

A Vaccine Purchase Commitment: Preliminary Cost-Effectiveness Estimates and Pricing Guidelines

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This paper reports some preliminary cost-effectiveness estimates for vaccine purchase commitments. Besides assessing the merit of a purchase program, this analysis can be used to examine the cost-effectiveness of purchasing vaccines with different characteristics, and thus to help establish eligibility requirements and identify prices at which vaccines with different characteristics might be purchased.

We estimate that a commitment to provide an annual market for an ideal vaccine averaging \$336 million per year for ten years, would cost about \$4 per Disability-Adjusted Life Year³ (DALY) saved for malaria, \$7 for tuberculosis and \$2 for AIDS. This is highly cost effective relative to other health programs. A purchase commitment would be highly cost effective even if it covered vaccines that departed significantly from the ideal.

This document is organized as follows. Section 1 discusses our general methodology for determining the cost effectiveness of a vaccine for a given set of vaccine characteristics. Section 2 discusses our assumptions about the DALY burden of disease, the marginal cost of delivering

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³ DALYs, disability-adjusted life years, are a standard measure of the burden of disease and are defined as the number of healthy years of life lost due to premature death and disability. The World Bank maintains that health interventions in developing countries that cost in the range of \$100 per DALY are “highly cost effective” (1993, pages 8, 64, and 68). Refer to Murray and Lopez (1996) for more details.

vaccines to different groups, the percentage of the population that would be reached by immunization programs, and the structure of a purchase commitment, including the amounts pledged by donors and the share of costs that could be covered through co-payments. Section 3 reports results on the cost effectiveness of a commitment to purchase vaccines. Section 4 discusses the sensitivity of our results to alternative assumptions about funding levels for the program, coverage rates, and discount rates. Section 5 discusses one possible way to allow the scale of the purchase commitment to vary with vaccine characteristics, such as efficacy levels and required number of doses.

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. The Excel spreadsheet `VPCCostEffectiveness.xls` contains the calculations to which this paper refers, and the “Technical Guide to Vaccine Cost Effectiveness Calculations” provides a detailed description of the spreadsheet analysis. The spreadsheet may be used to tailor the analysis to match the assumptions and needs of particular users. Note that “Creating Markets for New Vaccines: Rationale” and “Creating Markets for New Vaccines: Design Issues” report some results from an earlier version of the analysis discussed here. The results in this paper are based on more recent data and a more refined analysis, and thus supersede those reported in the earlier documents. (Results are qualitatively similar.)

