aids*, *malaria*, and *tb* worksheets, respectively.

Row 11. This multiplies the total new cohort DALYs saved in Row 10 by the new cohorts coverage rate.

Row 12. This calculates the present value of saving the number of DALYs in Row 11 in the first ten years at the real discount rate. This procedure is performed for the first ten years, because new cohorts are vaccinated for each of the ten years of the purchase program.

Row 13. The number of 1-10 year old children in covered countries.

Row 14. The total children vaccinated at the coverage rate. The default coverage rate for children is 30%.

Row 15. The total children vaccinated in the first ten years at the coverage rate. Row 14 is multiplied by one because children are only vaccinated at the beginning of the purchase program.

Row 16. The total children DALYs saved for each of the three vaccines comes from the *hiv-aids*, *malaria*, and *tb* worksheets, respectively.

Row 17. The total new cohort DALYs saved (Row 16) are multiplied by the children coverage rate.

Row 18. This calculates the present value of saving the number of DALYs in Row 17 for the program period at the real discount rate. Since children are vaccinated at the beginning of the period, the present value is simply the value in Row 17.

Row 19. The number of 10-35 years olds in a country.

Row 20. The total old cohorts vaccinated at the coverage rate. The default coverage rate for old cohorts is 30% (and 50% for malaria).

Row 21. The total old cohorts vaccinated in the first ten years at the coverage rate. Row 20 is multiplied by one because old cohorts are only vaccinated at the beginning of the purchase program (except for malaria where old cohorts are vaccinated for the entire purchase program, or ten years).

Row 22. The total old cohort DALYs saved for each of the three vaccines comes from the *hiv-aids*, *malaria*, and *tb* worksheets, respectively.

Row 23. This multiplies the total old cohort DALYs saved (Row 22) by the old cohorts coverage rate.

Row 24. This calculates the present value of saving the number of DALYs in Row 23 for the program period at the real discount rate. Since old cohorts are only vaccinated at the beginning of the period, the present value is simply the value in Row 23. For malaria, however, old cohorts are vaccinated for each of the ten years of the purchase program; therefore, this calculates the present value of saving the number of DALYs in Row 23 for ten years at the real discount rate.

Row 25. Lists the total number of new cohorts, children, and old cohorts vaccinated for the ten year program period.

Row 26. This sums the total DALYs saved for new cohorts, children, and old cohorts in Rows 12, 18, and 24.

11.1.2 TOTAL DISCOUNTED DALYS

Row 30. The total new cohort DALYs saved for each of the three vaccines comes from the *hiv-aids*, *malaria*, and *tb* worksheets, respectively.

Row 31. This multiplies the total new cohort DALYs saved in Row 30 by the new cohorts coverage rate.

Row 32. This calculates the present value of saving the number of DALYs in Row 31 at the real discount rate. Thus, the value in Row 31 is divided by the real discount rate. At the end of the ten year purchase program, countries will continue to vaccinate new cohorts. Therefore, DALYs saved are divided by the interest rate to obtain the total discounted DALYs saved.

Row 33. The total children DALYs saved for each of the three vaccines comes from the *hiv-aids*, *malaria*, and *tb* worksheets, respectively.

Row 34. This multiplies the total children DALYs saved in Row 33 by the children coverage rate.

Row 35. This calculates the present value of saving the number of DALYs in Row 34 at the real discount rate. Since children are vaccinated at the beginning of the program period, the present value is simply the value in Row 34.

Row 36. The total old cohort DALYs saved for each of the three vaccines comes from *the hiv-aids*, *malaria*, and *tb* worksheets, respectively.

Row 37. This multiplies the total old cohort DALYs saved in Row 36 by the old cohorts coverage rate.

Row 38. This calculates the present value of saving the number of DALYs in Row 37 at the real discount rate. Since old cohorts are only vaccinated at the beginning of the period, the present value is simply the value in Row 37. For malaria, however, old cohorts are vaccinated for twenty years in all; therefore, this calculates the present value of saving the number of DALYs in Row 37 for twenty years at the real discount rate.

Row 39. The total DALYs saved for new cohorts, children, and old cohorts (Rows 32, 35, and 38) are aggregated .

11.1.3 UNDISCOUNTED DALYS FOR THE FIRST TEN YEARS

This section directly corresponds with the calculations in Rows 7 to 26 for Discounted DALYs. The differences between the two sections are discussed here.

Row 12. The DALYs saved in Row 11 are multiplied by ten to obtain the number of new cohort DALYs saved for the duration of the vaccine program

Row 18. The DALYs saved in Row 17 are multiplied by one to obtain the number of children DALYs saved for the duration of the vaccine program.

Row 24. The DALYs saved in Row 23 are multiplied by one to obtain the number of old cohort DALYs saved for the duration of the vaccine program. For malaria, Row 23 is multiplied by ten since old cohorts are vaccinated for all ten years of the purchase program.

11.2 NON-COVERED COUNTRIES AND ALL COUNTRIES

Following the methods outlined above for Rows 7 through 39, the same set of calculations are performed for both non-covered countries and all countries.

12. Co-payments

This worksheet figures out the total co-payments that result from the vaccine purchase commitment.

12.1 DISCOUNTED CO-PAYMENTS FOR THE FIRST TEN YEARS

Row 4. The number of annual births in the covered countries where vaccination is cost effective.

Row 5. The total number of new cohorts vaccinated at the coverage rate. The default coverage rate for new cohorts is 75%.

Row 6. The total new cohorts vaccinated for the first ten years at the coverage rate. Row 5 is multiplied by ten because new cohorts are vaccinated for each of the ten years of the purchase program.

Row 7. New cohort co-payments received per year (unadjusted by the coverage rate) from the *hiv-aids*, *malaria*, and *tb* worksheets, respectively.

Row 8. Co-payments received per year at the new cohort coverage rate of 75%.

Row 9. Total co-payment received for new cohort vaccinations is the present value of Row 8 for ten years, because new cohorts are vaccinated for ten years.

Row 10. The number of 1-10 year old children in a country.

Row 11. The total children vaccinated at the coverage rate. The default coverage rate for children is 30%.

Row 12. The total children vaccinated for the first ten years at the coverage rate. Row 11 is multiplied by one because children are vaccinated only once.

Row 13. Child co-payments received per year (unadjusted by the coverage rate) from the *hiv-aids*, *malaria*, and *tb* worksheets, respectively.

Row 14. Co-payments received per year at the children coverage rate of 30%.

Row 15. Total co-payment received for child vaccinations is simply Row 14, because children are vaccinated for the first year only.

Row 16. The number of 10-35 year olds in covered countries.

Row 17. The total old cohorts vaccinated at the coverage rate. The default coverage rate for old cohorts is 30% (50% for malaria).

Row 18. The total old cohorts vaccinated for the first ten years at the coverage rate. Row 17 is multiplied by one because old cohorts are vaccinated only once. For malaria, Row 17 is multiplied by ten, because pregnant women are vaccinated for the duration of the program period.

Row 19. Old cohorts co-payments received per year (unadjusted by the coverage rate) from the *hiv-aids*, *malaria*, and *tb* worksheets, respectively.

Row 20. Co-payments received per year at the old cohort coverage rate of 30% (50% for malaria).

Row 21. Total co-payment received for old cohort vaccinations is simply Row 20. For HIV/AIDS and tuberculosis, there are vaccinations for the first year. For malaria, the present value of Row 20 for the first ten years is calculated.

Row 22. This reports the total number of people vaccinated from the *vaccinations* worksheet.

Row 23. The total co-payments received are the sum of Rows 9, 15, and 21.

12.2. TOTAL DISCOUNTED CO-PAYMENTS

Note that these calculations are exactly the same as those *for the first ten years*. Countries that participate in the vaccine purchase commitment only pay co-payments for the ten years of the purchase program. Therefore, the total co-payments are those for the first ten years are the same.

12.3. UNDISCOUNTED CO-PAYMENTS FOR THE FIRST TEN YEARS

These calculations are the same as those in the Discounted section with the following exceptions.

Row 9. The total co-payments received for new cohorts are the co-payments per year times ten.

Row 15. The total co-payments received for children are the co-payments per year times one.

Row 21. The total co-payments received for old cohorts are the co-payments per year times one. For malaria, the total co-payments received for old cohorts are the co-payments per year times ten.

13. Costs

This worksheet finds the total social costs (excluding co-payments) of vaccination for covered countries, non-covered countries, and all countries.

13.1 COSTS FOR COVERED COUNTRIES

13.1.1. DISCOUNTED COSTS FOR THE FIRST TEN YEARS

Row 7. The number of people born in covered countries annually.

Row 8. The total new cohorts vaccinated at the coverage rate. The default coverage rate for new cohorts is 75%.

Row 9. The total new cohorts vaccinated for the first ten years at the coverage rate. Row 8 is multiplied by ten because new cohorts are vaccinated for each of the ten years of the purchase program.

Row 10. This is the donor contribution per vaccination for AIDS, malaria, and tuberculosis respectively and comes from the *commitment* worksheet

Row 11. The total purchase cost of new cohort vaccinations is the present value of the number of vaccinations per year (Row 8) times the donor contribution per vaccination (Row 10) for the first ten years.

Row 12. The marginal manufacturing cost per vaccination is given on the *options* worksheet.

Row 13. The total marginal manufacturing cost of new cohort vaccinations is the present value of the number of vaccinations per year (Row 8) times the marginal manufacturing cost per vaccination (Row 12) for the first ten years.

Row 14. The delivery cost per new cohort vaccination is given on the *options* worksheet.

Row 15. The total delivery cost of new cohort vaccinations is the present value of the number of vaccinations per year (Row 8) times the delivery cost per vaccination (Row 14) for ten years.

Row 16. Therefore, the total cost of new cohort vaccinations is the sum of total purchase cost and delivery cost.   This is because, for the first ten years, the vaccine developer pays for marginal manufacturing costs. In other words, the total purchase cost already "includes" marginal manufacturing costs.

Row 17. The total cost of new cohort vaccination excluding marginal manufacturing costs is Row 16 minus Row 12, total marginal manufacturing cost.

Row 19. The number of 1-10 year old children in covered countries.

Row 20. The total children vaccinated at the coverage rate. The default coverage rate for new cohorts is 30%.

