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HIV/AIDS Treatment and Prevention in India

Modeling the Cost and Consequences

Mead Over, Peter Heywood,
Julian Gold, Indrani Gupta,
Subhash Hira, Elliot Marseille

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THE WORLD BANK
Washington, D.C.

1818 H Street, NW
Washington, DC 20433
Telephone 202-473-1000
Internet www.worldbank.org
E-mail feedback@worldbank.org

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Foreword

In 2004 India has as many HIV-infected people as any country in the world. And scientists tell us that an effective vaccine against AIDS is unlikely for at least another decade. Yet there is hope that the devastation of the AIDS epidemic can be slowed and even reversed in India. Awareness of the threat of AIDS and willingness to take precautions to prevent infection have both improved dramatically since 1990, with condom use on high-risk sexual contacts rising from almost zero in 1990 to 50 percent nationally and to up to 85 percent in some states. These changes have already prevented millions of infections. Further increases in condom use on high-risk contacts can prevent millions more infections.

Now as the epidemic matures, HIV–infected people are falling ill with AIDS in ever increasing numbers and looking to the Indian health care system for care and support. This new burden would be difficult for any government to cope with, but is particularly difficult in India where 80 percent of national health expenditure passes through the private sector.

In the area of treatment, there is new hope. India has benefited for years from the entrepreneurial dynamism of its private pharmaceutical industry. Companies like Cipla and Ranbaxy have developed innovative new processes for manufacturing complex pharmaceutical products and marketed those products in India and to the world in competition with similar but much higher priced brand name products developed in the OECD countries. The lower prices of the drugs in India have made it possible to consider for the first time the financing of antiretroviral therapy for its citizens.

The Government of India requested the World Bank to assemble a team of public health specialists, epidemiologists, and economists to analyze the

costs and benefits of several different options for use of antiretroviral medication. The team first presented the enclosed study to the Indian government in draft form in January, 2003.

The report analyzes three alternative plans for using and financing antiretroviral therapy (ART) in India. These alternative plans, or "scenarios," are a minimally interventionist plan to strengthen the private sector's ability to manage ART, a moderately interventionist plan to provide free ART to HIV-positive pregnant women and, if they are also infected, to their spouses and children, and a more generous plan to finance ART for the poorest 40 percent of all Indians with HIV infection. (The study refers to these three scenarios respectively as the "Adhere scenario," the "MTCT+ scenario" and the "BPL scenario.")

The study sounds several notes of caution to the Indian government. Serious consideration of these possible dangers will help the Government and its partners to avoid them.

First, the study finds that its favorable cost-effectiveness results will only be attainable if patients receive high quality medical care and thus are able to adhere quite strictly to the sometimes onerous ART regimens prescribed by their physicians. **Second,** the study assumes that patients will enter treatment relatively early rather than waiting until they are sick and harder to help. This will require a greatly expanded effort to reduce the social stigma associated with a positive HIV diagnosis and to attract people into voluntary counseling and testing centers so they learn their infection status and can be mapped into treatment programs. **Third,** the study shows that even if the Indian government succeeds in scaling up the most generous of the three options so that 2.1 million Indians are under government-financed ART in the year 2013, AIDS treatment alone will not materially slow the spread of HIV infection. Indeed, unless prevention efforts are greatly strengthened, the commitment to universal access will become more expensive with every passing year, as newly infected AIDS patients become eligible for ART and are added to those already using it. **Fourth,** the attractive cost-effectiveness results depend upon the assumption that India's achievements in increasing condom use on high-risk sexual contacts can be sustained despite the spreading news of freely accessible AIDS treatment. This assumption may be wrong. If people come to believe that the availability of treatment reduces the danger of casual or commercial sex and they therefore practice riskier sex, the new HIV infections resulting from this increased risk can more than offset the health gains from treatment and greatly increase the future budgetary implications of the government's commitment to it.

India must accept the challenge of treatment, take advantage of its national wealth of pharmaceutical and public health expertise and of the proffered assistance of international agencies and, using these resources, it must extend a therapeutic hand to its AIDS patients. But the notes of caution in this study must also be heeded. The government and its national and international partners must invest heavily in improving the voluntary counseling and testing network in order to recruit AIDS patients early enough to help them; and make sure that AIDS therapy is delivered with high standards that maximize the patient's chance of adhering to the drug regimens. Most importantly, the government and its partners must counteract any possible tendency for treatment availability to induce relaxation of prevention programs by vigorously initiating programs which strengthen positive synergy between treatment and prevention. Finally, the government must rigorously evaluate both the direct and the indirect effects of ART to ensure that the nation gains the benefits projected by this report and avoids the pitfalls it warns us against.

J. V. R. Prasada Rao
Secretary, Department of Health,
Ministry of Health and Family Welfare, India

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Executive Summary

Now that the daily cost of high quality AIDS drugs has fallen to less than one dollar a day, what would happen if the Indian government were to finance such treatment? This was the question posed to World Bank staff by an official of the National AIDS Control Organization (NACO). To answer this question, the World Bank assembled a team of Indian and international authors and asked them to estimate the costs and health benefits of three different national policy options. The result is the present study, which draws on the international literature, a set of background papers commissioned explicitly for this study and on the authors' own expertise. A first draft of this study was delivered to NACO and circulated to a limited number of people in the government in January 2003.

The three policies analyzed in this document include a minimalist policy in which the government strengthens private sector delivery, an intermediate policy of providing treatment for mothers who have AIDS and their spouses, and a generous policy of providing treatment to the poorest 40 percent of all AIDS patients. In January 2004 the Indian government adopted an AIDS financing policy which contains elements of all three of the hypothetical policies analyzed in this book. This study's projections of the total financial cost of the program and of the cost-effectiveness of the three options can help the government and its partners to plan the scale-up of the existing treatment program, to optimize the mix of components in order to improve its cost-effectiveness and to design monitoring and evaluation measures which provide feedback on program performance.

India has as many people infected with HIV as other countries. Of the roughly 3.8 million people with HIV, about 550,000 have AIDS and another 300,000 a year will develop AIDS over the next 15–20 years.* Al-

*Reference citations can be found in the text.

though several states have made progress in improving prevention, much more significant improvement is needed to slow the rate of growth of HIV/AIDS over the next 10–20 years.

Antiretroviral drugs, which control but do not cure HIV, are now available from generic manufacturers in India for less than $1 a day. Access to these drugs remains limited, however, partly because even this modest cost is high for most Indians. An increasingly strong and vocal lobby of national and international interest groups and agencies is urging the government to use public money to make antiretroviral therapy widely accessible. Even at current prices doing so would require a substantial increase in government health expenditures.

The government faces several policy questions. It must determine how much of its budget to allocate to health, how much of its health budget to allocate to AIDS, and how much of its AIDS budget to devote to antiretroviral therapy. The availability of donor resources for health or specifically for AIDS relieves somewhat but does not eliminate the government's resource constraint.

This report advises the government of India on the full range of costs and consequences likely to result from several plausible policy choices regarding government funding of antiretroviral therapy. It helps policymakers make decisions by:

- Reviewing the state of the epidemic and of treatment in India.
- Reviewing the effects and consequences of antiretroviral therapy.
- Using an epidemiological model to predict the course of the epidemic, including its consequences and costs, under current government policies.
- Using the same model to determine the consequences and costs of three alternative policies and compare their effects with the consequences and costs of maintaining current policies.

The Spread of HIV and the Development of Antiretroviral Drugs

HIV can be spread in three ways: through sexual contact, through mother-to-child transmission (birth and breastfeeding), and through the exchange of blood. Most infections in India are transmitted through vaginal or anal sexual contact. The risk of transmitting HIV during sex rises when the viral

load in genital secretions is high, which can occur if the blood viral load is high or if a genital sexually transmitted infection is present. The most effective ways to prevent sexual transmission of HIV are to use condoms, control other sexually transmitted diseases, and reduce the frequency of sexual partners.

Soon after infection, the viral concentration in the blood increases, remaining high for at least three to four weeks. During this time infectiousness may be at its peak. (The concentration of the virus in blood and genital secretions also increases during the late stages of the disease, but patients may be too ill by then to engage in regular sexual contact.) After four to six weeks the natural immune response is activated, HIV antibodies are produced, and a blood or saliva test for HIV comes out positive.

HIV infects many different cell types in the body, especially a set of immune system cells known as CD4+ T-helper lymphocytes (hereafter referred to as CD4 cells). The result is destruction of the infected cells, infection of more cells, and impairment of the immune function as the virus replicates. The immune system replaces some destroyed cells, but it becomes exhausted after a few years and HIV replicates unhindered, resulting in a slow decline in the number of CD4 cells and increased susceptibility to HIV–related illnesses, including opportunistic infections and cancers. The presence of opportunistic infections and cancers defines the onset of AIDS, with the mix of diseases and their timing varying. Until the advent of antiretroviral drugs, medical intervention for HIV infection was limited to preventing and treating opportunistic infections.

To develop a forecasting model, this report assumes that the average time between infection and the onset of symptoms and less threatening infections (the AIDS–related complex) is five years. In the absence of antiretroviral therapy, the average time from the appearance of the AIDS–related complex to the onset of an AIDS-defining illness is assumed to be four years; the average time from the onset of AIDS to death is assumed to be one year. The typical course of the illness from infection to death is thus 10 years.