1. Methodology

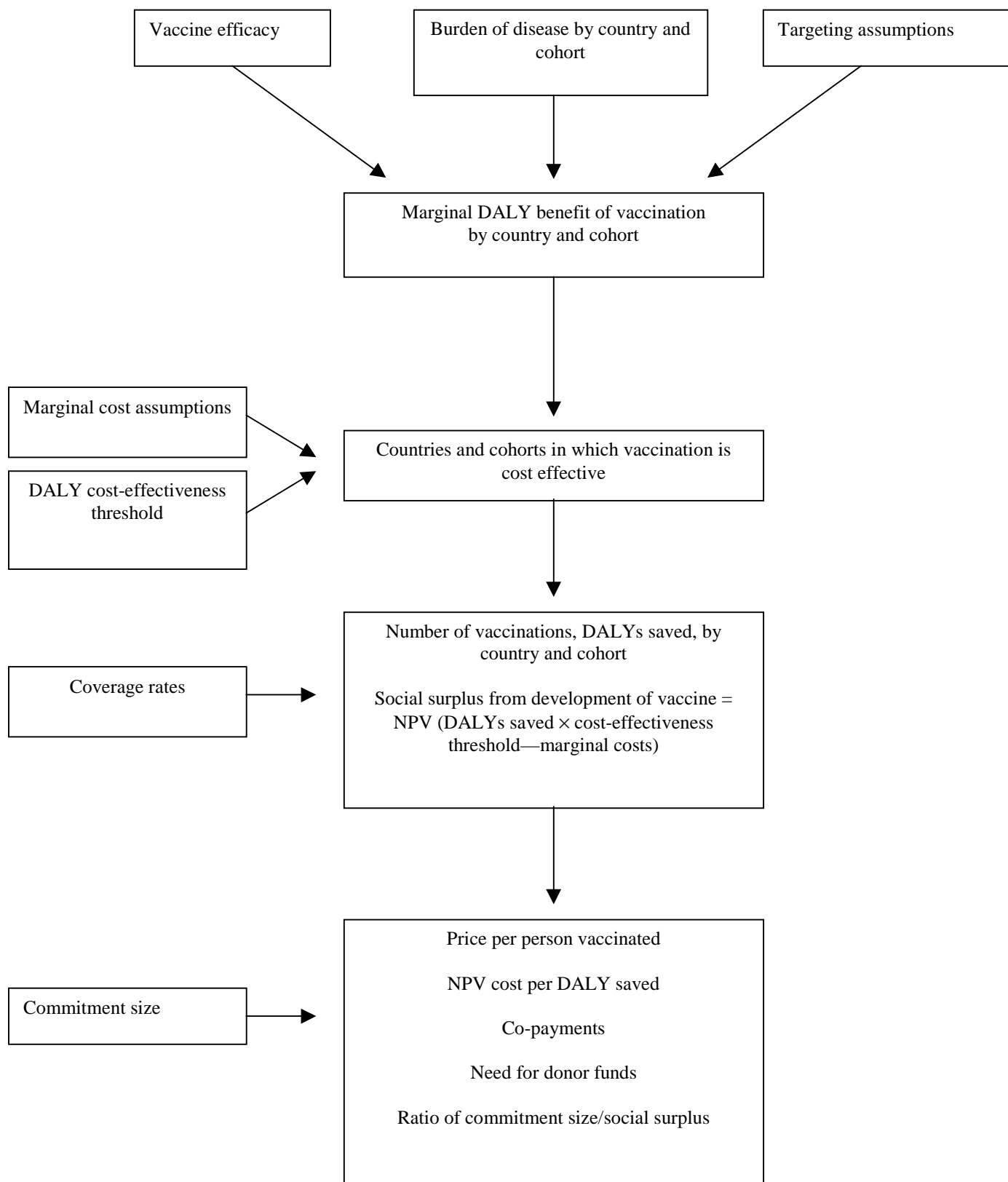
Before proceeding to the details of the calculation, it is worth first getting a sense of the big picture. The flow chart in Figure 1 gives an overview of how the calculation proceeds. Suppose a vaccine with given efficacy and other characteristics were developed tomorrow. The spreadsheet first calculates the countries and age groups in which it would be socially cost-effective to vaccinate given the marginal benefit and cost of vaccination. As discussed in “Creating Markets for New Vaccines: Design Issues,” a vaccine purchase commitment should cover all those for whom vaccination would be socially cost-effective at the marginal cost of vaccination. It would be a false economy to order fewer doses of vaccine and treat fewer people in order to reduce expenditure, because potential vaccine developers’ research decisions will be driven primarily by the total size of the market. If fewer doses are ordered, a greater price per dose will be needed on the remaining doses to maintain the same overall research incentives.

Given the countries and age groups in which vaccination is cost-effective, the actual number of vaccinations is calculated by multiplying the number of people in these demographic groups by the vaccination coverage rate.

The price per person immunized is derived by dividing the overall commitment size by the number of vaccinations.

The number of disability-adjusted life years saved is calculated by multiplying the number of vaccinations by vaccine efficacy, the DALY burden of disease faced by members of the demographic group over their lifetime or the lifetime of the vaccine, and a factor reflecting whether the immunizations are targeted within the demographic group to particularly high risk groups.

Figure 1: Overview of Cost Effectiveness Calculations



Dividing the discounted costs of purchasing and delivering the vaccine by the discounted total disability-adjusted life years saved by the vaccine gives the net present value of cost per DALY saved.

Our analysis focuses on the social cost-effectiveness of a vaccine purchase commitment. We therefore try to be comprehensive in calculating both costs and DALY savings. For example, our cost calculations include delivery costs and co-payments, even though these would be incurred by individual developing countries, not the program. Similarly, if a vaccine were developed due to the program, it would benefit non-program countries and would lead to delivery costs in those countries. We therefore count delivery costs and DALY savings in non-program countries that purchase vaccine.

Note that a vaccination program could cover both the annual flow of new cohorts and a backlog of the population already existing when the vaccine is developed. The backlog will have to be worked off over time, given the difficulty of manufacturing and delivering vaccine. The spreadsheet simply treats this as occurring in the first year and reports average annual purchases over the ten-year period as a whole. The calculation could be refined to explicitly allow time to work off the backlog, but this would not substantially affect the cost-effectiveness calculations.