Row 21. The total children vaccinated for ten years at the coverage rate. Row 20 is multiplied by one, because children are only vaccinated at the beginning of the purchase program.

Row 22. This is the donor contribution per vaccination for AIDS, malaria, and tuberculosis respectively.

Row 23. The total purchase cost of children vaccinations is the number of vaccinations (Row 20) times the donor contribution per vaccination (Row 22).

Row 24. The marginal manufacturing cost per vaccination is given on the *options* worksheet.

Row 25. The total marginal manufacturing cost of children vaccinations the number of vaccinations per year (Row 20) times the marginal manufacturing cost per vaccination (Row 24) since children are vaccinated only once.

Row 26. The delivery cost per child vaccination is given on the *options* worksheet.

Row 27. The total delivery cost of children vaccinations is the number of vaccinations per year (Row 20) times the delivery cost per vaccination (Row 26), since children are vaccinated once.

Row 28. Therefore, the total cost of child vaccinations is the sum of total purchase cost and delivery cost. This is because, for the first ten years, the vaccine developer pays for marginal manufacturing costs. In other words, the total purchase cost already “includes” marginal manufacturing costs.

Row 29. The total cost of child vaccinations excluding marginal manufacturing cost is Row 28 minus Row 25, total marginal manufacturing cost.

Row 31. The number of 10-35 years olds in covered countries.

Row 32. The total old cohorts vaccinated at the coverage rate. The default coverage rate for old cohorts is 30% (50% for malaria).

Row 33. The total old cohorts vaccinated for ten years at the coverage rate. For AIDS and tuberculosis, Row 32 is multiplied by one because old cohorts are vaccinated for only one year. For malaria, Row 32 is multiplied by ten as old cohorts are vaccinated for all ten years of the Commitment period.

Row 34. This is the donor contribution per vaccination for AIDS, malaria, and tuberculosis respectively.

Row 35. The total purchase cost of old cohort vaccinations is the number of vaccinations per year (Row 32) times the donor contribution per vaccination (Row 34). For malaria, the total purchase cost is the present value of the number of vaccinations per year (Row 32) times the donor contribution per vaccination (Row 34) for ten years.

Row 36. The marginal manufacturing cost per vaccination is given on the *options* worksheet.

Row 37. The total marginal manufacturing cost of old cohort vaccinations is the number of vaccinations per year (Row 32) times the marginal manufacturing cost per vaccination (Row 36). For malaria, the total marginal manufacturing cost of old cohort vaccinations is the present value of the number of vaccinations per year (Row 32) times the marginal manufacturing cost per vaccination (Row 36) for ten years.

Row 38. The delivery cost per old cohort vaccination is given on the *options* worksheet.

Row 39. The total delivery cost of old cohort vaccinations is the number of vaccinations per year (Row 32) times the delivery cost per vaccination (Row 38). For malaria, the total delivery cost of old cohort vaccinations is the present value of the number of vaccinations per year (Row 32) times the delivery cost per vaccination (Row 38) for ten years.

Row 40. Therefore, the total cost of old cohort vaccinations is the sum of total purchase cost and delivery cost. This is because, for the first ten years, the vaccine developer pays for marginal manufacturing costs. In other words, the total purchase cost already "includes" marginal manufacturing costs.

Row 41. The total cost of old cohort vaccination excluding marginal manufacturing cost is Row 40 minus Row 37, total marginal manufacturing cost.

Row 42. Total people vaccinated is from the vaccinations worksheet.

Row 43. The total cost of vaccinations is the sum of Rows 16, 28, and 40.

Row 44. The sum of the costs of purchasing the vaccine for new cohorts and existing cohorts of children and adults .

Row 45. The sum of the marginal costs of manufacturing the vaccine for new cohorts and existing cohorts of children and adults.

Row 46. The sum of vaccine delivery costs for new cohorts and existing cohorts of children and adults.

13.1.2 TOTAL DISCOUNTED COSTS

This section directly corresponds with the calculations in Rows 6 to 46. The differences between the two sections are discussed here.

Row 54. The total purchase cost of new cohort vaccinations is the present value of the number of new cohort vaccinations per year times the donor contribution per vaccination for ten years. This is because the Commitment terminates after ten years.

Row 56. The total marginal manufacturing cost of new cohort vaccinations is the number of vaccinations per year times the marginal manufacturing cost per vaccination which is divided by the real discount rate. This is because new cohorts are vaccinated each and every year.

Row 58. The total delivery cost of new cohort vaccinations is the number of vaccinations per year times the delivery cost per vaccination which is divided by the real discount rate. This is because new cohorts are vaccinated each and every year.

Row 59. The total costs of new cohort vaccinations is the sum of total purchase, marginal manufacturing, and delivery costs minus the total marginal manufacturing cost for ten years. In this way, the marginal manufacturing costs for the first ten years, which are included in the purchase cost, are not double counted.

Row 60. The total costs of new cohort vaccinations excluding marginal manufacturing is the sum of total purchase and delivery costs.

Row 65. The total purchase cost of child vaccinations is the number of vaccinations per year times the donor contribution per vaccination. This is because children are vaccinated once.

Row 67. The total marginal manufacturing cost of child vaccinations is the number of vaccinations per year times the marginal manufacturing cost per vaccination. This is because children are vaccinated once.

Row 69. The total delivery cost of child vaccinations is the number of vaccinations per year times the delivery cost per vaccination. This is because children are vaccinated once.

Row 70. The total costs of child vaccinations is the sum of total purchase, marginal manufacturing, and delivery costs minus the marginal manufacturing cost for ten years. In this way, the marginal manufacturing costs for the first ten years, which are included in the purchase cost, are not double counted.

Row 71. The total costs of child vaccinations excluding marginal manufacturing cost is the Row 70 minus the total marginal manufacturing costs.

Row 76. The total purchase cost of old cohort vaccinations is the number of vaccinations per year times the donor contribution per vaccination. For malaria, the total purchase cost of old cohort vaccinations is the present value of the number of vaccinations per year times the donor contribution per vaccination for ten years. This is because the Commitment only lasts for ten years.

Row 78. The total marginal manufacturing cost of old cohort vaccinations is the present value of the number of vaccinations per year times the marginal manufacturing cost per vaccination. For malaria, the total marginal manufacturing cost of old cohort vaccinations is the present value of the number of vaccinations per year times the marginal manufacturing cost per vaccination for twenty years. This is because old cohorts are vaccinated for twenty years.

Row 80. The total delivery cost of old cohort vaccinations is the present value of the number of vaccinations per year times the delivery cost per vaccination. For malaria, the total delivery cost of old cohort vaccinations is the present value of the number of vaccinations per year times the delivery cost per vaccination for twenty years. This is because old cohorts are vaccinated for twenty years.

Row 81. The total costs of old cohort vaccinations is the sum of total purchase, marginal manufacturing, and delivery costs minus the marginal manufacturing costs for ten years. In this way, the marginal manufacturing costs for the first ten years, which are included in the purchase cost, are not double counted.

Row 82. The total costs of old cohort vaccinations excluding marginal manufacturing cost is Row 81 minus total marginal manufacturing cost.

The following calculations are needed for the *proportional commitment* worksheet:

Row 89. This adds the total delivery and manufacturing costs for covered countries.

Row 90-92. This displays the total purchase costs of for new cohort, children, and old cohort vaccinations, respectively, using the purchase price from the *proportional commitment* worksheet.

Row 93. The costs for covered countries for the first ten years of the purchase program using purchase price from the *proportional commitment* worksheet. These consist in both the delivery and purchase costs.

Row 94. The total costs for covered countries using the purchase price from the *proportional commitment* worksheet. These consist in the total delivery, manufacturing, and purchase costs minus the manufacturing costs for the first ten years.

13.1.3 UNDISCOUNTED COSTS FOR THE FIRST TEN YEARS

This section directly corresponds with the calculations in Rows 6 to 46. The differences between the two sections are discussed here.

Row 11. The total purchase cost of new cohort vaccinations is the number of annual vaccinations times the donor contribution per vaccination multiplied by ten. This is because new cohorts are vaccinated for each year of the purchase period.

Row 13. The total marginal manufacturing cost of new cohort vaccinations is the number of annual vaccinations times the marginal manufacturing cost per vaccination multiplied by ten. This is because new cohorts are vaccinated for each year of the purchase period.

Row 15. The total delivery cost of new cohort vaccinations is the number of annual vaccinations times the delivery cost per vaccination multiplied by ten This is because new cohorts are vaccinated for each year of the purchase period.

Row 23. The total purchase cost of child vaccinations is the number of annual vaccinations times the donor contribution per vaccination. This is because children are vaccinated once.

Row 25. The total marginal manufacturing cost of child vaccinations is the number of annual vaccinations times the marginal manufacturing cost per vaccination. This is because children are vaccinated once.

Row 27. The total delivery cost of child vaccinations is the number of annual vaccinations times the delivery cost per vaccination. This is because children are vaccinated once.

Row 35. The total purchase cost of old cohort vaccinations is the number of annual vaccinations times the donor contribution per vaccination. For malaria, the total purchase cost of old cohort vaccinations is the number of annual vaccinations times the donor contribution per vaccination multiplied by ten. This is because old cohorts are vaccinated for each year of the purchase period.

Row 37. The total marginal manufacturing cost of old cohort vaccinations is the number of annual vaccinations times the marginal manufacturing cost per vaccination. For malaria, the total marginal manufacturing cost of old cohort vaccinations is the number of annual vaccinations times the marginal manufacturing cost per vaccination multiplied by ten. This is because old cohorts are vaccinated for each year of the purchase period.

Row 39. The total delivery cost of old cohort vaccinations is the number of annual vaccinations times the delivery cost per vaccination. For malaria, the total delivery cost of old cohort vaccinations is the number of annual vaccinations times the delivery cost per vaccination multiplied by ten. This is because old cohorts are vaccinated for each year of the purchase period.

13.2 COSTS FOR NON-COVERED COUNTRIES AND COSTS FOR ALL COUNTRIES

These sections are analogous to the Costs for Covered Countries, except that they use the price per vaccination (*commitment* Row 10) instead of the donor contribution per vaccination. This is because these countries are unsubsidized by the vaccine purchase commitment. They purchase the vaccine on their own. Also, the total cost of vaccination of non-covered countries is the sum of the total purchase and manufacturing costs. This is because this analysis only considers manufacturing and delivery costs as social costs.