With the development of antiretroviral drugs in the late 1980s, medical intervention could suppress the virus and partially restore immune function, slowing disease progression and improving quality of life. Three groups of drugs interrupt viral replication. Initially, single drugs or two-drug combinations were used, but resistance to them developed rapidly and they became ineffective. Since the late 1990s, the use of three or more drugs in combination has achieved sustained viral suppression for several years,

provided there is strict adherence to the drug regimen. In good clinical practice these drugs are initiated when immune suppression is advanced (that is, when the CD4 count is about 200 per cubic millimeter, a level reached, on average, five years after infection).

Few data are available on the impact of antiretroviral therapy on life expectancy in developing countries. Based on data from Western countries, this report assumes that the inexpensive version of "triple-drug" therapy most widely available in India increases the time from the onset of AIDS–related complex to the onset of AIDS from four to eight years; the time between the onset of AIDS and death remains one year. The use of antiretroviral drugs in accordance with strict guidelines thus increases the average time from infection to death from 10 to 14 years.

Initially, antiretroviral drugs were available only in rich countries—and then only at an annual cost of more than $20,000 per person. Now that Indian pharmaceutical firms are manufacturing generic versions of advanced therapies and selling them for about $240 per person per year, national and international interest groups are lobbying the government to increase access to antiretroviral therapy. Proposals range from simply encouraging the use of antiretroviral therapy by patients of private physicians to providing free antiretroviral therapy to all people infected with HIV.

The Current State of the Epidemic in India

The first serological evidence of HIV infection in India appeared in 1986. HIV has since been detected in 29 of India's 32 states and territories. In six states and territories the prevalence of HIV in women attending antenatal clinics exceeds 1 percent, categorizing the epidemic as "generalized."

The Indian government estimated that 3.8 million people were infected with HIV in 2002, with the highest prevalence rates in Andhra Pradesh, Karnataka, Maharashtra, Manipur, Nagaland, and Tamil Nadu. But estimates of the number of people who are HIV–positive are very sensitive to the assumptions, many of them untested, on which these estimates are based. Under quite plausible alternate assumptions, the total number of people with HIV could be 4.8 or even 6.5 million.

The World Health Organization (WHO) estimates that HIV/AIDS caused 2 percent of all deaths and 6 percent of deaths due to infectious diseases in India in 1998. If current HIV/ AIDS policies continue, by 2033

AIDS will account for an estimated 17 percent of all deaths and 40 percent of deaths from infectious disease.

Since heterosexual contact accounted for about 84 percent of all HIV infections in India in 2000, the contribution of AIDS to Indian mortality could be largely eliminated by consistent condom use. A recent behavioral survey shows wide variation in rates of condom use across states. Use by urban males in the general population ranges from 16 percent in Uttar Pradesh to almost 90 percent in Goa. Females report lower usage rates than males, in both urban and rural populations, and rates are lower in rural areas (for both males and females) than in urban areas. While clients of female sex workers report relatively high rates of use with commercial partners (57.5 percent), only 21.8 percent report using condoms with their regular partners, and use is even lower with nonregular partners. Longitudinal behavioral data from Tamil Nadu, where AIDS control activities began in 1995, show substantial positive behavior change, principally increases in condom use, among high-risk groups.

Following the launch of generic antiretroviral drugs by Indian pharmaceutical companies in 2000 and the decline in the costs of these drugs, an increasing number of people with HIV/AIDS have been using antiretroviral therapy. Of the estimated 550,000 people with AIDS in India, 370,000 reside in 60 major cities. Physicians in these cities are treating 90,000 of these people, 11,700 of whom (8,700 males and 3,000 females) are receiving antiretroviral therapy. Most of the antiretroviral therapy is "unstructured," that is, does not conform to the guidelines of the WHO and the National AIDS Control Organisation of India (NACO).

Possible Consequences of Antiretroviral Therapy

Public policymakers need to consider both the direct and indirect effects of antiretroviral therapy policy. Direct effects are those that improve health and increase lifespan for the patients receiving the therapy. Indirect effects are those that affect the transmission of HIV, that is, the infection of new people. The existence of these indirect, or "spillover," effects provides one of the strongest rationales for government intervention. The presence of positive spillover effects indicates that the unregulated market will produce too little of a commodity. Consumption of such commodities should therefore be subsidized or otherwise encouraged by governments. Conversely, commodities with negative spillover effects should be taxed or otherwise

discouraged. Assessing the positive and negative spillover effects of antiretroviral therapy is thus an important part of designing public policy.

Antiretroviral Therapy May Reduce Infectiousness

Antiretroviral therapy may reduce infectiousness, and therefore transmission, by reducing the total amount of the virus in body fluids and genital secretions. Antiretroviral drugs do reduce the amount of virus in the blood, but the evidence linking the amount of virus in the blood to reduced transmission is not convincing. Although the effect of antiretroviral therapy on infectiousness is thus unclear, this report uses the optimistic assumptions that structured therapy eliminates transmission for five years and unstructured therapy reduces it by 50 percent for up to three years.

Antiretroviral Therapy May Strengthen Prevention

Increased availability of antiretroviral therapy could strengthen prevention by motivating people to come forward for voluntary counseling and testing, resulting in more prevention counseling, less high-risk behavior, and lower transmission. The evidence in support of such an effect is weak, however, and the effect is likely to be context specific.

Antiretroviral Therapy Increases Drug Resistance

Users of antiretroviral therapy sometimes react adversely to the drugs, when they start them or after months of use. These adverse reactions or other psychosocial problems impede adherence to the prescribed regimen. In the absence of strict adherence to a three-drug regimen, most people develop drug-resistant strains of the virus, which can then spread. In Mumbai 18 percent of people newly diagnosed with HIV were resistant to at least one antiretroviral drug. This figure is higher than the 14 percent of new infections estimated to be resistant in North America in 2001. These high rates of resistance among the newly infected are likely to increase as resistant strains accumulate in the population.

Antiretroviral Therapy Lengthens the Period of Infectiousness

High levels of adherence to recommended antiretroviral therapy drug regimen are expected to result in four additional years of life and in better health during those years, including a return to usual levels of sexual activ-

ity. Increased longevity can thus increase the chance that an individual can pass on the infection.

Antiretroviral Therapy May Increase Risky Sexual Behavior

The availability of antiretroviral therapy may induce both people being treated and the general population to engage in riskier sexual behavior—a phenomenon referred to as "disinhibition." North American and European studies of men who have sex with men indicate an increase in the proportion of people having unprotected sex since antiretroviral therapy became available. Evidence from Kenya on heterosexual behavior suggests that substantial disinhibition occurs if the availability of antiretroviral therapy is announced without strengthening prevention measures.

The Configuration of Antiretroviral Therapy Provision

The manner in which antiretroviral therapy is provided, or the configuration of therapy, determines its costs and consequences. Three attributes of a country's antiretroviral therapy policy—population coverage, the relative mix of public-private services, and the extent of HIV transmission–minimizing features—are critical to policy design and analysis.

Population coverage refers to the number of eligible people receiving any form of antiretroviral therapy (ranging from self-medication to model clinical practice) as a percentage of the total number of people eligible for such therapy. Coverage can be increased by expanding availability to all or only to specific groups, such as pregnant women or poor people. A person is eligible for antiretroviral therapy if he or she either has AIDS or is HIV–positive and has significant AIDS–related illnesses or a CD4 count of less than 200 per cubic millimeter. On average this period of eligibility includes about 5 of the 10 years between initial HIV infection and death. Thus as many as half of people who are HIV–positive are eligible for antiretroviral therapy (the proportion is lower early in the epidemic, higher later in the epidemic). This report conservatively assumes that 1.9 million, or 50 percent of the estimated 3.8 million Indians who are HIV–positive (including people with AIDS), are eligible for antiretroviral therapy. Only 12,000 are currently on antiretroviral therapy of any kind, indicating coverage of less than 1 percent.

The second attribute of antiretroviral therapy provision is the degree to which it is financed and provided by the public sector. The Indian government subsidizes an estimated 20 percent of total health care costs, but the percentage of antiretroviral therapy costs funded by the public sector has been smaller. Given that people with HIV/AIDS are often refused treatment at public hospitals, public spending probably represents an even smaller percent of total spending on antiretroviral therapy.

While the way in which antiretroviral therapy is delivered varies from country to country, the essential elements of model clinical practice, referred to in this report as "structured treatment," consist of the following features:

- Standardized, competency-based training of physicians in antiretroviral therapy management.
- Prescription of a standard triple-drug regimen.
- Support from a multidisciplinary team that includes a counselor and a nutritionist.
- Regular clinical and lab-based monitoring of the patient's treatment status.
- Counseling to prevent transmission.
- Prophylaxis for opportunistic illnesses when indicated.
- Diagnosis and treatment of opportunistic illnesses.

Most antiretroviral therapy provided in India is "unstructured," that is, it does not follow these guidelines. Such therapy reaches few people and is unconnected to prevention programs.

As typically practiced, structured treatment does little to address the risk behavior of either patients being treated or people not under treatment. Since a sufficient increase in the risk behavior of people not under treatment could easily cause health consequences that offset the beneficial effects of antiretroviral therapy, it is imperative that delivery of antiretroviral therapy be designed to prevent increased risk behavior in both groups.

Transmission-minimizing antiretroviral therapy consists of three elements: structured antiretroviral therapy, incentives to state and local government and community leaders to strengthen prevention programs, and monitoring and evaluation (including independent third-party evaluation)

of the effectiveness of both treatment and prevention programs and of the extent to which they contribute to one another. In a well-functioning transmission-minimizing antiretroviral therapy program, these three elements work together to decrease transmission as well as improve treatment.