For any set of vaccine characteristics, the spreadsheet specifies a price and quantity. However, given the many uncertainties in calculations of the necessary number of doses, an actual purchase commitment should cover a smaller number of doses at a somewhat greater price, with an option for the program to buy additional vaccine at a discounted price at the program's discretion, given appropriate warning time for the manufacturers. For example, the commitment could be conditional on the manufacturers' agreement to provide additional doses at

\$0.50 per immunized person, provided the order was placed at least 2 years in advance, that purchases of these additional doses would continue for 5 years, and that the vaccine would only be made available in countries with per capita incomes below a cutoff.

2. Assumptions

DALY Burden of Disease and Benefits of Vaccination

We estimate the DALYs potentially saved as a result of the program using data on disease burden from the World Health Report (WHO, 2000). This source estimates the DALY burden of various diseases in regions such as Africa and the Americas.⁴ Geographic heterogeneity in burden of disease will lead us to underestimate the scope for targeting vaccine delivery, and thus the cost-effectiveness of a vaccine. (To see the logic in an extreme case, note that if a disease is spread evenly throughout a country, it is necessary to vaccinate everyone to protect the population, whereas if it is concentrated in one region, it may be possible to protect the population by immunizing only people in that area.) We have made very rough attempts to disaggregate the burden to individual countries within regions using data from World Health Organization (2000) for tuberculosis, UNAIDS (2000) for HIV/AIDS, and World Health Organization (1997) for malaria.⁵ Within each country we allocate the burden to different age groups using the same proportions as in Murray and Lopez (1996).

⁴ WHO provides information on the DALY burden of disease, which is calculated under the assumption that people would face a very favorable (Japanese) 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. This would bias estimated cost-effectiveness upward. To correct for this, we use the rough and ready approximation that the benefit of eliminating a disease in a country equals the burden of disease times the ratio of the present discounted value of a stream of benefits received over the expected lifespan in the country to the present discounted value of a stream of benefits received over the expected Japanese lifespan.

⁵ For tuberculosis and HIV/AIDS, these sources give number of infections by country, and we allocate the DALY

Immunization protects people over time, and we follow Murray and Lopez in applying a three-percent real discount rate to make our results comparable to other studies of the cost-effectiveness of health interventions.

The spreadsheet analysis assumes that immunization protects the individual to the extent determined by vaccine efficacy. However, we do not take into account the DALYs saved from reductions in secondary infections. For tuberculosis and HIV, vaccination may prevent many secondary infections, but the number is extremely difficult to estimate. Hence we follow the extremely conservative course of ignoring these benefits in cost-effectiveness calculations.⁶

Delivery Costs

Delivery costs depend on the target group, the number of required doses, and whether a vaccine could be added to the standard package of vaccines that are delivered under the EPI package. That package, which includes 3 contacts with each child, costs \$15, or \$5 for every contact [World Bank, 1993]. The majority of this cost is due to delivery costs, as the price of the EPI vaccines is very low. The World Bank estimated that adding the one-dose yellow fever vaccine and the fairly expensive three dose hepatitis B vaccine to the EPI package would increase the cost of the package by 15 percent, or \$2.25, including both the purchase price and

burden in the same proportion. For malaria, the World Health Organization (1997) reports only qualitative levels of prevalence. Percentages of the population living in low- and high-risk areas are reported for each country. Based on these probabilities and data on incidence of malaria in limited countries, we gave a weight of 1 to low-risk and 10 to high-risk areas and weighted according to the population living in low- and high-risk regions. The regional DALYs were then allocated to individual countries in proportion to these proportion of burden numbers. Although the calculation is very rough, it affects only the distribution of burden among countries, not overall burden. Sensitivity analysis we have conducted shows that the distribution of burden among countries is not sensitive to the particular weights chosen for the high- and low-risk probabilities.

⁶ Malaria has such a high reproductive rate in some parts of Africa that the chain of transmission is unlikely to be significantly disrupted by vaccination programs with realistic coverage rates. Studies have shown that even a dramatic reduction in the number of infected mosquitoes have little impact on the prevalence of the disease [Loutan et al.].

the delivery cost [World Bank, 1993]. This works out to \$1.12 per vaccine. We assume that for an ideal vaccine which could be delivered along with the EPI package, the additional delivery cost of adding the vaccine to the package is \$0.40 per required dose. To find the cost-effectiveness of vaccines with other characteristics, users can specify extra delivery costs.

Manufacturing and delivery costs are assumed to be constant in real terms over time. We assume that coverage of new cohorts of children will be the same as for the EPI package (i.e., that three-quarters of each new cohort of children will be immunized). Of course, availability of malaria, tuberculosis, or HIV vaccines might spur more people to seek vaccination.