14. COST PER DALY SAVED

This worksheet summarizes the number of people vaccinated, DALYs saved, cost of vaccinations, and co-payments received and calculates the cost per DALY saved of the program for both the total and the first ten years of the program.

14.1. COST PER DALY SAVED FOR THE FIRST TEN YEARS

Row 4. Total number of people vaccinated comes from the *vaccinations* worksheet.

Row 5. Total cost of vaccinations comes from the *costs* worksheet.

Row 6. Total DALYs saved comes from the *dalys saved* worksheet.

Row 7. Total cost per new cohort vaccination is the discounted total cost of new cohort vaccinations divided by the number of new cohort vaccinations.

Row 8. Total cost per child vaccination is the discounted total cost of child vaccinations divided by the number of child vaccinations.

Row 9. Total cost per old cohort vaccination is the discounted total cost of old cohort vaccinations divided by the number of old cohort vaccinations.

Row 10. Total cost per DALY saved is the total cost of vaccinations divided by the total DALYs saved.

Row 12. The total co-payments received from participating countries comes from the *co-payments* worksheet.

Row 13. This is the total co-payments plus the total costs for ten years. Please remember that the total costs for covered countries did not include any co-payments.

Row 14. The total cost of vaccinations (including co-payments) per DALY saved is then Row 13 divided by Row 6.

14.2.TOTAL DISCOUNTED COSTS PER DALY SAVED

Row 18. The total cost of vaccinations comes from the *costs* worksheet.

Row 19. The total DALYs saved comes from the *dalys saved* worksheet.

Row 20. The total cost per DALY saved is the total cost of vaccinations divided by the total DALYs saved.

Row 22. The total co-payments comes from the *co-payments* worksheet.

Row 23. This is the total co-payments plus the total cost of vaccinations.

Row 24. The total cost of vaccinations per DALY saved is Row 23 divided by Row 19.

15. Program

This worksheet summarizes various characteristics of the vaccine purchase commitment itself such as annual commitment size, amount of donor contributions, and the amount of co-payments. Refer to the *proportional commitment* worksheet for the purchase prices, number of vaccinations, and cost effectiveness results when the size of commitment for a vaccine with given characteristics is set to be proportional to the social surplus generated by the vaccine.

15.1 COMMITMENT SIZE

Row 4. The annual size of commitment that appears as a parameter on the *options* worksheet is listed here.

Row 5. The annual commitment size is multiplied by ten to get the total commitment size for the duration of the purchase program.

15.2 CO-PAYMENTS AND DONOR CONTRIBUTIONS

Row 6. This displays the total co-payments received (for all ten years) under the program.

Row 7. This is Row 5 minus Row 6. It is the amount of donor contributions needed given the commitment size specified in Row 5 and the level of co-payments.

Row 8. The total amount of donor contributions is divided by ten to get the average annual donor contributions needed per year. This spreadsheet is not set up to analyze the time path of donor contributions, since it treats all vaccinations of existing cohorts as occurring in year one. In reality, existing cohorts would have to be vaccinated over time. Further refinement of the model could address the schedule of donor contributions and vaccinations since, in practice, they would have to be smoothed out over the duration of the purchase program.

15.3 AVERAGE CO-PAYMENT, DONOR CONTRIBUTION, AND PURCHASE PRICE PER PERSON VACCINATED

Row 9. This lists the total vaccinations over ten years from the *vaccinations* worksheet.

Row 10. The dollar amount per vaccination that the program pays to the vaccine developer is the total commitment size divided by the number of vaccinations for ten years assuming that co-payments do not exceed the commitment size in Row 5.

Row 11. The average co-payment received is the total co-payments divided by the total number of vaccinations.

Row 12. The donor contribution per vaccination is the total amount of donor contributions divided by the total number of vaccinations for ten years.

Row 13. The calculation gives the average co-payment as a ratio of price per vaccination, that is Row 11 divided by Row 10. It is a measure of how large the co-payment share of the vaccine purchase commitment is relative to the donation share.

16. HIV-AIDS

This worksheet evaluates the cost effectiveness of vaccinations for HIV/AIDS; obtains the number of vaccinations and DALYs saved for both covered and non-covered countries; and calculates the amount of co-payments received.

16.1 NEW COHORTS IN COVERED COUNTRIES

Column B lists the lifetime burden of HIV/AIDS in DALYs per new cohort from the *hiv-aids new cohorts* worksheet. This number can be considered the marginal benefit of a successful intervention if the vaccine is perfectly effective. Remember that the *options* worksheet estimates the marginal cost of manufacturing and delivering an additional vaccination given high production volume.

Column C actually performs the cost-effective evaluation for the covered under the program (their GNP per capita is below the "cutoff" value). It compares the (1) marginal benefit, i.e. the lifetime burden per new cohort, multiplied by the level of vaccine efficacy and the ratio of DALY burden (see *options* documentation) with (2) the marginal cost. If the marginal cost is greater than the lifetime burden adjusted for efficacy, then new cohorts born in a country do not receive vaccinations. If the lifetime burden adjusted for efficacy is equal to or greater than the marginal cost, then the worksheet displays the number of births in one year in the country. This number is adjusted for the vaccine coverage rate on a subsequent worksheet. The costs and benefits that are compared here are in the same units—DALYs per person vaccinated. Recall that on the *options* worksheet the marginal cost of vaccinating an additional person is divided by the DALY cost effectiveness cutoff to transform the marginal cost per person vaccinated into DALY terms.

Column D finds the co-payments that a country will pay for new cohort vaccinations (unadjusted by the coverage rate). This is simply the number of vaccinations multiplied by the per capita GNP multiplied by the co-payment factor on the *options* worksheet.

Column E gives the number of DALYs saved for those new cohorts that receive effective vaccinations. This is the lifetime burden per newly born person times the number of vaccinations times the vaccine efficacy times the ratio of DALY burden (see the notes for the *options* worksheet).

Column F records which countries receive new cohort vaccinations.

16.2 NEW COHORTS IN NON-COVERED COUNTRIES

Columns G through I are analogous to the previous section.

16.3 CHILDREN IN COVERED COUNTRIES

Column J lists the lifetime burden of HIV/AIDS in DALYs per child from the *hiv-aids children* worksheet. This number can be considered the marginal benefit of a successful vaccination. Remember that the *options* worksheet estimates the marginal cost of manufacturing and delivering an additional vaccination given high production volume.

Column K actually performs the cost-effective evaluation for the countries that may participate in the program (their GNP per capita is below the "cutoff" value). It compares the (1) marginal benefit, i.e. lifetime burden per child, multiplied by the level of vaccine efficacy and the ratio of DALY burden (see *options* description) with (2) the marginal cost. If the marginal cost is greater than the lifetime burden adjusted for efficacy, then a country does not receive funding for child vaccinations under the program. If the lifetime burden adjusted for efficacy is equal to or greater than the marginal cost, then the column displays the number of 1 to 10 year olds in the country. This number is adjusted for the vaccine coverage rate on a subsequent worksheet. The costs and benefits that are compared here are in the same units—DALYs per person vaccinated. Recall that on the *options* worksheet the marginal cost of vaccinating an additional person is divided by the DALY cost effectiveness cutoff to transform the marginal cost per person vaccinated into DALY terms.

Column L finds the co-payments that a country will pay for children vaccinations (unadjusted by the coverage rate). This is simply the number of vaccinations multiplied by the per capita GNP multiplied by the co-payment factor on the *options* worksheet.

Column M gives the number of DALYs saved for those children that receive effective vaccinations. This is the lifetime burden per child times the number of vaccinations times the vaccine efficacy times the ratio of DALY burden (see notes for the *options* worksheet).

Column N records which countries receive children vaccinations.

16.4 CHILDREN IN NON-COVERED COUNTRIES

Columns O to Q are analogous to the previous section.

16.5 OLD COHORTS IN COVERED COUNTRIES

Column R lists the lifetime burden of HIV/AIDS in DALYs per old cohort from the *hiv-aids old cohorts* worksheet. This number can be considered the marginal benefit of a successful untargeted vaccination. Remember that the *options* worksheet estimates the marginal cost of manufacturing and delivering an additional vaccination given high production volume.

Column S actually performs the cost-effective evaluation for the countries that may participate in the Commitment (their GNP per capita is below the "cutoff" value). It compares the (1) marginal benefit, i.e. lifetime burden per old cohort, multiplied by the level of vaccine efficacy, the targeting parameter, and the ratio of DALY burden (see *options* documentation) with (2) the marginal cost. If the cutoff is greater than the lifetime burden adjusted for efficacy, then a country does not receive funding for old cohort vaccinations. If the lifetime burden adjusted for efficacy is equal to or greater than the marginal cost, then the column displays the number of 10 to 35 year olds in the country. This number is adjusted for the vaccine coverage rate on a subsequent worksheet. The costs and benefits that are compared here are in the same units—DALYs per person vaccinated. Recall that on the *options* worksheet the marginal cost of vaccinating an additional person is divided by the DALY cost effectiveness cutoff to transform the marginal cost per person vaccinated into DALY terms..

Column T finds the co-payments that a country will pay for old cohort vaccinations (unadjusted by the coverage rate). This is simply the number of vaccinations multiplied by the per capita GNP multiplied by the co-payment factor on the *options* worksheet.

Column U gives the number of DALYs saved for those old cohorts that receive effective vaccinations. This is the lifetime burden per old cohort times the number of vaccinations times the vaccine efficacy times the ratio of DALY burden (see notes for the *options* worksheet).

Column V records which countries receive old cohort vaccinations.

16.6 OLD COHORTS IN NON-COVERED COUNTRIES

Columns W to Y are analogous to the previous section.

16.7 COUNTRIES RECEIVING VACCINATIONS

Columns Z through AD list the covered countries receiving any vaccination, non-covered countries receiving any vaccination, any country receiving any vaccination, IDA eligibility for Commitment participating countries, and IDA eligibility for non-Commitment participating countries, respectively.

16.8 CO-PAYMENTS FOR COVERED COUNTRIES

Column AE shows the co-payments per person vaccinated that each covered country would pay under the purchase program. If a covered country does not receive funding for a particular vaccine or if the country is not covered, then this variable equals zero.