The Epidemiological Projection Model

HIV/AIDS is a slow epidemic, and the effects of policies will be felt over time. Some effects occur immediately. The infectiousness of people receiving high-quality structured antiretroviral therapy declines rapidly, for example, reducing the likelihood that they will infect their sex partners. Other effects are less immediate, and some may be deleterious. After a few years the average person receiving antiretroviral therapy develops resistant strains of HIV, which can spread to others. Behavioral effects also occur slowly and cumulate. If antiretroviral therapy changes risk behavior, the rate of transmission will also vary, leading to changes in the epidemic path, some of which will be experienced only after several decades. The analysis reported here projects 30 years into the future—a period long enough to see temporary trends reverse themselves as a result of longer-run influences on the epidemic.

This report modifies an epidemiological model used to project the course of the Indian epidemic. The model draws on the international and Indian HIV/AIDS literature to set epidemiological and biological parameters for transmission, disease progression, and the pathways from infection to death, depending on whether the person is infected with a resistant or nonresistant virus and whether he or she has access to antiretroviral therapy at the onset of symptoms. The model consist of 50 separate parameters, each of which was calibrated based on the most recent Indian data available.

The spread of the epidemic depends on the rates of sexual contact between low-risk men and women and between sex workers and their clients. These sexual contact rates, combined with the assumptions described above, determine the rate of growth of HIV prevalence, the demand for antiretroviral therapy, and the costs and consequences of any antiretroviral therapy policy.

The model assumes that in 1998, at the start of the simulation run, 15 percent of the adult male population (37.5 million men) were clients of sex workers, with each client purchasing 50 sexual contacts a year. It also assumes that 1.1 percent of the adult female population (2.8 million women)

were sex workers, so that the average sex worker conducted about 675 commercial sex transactions a year. Condoms are assumed to have been used in half these commercial sex transactions, reducing the probability of infection to zero in those cases.

Baseline Scenario

The baseline scenario uses the assumptions of the epidemiological model plus a set of assumptions about how rapidly the Indian population will adopt antiretroviral therapy without any change in policy. It is based on the assumption that under current policies, unstructured antiretroviral therapy will:

- Grow steadily until half of symptomatic Indians are using some form of antiretroviral therapy by 2012 and 80 percent are doing so by 2018.
- Attain lower rates of patient compliance than structured care, therefore yielding lower health benefits for patients.
- Facilitate the spread of resistant viral strains.
- Decline in quality as it becomes more widely used. By the time adoption reaches 80 percent, most of the health gains will have been eroded.

Given the very low rates of health insurance in India, the baseline model assumes that the growth of structured antiretroviral therapy will be slow (2 percent a year), restricted by the limited capacity to raise funds from private sources and the need to reallocate and train manpower.

Alternative Policy Scenarios

The estimated epidemiological consequences of three policy options—ADHERE, MTCT+, and Below the Poverty Line—are evaluated and compared with the baseline model.

ADHERE aims to maintain the quality of unstructured antiretroviral therapy at its current level, that is, to prevent the erosion of the quality of unstructured care projected under the baseline scenario. This policy would provide government financing to train private physicians and laboratories in the basic techniques of antiretroviral therapy and diagnostic testing and subsidize laboratory tests, the procedures for which patients are least willing to pay. The effect of this policy on the epidemic would be the net result

of two offsetting effects on transmission: the decrease in the proportion of patients who have and can transmit resistant strains of HIV and the increase in the opportunity of each patient to infect others.

MTCT+ would provide government-financed antiretroviral therapy for some mothers and their husbands who meet the criteria for beginning antiretroviral therapy. An estimated 54,000 HIV–infected children are born in India each year. Under this policy the government would introduce a program to prevent mother-to-child transmission and scale it up to cover all HIV–infected pregnant women treated in the public sector. The program would test all women who present themselves at government-owned antenatal clinics and implement a nevirapine-based preventive strategy to reduce mother-to-child transmission for women who test positive for HIV. Few women testing positive will yet have AIDS or be eligible for antiretroviral therapy. The model assumes that:

- The public sector screens half of all pregnant women.
- The average HIV–positive woman is not eligible for antiretroviral therapy until two and a half years after screening.
- Women already in unstructured antiretroviral therapy begin structured antiretroviral therapy immediately.
- Women with resistant viruses are not recruited into the program.
- The program succeeds in recruiting at least 25 percent of HIV–positive women and about half of their husbands.

An alternative to targeting HIV–positive mothers would be to target the poorest HIV–positive adults. Under this third policy option, which we call the Below the Poverty Line policy, a mechanism is assumed to be in place for identifying the poorest people with symptomatic HIV infection and financing their access to antiretroviral therapy. This policy would provide subsidized access to structured care for 40 percent of people with HIV. By 2033 the model projects that 7 million people would be receiving antiretroviral therapy, of whom 4.7 million would be receiving structured care financed by the government and 2.3 million would be receiving unstructured care. The effect of the policy is first assessed assuming that it induces no behavioral changes. That assumption is then relaxed to assess the effects if the policy increases or decreases condom use.

Costs of Antiretroviral Therapy

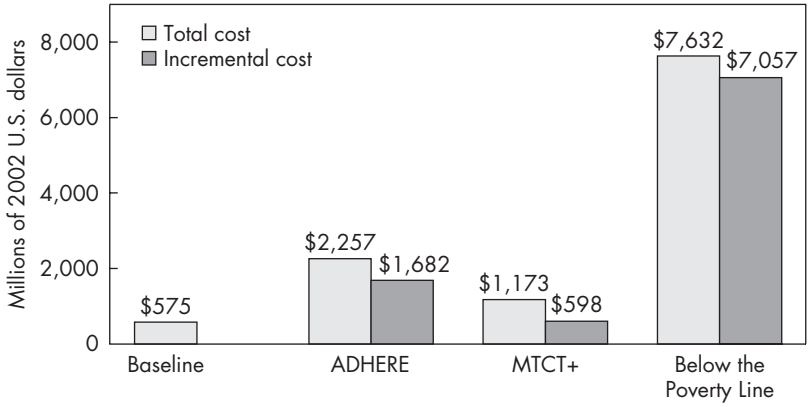
In the absence of detailed information on program costs, this report uses a small set of basic cost assumptions to estimate the costs and cost-effectiveness of alternative antiretroviral therapy policies. It assumes that the ADHERE policy would cost $100 for every patient-year of structured or unstructured treatment and that the MTCT+ and Below the Poverty Line programs would cost $500 per patient-year for patients in structured therapy. These figures include the cost of drugs, clinic visits, and laboratory tests that enable physicians to monitor treatment success and patient adherence. The estimated costs are net of the offsetting reduction in costs due to the avoided or postponed costs of treating opportunistic illnesses for the 20 percent of people with HIV/AIDS who would have used public sector facilities. Under these assumptions, government financing of antiretroviral therapy would increase the present value of future health expenditures through 2033 by between $598 million (for the MTCT+ program) and $7,057 million (for the Below the Poverty Line program) (figure 1).

Conclusions

How much should the Indian government contribute to financing high-quality structured antiretroviral therapy? Providing such therapy without a concomitant increase in the subsidy to patients with cancer, renal disease, hepatitis, or other serious illnesses requires justification. Public financing of structured antiretroviral therapy is justified on the ground that, unlike many other serious diseases, HIV is communicable and treatment can slow transmission. Antiretroviral therapy has both positive and negative effects on transmission, however. Making the case for government-subsidized antiretroviral therapy thus requires careful consideration of the evidence, as well as estimates of the costs and effects of alternative policies.

Which of the three policy options studied makes most sense for India? ADHERE is designed to maximize the quality of unstructured care occurring primarily in the private sector. Since unstructured care tends to be less successful at sustaining adherence, it tends to fail sooner than structured care and to lead more frequently to the transmission of resistant strains of HIV. As a larger proportion of infected people carry a

Figure 1 Present Value of Cost to Government through 2033 of Adopting Alternative Antiretroviral Therapy Policies



Note: Discount rate is 10 percent.
Source: Authors' estimates.

resistant virus, even the limited health gains available from antiretroviral therapy today will cease to be available in the future. To allow unstructured care to grow without restriction or assistance is to allow India's dynamic private medical sector to exhaust too quickly the value of existing generic drugs, when replacements are likely to be much more expensive. There are thus efficiency arguments for subsidizing complementary inputs that will improve the quality of privately financed unstructured care. The estimate of $100 per patient-year for these complementary inputs for all people in either structured or unstructured care results in a present value of projected expenditure of $1.7 billion dollars, a substantial sum that reduces the life-years lost from the epidemic by 6 percent. In the absence of a positive or negative behavioral response to antiretroviral therapy, the ADHERE policy is the most cost-effective of the three policies considered. However, as a way for the Indian government to purchase health, it is estimated to be about 10 times as expensive as other alternatives.

In contrast to the ADHERE policy's appeal to efficiency criteria, both the MTCT+ and the Below the Poverty Line policies look to equity grounds for justification. Both programs cost more per life-year saved than

ADHERE and are thus expensive in both absolute terms and relative to alternative uses for the same budgets.