As noted above, in addition to each year's annual cohort of new births, there is also a backlog of existing population which could be vaccinated over time. Delivering a vaccine to older children and adults will be more expensive since a delivery system is not already in place. It is likely to be relatively cheaper to vaccinate those who are already gathered in one place, such as children in school and pregnant women attending pre-natal clinics. Reaching other groups is likely to be more expensive.

The delivery cost is also likely to rise with the percentage of the population which is targeted, as some people will be easy to reach, such as those who live in cities and regularly use the health care system, while others will be more difficult to reach, such as those who live in remote areas and are unwilling to come to clinics.

Given that expanding the program beyond those relatively easy to reach will be difficult, we assume that only a minority of the existing population will be reached. In particular, we assume that 30 percent of the population aged 1-35 will be immunized against tuberculosis and AIDS. The delivery cost for reaching 30 percent of children aged 1-10, many of whom will be in school, is assumed to be \$2, while the delivery cost for reaching 30 percent of people aged 11-35

is assumed to be \$3.33, two-thirds of the average cost of a contact with the EPI program, which reaches 74% coverage worldwide.⁷

We assume a malaria vaccine would be targeted to children under 5 and to first-time mothers, the two groups for which the disease is most often fatal.⁸ Clinics already exist which provide medical services to pregnant women in many developing countries. We therefore assume that 50 percent of women pregnant with their first child will be immunized against malaria each year for the first 20 years at a cost of \$2 per woman. After twenty years, most first-time mothers will have already been immunized as children. We have assumed that ¼ of births are to first-time mothers. We also assume that 50 percent of one to five year olds are vaccinated against malaria. For HIV/AIDS and tuberculosis, we assume that 30 percent of the stock of unimmunized 11 to 35 year olds, and 75 percent of children in new cohorts will be vaccinated.

We assume that once economies of scale have been fully realized and there has been time to optimize the manufacturing process, the costs of manufacturing one additional dose of vaccine will be \$0.50. Although R&D is very expensive and risky, and manufacturing costs may be substantial initially, once start-up costs have been incurred, the long-run costs involved with expanding large scale production are quite low. The package of five vaccines in the Expanded Program on Immunization (EPI) schedule sells for \$0.50 per dose and vaccines would be purchased in bulk under the program. On the other hand, newer conjugate vaccines may well be more expensive to produce. Thus \$0.50 in marginal manufacturing costs per dose given initial high production levels seems a reasonable estimate. Of course, the prices actually paid for

⁷ Under our assumptions, it is cost effective to vaccinate newborns against HIV/AIDS rather than to wait until they become older, even though this means delivery costs must be incurred sooner, because it is much cheaper to immunize people as part of the EPI program.

⁸ Young children have not yet developed limited natural immunity, and primiparous women have weakened immune systems.

vaccines would have to be much higher to cover R&D costs, risk, and costs of building and optimizing manufacturing capacity.

Fund Size and Co-Payment Rules

The commitment consists of both the co-payments received from participating countries and donor contributions. Mercer Management Consulting, a respected pharmaceutical consulting firm, 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 in any case after ten years competing vaccines are likely to emerge 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 our default case, the annual commitment size is \$336 million dollars. (It is set in nominal terms, which is part of the reason for setting it greater than \$250 million.)

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. However, requiring a greater co-payment from countries with a greater burden of disease seems inequitable and is likely to be politically infeasible.)

We assume co-payments per immunized person of 0.102 percent of per capita Gross National Product (GNP) for HIV/AIDS, 0.025 percent of per capita GNP for tuberculosis, and 0.056 percent of per capita GNP for malaria. (These percentages are chosen to be proportional to the DALY benefits of each vaccine per person immunized, since willingness to pay presumably increases with DALY benefits per person vaccinated.) For concreteness, this implies that for a low-income country, such as Kenya, with GNP per capita of \$350, the co-payment per immunization would be \$0.36, \$0.09, and \$0.20 for HIV/AIDS, tuberculosis, and malaria, respectively.

Cost-Effectiveness Threshold

Vaccines would only be administered on a wide scale in those countries where a mass vaccination program would be cost effective. The cost effectiveness threshold 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 with costs ranging from \$25 to \$150 per DALY and terms these interventions "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 ratio of U.S. to developing country DALY thresholds far exceeds the corresponding ratio of GDP, implying that the DALY threshold may be considered conservative. This threshold is used to determine to what age groups and countries vaccination programs should be targeted.