17. HIV-AIDS New Cohorts

This purpose of this worksheet is to obtain the expected lifetime DALY burden of HIV-AIDS for the typical newly born person in each country. Default parameters are set for an ideal vaccine that would prevent mother to infant transmission of HIV/AIDS. If a vaccine would not do this or would only prevent transmission in breast milk, the user should change the "scaling factor for benefits ages 0-4" parameter.

17.1 DERIVATION OF BURDEN BY COUNTRY

This worksheet first displays the number of HIV positive individuals and proportion of HIV positive individuals from the 'hiv-aids cases' page for each country (columns D and F, respectively).

Then estimates for the *distribution* of DALY burden by sex and age group are calculated. Murray and Lopez (1996a) provide 1990 data on male/female and age group burden of disease according to their regional categories (Murray and Lopez, 1996a, Annex Table 9, pages 541, 545, 549, 553, 557, 561, 565, and 569).

Columns G through N assign each country the Murray and Lopez regional data with accordance to their regional codes. Columns O through V convert the regional numbers into proportions. In the absence of more detailed data, the regional proportions are used as the best estimate for country-level proportions of burden by sex and age.

Column W lists the 1999 regional burden of HIV/AIDS figures (in DALYs) from the World Health Report (WHO 2000), Statistical Annex Table 4. (The data appear in column Z in rows 190 to 203. The numbers are listed according to WHO's categories and sub-categories based on region and mortality stratum.)

In column X, an estimate of a country's DALY burden of HIV/AIDS is derived by multiplying the WHO regional total by the country's proportion of burden (from the *hiv-aids cases* page). To get country burden by sex in Y and Z, the country burden (in X) is multiplied by that country's regional proportion of burden by sex (in P and Q).

17.2 NEW COHORT LIFETIME BURDEN

17.2.1 FORMULA FOR LIFETIME BURDEN

In AA to AE, the burden per person of HIV/AIDS is found in the age categories 0-4, 5-14, 15-44, 45-59, and 60+ years old (these are the categories given by Murray and Lopez). The country burden is multiplied by the age category's share of burden in the country's region. Then this number is divided by the proportion of the age group in the total country population to obtain an average burden per person in the given age group.

Then the worksheet performs the steps necessary to calculate the lifetime burden for new cohorts, the final outcome of which is displayed in column AF. The lifetime burden for new cohorts can be interpreted as the discounted average number of disability-adjusted life years lost due to HIV/AIDS for a person born in a particular country. In general,

Lifetime new cohort burden=
$burden_{0\text{-}4} + burden_{0\text{-}4}/(1+r) + burden_{0\text{-}4}/[(1+r)^2] + burden_{0\text{-}4}/[(1+r)^3] +$
$burden_{0\text{-}4}/[(1+r)^4] + burden_{5\text{-}14}/[(1+r)^5] +$
$burden_{5\text{-}14}/[(1+r)^6] + \ldots + burden_{\text{country's last age group}}/[(1+r)^{\text{country life expectancy}}]$,

where r is the real discount rate and $burden_i$ is the burden per person of age group i (i=0-4, 5-14, 15-44, 45-59, 60+).

To make this calculation easier, the lifetime new cohort burden is broken apart by age group and the results are summed for each age group. In concrete terms,

Column BB=
$burden_{0\text{-}4} + burden_{0\text{-}4}/(1+r) + burden_{0\text{-}4}/[(1+r)^2] + burden_{0\text{-}4}/[(1+r)^3] +$
$burden_{0\text{-}4}/[(1+r)^4]$

Column BC=
$burden_{5\text{-}14}/[(1+r)^5] + burden_{5\text{-}14}/[(1+r)^6] + \ldots + burden_{5\text{-}14}/[(1+r)^{14}]$

Column BD=
$burden_{15\text{-}44}/[(1+r)^{15}] + burden_{15\text{-}44}/[(1+r)^{16}] + \ldots + burden_{5\text{-}14}/[(1+r)^{44}]$

Column BE=
$burden_{45\text{-}59}/[(1+r)^{45}] + burden_{45\text{-}59}/[(1+r)^{46}] + \ldots + burden_{45\text{-}59}/[(1+r)^{59}]$

Column BF=
$burden_{60+}/[(1+r)^{60}] + burden_{60+}/[(1+r)^{61}] + \ldots + burden_{60+}/[(1+r)^{\text{country life expectancy}}]$

Please note that for some countries with a life expectancy less than 60, Column BF (or even BE and BF) will contain zeros. The lifetime burden is only calculated up to a country's life expectancy.

17.2.2 TECHNICAL IMPLEMENTATION OF FORMULA

Now the technical implementation of the above formulas will be explained. The form of the burden calculation for age group *i* (any column from BB to BF) is the following:

=(-PV(real interest rate, years in annuity, payment ,,1))/((1+real interest rate)^years to discount)

The present value (PV) calculation requires four parameters: the real interest rate, the number of periods in the annuity, the “payment” made each period, and a dummy variable that indicates “payments” are due at the beginning of each period. See Microsoft Excel's Help for a more lengthy description of this function. The real interest rate comes from the *options* worksheet. The “payment” each period is the burden per person of age group *i* (in columns AA to AE). The number of periods in the annuity comes from two calculations: the “intermediate calculation” and “years in annuity.” Basically, the objective is to obtain the number of years within the given age interval after which vaccination begins. For example, for the 15-44 year old category, the answer is 30 if vaccination begins at birth (45-15=30). The “intermediate calculation” evaluates the number of years in a given age interval. The “years in annuity” calculation adjusts the value from the “intermediate calculation” in case vaccination has started *after* the given age period. This is the basic structure of the present value function.

Also, because the present value calculation is individually performed for each age period, the present value results must be adjusted in the following way. The present value DALYs for each age period is divided by [(1 + real interest rate) ^ years to discount]. In essence, “years to discount” gives the number of years between the age at which vaccination begins and the age at which the given age period begins. Example: for the 15-44 year old category the answer is 15 if the vaccination begins at birth (15-0= 15). This adjustment is needed since the PV function has not accounted for the 15 years that have passed after vaccination begins and before the start of the 15-44 age group (i.e. the PV function has discounted such that the 15-44 age period were 15 years closer to present time).

Finally, the discounted DALYs are summed for the five age groups, which are BB to BF. The result is the lifetime burden for new cohorts in AF.

One side note: this accounts for the fact that the life expectancy of countries varies widely. In many countries few people will live past 60 years of age. Therefore, in general, the population cannot accrue DALYs beyond 60 years of age. The "intermediate calculation II" corrects for this fact. It counts the number of years in an age period that fall below a country's life expectancy. Example: Suppose the 65-69 age category is considered. If the life expectancy in a country is 67, then the "intermediate calculation II" gives 2. If the life expectancy is 60, then the "intermediate calculation II" yields –5. If the life expectancy is 80, then it yields 5. The "years in annuity" calculation lists only the zero or positive values from the "intermediate calculation II." In this way, the calculations adjust for those countries that have a low average life expectancy. Further refinement of this work could incorporate heterogeneity in life expectancy within countries.

17.3 LIFETIME BURDEN EXAMPLE

Consider an example for Angola: For the 5-14 age group: The intermediate calculation is 10, because there are ten years in the age interval. The years in annuity calculation is also 10, because vaccination begins before the 5-14 period. The burden of AIDS per person of age 5-14 is 0.0062. Therefore, the present value of 0.0062 DALYs per year for ten years at a three percent interest rate is 0.0544 DALYs. However, since the beginning of this period occurs five years after vaccination of new cohorts begins, 0.0443 must be multiplied by [1/(1 + 0.03)^ 5]. The number 5 comes from the "years to discount" calculation. This is essentially the number of years between the age at which vaccination begins and the age at which the given period begins. For the 5-14 category years to discount equals 5 (5-0=5). Therefore, 0.0470 DALYs are the total discounted DALYs for the 5-14 age group. This procedure is followed for each of the age categories, 0-4, 5-14, 15-44, 45-59, and 60+ and the results are summed to obtain the lifetime burden per new cohort in Angola, which is 1.2624 DALYs.

17.4 PREPARATION FOR CHILDREN AND OLD COHORT LIFETIME BURDEN CALCULATIONS

Next, in preparation for the calculations for children and old cohorts, the present value calculations are performed in five year age intervals in columns CV to DK. The calculations that provide input parameters for the PV function (intermediate and years in annuity procedures) are the same as those for new cohorts (see BH to CU).

18. HIV-AIDS children

This worksheet finds the average lifetime burden of HIV/AIDS for a child between the ages of 1 and 10.

Columns B through Q display the present value calculations that were obtained in columns CV to DK on the *hiv-aids new cohorts* worksheet. Since the data pertains to five-year ranges, it is assumed that all individuals are in the middle of their particular age range. Thus, it is assumed that all children between the ages of 5 and 10 in a country are all 7.5 years old.

The discounted burden per person in each age range (0-4 and 5-10) is calculated for an entire life span. A weighted average of the age category burden figures is taken according to the population distribution in each country and divide by the proportion of 1-10 year olds in the country to obtain the lifetime burden per child.

19. HIV-AIDS Old Cohorts

This worksheet finds the average lifetime burden of HIV/AIDS for an individual between the ages of 10 and 35. First, the average lifetime burden is found for an individual in each age category. It is assumed that this person is in the middle of the age range; that is, of people that are between 20 and 25, all are 22.5 years old. To do this, the present value of burden that remains in the rest of her/his life for each span of five years in the lifetime is discounted. These discounted burden estimates are summed to get the lifetime burden of the median person in the age range. This procedure is performed for all age categories.

Then the weighted average of the age range lifetime burdens for people from 10 to 35 is taken according to population distribution and divided by the proportion of 10 to 35 year olds in the country. This yields the average lifetime burden of HIV/AIDS per person between the ages 10 and 35.

20. Malaria

This worksheet evaluates the cost effectiveness of vaccinations for malaria; obtains the number of vaccinations and DALYs saved for both covered and non-covered countries; and calculates the amount of co-payments received.

20.1 NEW COHORTS IN COVERED COUNTRIES

Column B lists the lifetime burden of malaria in DALYs per new cohort from the *malaria new cohorts* worksheet. This number can be considered the marginal benefit of a successful intervention if the vaccine is perfectly effective. Remember that the *options* worksheet estimates a “cutoff”—the marginal cost of manufacturing and delivering an additional vaccination given high production volume.