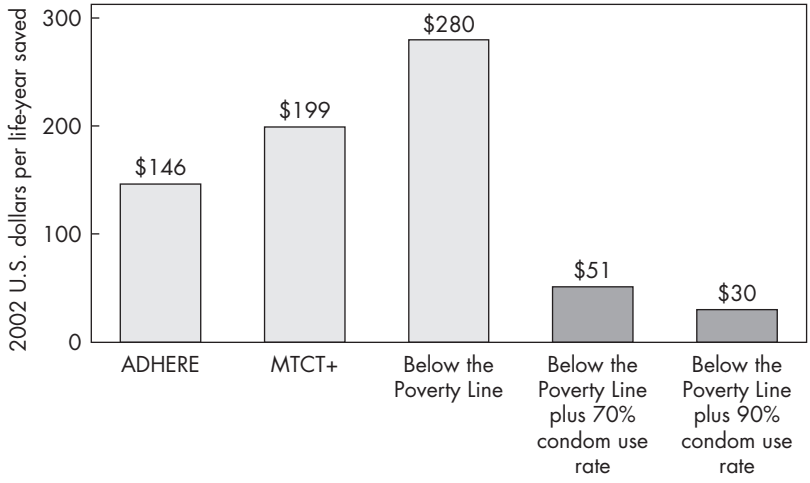
In addition to the biological effects of treatment, both medical and transmission reducing, the report analyzes the potential spillover effects that would occur if the high-risk population relaxes its prevention efforts in response to the availability of treatment. While evidence from developing countries is limited, it is possible that condom use among those at highest risk could decline by as much as 10 percentage points or increase by as much as 40 percentage points as a result of the availability of antiretroviral treatment. Sensitivity analysis across this range reveals that spillover effects of this magnitude would overwhelm the direct biological benefits of treatment. If condom use among high-risk groups in the general population drops by 10 percentage points in response to the availability of treatment, the number of new infections in 2013 would increase by 1 million, with commensurate increases in the costs of treatment. Increased condom use would greatly increase the benefits and reduce the costs of any treatment policy.

This report proposes coupling the most ambitious of the three proposed programs, the Below the Poverty Line program, with incentives to motivate state-level government and medical decisionmakers to dramatically increase condom use. It suggests that India could design a mechanism that would increase condom use during high-risk contacts from the current rate of 50 percent to 70 percent. Assuming that the change in behavior could not have been achieved without the incentives provided in the antiretroviral therapy program—and that the costs of this improved prevention effort had already been allocated—all of the epidemiological benefits to the change and none of its costs could be attributed to the transmission-minimizing antiretroviral therapy policy. Under these admittedly very favorable assumptions, the cost per life-year saved of the antiretroviral therapy program falls to just $51 (figure 2). If the rate of condom use rose to 90 percent, the cost per life-year saved by the Below the Poverty Line policy would fall to about $30.

Recommendations

Even at very low prevailing prices for generic antiretroviral therapy medications in India, financing such therapy is very expensive and produces only a small percentage reduction in the burden of the AIDS epidemic. While

Figure 2 Cost per Life-Year Saved of Alternative Antiretroviral Therapy Policies



Note: Discount rate is 10 percent.
Source: Authors' estimates.

more cost-effective than ever before, antiretroviral therapy still costs more than $100 per life-year saved—much more than many other life-saving interventions.

In view of the relatively large costs and potentially dangerous spillover effects of financing antiretroviral therapy, this report recommends that the government proceed cautiously. It recommends that the government:

- Collect better statistics on the current prevalence and incidence of HIV infection in India in order to improve the accuracy of planning exercises like the present one.
- Support improvements to the quality of unstructured antiretroviral therapy provided by the private sector in order to minimize its negative spillover effects at the lowest possible cost to the government. Under the assumptions made in this report, such a policy is the most cost-effective approach to antiretroviral therapy.
- Evaluate both the costs and the effects of prevention programs. If the government finds that prevention programs are stalled and can no longer

be extended at a cost of $10–$20 per life-year saved, the case for antiretroviral therapy, especially transmission-minimizing antiretroviral therapy, would be strengthened.

- Evaluate the costs and effects of alternative antiretroviral therapy programs. It would be useful to know what modes of treatment maximize patient adherence to a drug regimen in India.
- Support measurement of the prevalence of resistant strains of the virus among people with HIV.
- To ensure that condom use increases rather than declines, monitor the behavioral effects of awareness of improved access to antiretroviral treatment on risk behavior of those not under treatment, especially high-risk groups.
- In consultation with all state and national stakeholders, design and implement an institutional arrangement that rewards effective prevention programs, thereby ensuring that the availability of treatment has beneficial (rather than perverse) spillover effects.

List of Acronyms and Abbreviations

ADHERE	national antiretroviral therapy capacity building program
AIDS	acquired immune deficiency syndrome
CIDA	Canadian International Development Agency
DFID	Department for International Development (United Kingdom)
HAART	highly active antiretroviral therapy
HIV	human immunodeficiency virus
MTCT	mother-to-child transmission
MTCT+	program to provide antiretroviral therapy to mothers identified as HIV–positive in the MTCT prevention program
NACO	National AIDS Control Organisation of India
NACP	National AIDS Control Programme
NGO	nongovernmental organization
USAID	United States Agency for International Development
WHO	World Health Organization

CHAPTER 1

Introduction

Now that the daily cost of high quality AIDS drugs has fallen to less than one dollar a day, what would happen if the Indian government were to finance such treatment? This was the question posed to World Bank staff by an official of the National AIDS Control Organization (NACO). To answer this question, the World Bank assembled a team of Indian and international authors and asked them to estimate the costs and health benefits of three different national policy options. The result is the present study, which draws on the international literature, a set of background papers commissioned explicitly for this study and on the authors' own expertise. A first draft of this study was delivered to NACO and circulated to a limited number of people in the government in January 2003.

The three policies analyzed in this document include a minimalist policy in which the government strengthens private sector delivery, an intermediate policy of providing treatment for mothers who have AIDS and their spouses, and a generous policy of providing treatment to the poorest 40 percent of all AIDS patients. In January 2004 the Indian government adopted an AIDS financing policy which contains elements of all three of the hypothetical policies analyzed in this book. This study's projections of the total financial cost of the program and of the cost-effectiveness of the three options can help the government and its partners to plan the scale-up of the existing treatment program, to optimize the mix of components in order to improve its cost-effectiveness and to design monitoring and evaluation measures which provide feedback on program performance.

India is burdened with a larger HIV/AIDS epidemic than any other country in the world. More than 4 million Indian adults are infected with the human immunodeficiency virus (HIV), according to official government estimates, and the actual number people with HIV may be as high as 6.5 million.

Among people with HIV, an unknown number—somewhere between 100,000 and 1,000,000 suffer from AIDS.

The Indian government is committed to preventing HIV infection, and it has greatly expanded its efforts to prevent the disease since 1997. Although no rigorous evaluations of the effectiveness of the government's strategy have been conducted, the Behavior Surveillance Survey (Org-Mark Quest 2002) documents moderate levels of condom use in many parts of the country, especially among people whose sexual behavior places them most at risk. The limited HIV surveillance system in India suggests that HIV prevalence among pregnant women may be leveling off, but the data are too sketchy, and the apparent trend too recent, to be relied on.[1] Without additional data collection and more rigorous analysis, it is impossible to distinguish a true reduction in new infections from several other causes of an apparent leveling off of prevalence. For example, since HIV–infected women are less likely to become pregnant, infections among all women could be rising while the prevalence rate measured among pregnant women is leveling off.

Whether or not the incidence of new infections has leveled off, the effect of existing infections on the number of new AIDS cases is predictable. In the absence of certain types of treatment, roughly 5–7 percent of people with HIV will develop AIDS every year. Given the range of values for the number of people with HIV of 4–7 million, this means that 200,000–490,000 adults with AIDS will hit the Indian health care system each year for the next 15–20 years. If India's prevention programs fail to halt the expansion of the AIDS epidemic, these numbers could double or triple over this period.

Antiretroviral Therapy

HIV slowly attacks the immune system, causing people infected with the virus to gradually succumb to a variety of illnesses they would normally be able to resist. Medical treatment for HIV infection consists partly of treatment of these "opportunistic" illnesses and partly of efforts to combat HIV directly so that the body's natural defenses can resume their role in fending off such illnesses.

Advanced pharmaceutical products that combat HIV are referred to as antiretroviral therapy. Antiretroviral therapy does not cure HIV infection, but it can add one to many additional years of life. Based on a review of the evidence, this report concludes that antiretroviral therapy will add two to

five years of life, depending on patient adherence and the quality of patient management.

Fifteen years ago no medical treatments other than treatment of opportunistic infections and cancers were available to slow the progression from HIV infection to AIDS or from AIDS to death. Ten years ago antiretroviral therapy was available in rich countries, but its effectiveness was limited and it cost more than $20,000 per patient-year (Over and Piot 1993). In 1996 the effectiveness of antiretroviral therapy improved substantially, and it cost as little as $10,000 per patient-year in Thailand and other developing countries able to bargain effectively with multinational pharmaceutical firms (Prescott 1997; World Bank 1997).

Today Indian pharmaceutical firms are manufacturing generic versions of advanced therapies and selling them for less than $1 a day. About 11,700 Indians are currently taking such medications, paying the costs of the drug and of the concomitant medical care out of their own pockets. National and international interest groups are lobbying the Indian government to expand access to antiretroviral therapy. Proposals range from simply promoting the use of antiretroviral therapy by patients of private physicians to government provision of free antiretroviral therapy to all people with HIV (Moatti and others 2002). As time passes these interest groups will gain strength, and the cost and difficulty of administering antiretroviral therapy will continue to decline. As a result, pressure on the Indian government to finance or provide expanded access is likely to intensify.