Per Capita Income Cutoff

A program eligibility cutoff determines the set of countries that may participate in the program. If a country has per capita GNP lower than this cutoff, then the country may participate in the vaccine purchase commitment. Note that not all countries 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).

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 malaria vaccine could be targeted to geographic areas with a particularly high burden of malaria. A tuberculosis vaccine could be targeted to people in prisons and urban slums with high prevalence of the disease. An HIV/AIDS vaccine could be targeted to soldiers and sex workers. We assume that there is no effective targeting for new cohorts or children, but that targeting for old cohorts is possible. Murray and Lopez’s (1996)

figures indicate that the malaria burden for 15-44 year old females is about 25% higher than that for 15-44 year old males. If 1/20th of these women are first-time mothers, and if the entire excess burden is due to this group, then this implies their malaria burden is about five times higher than the average burden for a 15-44 year old person. Therefore, we set the default value for targeting first-time pregnant women to five. We set the default targeting parameter for old cohorts for HIV/AIDS and tuberculosis to two, implying that vaccination of 30% of the relevant populations with a 100% effective vaccine could protect against 60% of the burden of the disease.

3. Cost-Effectiveness Results Given Specified Vaccine Characteristics and Commitment Size

We first calculate the cost-effectiveness of a commitment to purchase an ideal vaccine and then consider commitments to purchase imperfect vaccines. An ideal vaccine would require a single dose and would be perfectly efficacious against all strains of the disease.

Number of Vaccinations

Using the assumptions above on the DALY burden of disease and costs of vaccine manufacturing and delivery, we calculate the marginal cost per DALY of vaccination for each of three different age groups in each country. Sixty-one covered countries have a high enough malaria burden that immunization of new cohorts would be cost effective. Widespread immunization of new cohorts would be cost effective in 108 covered countries for tuberculosis and in seventy-five covered countries for HIV.

Overall, we find that in the first 10 years of the program, it would be cost effective to vaccinate 773 million people against malaria, 1,617 million people against tuberculosis, and 882 million people against HIV (Table 2).

Purchase Cost, Co-Payments, and Cost-Effectiveness

Given an average annual market of \$336 million for each disease, and the number of immunizations projected above, the price per immunization would be \$4.35 for malaria, \$2.08 for tuberculosis, and \$3.81 for AIDS. The total value of co-payments over 10 years would be \$200 million for malaria, \$255 million for tuberculosis, and \$451 million for AIDS.

After the 10 years of the program we assume that competing vaccines will be developed, and prices will fall. With competition, we assume that the vaccines can be purchased by governments or organizations such as UNICEF at a price equal to the manufacturing cost, which is assumed to be \$0.50 per immunization. The net present value (NPV) of purchase and delivery costs for covered countries, over 10 years, would be \$ 3.5 billion for malaria, \$5.5 billion for tuberculosis, and \$4.0 billion for HIV.

The program would be highly cost effective in covered countries even in the short run, with a NPV cost per discounted DALY saved over the first 10 years of \$6.37 for malaria, \$11.00 for tuberculosis, and \$3.71 for HIV. However, the benefits of the program will continue beyond 10 years. Overall the NPV cost per discounted DALY would be \$3.63 for malaria, \$7.39 for tuberculosis, and \$2.24 for HIV.

Note that tuberculosis vaccines are the least cost effective. This is because, compared to malaria and HIV, tuberculosis is geographically diffuse, and a vaccination program would therefore have a lower ratio of DALYs saved through immunization to delivery costs incurred.

Commitments to Purchase Less than Ideal Vaccines

Table 3 shows that commitments to purchase even highly imperfect malaria and HIV vaccines would be cost-effective under our assumptions. Note that as the efficacy of a vaccine declines, the number of people for whom vaccinations are cost effective at the threshold cost per DALY declines. 30% effective vaccines for HIV and malaria vaccines would cost \$10 or less per DALY. Although even vaccines of low efficacy would be cost-effective under the assumptions of the model, it is worth noting that some people feel that such vaccines should not be used due to factors not captured in this model. For example, some people feel that the distribution of a 50 percent effective malaria vaccine could undermine confidence in the vaccination system, reducing take-up of other vaccines. In our view, it is more likely that the availability of even an imperfect malaria vaccine would encourage more people to come to clinics for vaccination, thus boosting take-up rates for other vaccines. To take another example, some argue that the availability of an imperfect HIV vaccine would encourage people to take more risks. On the other hand, in high prevalence countries the behavioral response among the high-risk people who constitute the core groups critical to the spread of the epidemic could be precisely the opposite, with an imperfect vaccine helping to alleviate a fatalistic attitude about the disease and encouraging people to be more careful. In any case, if such factors are thought to be important, one approach might be to require a market test in addition to specifying technical

eligibility and pricing criteria. Then if the health authorities in a particular country were worried about such problems with imperfect vaccines, they could refuse to participate in the program and payments to the vaccine developer would be reduced accordingly.