Column C actually performs the cost-effective evaluation for the covered under the program (their GNP per capita is below the “cutoff” value). It compares the (1) marginal benefit, i.e. the lifetime burden per new cohort multiplied by the level of vaccine efficacy and the ratio of DALY burden (see *options* description) with (2) the marginal cost. If the marginal cost is greater than the lifetime burden adjusted for efficacy, then new cohorts born in a country do not receive vaccinations. If the lifetime burden adjusted for efficacy is equal to or greater than the marginal cost, then the worksheet displays the number of births in one year in the country. This number is adjusted for the vaccine coverage rate on a subsequent worksheet. The costs and benefits that are compared here are in the same units—DALYs per person vaccinated. Recall that on the *options* worksheet the marginal cost of vaccinating an additional person is divided by the DALY cost effectiveness cutoff to transform the marginal cost per person vaccinated into DALY terms.

Column D finds the co-payments that a country will pay for new cohort vaccinations (unadjusted by the coverage rate). This is simply the number of vaccinations multiplied by the per capita GNP multiplied by the co-payment factor on the *options* worksheet.

Column E gives the number of DALYs saved for those new cohorts that receive effective vaccinations. This is the lifetime burden per new cohorts times the number of vaccinations times the vaccine efficacy times the ratio of DALY burden (see notes for the *options* worksheet).

Column F records which countries receive new cohort vaccinations.

20.2 NEW COHORTS IN NON-COVERED COUNTRIES

Columns G to I are analogous to the previous section.

20.3 CHILDREN IN COVERED COUNTRIES

Column J lists the lifetime burden of malaria in DALYs per child from the *malaria children* worksheet. This number can be considered the marginal benefit of a successful intervention if the vaccine is perfectly effective. Remember that the *options* worksheet estimates a “cutoff”—the marginal cost of manufacturing and delivering an additional vaccination given high production volume.

Column K actually performs the cost-effective evaluation for the countries that may participate in the program (their GNP per capita is below the “cutoff” value). It compares the (1) marginal benefit, i.e. lifetime burden per child, multiplied by the level of vaccine efficacy and the ratio of DALY burden (see *options* documentation) with (2) the marginal cost. If the marginal cost is greater than the lifetime burden adjusted for efficacy, then a country does not receive funding for child vaccinations under the program. If the lifetime burden adjusted for efficacy is equal to or greater than the marginal cost, then the column displays the number of 1 to 5 year olds in the country. This number is adjusted for the vaccine coverage rate on a subsequent worksheet. The costs and benefits that are compared here are in the same units—DALYs per person vaccinated. Recall that on the *options* worksheet the marginal cost of vaccinating an additional person is divided by the DALY cost effectiveness cutoff to transform the marginal cost per person vaccinated into DALY terms.

Column L finds the co-payments that a country will pay for children vaccinations (unadjusted by the coverage rate). This is simply the number of vaccinations multiplied by the per capita GNP multiplied by the co-payment factor on the *options* worksheet.

Column M gives the number of DALYs saved for those children that receive effective vaccinations. This is the lifetime burden per child times the number of vaccinations times the vaccine efficacy times the ratio of DALY burden (see notes for the *options* worksheet).

Column N records which countries receive children vaccinations.

20.4 CHILDREN IN NON-COVERED COUNTRIES

Columns O to Q are analogous to the previous section.

20.5 OLD COHORTS IN COVERED COUNTRIES

Column R lists the lifetime burden of malaria in DALYs per old cohort from the *malaria old cohorts* worksheet. Recall that the only adults immunized against malaria are women pregnant with their first child. This number can be considered the marginal benefit of a successful untargeted vaccination if the vaccine is perfectly effective. Remember that the *options* worksheet estimates the marginal cost of manufacturing and delivering an additional vaccination given high production volume.

Column S actually performs the cost-effective evaluation for the countries that may participate in the Commitment (their GNP per capita is below the "cutoff" value). It compares the (1) marginal benefit, i.e. lifetime burden per old cohort, multiplied by the level of vaccine efficacy, the targeting parameter, and the ratio of DALY burden (see *options* documentation) with (2) the marginal cost. If the cutoff is greater than the lifetime burden adjusted for efficacy, then a country does not receive funding for old cohort vaccinations. If the lifetime burden adjusted for efficacy is equal to or greater than the marginal cost, then the column displays the number of annual births divided by four in a country. Thus, it is assumed that one-fourth of all births in a country are to first-time mothers. This number is adjusted for the vaccine coverage rate on a subsequent worksheet. The costs and benefits that are compared here are in the same units—DALYs per person vaccinated. Recall that on the *options* worksheet the marginal cost of vaccinating an additional person is divided by the DALY cost effectiveness cutoff to transform the marginal cost per person vaccinated into DALY terms.

Column T finds the co-payments that a country will pay for old cohort vaccinations (unadjusted by the coverage rate). This is simply the number of vaccinations multiplied by the per capita GNP multiplied by the co-payment factor on the *options* worksheet.

Column U gives the number of DALYs saved for those old cohorts that receive effective vaccinations. This is the lifetime burden per old cohort times the number of vaccinations times the vaccine efficacy times the ratio of DALY burden (see notes for the *options* worksheet).

Column V records which countries receive old cohort vaccinations.

20.6 OLD COHORTS IN NON-COVERED COUNTRIES

Columns W to Y are analogous to the previous section.

20.7 COUNTRIES RECEIVING VACCINATIONS

Columns Z through AD list the Commitment participating countries receiving any vaccination, non-covered countries receiving any vaccination, any country receiving any vaccination, IDA eligibility for covered countries, and IDA eligibility for non-covered countries, respectively.

20.8 CO-PAYMENTS FOR COVERED COUNTRIES

Column AE shows the co-payments per person vaccinated that each covered country would pay under the purchase program. If a covered country does not receive funding for a particular vaccine or if the country is not covered, then this variable equals zero.

21. Malaria New Cohorts

This purpose of this worksheet is to obtain the expected lifetime DALY burden of malaria for the typical newly born person in each country.

21.1 DERIVATION OF BURDEN BY COUNTRY

This worksheet first displays the country's share of regional malaria burden from the *malaria cases* page for each country (column D).

Then estimates for the *distribution* of DALY burden by sex and age group are calculated. Murray and Lopez (1996a) provide 1990 data on male/female and age group burden of disease according to their regional categories (The numbers are listed in a table located in E190. See Murray and Lopez (1996a), Annex Table 9, pages 541, 545, 549, 553, 557, 561, 565, and 569).

Columns E through Q assign each country the Murray and Lopez regional data with accordance to their regional codes. Unlike the case with HIV/AIDS and tuberculosis, the age group regional burden of malaria needs to be broken down further by sex. This is because only women pregnant with their first child are vaccinated as opposed to all adults between the ages 10 and 35. Columns R through AD convert the regional numbers into proportions. In the absence of more detailed data, the regional proportions are used as the best estimate for country-level proportions of burden by sex and age.

Column AE lists the 1999 regional burden of malaria figures (in DALYs) from the World Health Report (WHO 2000), Statistical Annex Table 4. (The data appear in a table in column AH in rows 190 to 203. The numbers are listed according to WHO's categories and sub-categories based on region and mortality stratum, respectively.)

In column AF, an estimate of a country's DALY burden of malaria is estimated by multiplying the WHO regional total by the country's proportion of burden (from the *malaria cases* worksheet). To get country burden by sex in AG and AH, the country burden (in AF) is multiplied by that country's regional proportion of burden by sex (in S and T).

21.2 NEW COHORT LIFETIME BURDEN

21.2.1 FORMULA FOR LIFETIME BURDEN

In AI to AR, then the burden per person of malaria is found in the age categories 0-4, 5-14, 15-44, 45-59, and 60+ years old (these are the categories given by Murray and Lopez). The country burden is multiplied by the age category's share of burden in the country's region. Then this number is divided by the proportion of the age group in the total country population to obtain an average burden per person in the given age group.

The worksheet then goes through the steps necessary to calculate the lifetime burden for new cohorts, the final outcome of which is displayed in column AS. The lifetime burden for new cohorts can be interpreted as the discounted average number of disability-adjusted life years lost due to malaria for a person born in a particular country. In general,

Lifetime new cohort burden=
$burden_{0\text{-}4} + burden_{0\text{-}4}/(1+r) + burden_{0\text{-}4}/[(1+r)^2] + burden_{0\text{-}4}/[(1+r)^3] +$

$\text{burden}_{0\text{-}4}/[(1+r)^4] + \text{burden}_{5\text{-}14}/[(1+r)^5] +$
$\text{burden}_{5\text{-}14}/[(1+r)^6] + \ldots + \text{burden}_{\text{country's last age group}}/[(1+r)^{\text{country life expectancy}}]$,

where r is the real discount rate and $burden_i$ is the burden per person of age group i (i=0-4, 5-14, 15-44, 45-59, 60+).

To make this calculation easier, the lifetime new cohort burden are broken apart by age group and the results are summed for each age group. In concrete terms,

Column BO=
$\text{burden}_{0\text{-}4} + \text{burden}_{0\text{-}4}/(1+r) + \text{burden}_{0\text{-}4}/[(1+r)^2] + \text{burden}_{0\text{-}4}/[(1+r)^3] +$
$\text{burden}_{0\text{-}4}/[(1+r)^4]$

Column BP=
$\text{burden}_{5\text{-}14}/[(1+r)^5] + \text{burden}_{5\text{-}14}/[(1+r)^6] + \ldots + \text{burden}_{5\text{-}14}/[(1+r)^{14}]$

Column BQ=
$\text{burden}_{15\text{-}44}/[(1+r)^{15}] + \text{burden}_{15\text{-}44}/[(1+r)^{16}] + \ldots + \text{burden}_{5\text{-}14}/[(1+r)^{44}]$

Column BR=
$\text{burden}_{45\text{-}59}/[(1+r)^{45}] + \text{burden}_{45\text{-}59}/[(1+r)^{46}] + \ldots + \text{burden}_{45\text{-}59}/[(1+r)^{59}]$

Column BS=
$\text{burden}_{60+}/[(1+r)^{60}] + \text{burden}_{60+}/[(1+r)^{61}] + \ldots + \text{burden}_{60+}/[(1+r)^{\text{country life expectancy}}]$

Please note that for some countries with a life expectancy less than 60, Column BS (or even BS and BR) will contain zeros. The lifetime burden is calculated up to a country's life expectancy.