Scope of the Report

This report advises the Indian government on the full range of costs and consequences likely to result from several possible policies for public funding of antiretroviral therapy. In traditional cost-benefit analysis, dollar values are attached to all costs and consequences in order to rank different policy options according to their net present values.[2] Because of the difficulty of attaching dollar values to prevented HIV infections and saved lives, this report avoids this approach in favor of presenting, as completely as possible in a short report, the full range of consequences and a variety of cost-effectiveness measures for each policy. While this approach arguably shirks part of the responsibility of the policy analyst, it has the advantage of transparency. At the cost of somewhat greater complexity of presentation, the report allows readers to appreciate all the elements of the decision problem

facing the Indian government, enabling each reader to arrive at his or her own conclusion regarding the policy the Indian government should pursue. While the reader is left with the ultimate task of ranking the policy options, the report team's views are presented in chapter 6.

The analysis is based on a quantitative model of the HIV epidemic and of the treatment choices facing people infected with HIV. The model is used to estimate the impact of three different policy options on the number of people with HIV, the length of life of people with HIV, the costs of hospitalization for opportunistic illnesses, the number of years of orphanhood, the budgetary costs to the Indian government, and the positive and negative effects of antiretroviral therapy on prevention activities. Because the long incubation period of AIDS means that consequences of today's policy choices will play out over decades, the analysis projects out 30 years. By presenting the estimated costs and consequences with and without discounting, the report highlights the importance of evaluating longer-term and shorter-term effects. The model parameters are drawn from the international AIDS literature and from expert opinion on the Indian HIV epidemic. Sensitivity analysis reveals the robustness of the results to alternative assumptions about these parameters.

Since the impact of a policy choice can be defined only in comparison to what would have happened in the absence of the choice, the foundation for the analysis is a baseline projection of the future course of AIDS treatment given no government policy change on antiretroviral therapy. An important feature of the baseline is the assumption that the current number of people with HIV who are paying for antiretroviral therapy out of their own pockets will grow rapidly as news of its availability and potential efficacy spreads and its price continues to drop. This trend and its consequences are the context for any government policy actions. Government policies are likely to succeed only if they build on and reinforce the positive features of private provision while reducing its negative consequences (see box 1.1).

Against this baseline projection the report analyzes the impact of three government policies: national antiretroviral therapy capacity building (ADHERE), antiretroviral therapy for mothers with AIDS and their partners (MCT+), and antiretroviral therapy for the poorest people with AIDS (Below the Poverty Line). The costs and consequences of each of these scenarios are calculated. The report also examines the sensitivity of the results for the Below the Poverty Line option to possible changes in behavior that occur as a result of the program.

Box 1.1 Is Government Financing of AIDS Treatment in Poor Countries Ethical?

Some observers believe it is possible to take a position on whether the governments of poor countries should fund AIDS treatment based on ethics alone, without elaborate analysis. The views of advocates and opponents of government financing of AIDS treatment on ethical grounds can be simplistically described in terms of the lifeboat metaphor.

Supporters of government-financed antiretroviral therapy argue that refusal to finance AIDS treatment is like pushing people with HIV out of the lifeboat. Opponents of government financing argue that the lifeboats in poor countries are already full. Allowing antiretroviral therapy patients on board would force the government to push out children currently saved by vaccination programs, poor people currently saved from a lifetime of poverty, and people currently protected from AIDS transmission by vigorous HIV prevention programs.

Advocates of government funding of antiretroviral therapy treatment argue that such funding need not push anyone out of the lifeboat, because the lifeboat can be expanded by transfers from rich countries. Such transfers, they argue, are not available for expanding other life-saving programs. Financing antiretroviral therapy would thus expand the lifeboat, by facilitating HIV prevention and strengthening the overall health sector.

Opponents of government financing argue that governments and donors have an ethical responsibility to give priority to financing public goods, that is, goods that are nonrivalrous and nonexcludable or have positive externalities.* These are goods with spillover effects, which markets will either oversupply or undersupply. Goods the market undersupplies include infrastructure, such as roads and clean water; a strong legal system to enforce contracts; and support for immunization and other public health systems. Goods that markets oversupply include industrial pollution. According to this view, the government should not finance antiretroviral therapy unless it can be shown to facilitate prevention. If antiretroviral therapy hampers prevention, as some experts claim, the ethical role of government would be to seek to limit its negative spillover effects on the rest of society.

Proponents of government-financed antiretroviral therapy financing would counter that markets in poor countries do not supply affordable insurance against catastrophic health care. Government financing of antiretroviral therapy would partially correct this market failure.

(continued)

Box 1.1 continued

Opponents of government financing would respond by noting that this failure of insurance markets in poor countries extends to all catastrophic health care costs, such as those arising from childbirth, road accident trauma, cancer, and even simple surgical procedures, such as appendectomies. One approach to this problem, adopted to various degrees in poor countries, has been for governments to provide highly subsidized or free hospital care, especially for the poor. But the low quality of this publicly financed inpatient care in poor countries represents a longstanding challenge to governments and donors. Opponents of public funding of antiretroviral therapy would argue that efforts to strengthen these health care systems should first shore up the delivery of more common and effective health care services before undertaking the management of antiretroviral therapy.

Advocates of government financing of antiretroviral therapy would reiterate their assertion that provision of antiretroviral therapy in low-resource settings will have positive synergies for the health care system. Opponents would retort that there is no evidence for such synergies, that indeed introducing antiretroviral therapy is likely to divert resources away from other critically needed public health interventions.

The starting point of this debate was abstract and based on ethical principles, which seemed not to require factual support. However, as the argument has deepened, it has become apparent that each side depends increasingly on assertions of statements that are subject to empirical verification. Furthermore, some of these "facts," such as the price of antiretroviral drugs, change over time, while others, such as whether such therapy facilitates or hampers prevention, are likely to vary from context to context.

This report avoids basing its arguments on ethical principles, about which reasonable people can disagree. Instead, it attempts to estimate the empirically probable impacts on the most relevant indicators of various alternative antiretroviral therapy policies in India today. Where empirical issues are unresolved or subject to change, it uses sensitivity analysis to show how the results change under various possible values. It is hoped that this approach will contribute to the policy debate in two ways. First, it will allow the debate to focus on the consequences of alternative policies rather than on the endlessly debatable abstract ethical properties of the policies. Second, it will highlight areas in

which additional empirical data could most help policymakers choose a policy between the extremes supported by advocates and opponents of government-financed antiretroviral therapy.

*A "nonrivalrous" good is one whose consumption by one person does not limit its consumption by others. A "nonexcludable" good is one from which nonpaying individuals cannot be excluded. A pure public good has both of these properties. Some public goods have one property but not the other. A bridge, for example, is nonrivalrous (in the absence of crowding) but excludable. Medical treatment has neither property and is therefore a private good. "Externalities" are spillover effects of a market transaction on people other than the buyer and seller. Medical treatment of a sexually transmitted disease is a private good with positive externalities, because the treated person is less of a danger to future sexual partners. Whether antiretroviral therapy has positive or negative externalities is a matter of debate and may depend on the setting (Over 1999).

Notes

1. "Incidence" refers to the flow of new infections during a stated period of time. "Prevalence" refers to the stock of existing infections at a point in time. Either measure can be low while the other is high. Within a given population, incidence is the better gauge of the advance or retreat of an epidemic, but prevalence is usually much easier to measure.
2. Net present value is defined as the dollar value of the discounted stream of future benefits of a policy choice less the dollar value of the discounted stream of future costs. If all benefits and costs occur in the same year, calculating the net benefits of a program is simple. However, in the case of an HIV epidemic, costs incurred in a given year have consequences that range over decades. To compare the stream of future benefits to the stream of future costs, each stream is first discounted to a present value and then the present value of future costs is subtracted from the present value of future benefits. The discount rate chosen for calculating the net present value of health investments is typically 3–10 percent.

CHAPTER 2

India's HIV/AIDS Epidemic

This chapter provides an overview of India's HIV/AIDS epidemic and the responses by the government, donors, the private pharmaceutical sector, and people with HIV/AIDS.

The Epidemiology of HIV in India

HIV is spread in three ways: through sexual contact, from mother to child (during birth and breastfeeding), and through the exchange of blood. India's National AIDS Control Organisation (NACO), the federal government agency responsible for tracking and controlling the HIV/AIDS epidemic, estimates that in 2000, 84 percent of new infections are contracted through sexual contact.

Although it is generally believed that HIV first appeared in India among intravenous drug users in the northeast states, the first serological evidence of infection in India appeared in 1986 among female sex workers in Tamil Nadu. Later in the 1980s HIV was detected in a range of population groups and locations: the epidemic was underway. Today HIV has been detected in 29 of India's 32 states and territories. The epidemic is generalized (that is, the prevalence among pregnant women attending antenatal clinics exceeds 1 percent) in six states and territories (Andhra Pradesh, Karnataka, Maharashtra, Manipur, Nagaland, and Tamil Nadu). In these states and territories as well as in Manipur and Kerala, the prevalence of HIV in patients at sexually transmitted disease clinics exceeds 5 percent.

Both HIV-1 and its less pathogenic relative, HIV-2, are found in India, although most infections are HIV-1. For HIV-1 the predominant subtype is C, the same subtype that predominates in Africa.