We also test the sensitivity of our results to the number of doses needed to maintain vaccine effectiveness. As the number of doses increases, the cost of delivery increases and the percentage of target groups that actually receive an effective vaccine decreases. Therefore, the number of people that receive vaccinations and the number of DALYs saved decrease. Increasing the number of required vaccine doses from increases the total discounted cost per DALY and reduces the number of DALYs saved substantially.

It is possible that an HIV/AIDS vaccine may not be effective against all subtypes of HIV/AIDS. The third panel of Table 3 illustrates the possibility in which an HIV/AIDS vaccine is effective against various sets of subtypes. It makes a big difference whether or not the vaccine will be effective against clade C, which is the HIV-1 subtype that predominates in Sub-Saharan Africa. The cost per DALY saved increases by a factor of six when the vaccine is only effective against clade B, which is most common in the Americas and Europe. Even more striking is the result that when the vaccine works for all clades, 90% of the DALYs saved come from areas with clade C.

4. Sensitivity Analysis

Estimating DALY burdens and assessing the marginal cost of vaccination involves many difficult judgments, and it would be a mistake to attach even a moderate degree of precision to

these estimates. Yet the program remains highly cost effective under a variety of sensitivity checks.

Table 4 shows that changing the cost-effectiveness threshold at which people are vaccinated has only a minor impact on the discounted cost of the program per DALY saved. The number of people vaccinated does not fall dramatically if the cost-effectiveness threshold is set at \$15/DALY.

Table 4 then shows how the cost-effectiveness of the program varies with the size of the market promised to vaccine developers. Doubling the size of the market promised to vaccine developers increases the cost per DALY by considerably less than a factor of two. This is because delivery costs represent a large share of overall costs, and they are unaffected by increasing the price paid to vaccine developers.

The third section displays the effect of changing the real discount rate used in the cost-effectiveness analysis. Most cost-effectiveness analyses of health programs assume a 3 percent discount rate, and to maintain consistency with this literature, we also assume a 3 percent discount rate. However, the program would still be highly cost effective at a 5 percent discount rate. Note that to maintain rough consistency with analyses of other health interventions, cost-effectiveness should be interpreted more favorably if the discount rate is raised.

We then show several scenarios with different vaccination rates. The first line shows the base case with 75% of new cohorts vaccinated for HIV/AIDS, malaria, and tuberculosis. In this case, 50% of pregnant women and 1-5 year old children vaccinated for malaria; and 30% of old cohorts and 1-10 year old children vaccinated for HIV/AIDS and tuberculosis. The second line shows a vaccination rate of approximately 2/3 the base case, with 50% of new cohorts vaccinated for HIV/AIDS, malaria, and tuberculosis; 33% of pregnant

women and 1-5 year old children vaccinated for malaria; and 20% of old cohorts and 1-10 year old children vaccinated for HIV/AIDS and tuberculosis. While the number of vaccinations and DALYs saved would decrease somewhat in the latter scenario, the program would remain highly cost effective.

The last section in Table 4 shows effects of changes in the marginal delivery costs of vaccination. The base case assumes that delivery costs are \$0.40 for new cohorts, \$2 for children, \$2 for pregnant women with their first child and \$3.33 for other old cohorts. For an HIV/AIDS and malaria vaccine, a 100% increase in the delivery costs does not change the discounted cost per DALY saved, number of vaccinations, or number of DALYs saved by a significant amount. For a tuberculosis vaccine, the discounted cost per DALY saved increases by about two dollars and the number of DALYs saved and vaccinations decrease by about 20%. Obviously, raising delivery costs per dose would have a bigger effect if more doses were required.

In general, our cost-effectiveness estimates are likely to be conservative, as we have not taken into account some important but difficult to quantify effects. 1) As noted above, immunization programs are likely to reduce secondary infections, particularly for HIV and tuberculosis. 2) We have assumed that the population and prevalence of the diseases are at steady state. Given the fixed costs of research and development, population growth will tend to improve the cost-effectiveness of the program. 3) HIV prevalence is growing rapidly, which would lower the cost of the program per DALY saved. 4) It is possible that with widespread immunization, the diseases would be eradicated, at least in some regions. In this case the benefits of the program would continue while the delivery and manufacturing costs would fall.