21.2.2 TECHNICAL IMPLEMENTATION OF FORMULA

Now the technical implementation of the above formulas will be explained. The form of the burden calculation for age group *i* (any column from BO to BS) is the following:

=(-PV(real interest rate, years in annuity, payment ,,1))/((1+real interest rate)^years to discount)

The present value (PV) calculation requires four parameters: the real interest rate, the number of periods in the annuity, the “payment” made each period, and a dummy variable that “payments” are due at the beginning of each period. See Microsoft Excel's Help for a more lengthy description of this function. The real interest rate comes from the *options* worksheet, Row 8. The “payment” each period is the burden per person of age group *i* (in columns AI to AR). The number of periods in the annuity comes from two calculations: the “intermediate calculation” and “years in annuity.” Basically, it is necessary to obtain the number of years within the given age interval after which vaccination begins. For example, for the 15-44 year old category, the answer is 30 if vaccination begins at birth (45-15=30). The “intermediate calculation” evaluates the number of years in a given age interval. The “years in annuity” calculation adjusts the value from the “intermediate calculation” in case vaccination has started *after* the given age period. This is the basic structure of the present value function.

Also, because the present value calculation is individually performed for each age period, the present value results must be adjusted in the following way. The present value DALYs for each age period are divided by [(1 + real interest rate) ^ years to discount]. In essence, “years to discount” gives the number of years between the age at which vaccination begins and the age at which the given age period begins. Example: for the 15-44 year old category the answer is 15 if the vaccination begins at birth (15-0= 15). This adjustment is necessary as the PV function has not accounted for the 15 years that have passed after vaccination begins and before the start of the 15-44 age group (i.e. the PV function has discounted such that the 15-44 age period were 15 years closer to present time).

Finally, the discounted DALYs are summed for the five age groups, which are BO to BS. The result is the lifetime burden for new cohorts in AS.

One side note: the spreadsheet accounts for the fact that the life expectancy of countries varies widely. In many countries few people will live past 60 years of age; therefore, in general, the population cannot accrue DALYs beyond 60 years of age. The “intermediate calculation II” corrects for this fact. It counts the number of years in an age period that fall below a country’s life expectancy. Example: Suppose the 65-69 age category is considered. If the life expectancy in a country is 67, then the “intermediate calculation II” gives 2. If the life expectancy is 60, then the “intermediate calculation II” yields –5. If the life expectancy is 80, then it yields 5. The “years in annuity” calculation lists only the zero or positive values from the “intermediate calculation II.” In this way, the calculations adjust for those countries that have a low average life expectancy. Further refinement of this work could incorporate heterogeneity in life expectancy within countries.

21.3 LIFETIME BURDEN EXAMPLE

Consider an example for Angola: For the 5-14 age group: The intermediate calculation is 10, because there are ten years in the age interval. The years in annuity calculation is also 10, because vaccination begins before the 5-14 period. The burden of malaria per person of age 5-14 is 0.02156 (average of male and female burden). Therefore, the present value of 0.02156 DALYs per year for ten years at a three percent interest rate is 0.1894 DALYs. However, since the beginning of this period occurs five years after vaccination of new cohorts begins, 0.1894 must be multiplied by [1/(1 + 0.03)^ 5]. The number 5 comes from the “years to discount” calculation. This is essentially the number of years between the age at which vaccination begins and the age at which the given period begins. For the 5-14 category years to discount equals 5 (5-0=5). Therefore, 0.1634 DALYs are the total discounted DALYs for the 5-14 age group. This procedure is followed for each of the age categories, 0-4, 5-14, 15-44, 45-59, and 60+ and the results are added to obtain the lifetime burden per new cohort in Angola, which is 1.8140 DALYs.

21.4 PREPARATION FOR CHILDREN AND OLD COHORTS LIFETIME BURDEN CALCULATIONS

Next, in preparation for the calculations for children and old cohorts, the present value calculations are performed in five year age intervals in columns DI to DX. The calculations that provide input parameters for the PV function (intermediate and years in annuity procedures) are the same as those for new cohorts (see BU to DH).

22. Malaria children

This worksheet finds the lifetime burden of malaria for a child between the ages of 0 and 5.

Columns B through Q display the present value calculations based on saving the average of the burden per person for males and females age 0 to 4. Since the data relates to five-year ranges, it is assumed that all individuals are in the middle of their particular age range. Thus, it is assumed that all children between the ages of 0 and 5 in a country are all 2.5 years old.

The discounted burden per person in the 0-4 age range is calculated for an entire life span. These discounted burden numbers are summed to get the lifetime burden of malaria for a child between the ages of 0 and 5.

23. Malaria Old Cohorts

This worksheet finds the average lifetime burden of malaria for pregnant women between the ages of 15 and 50. First, the average lifetime burden is found for an individual in each age category. It is assumed that this person is in the middle of the age range; that is, of people that are between 20 and 25, all are 22.5 years old. To do this, the present value of burden that remains in the rest of her life for each span of five years in the lifetime is discounted. These discounted burden estimates are summed to get the lifetime burden of the median person in the age range. This procedure is performed for all age categories.

Then the weighted average of the age range lifetime burdens is taken for pregnant women from 15 to 50 according to the fertility distribution. This yields the average lifetime burden of malaria per pregnant woman between the ages 15 and 50.

24. TB

This worksheet evaluates the cost effectiveness of tuberculosis interventions; obtains the number of vaccinations and DALYs saved for both covered and non-covered countries; and calculates the amount of co-payments from covered countries.

24.1 NEW COHORTS IN COVERED COUNTRIES

Column B lists the lifetime burden of tuberculosis in DALYs per new cohort from the *tb new cohorts* worksheet. This number can be considered the marginal benefit of a successful intervention if the vaccine is perfectly effective. Remember that the *options* worksheet estimates a "cutoff"—the marginal cost of manufacturing and delivering an additional vaccination given high production volume.

Column C actually performs the cost-effective evaluation for the covered under the program (their GNP per capita is below the "cutoff" value). It compares the (1) marginal benefit, i.e. the lifetime burden per new cohort, multiplied by the targeting parameter, the level of vaccine efficacy and the ratio of DALY burden (see *options* description) with (2) the marginal cost. If the marginal cost is greater than the lifetime burden adjusted for efficacy, then new cohorts born in a country do not receive funding for vaccinations. If the lifetime burden adjusted for efficacy is equal to or greater than the marginal cost, then the worksheet displays the number of births in one year in the country. This number is adjusted for the vaccine coverage rate on a subsequent worksheet. The costs and benefits that are compared here are in the same units—DALYs per person vaccinated. Recall that on the *options* worksheet the marginal cost of vaccinating an additional person is divided by the DALY cost effectiveness cutoff to transform the marginal cost per person vaccinated into DALY terms.

Column D finds the co-payments that a country will pay for new cohort vaccinations (unadjusted by the coverage rate). This is simply the number of vaccinations multiplied by the per capita GNP multiplied by the co-payment factor on the *options* worksheet.

Column E gives the number of DALYs saved for those new cohorts that receive effective vaccinations. This is the lifetime burden per new cohorts times the number of vaccinations times the vaccine efficacy times the ratio of DALY burden (see notes for the *options* worksheet).

Column F records which countries receive new cohort vaccinations.

24.2 NEW COHORTS IN NON-COVERED COUNTRIES

Columns G to I are analogous to the previous section.

24.3 CHILDREN IN COVERED COUNTRIES

Column J lists the lifetime burden of tuberculosis in DALYs per child from *the tb children* worksheet. This number can be considered the marginal benefit of a successful intervention if the vaccine is perfectly effective. Remember that the *options* worksheet estimates a “cutoff”—the marginal cost of manufacturing and delivering an additional vaccination given high production volume.

Column K actually performs the cost-effective evaluation for the countries that may participate in the program (their GNP per capita is below the “cutoff” value). It compares the (1) marginal benefit, i.e. lifetime burden per child, multiplied by the level of vaccine efficacy and the ratio of DALY burden (see *options* description) with (2) the marginal cost. If the marginal cost is greater than the lifetime burden adjusted for efficacy, then a country does not receive funding for child vaccinations under the program. If the lifetime burden adjusted for efficacy is equal to or greater than the marginal cost, then the column displays the number of 1 to 10 year olds in the country. This number is adjusted for the vaccine coverage rate on a subsequent worksheet. The costs and benefits that are compared here are in the same units—DALYs per person vaccinated. Recall that on the *options* worksheet the marginal cost of vaccinating an additional person is divided by the DALY cost effectiveness cutoff to transform the marginal cost per person vaccinated into DALY terms.

Column L finds the co-payments that a country will pay for children vaccinations (unadjusted by the coverage rate). This is simply the number of vaccinations multiplied by the per capita GNP multiplied by the co-payment factor on the *options* worksheet.

Column M gives the number of DALYs saved for those children that receive effective vaccinations. This is the lifetime burden per child times the number of vaccinations times the vaccine efficacy times the ratio of DALY burden (see notes for the *options* worksheet).

Column N records which countries receive children vaccinations.

24.4 CHILDREN IN NON-COVERED COUNTRIES

Columns O to Q are analogous to the previous section.

24.5 OLD COHORTS IN COVERED COUNTRIES

Column R lists the lifetime burden of HIV/AIDS in DALYs per old cohort from the *hiv-aids old cohorts* worksheet. This number can be considered the marginal benefit of a successful untargeted vaccination if the vaccine is perfectly effective. Remember that the *options* worksheet estimates the marginal cost of manufacturing and delivering an additional vaccination given high production volume.

Column S actually performs the cost-effective evaluation for the countries that may participate in the Commitment (their GNP per capita is below the "cutoff" value). It compares the (1) marginal benefit, i.e. lifetime burden per old cohort, multiplied by the level of vaccine efficacy, the targeting parameter, and the ratio of DALY burden (see *options* documentation) with (2) the marginal cost. If the cutoff is greater than the lifetime burden adjusted for efficacy, then a country does not receive funding for old cohort vaccinations. If the lifetime burden adjusted for efficacy is equal to or greater than the marginal cost, then the column displays the number of 10 to 35 year olds in the country. This number is adjusted for the vaccine coverage rate on a subsequent worksheet. The costs and benefits that are compared here are in the same units—DALYs per person vaccinated. Recall that on the *options* worksheet the marginal cost of vaccinating an additional person is divided by the DALY cost effectiveness cutoff to transform the marginal cost per person vaccinated into DALY terms.