As in many other low-income countries, HIV in India is overwhelmingly transmitted heterosexually. The main change in the past 10 years has been the decline in infections caused by contaminated blood (from 10 percent to 2 percent, the result of vastly improved screening of blood) and by injection of drugs (from 9 percent to 3 percent). Less than 1 percent of infections were reportedly the result of men having sex with men (Indrayan 2003). Perinatal transmission must be increasing as a proportion of all infections, but India's current information system is not picking up the change. Men having sex with men may also be underestimated due to the stigma attached to homosexuality in India.

NACO estimates the number of people with HIV in India at 3.8 million in 2002. Estimates by state (table 2.1) are derived from the sentinel surveillance of women attending antenatal clinics and men attending sexually transmitted disease clinics, based on the assumptions identified in box 2.1.

How accurate is the estimate of 3.8 million people with HIV? As box 2.1 demonstrates, small changes in the assumptions used to estimate the number of infections yield quite different, and typically larger, estimates.

Table 2.1 Estimated Number of People with HIV/AIDS, by State, 2002

STATE	NUMBER OF PEOPLE WITH HIV/AIDS	STATE	NUMBER OF PEOPLE WITH HIV/AIDS
A and N Islands	538	Lakshadweep	211
Andhra Pradesh	752,204	Madhya Pradesh	85,503
Arunachal Pradesh	2,336	Maharashtra	852,901
Assam	44,905	Manipur	48,906
Bihar	35,214	Meghalaya	4,626
Chandigarh	6,346	Mizoram	2,990
Chhatisgarh	28,142	Nagaland	9,437
D and N Haveli	292	Orissa	35,052
Daman and Diu	259	Pondicherry	2,116
Delhi	58,328	Punjab	58,913
Goa	7,920	Rajasthan	137,432
Gujarat	155,723	Sikkim	840
Haryana	45,000	Tamil Nadu	514,513
Himachal Pradesh	2,323	Tripura	3,680
Jammu and Kashmir	10,782	Uttar Pradesh	317,172
Jharkhand	8,898	Uttaranchal	18,044
Karnataka	414,519	West Bengal	57,545
Kerala	33,866		
		Total	3,757,477

Source: National AIDS Control Organisation 2002.

Box 2.1 Sources, Limitations, and Assumptions behind Current Estimates of HIV Incidence and Prevalence in India, 2002

Since 1987 NACO has estimated the total number of HIV infections using data from two sources. Data for women come from sentinel surveillance at about 200 antenatal clinics. Data for men come from sentinel surveillance at about 166 sexually transmitted disease clinics.

The estimation model for 2002 divides the Indian population into 24 groups based on four dimensions: high, moderate, or low prevalence of HIV within the state; the distribution of the population between high-risk and low-risk

Sensitivity of HIV/AIDS Estimates to Assumptions

	HIV PREVALENCE RATIOS SEXUALLY TRANSMITTED DISEASE (HIGH RISK)				HIV PREVALENCE RATIOS ANTENATAL CLINIC (LOW RISK)				ESTIMATED NUMBER OF PEOPLE WITH HIV/AIDS (MILLIONS)
ASSUMPTIONS	URBAN MALE	URBAN FEMALE	RM	RF	URBAN MALE	URBAN FEMALE	RM	RF	
Original NACO									
High-prevalence states	$\mathbf{X_i}$	$0.83X_i$	$0.33X_i$	$0.27X_i$	$1.2Y_i$	$\mathbf{Y_i}$	$0.15Y_i$	$0.125Y_i$	3.75
Moderate-prevalence states	$\mathbf{X_j}$	$0.50X_j$	$0.33X_j$	$0.16X_j$	$2.0Y_j$	$\mathbf{Y_j}$	$0.25Y_j$	$0.125Y_j$	
Low-prevalence states	$\mathbf{X_k}$	$0.33X_k$	$0.33X_k$	$0.11X_k$	$3.0Y_k$	$\mathbf{Y_k}$	$0.375Y_k$	$0.125Y_k$	
Alternative 1									
High-prevalence states	$\mathbf{X_i}$	X_i	X_i	X_i	$1.20Y_i$	$\mathbf{Y_i}$	$0.15Y_i$	$0.125Y_i$	4.8
Moderate-prevalence states	$\mathbf{X_j}$	X_j	X_j	X_j	$2.00Y_j$	$\mathbf{Y_j}$	$0.25Y_j$	$0.125Y_j$	
Low-prevalence states	$\mathbf{X_k}$	X_k	X_k	X_k	$3.00Y_k$	$\mathbf{Y_k}$	$0.375Y_k$	$0.125Y_k$	
Alternative 2									
High-prevalence states	$\mathbf{X_i}$	X_i	X_i	X_i	Y_i	Y_i	Y_i	Y_i	6.5
Moderate-prevalence states	$\mathbf{X_j}$	X_j	X_j	X_j	Y_j	Y_j	Y_j	Y_j	
Low-prevalence states	$\mathbf{X_k}$	X_k	X_k	X_k	Y_k	Y_k	Y_k	Y_k	

Note: Bold numbers denote data; far right column presents conclusions; all other numbers present assumptions. X denotes data on women; Y denoted data on men. The subscripts *i*, *j*, and *k* refer to the high-, moderate-, and low-prevalence states.
Source: Indrayan 2002.

(continued)

groups; the urban/rural distribution; and the male/female distribution. The size of the population in each of the 24 cells is not based on surveillance data but simply assumed. The ratio between the prevalence rate of urban males and the other three high-risk categories is also assumed, as are the ratios between urban females and the other three low-risk categories. Thus of the 36 numbers that go into calculating the total number of cases, only six are based on the sentinel surveillance system. The remaining 30 are untested assumptions. Changing a few of these assumptions could change the NACO estimate of 3.8 million people with HIV to 4.8 or even 6.5 million people.

Where data are unavailable, assumptions must be made. Indeed, this report makes generous use of assumptions. However, data have become available to estimate many of the 30 missing figures in NACO's model. Furthermore, India's medical research capacity is more than adequate to conduct additional surveys that might prove necessary. These data are needed to monitor the spread of the epidemic and to form the basis for an improved policy response. Since such information is a national public good, the surveys should be supported at the national level. This report recommends that the Indian national government support such surveys and estimation as a matter of urgency.

Source: Indrayan 2002.

In an effort to understand current AIDS treatment patterns in India, authors of a background paper for this report conducted two related surveys of doctors known to be interested in treatment of AIDS. (Hira 2003). The first sent a mail survey to 930 doctors on the mailing list *of AIDS UPDATE*, a publication produced by the AIDS Research and Control Center in Mumbai. Three hundred doctors responded to the survey. The second surveyed 339 doctors visited by representatives of a generic pharmaceutical company manufacturing antiretroviral drugs. Respondents were from 60 towns and cities with populations of at least 100,000. Each doctor completed a questionnaire that included questions on characteristics of the doctors and their knowledge of, attitudes toward, and practices (including prescribing practices) for using antiretroviral drugs. Respondents were also asked to estimate the number of AIDS cases in their town or city. For each town and city, the median estimated number of AIDS cases was

Table 2.2 Estimated Number of People with AIDS in 60 Indian Cities, 2002 (thousands)

CITY	NUMBER OF CASES	CITY	NUMBER OF CASES
Ahmedabad	15.0	Loni	0.2
Ahmednagar	0.5	Lucknow	50.0
Akola	1.0	Madurai	6.5
Allahabad	10.0	Meerut	5.0
Amritsar	0.5	Miraj	3.0
Aurangabad	1.0	Mumbai	10.0
Bagdogra	0.1	Mysore	1.0
Bangalore	20.0	Nagpur	2.3
Baramati	1.0	Namakkal	10.0
Belgaum	1.0	Nanded	0.7
Bellary	1.3	Nashik	5.0
Bhavnagar	3.8	Navi Mumbai	1.0
Bhiwandi	0.5	Patiala	0.1
Chennai	10.0	Patna	10.1
Chinchwad	0.6	Pondicherry	0.2
Coimbatore	0.4	Pune	10.0
Cuttack	0.1	Rajkot	1.9
Delhi	45.0	Salem	1.0
Erode	1.0	Sangli	8.0
Guntur	8.0	Shimla	0.0
Hubli	10.0	Solapur	3.0
Hyderabad	35.0	Surat	45.0
Imphal	0.5	Thane	4.3
Indore	1.0	Trichur	0.1
Jaipur	1.0	Trivandrum	0.1
Jalna	0.5	Vadodara	1.0
Jammu	0.1	Varanasi	0.2
Karimnagar	3.0	Vijaywada	8.8
Kolar	1.0	Visakhapatnam	2.5
Kolhapur	1.0		
Kolkata	5.0	Total	369.5

Note: These estimates may be unrealistically high for Delhi, Lucknow, Patna, and Surat and unrealistically low for Mumbai.
Source: Hira 2003.

determined and then aggregated across all 60 cities (table 2.2). Summing the median estimates for the 60 cities yields a figure of 369,500 people with AIDS. Assuming that rural areas have about half that number of cases yields a rough estimate of 554,300 for the total number of people with AIDS in India.[1] Assuming that the number of AIDS cases is 10–15 percent, the total number of adults with HIV yields a range for the number of people with HIV of 3.7–5.5 million. The midpoint of this range is 4.6 million,

which is in rough agreement with the middle of the three estimates in the table in box 2.1.

Respondents were also asked how many HIV/AIDS patients they currently managed and how many were on antiretroviral therapy. The responses indicated that 362 doctors were managing 90,000 HIV–positive patients, 11,700 of whom (8,700 males and 3,000 females) were on antiretroviral therapy.