4. Allowing the Scale of the Commitment to Vary with Vaccine Characteristics

One important issue in designing a commitment program is how to compensate developers of less than ideal vaccines. Many approaches are possible. For example, one approach would be to set eligibility rules based on a vaccine cost-effectiveness requirement, but not to vary the scale of the commitment with vaccine characteristics. In this case, vaccines would be eligible as long as they had certain pre-defined characteristics, chosen, for example, in order to produce an NPV of cost per DALY of less than \$10. The spreadsheet can be used to identify such vaccines along the lines shown in Table 4.

The spreadsheet can also be used to examine the consequences of an alternative approach to vaccine pricing based on the concept of making the total payments to a vaccine developer proportional to the social surplus generated by the vaccine. To be precise, we define the social surplus generated by a vaccine to be the discounted number of DALYs that would be saved by the vaccine multiplied by the cost-effectiveness threshold, (in the default case, this is equal to \$25/DALY), minus the social costs incurred in manufacturing and delivering the vaccine once it has been developed. Under this approach, the payment to the developer of an imperfect vaccine is equal to the ratio of the social surplus generated by the vaccine to the social surplus that would have been generated by an ideal vaccine times the total size of the commitment that would have been provided for an ideal vaccine.

The worksheet “Proportional Commitment” shows these calculations. Note that in using this worksheet, the user must manually enter several parameters needed to calculate the social surplus associated with the ideal vaccine. The default values of these parameters are set to correspond to those that would be generated for an ideal vaccine given all other default

assumptions in the spreadsheet. However, if the user changes some of the default assumptions in the spreadsheet, such as coverage rates, and then wishes to use the proportional commitment worksheet, it would be necessary to first calculate the relevant parameters from an ideal vaccine using the spreadsheet, manually enter them into the worksheet, and then change the characteristics of the specified vaccine under consideration.

For example, a user may wish to see the price at which a vaccine with 80% efficacy would be purchased. To address this question, change the default values for vaccine efficacy on the options worksheet to 80% and go to the proportional commitment worksheet to view the results. The size of purchase commitment per year is \$265,788,214 for HIV/AIDS and the purchase price is \$3.05. For an AIDS vaccine that requires three additional doses, the purchase commitment would be \$152,792,487 and the purchase price would be \$5.31. Also, for an AIDS vaccine that requires one additional dose and is 70% efficacious, the purchase commitment would be \$173,435,554 and the purchase price would be \$3.44. These examples use the ideal vaccine generated by the default values on the options worksheet.

Questions and Comments

Would be much appreciated. Please contact Michael Kremer (mkremer@fas.harvard.edu) or Andy Francis (afrancis@brook.edu).

Cost Effectiveness

Table 1. Base Case Assumptions

Real discount rate	0.03
Inflation	0.02
Groups targeted from existing cohorts: hiv/aids	1 to 35 year olds
Groups targeted from existing cohorts: malaria	1 to 5 year olds, first-time
Groups targeted from existing cohorts: tuberculosis	mothers
Coverage for new cohorts	1 to 35 year olds
Coverage for existing cohorts: hiv/aids and tuberculosis	75%
Coverage for existing cohorts: malaria	30%
Coverage for existing cohorts: tuberculosis	50%
Average annual purchase cost per disease (millions)	\$336
Manufacturing cost per person immunized	\$0.50
Per dose delivery cost: new cohorts	\$0.40
Per dose delivery cost: 1-10 year olds, pregnant women	\$2.00
Per dose delivery cost: 11-35 year olds	\$3.33