Column T finds the co-payments that a country will pay for old cohort vaccinations (unadjusted by the coverage rate). This is simply the number of vaccinations multiplied by the per capita GNP multiplied by the co-payment factor on the *options* worksheet.

Column U gives the number of DALYs saved for those old cohorts that receive effective vaccinations. This is the lifetime burden per old cohort times the number of vaccinations times the vaccine efficacy times the ratio of DALY burden (see notes for the *options* worksheet).

Column V records which countries receive old cohort vaccinations.

24.6 OLD COHORTS IN NON-COVERED COUNTRIES

Columns W to Y are analogous to the previous section.

24.7 COUNTRIES RECEIVING VACCINATIONS

Columns Z through AD list the covered countries receiving any vaccination, non-covered countries receiving any vaccination, any country receiving any vaccination, IDA eligibility for covered countries, and IDA eligibility for non-covered countries, respectively.

24.8 CO-PAYMENTS FOR COVERED COUNTRIES

Column AE shows the co-payments per person vaccinated that each covered country would pay under the purchase program. If a covered country does not receive funding for a particular vaccine or if the country is not covered, then this variable equals zero.

25. TB New Cohorts

This purpose of this worksheet is to obtain the expected lifetime DALY burden of tuberculosis for the typical newly born person in each country.

25.1 DERIVATION OF BURDEN BY COUNTRY

This worksheet first displays each country's tb cases and share of regional burden from the *tb cases* page for each country (columns D and F, respectively).

Then estimates of the *distribution* of DALY burden by sex and age group are calculated. Murray and Lopez (1996a) provide 1990 data on male/female and age group burden of disease according to their regional categories (Murray and Lopez (1996a), Annex Table 9, pages 541, 545, 549, 553, 557, 561, 565, and 569).

Columns G through N assign each country the Murray and Lopez regional data with accordance to their regional codes. Columns O through V convert the regional numbers into proportions. In the absence of more detailed data, the regional proportions are used as the best estimate for country-level proportions of burden by sex and age.

Column W lists the 1999 regional burden of tuberculosis (in DALYs) from the World Health Report (WHO 2000), Statistical Annex Table 4. (The data appear in column Z in rows 190 to 203. The numbers are listed according to WHO's categories and sub-categories based on region and mortality stratum.)

In column X, an estimate of a country's DALY burden of tuberculosis is derived by multiplying the WHO regional total by the country's proportion of burden (from the *tb cases* worksheet). To get country burden by sex in Y and Z, the country burden (in X) is multiplied by that country's regional proportion of burden by sex (in P and Q).

25.2 NEW COHORTS LIFETIME BURDEN

25.2.1 FORMULA FOR LIFETIME BURDEN

In AA to AE, then the burden per person of tuberculosis is found in the age categories 0-4, 5-14, 15-44, 45-59, and 60+ years old (these are the categories given by Murray and Lopez). The country burden is multiplied by the age category's share of burden in the country's region. This number is then divided by the proportion of the age group in the total country population to obtain an average burden per person in the given age group.

The worksheet then goes through the steps necessary to calculate the lifetime burden for new cohorts, the final outcome of which is displayed in column AF. The lifetime burden for new cohorts can be interpreted as the discounted average number of disability-adjusted life years lost due to tuberculosis for a person born in a particular country. In general,

Lifetime new cohort burden=
burden $_{0\text{-}4}$ + burden $_{0\text{-}4}$ /(1+r) + burden $_{0\text{-}4}$/[(1+r)^2] + burden $_{0\text{-}4}$/[(1+r)^3] +
burden $_{0\text{-}4}$/[(1+r)^4] + burden $_{5\text{-}14}$/[(1+r)^5] +
burden $_{5\text{-}14}$/[(1+r)^6] + … + burden $_{\text{country's last age group}}$ /[(1+r)^country life expectancy],

where *r* is the real discount rate and *burden* $_i$ is the burden per person of age group *i*
(i=0-4, 5-14, 15-44, 45-59, 60+).

To make this calculation easier, the lifetime new cohort burden is broken apart by age group and the results are summed for each age group. In concrete terms,

Column BB=
burden $_{0\text{-}4}$ + burden $_{0\text{-}4}$ /(1+r) + burden $_{0\text{-}4}$/[(1+r)^2] + burden $_{0\text{-}4}$/[(1+r)^3] +
burden $_{0\text{-}4}$/[(1+r)^4]

Column BC=
burden $_{5\text{-}14}$/[(1+r)^5] + burden $_{5\text{-}14}$/[(1+r)^6] + … + burden $_{5\text{-}14}$/[(1+r)^14]

Column BD=
burden $_{15\text{-}44}$/[(1+r)^15] + burden $_{15\text{-}44}$/[(1+r)^16] + … + burden $_{5\text{-}14}$/[(1+r)^44]

Column BE=
burden $_{45\text{-}59}$/[(1+r)^45] + burden $_{45\text{-}59}$/[(1+r)^46] + … + burden $_{45\text{-}59}$/[(1+r)^59]

Column BF=
burden $_{60+}$/[(1+r)^60] + burden $_{60+}$/[(1+r)^61] + … + burden $_{60+}$ /[(1+r)^country life expectancy]

Please note that for some countries with a life expectancy less than 60, Column BF (or even BE and BF) will contain zeros. The lifetime burden is only calculated up to a country's life expectancy.

25.2.2 TECHNICAL IMPLEMENTATION OF FORMULA

Now the technical implementation of the above formulas will be explained. The form of the burden calculation for age group *i* (any column from BB to BF) is the following:

=(-PV(real interest rate, years in annuity, payment ,,1))/((1+real interest rate)^years to discount)

The present value (PV) calculation requires four parameters: the real interest rate, the number of periods in the annuity, the "payment" made each period, and a dummy variable that "payments" are due at the beginning of each period. See Microsoft Excel's Help for a more lengthy description of this function. The real interest rate comes from the *options* worksheet, Row 8.

The “payment” each period is the burden per person of age group *i* (in columns AA to AE). The number of periods in the annuity comes from two calculations: the “intermediate calculation” and “years in annuity.” Basically, the objective is to obtain the number of years within the given age interval after which vaccination begins. For example, for the 15-44 year old category, the answer is 30 if vaccination begins at birth (45-15=30). The “intermediate calculation” evaluates the number of years in a given age interval. The “years in annuity” calculation adjusts the value from the “intermediate calculation” in case vaccination has started *after* the given age period. This is the basic structure of the present value function.

Also, because the present value calculation is individually performed for each age period, the present value results must be adjusted in the following way. The present value DALYs for each age period are divided by [(1 + real interest rate) ^ years to discount]. In essence, “years to discount” gives the number of years between the age at which vaccination begins and the age at which the given age period begins. Example: for the 15-44 year old category the answer is 15 if the vaccination begins at birth (15-0= 15). This adjustment is necessary since the PV function has not accounted for the 15 years that have passed after vaccination begins and before the start of the 15-44 age group (i.e. the PV function has discounted such that the 15-44 age period were 15 years closer to present time).

Finally, the discounted DALYs are summed for the five age groups, which are BB to BF. The result is the lifetime burden for new cohorts in AF.

One side note: the calculations account for the fact that the life expectancy of countries varies widely. In many countries few people will live past 60 years of age; therefore, in general, the population cannot accrue DALYs beyond 60 years of age. The "intermediate calculation II" corrects for this fact. It counts the number of years in an age period that fall below a country's life expectancy. Example: Suppose the 65-69 age category is considered. If the life expectancy in a country is 67, then the "intermediate calculation II" gives 2. If the life expectancy is 60, then the "intermediate calculation II" yields –5. If the life expectancy is 80, then it yields 5. The "years in annuity" calculation lists only the zero or positive values from the "intermediate calculation II." In this way, the spreadsheet adjusts for those countries that have a low average life expectancy. Further refinement of this work could incorporate heterogeneity in life expectancy within countries.

25.3 LIFETIME BURDEN EXAMPLE

Consider an example for Angola: For the 5-14 age group: The intermediate calculation is 10, because there are nine years in the age interval. The years in annuity calculation is also 10, because vaccination begins before the 5-14 period. The burden of tuberculosis per person of age 5-14 is 0.0048. Therefore, the present value of 0.0048 DALYs per year for ten years at a three percent interest rate is 0.0425 DALYs. However, since the beginning of this period occurs five years after vaccination of new cohorts begins, 0.0425 must be multiplied by [1/(1 + 0.03)^ 5]. The number 5 comes from the "years to discount" calculation. This is essentially the number of years between the age at which vaccination begins and the age at which the given period begins. For the 5-14 category years to discount equals 5 (5-0=5). Therefore, 0.0366 DALYs are the total discounted DALYs for the 5-14 age group. This procedure is followed for each of the age categories, 0-4, 5-14, 15-44, 45-59, and 60+ and the results are added to obtain the lifetime burden per new cohort in Angola, which is 0.2419 DALYs.

25.4 PREPARATION FOR CHILDREN AND OLD COHORTS LIFETIME BURDEN CALCULATIONS

Next, in preparation for the calculations for children and old cohorts, the present value calculations are performed in five year age intervals in columns CV to DK. The calculations that provide input parameters for the PV function (intermediate and years in annuity procedures) are the same as those for new cohorts (see BH to CU).

26. TB children

This worksheet finds the average lifetime burden of tuberculosis for a child between the ages of 1 and 10.

Columns B through Q display the present value calculations from columns CV to DK on *tb new cohorts*. Since the data pertain to five-year ranges, it is assumed that all individuals are in the middle of their particular age range. Thus, it is assumed that all children between the ages of 5 and 10 in a country are all 7.5 years old.

The discounted burden per person in each age range (0-4 and 5-10) is calculated for an entire life span. A weighted average of the age category burden figures is taken according to the population distribution in each country and divide by the proportion of 1-10 year olds in the country to obtain the lifetime burden per child.