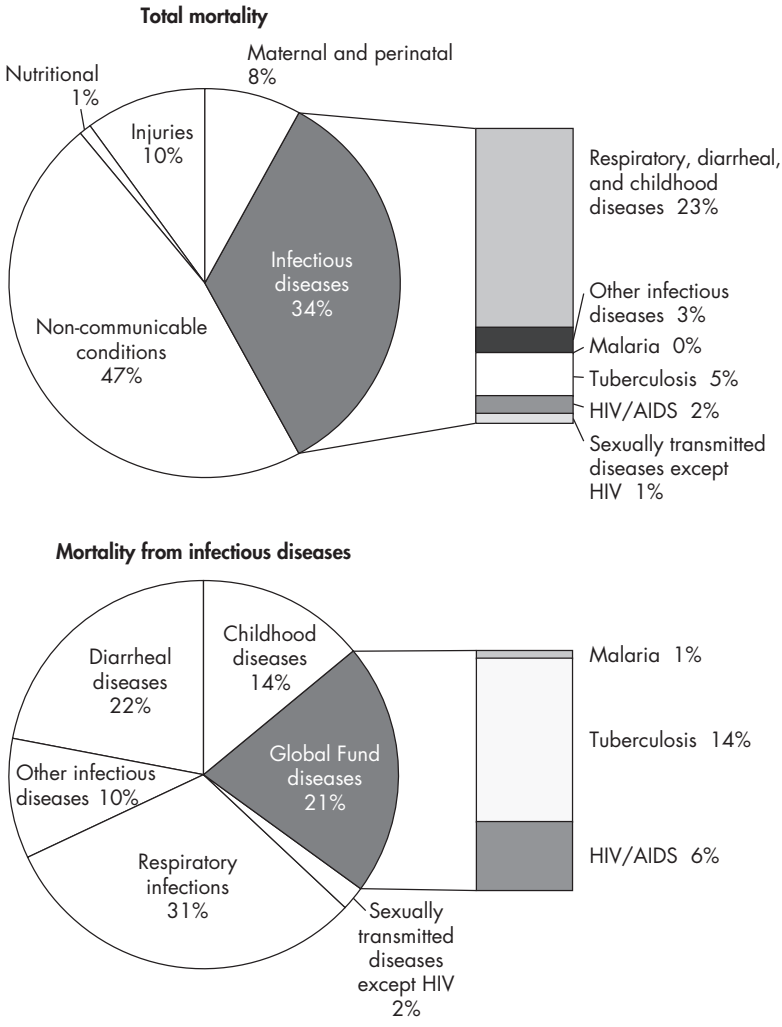
Estimates of the numbers of people with HIV and AIDS are critical for projecting the costs and consequences of alternative antiretroviral therapy policies. It is unfortunate that these estimates are unreliable in India today. This report calibrated the simulation model to yield an estimate of about 3.8 million people with HIV and 550,000 people with AIDS in 2002. If better data suggest different figures, the model can be adjusted accordingly.

The 2000 World Health Organization (WHO) annual report updated previous World Bank/WHO estimates of the global burden of disease to 1998, as measured by deaths and disability-adjusted life-years lost. According to the report, 9.4 million deaths occurred in India in 1998, of which 1.9 percent, or 179,365, were from AIDS (figure 2.1).[2] HIV/AIDS accounted for only 6 percent of deaths from infectious disease. AIDS, tuberculosis, and malaria—the three diseases targeted by the recently established Global Fund for AIDS, Tuberculosis and Malaria—accounted for 21 percent of the communicable disease burden in 1998, of which AIDS accounted for 30 percent.

HIV/AIDS is increasing faster than any other disease category in India. The 2002 *World Health Report* estimates that by 2001 AIDS deaths accounted for 3.1 percent of all deaths in the high-mortality Southeast Asian countries, an increase in the AIDS share of more than 50 percent in three years (WHO 2002). Assuming that all other diseases grow in proportion to the population and AIDS deaths grow at the rate predicted in the model of the baseline projection scenario used for this report, AIDS is projected to account for 17 percent of all deaths and 40 percent of deaths from communicable diseases by 2033 (figure 2.2). Among the three diseases targeted by the Global Fund, AIDS will account for 80 percent of all deaths.

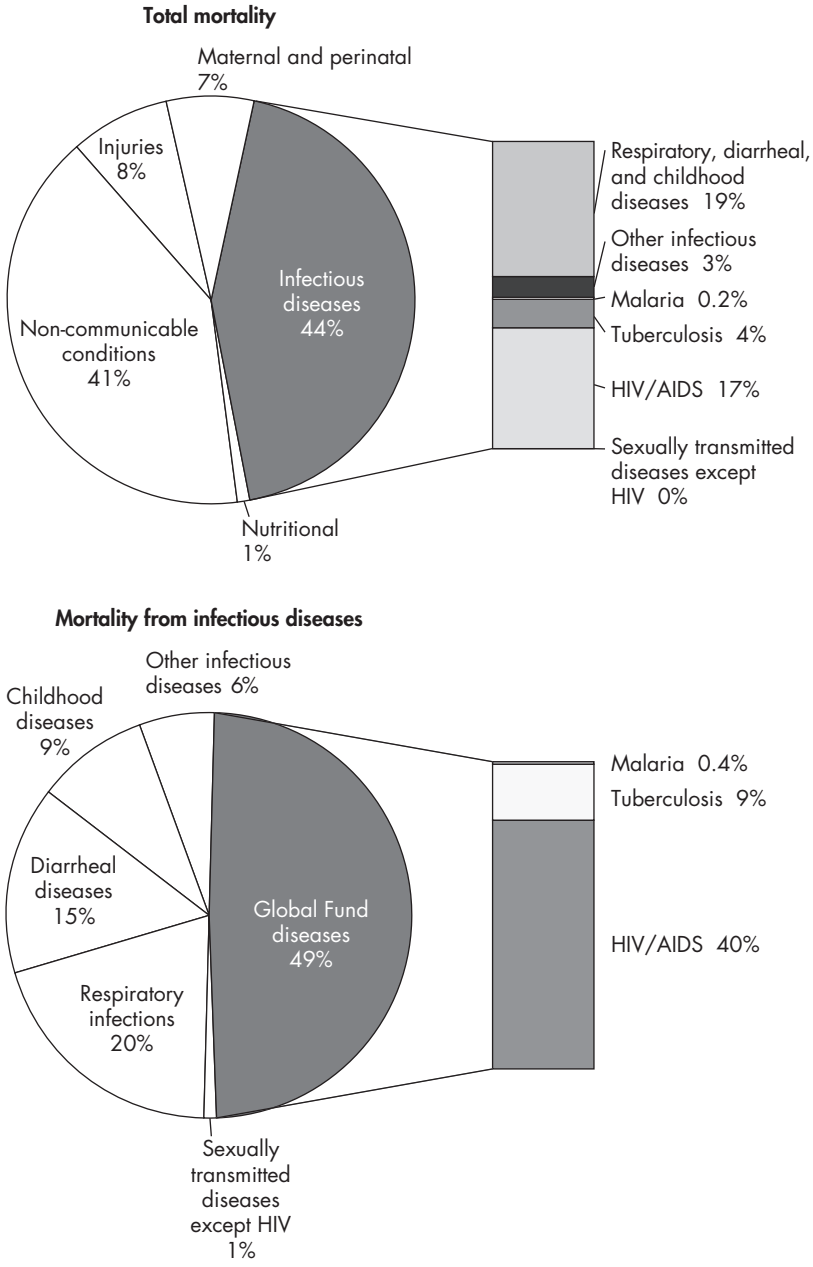
These deaths are associated with a projected prevalence of HIV among adults of 4 percent in 2033. Although 4 percent is a large prevalence rate—more than four times the current rate in India—it is much lower than prevalence rates already observed elsewhere in the world. Should the baseline scenario prove optimistic, AIDS would account for an even larger proportion of deaths than depicted in figure 2.2. If, for example, prevalence were to

Figure 2.1 Mortality in India, by Cause, 1998



Source: World Health Organization 2000.

Figure 2.2 Projected Mortality in India, by Cause, 2033



Source: Authors' estimates.

rise to 7 percent, AIDS deaths would represent 22 percent of total deaths and 47 percent of infectious deaths in 2033.

Responses to the Epidemic

Since the first cases of AIDS appeared in India in the late 1980s, Indian society and the Indian government have addressed the epidemic with increasing concern and resources.

Preventing the Spread of HIV/AIDS

The government of India has made a commitment to design and implement HIV prevention and control activities in all states. Phase I of the prevention effort began in 1992, supported by a World Bank credit of $84 million. During this stage funding focused on preventing transmission through blood and blood products and on increasing awareness of the danger of risky sex and needle exchange.

Phase II of the National AIDS Control Programme (NACP) began in 1999, supported by a World Bank credit of $191 million plus Indian government funding of $14 million. Phase II is a 100 percent centrally sponsored scheme. Substantially decentralized, the program is being implemented in 35 states and union territories and 3 municipal corporations through state AIDS control societies.[3] These societies implement the programs; NACO has assumed joint responsibility for activities such as epidemiological surveillance for sexually transmitted diseases and HIV/AIDS, training and capacity building, operational research, and monitoring and evaluation. NACO is also responsible for policy-level guidance, program oversight, allocation of public funds to the states, approval of proposed control activities, and coordination with other donor partners. NACO works closely with the states and coordinates advocacy meetings. The Prime Minister and the chief ministers of some high-prevalence states are engaged in frequent dialogue about the problems associated with controlling the epidemic. Issues related to HIV/AIDS are highlighted through intersectoral coordination and other mechanisms.