Table 2. Results

COVERED COUNTRIES	HIV/AIDS	Malaria	Tuberculosis	Total
For the first ten years				
Vaccinations (millions)	882	773	1,617	3,272
Price to developer per vaccination	\$3.81	\$4.35	\$2.08	\$3.09
Average co-payment per vaccination	\$0.51	\$0.26	\$0.16	\$0.28
Average donor contributions needed per year (millions)	\$291	\$316	\$311	\$919
Discounted DALYs saved (millions)	1,180	569	520	2,268
NPV cost per discounted DALY saved (including co-payments)	\$3.71	\$6.37	\$11.00	\$5.69
Total				
Discounted DALYs saved (millions)	2409	1331	1010	4750
NPV cost per discounted DALY saved (including co-payments)	\$2.24	\$3.63	\$7.39	\$3.73
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NON-COVERED COUNTRIES	HIV/AIDS	Malaria	Tuberculosis	Total
For the first ten years				
Vaccinations (millions)	201	19	81	301
Discounted DALYs saved (millions)	208	6	18	233
NPV cost per discounted DALY saved	\$1.75	\$3.86	\$6.73	\$2.19
Total				
Discounted DALYs saved (millions)	403	15	34	453
NPV cost per discounted DALY saved	\$1.54	\$3.74	\$7.33	\$2.05
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ALL COUNTRIES	HIV/AIDS	Malaria	Tuberculosis	Total
For the first ten years				
Vaccinations (millions)	1084	792	1698	3573
Discounted DALYs saved (millions)	1388	575	538	2501
NPV cost per discounted DALY saved	\$3.41	\$6.34	\$10.85	\$5.36
Total				
Discounted DALYs saved (millions)	2812	1346	1044	5202
NPV cost per discounted DALY saved	\$2.14	\$3.63	\$7.39	\$3.58

Table 3: Cost Effectiveness of Commitments to Purchase Vaccines with Various Characteristics

Entries in each cell are (**\$C/D**), the total cost per DALY saved for all countries, (**V**), the total number of people Vaccinated over the first ten years (in millions) for covered countries, and (**D**), the number of discounted DALYs saved over the first ten years (in millions) for covered countries.

In each case we assume that the purchase commitment per year is \$336 million.

Parameter	HIV/AIDS			Malaria			Tuberculosis		
	\$C/D	V	D	\$C/D	V	D	\$C/D	V	D
Vaccine efficacy									
30%	\$5.77	630	333	\$10.59	431	161	\$22.02	1159	127
50%	\$3.92	823	585	\$6.83	649	276	\$13.38	1276	231
80%	\$2.63	872	943	\$4.50	757	454	\$9.12	1578	413
100%	\$2.14	882	1180	\$3.63	773	569	\$7.39	1617	520
Number of doses									
1	\$2.14	882	1180	\$3.63	773	569	\$7.39	1617	520
2	\$3.10	658	937	\$5.21	519	442	\$11.07	1021	369
3	\$3.61	404	710	\$6.25	283	344	\$15.29	760	277
5	\$4.94	150	432	\$9.30	137	209	\$23.15	261	93
HIV Subtypes									
Clade B only	\$13.03	585	196	\$3.63	773	569	\$7.39	1617	520
Clade C only	\$1.96	691	1094	\$3.63	773	569	\$7.39	1617	520
All clades	\$2.14	882	1180	\$3.63	773	569	\$7.39	1617	520

Table 4: Sensitivity Analysis

Entries in each cell are (**\$C/D**), the total cost per DALY saved for all countries, (**V**), the total number of people Vaccinated over the first ten years (in millions) for covered countries, and (**D**), the number of discounted DALYs saved over the first ten years (in millions) for covered countries.

Parameter	HIV/AIDS			Malaria			Tuberculosis		
	\$C/D	V	D	\$C/D	V	D	\$C/D	V	D
Cost-effectiveness threshold for coverage									
\$15 per DALY	\$1.99	839	1172	\$3.43	659	554	\$6.74	1312	465
\$25 per DALY	\$2.14	882	1180	\$3.63	773	569	\$7.39	1617	520
\$50 per DALY	\$2.28	942	1182	\$4.04	1038	578	\$7.77	1671	525
\$100 per DALY	\$2.37	999	1185	\$4.10	1063	578	\$7.87	1673	525
Size of fund									
\$250 million	\$1.87	882	1180	\$3.08	773	569	\$6.64	1617	520
\$336 million	\$2.14	882	1180	\$3.63	773	569	\$7.39	1617	520
\$500 million	\$2.67	882	1180	\$4.68	773	569	\$8.81	1617	520
Real interest rate									
3%	\$2.14	882	1180	\$3.63	773	569	\$7.39	1617	520
5%	\$3.16	870	914	\$4.56	755	517	\$11.76	1304	310
Coverage rate									
base case	\$2.14	882	1180	\$3.63	773	569	\$7.39	1617	520
2/3 base	\$2.68	588	786	\$4.71	515	379	\$8.85	1078	347
Delivery costs									
base case	\$2.14	882	1180	\$3.63	773	569	\$7.39	1617	520
50% increase	\$2.47	869	1177	\$4.09	756	567	\$8.32	1388	478
100% increase	\$2.72	845	1172	\$4.24	657	554	\$9.38	1302	463