27. TB Old Cohorts

This worksheet finds the average lifetime burden of tuberculosis for an individual between the ages of 10 and 35. First, the average lifetime burden is found for an individual in each age category. It is assumed that this person is in the middle of the age range; that is, of people that are between 20 and 25, all are 22.5 years old. To do this, the present value of burden that remains in the rest of her/his life for each span of five years in the lifetime is discounted. These discounted burden estimates are summed to get the lifetime burden of the median person in the age range. This procedure is performed for all age categories.

Then the weighted average of the age range lifetime burdens is taken for people from 10 to 35 according to population distribution and divided by the proportion of 10 to 35 year olds in the country. This yields the average lifetime burden of tuberculosis per person between the ages 10 and 35.

28. Proportional Commitment

This worksheet implements one approach to vaccine pricing which set the size of the purchase commitment for a vaccine with particular characteristics proportional to the social surplus created by the vaccine, where the social surplus is defined as the number of discounted DALYs saved by a vaccine times the cost effectiveness threshold in dollars per DALY minus the total discounted manufacturing and delivery costs.

The spreadsheet first calculates the number of vaccinations that would be cost effective given any set of vaccine characteristics selected. It then calculates the total social surplus generated by such a vaccine. Under the approach to vaccine pricing implemented on this worksheet, the total commitment size is then set to equal the commitment size for an ideal vaccine times the ratio of social surplus generated by a vaccine with the selected characteristics to that generated by the ideal vaccine.

This worksheet can be used to calculate the size of purchase commitment associated with any particular set of vaccine characteristics as well as the implied vaccine price and cost effectiveness.

1. The user must first define the ideal vaccine. Go to the options worksheet and change any of the parameters. The suggested ideal vaccine is the one that corresponds with the default values of the parameters.

2. After creating an ideal vaccine, copy the values for the size of commitment and social surplus at the bottom of the options worksheet. Simply highlight the cells in the red box, right click on them, and choose "copy."

3. Go to the proportional commitment worksheet, which is the last one in the Excel file. Find the red box in the "Ideal Vaccine" section. Right click on the upper left-hand cell in the red box and choose "Paste Special." Another box will appear. Click on "Values only" and choose "OK."

4. Return to the options worksheet. To create a specified vaccine, change any of the parameters under the heading "Vaccine Characteristics."

5. Go to the proportional commitment worksheet again. The spreadsheet will have calculated the size of the purchase commitment and purchase price for the specified vaccine along with other general results. View the results at the bottom of the worksheet.

To formalize this approach to determining the size of commitment for a vaccine with specified characteristics, define these variables and terms:

Specified vaccine A vaccine corresponding to any combination of the parameters under "Characteristics of the Vaccine." The subscript "specified" refers to the case.

Ideal vaccine A vaccine corresponding to the one generated by setting all the parameters on the options worksheet to their default values. The subscript "ideal" refers to this case.

F	size of purchase commitment per year
T	$ per DALY cost effectiveness threshold
D	total discounted DALYs saved
C	total NPV marginal costs (total delivery and marginal manufacturing costs)
P	purchase price per vaccinated person
V	number of people vaccinated for the first ten years
S	the social surplus generated by a vaccine

If the size of the purchase commitment is set proportional to the social surplus created by the vaccine, then

$$\frac{F_{specified}}{(T * D_{specified} - C_{specified})} = \frac{F_{ideal}}{(T * D_{ideal} - C_{ideal})}$$

Equivalently, the size of purchase commitment for a specified vaccine is

$$F_{specified\ vaccine} = \frac{F_{ideal} * (T * D_{specified} - C_{specified})}{(T * D_{ideal} - C_{ideal})}$$

Given the size of the purchase commitment for a specified vaccine and the number of people immunized, it is straight-forward to calculate the implied price per person immunized.

$$\mathbf{P}_{\textbf{specified vaccine}} = \frac{\mathbf{F}_{\textbf{specified}} * \mathbf{10}}{\mathbf{V}_{\textbf{specified}}}$$

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Appendix A:
World Health Organization List of Member States by Region and Mortality Stratum (WHO 2000, pages 204-5)

AFR1: African Region
High child, high adult

Algeria	Guinea-Bissau
Angola	Liberia
Benin	Madagascar
Burkina Faso	Mali
Cameroon	Mauritania
Cape Verde	Mauritius
Chad	Niger
Comoros	Nigeria
Equatorial Guinea	Sao Tome & Principe
Gabon	Senegal
Gambia, The	Seychelles
Ghana	Sierra Leone
Guinea	Togo

AFR2: African Region
High child, very high adult

Botswana	Malawi
Burundi	Mozambique
C African Rep	Namibia
Congo	Rwanda
Congo, DR	South Africa
Cote d'Ivoire	Swaziland
Eritrea	Tanzania
Ethiopia	Uganda
Kenya	Zambia
Lesotho	Zimbabwe

AMR1: Region of the Americas
Very low child, very low adult

Canada
Cuba
USA

AMR2: Region of the Americas
Low child, low adult

Antigua and Barbuda	Guyana
Argentina	Honduras
Bahamas, The	Jamaica
Barbados	Mexico
Belize	Panama
Brazil	Paraguay
Chile	St. Kitts and Nevis
Colombia	St. Lucia
Costa Rica	St. V. & Grenadines
Dominica	Suriname
Dominican Republic	Trinidad and Tobago
El Salvador	Uruguay
Grenada	Venezuela

AMR3: Region of the Americas
High child, high adult

Bolivia	Haiti
Ecuador	Nicaragua
Guatemala	Peru

EMR1: Eastern Mediterranean Region
Low child, low adult

Bahrain	Oman
Cyprus	Qatar
Iran	Saudi Arabia
Jordan	Syrian Arab Republic
Kuwait	Tunisia
Lebanon	United Arab Emirates
Libya	

EMR2: Eastern Mediterranean Region

High child, high adult

Afghanistan	Pakistan
Djibouti	Somalia
Egypt	Sudan
Iraq	Yemen, Republic of
Morocco	

EUR1: European Region

Very low child, very low adult

Andorra	Italy
Austria	Luxembourg
Belgium	Malta
Croatia	Monaco
Czech Republic	Netherlands
Denmark	Norway
Finland	Portugal
France	Slovenia
Germany	Spain
Greece	Sweden
Iceland	Switzerland
Ireland	United Kingdom
Israel	

EUR2: European Region

Low child, low adult

Albania	Poland
Armenia	Romania
Azerbaijan	Slovak ia
Bosnia & Herzegovina	Tajikistan
Bulgaria	Turkey
Georgia	Turkmenistan
Kyrgyzstan	Uzbekistan
Macedonia	Yugoslavia

EUR3: European Region

Low child, high adult

Belarus	Lithuania
Estonia	Republic of Moldova
Hungary	Russian Federation
Kazakhstan	Ukraine
Latvia	

SEAR1: South-East Asia Region

Low child, low adult

Indonesia
Sri Lanka
Thailand

SEAR2: South-East Asia Region

High child, high adult

Bangladesh	Myanmar
Bhutan	Nepal
India	North Korea
Maldives	

WPR1: Western Pacific Region

Very low child, very low adult

Australia	New Zealand
Brunei Darussalam	Singapore
Japan	

WPR2: Western Pacific Region

Low child, low adult

Cambodia	Papua New Guinea
China	Philippines
Fiji	Republic of Korea
Kiribati	Samoa
Lao	Solomon Islands
Malaysia	Tonga
Micronesia	Vanuatu
Mongolia	Viet Nam
Palau	

Appendix B:
Murray and Lopez List of Countries by Region (1996)

chn: China

China

eme: Established Market Economies

Andorra	Japan
Australia	Luxembourg
Austria	Monaco
Belgium	Netherlands
Canada	New Zealand
Denmark	Norway
Finland	Portugal
France	Spain
Germany	Sweden
Greece	Switzerland
Iceland	United Kingdom
Ireland	USA
Italy	

fse: Formerly Socialist Economies of Europe

Albania	Macedonia
Belarus	Poland
Bosnia/Herzegovina	Republic of Moldova
Bulgaria	Romania
Croatia	Russian Federation
Czech Republic	Slovak ia
Estonia	Slovenia
Hungary	Ukraine
Latvia	Yugoslavia
Lithuania	

ind: India

India

lac: Latin America and the Caribbean

Antigua and Barbuda	
Argentina	Guyana
Bahamas, The	Haiti
Barbados	Honduras
Belize	Jamaica
Bolivia	Mexico
Brazil	Nicaragua
Chile	Panama
Colombia	Paraguay
Costa Rica	Peru
Cuba	St. Kitts and Nevis
Dominica	St. Lucia
Dominican Republic	St. V. & Grenadines
Ecuador	Suriname
El Salvador	Trinidad and Tobago
Grenada	Uruguay
Guatemala	Venezuela

mec: Middle Eastern Crescent

Afghanistan	Libya
Algeria	Malta
Armenia	Morocco
Azerbaijan	Oman
Bahrain	Pakistan
Cyprus	Qatar
Egypt	Saudi Arabia
Georgia	Syrian Arab Republic
Iran	Tajikistan
Iraq	Tunisia
Israel	Turkey
Jordan	Turkmenistan
Kazakhstan	United Arab Emirates
Kuwait	Uzbekistan
Kyrgyzstan	Yemen, Republic of
Lebanon	

oai: Other Asia and Islands

Bangladesh	North Korea
Bhutan	Palau
Brunei Darussalam	Papua New Guinea
Cambodia	Philippines
Fiji	Republic of Korea
Indonesia	Samoa
Kiribati	Seychelles
Lao	Singapore
Malaysia	Solomon Islands
Maldives	Sri Lanka
Mauritius	Thailand
Micronesia	Tonga
Mongolia	Vanuatu
Myanmar	Viet Nam
Nepal	

ssa: Sub-saharan Africa

Angola	Lesotho
Benin	Liberia
Botswana	Madagascar
Burkina Faso	Malawi
Burundi	Mali
C African Rep	Mauritania
Cameroon	Mozambique
Cape Verde	Namibia
Chad	Niger
Comoros	Nigeria
Congo	Rwanda
Congo, DR	Sao Tome & Principe
Cote d'Ivoire	Senegal
Djibouti	Sierra Leone
Equatorial Guinea	Somalia
Eritrea	South Africa
Ethiopia	Sudan
Gabon	Swaziland
Gambia, The	Tanzania
Ghana	Togo
Guinea	Uganda
Guinea-Bissau	Zambia
Kenya	Zimbabwe