In 2002 the government finalized and released the National AIDS Control Policy and the National Blood Policy. These policies were drafted following a wide a range of consultations with governmental and nongovernmental organizations, experts, and partner agencies.

The objective of the national policy is to prevent the epidemic from spreading farther and to reduce its impact on infected people and the general population. The policy envisages zero new infections by 2007. To achieve this, it has established several specific goals:

- Prevent the spread of HIV/AIDS and reduce its personal and social impact. Main activities include control of sexually transmitted diseases; promotion of condom use; provision of testing, counseling, care, and support for people with HIV/AIDS; surveillance; harm minimization for injecting drug users; provision of safe blood and blood products; and support of research and product development.
- Generate ownership of the control program by government and nongovernmental organizations at the national, state, and local levels.
- Create an enabling environment for prevention and treatment efforts.
- Decentralize HIV/AIDS control activity.
- Strengthen program management at all levels.
- Promote introduction of control activities in other government programs.
- Provide support to vulnerable groups.
- Provide support, including treatment, to people with HIV/AIDS.
- Work with multilateral and bilateral donors.
- Promote better understanding of HIV/AIDS, especially among high-risk groups.

Program implementation depends on the capacities of state units. Capacity, political commitment, and administrative leadership vary across states, but most of the state AIDS control societies are weak and need substantial technical support. Administrative and financial management capabilities have been strengthened adequately, but technical and management assistance are needed in strategic planning, priority setting, and provision of key service delivery inputs to targeted interventions through public and private sector agencies.

The main intervention strategy is to use nongovernmental organizations (NGOs) to deliver these interventions. State AIDS control societies have identified 660 NGOs to deliver targeted interventions among high-risk groups. These NGOs need technical support in understanding the

complexities of HIV/AIDS issues and inputs for accelerating prevention-oriented outcomes.

The key challenge in scaling up targeted interventions is understanding the level of effort needed to identify the scope and location of high-risk groups, determine what expansion of activities is required to expand coverage of high-risk populations, and identify and contract a sufficient number of credible and committed NGOs to deliver those targeted interventions.

The main targeted interventions are condom promotion, improved access to sexually transmitted disease services, and communication about behavior. These strategies are currently implemented on an ad hoc basis, and coverage is much below what is required. The challenge is to provide the support needed to scale up well-designed and high-quality targeted interventions.

Prevention interventions in the general population emphasize increasing awareness and improving access to condoms, voluntary counseling and testing services, and safe blood. The NACP has effectively addressed blood safety issues through a variety of measures at the policy and program levels.

Sources of Finance for AIDS Prevention

India's annual AIDS budget program from all sources is about $57 million (table 2.3). More than 80 percent of program resources are financed by the government, with one-fifth coming from government revenue and four-fifths from a World Bank credit. About 20 percent of the budget is financed by grants from bilateral donors. India receives additional support for its AIDS program from various NGOs. Figures on the level of such support are not available.

Virtually all of the $57 million of support is for prevention activities, including prevention of mother-to-child transmission through the use of short courses of antiretroviral medication.

Table 2.3 Financing of India's National HIV/AIDS Control Program, 2002

SOURCE	MILLIONS OF U.S. DOLLARS PER YEAR
Government of India	
Current budget	7.8
World Bank credit	38.2
Subtotal	46.0
Donors	
United Kingdom (DFID)	4.2
United States (USAID)	4.8
Canada (CIDA)	1.6
Subtotal	10.6
Total	56.6

Source: World Bank estimates.

Current government spending on treatment of AIDS patients in public hospitals is not part of the AIDS budget and therefore difficult to estimate. Very little treatment expenditure is used to purchase antiretroviral medication.

The federal budget for health and social welfare is about $1,300 million a year, of which about $300 million is allocated to health. While states currently finance most AIDS care and treatment in public hospitals, it is expected that financing for antiretroviral therapy would come from the federal government.

Prevention Efforts among People at Risk of or Living with HIV/AIDS

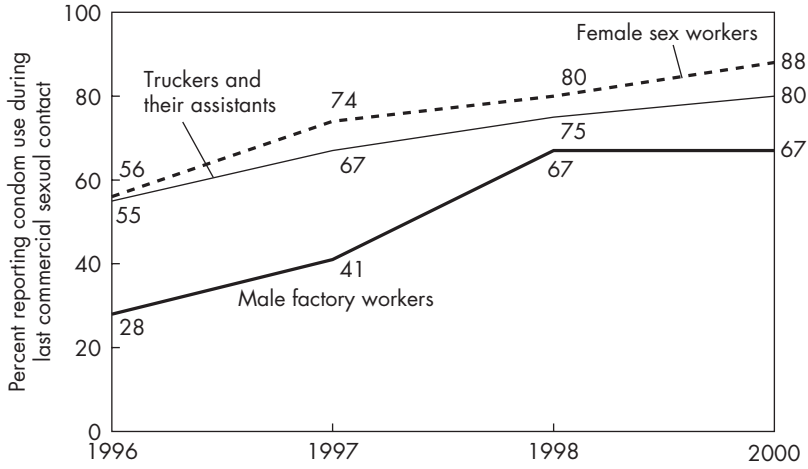
The best way to understand how the Indian population has responded to the HIV/AIDS epidemic and to news of the danger from unprotected sex or needle sharing would be to study the change in risk behavior of a given population group over time. Unfortunately, longitudinal data (that is, data over time on a given population group) on behavior that increases the risk of HIV infection are rare in India. Longitudinal data on condom use among sex workers in Tamil Nadu are available. Other sources also provide information on changes in risk behavior in response to the HIV/AIDS epidemic (APAC).

AIDS control activities in Tamil Nadu began in 1995, with substantial support from the United States Agency for International Development (USAID). Activities emphasized changing the behavior of high-risk groups, such as female sex workers, truckers and their assistants, and male factory workers.

NGOs are the main vehicle for implementing control activities targeting high-risk groups. They emphasize social marketing of condoms, training of peer educators for sex workers, and strengthening of counseling and communication skills.[4] The state government conducts annual behavioral surveillance surveys in a sample of respondents from high-risk groups in nine towns (figure 2.3). Those surveys indicate that condom use increased substantially in all groups between 1996 and 2000 but leveled off for male factory workers between 1998 and 2000.

A recent behavioral surveillance survey conducted in 22 Indian states and territories (Org-Mark Quest 2002) reveals that condom use varies widely across states. Use by urban males in the general population, for example, ranges from 16 percent in Uttar Pradesh to almost 90 percent in Goa. In both urban and rural areas, females report lower rates of condom use than males during the same encounters, and condom use is lower in rural areas (for both

Figure 2.3 Condom Use by High-Risk Groups in Tamil Nadu Following Introduction of HIV/AIDS Prevention Programs, 1996–2000



Source: APAC 2002.

males and females) than in urban areas. For India to attain a national average of 75 percent, condom use would have to increase 20–25 percentage points.

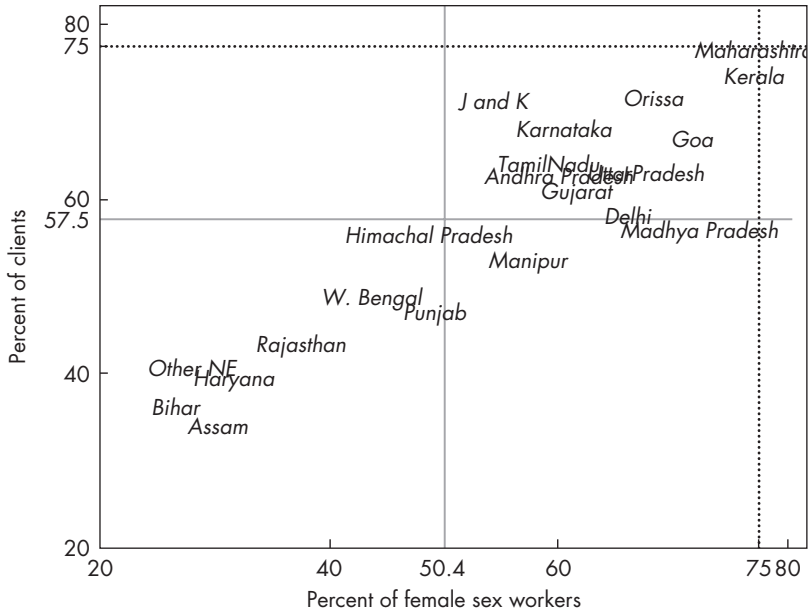
In 21 of the 22 states surveyed, estimates of condom use during contacts with female sex workers are available from both sex workers and their clients (figure 2.4). Clients of female sex workers report relatively high rates of use with commercial partners (57.5 percent), but these rates fall to 21.8 percent with regular partners and just 6.8 percent with nonregular partners (Org-Mark Quest 2002). Although sex workers typically report higher rates than their clients, the high correlation between the reported rates suggests that the survey methodology is sound.

The behavior of injecting drug users and people with HIV/AIDS has an important effect on the growth of the AIDS epidemic. Unfortunately, no information on the sexual or injecting behavior of these groups is currently available for India.

Treating People with HIV/AIDS

With the advent of generic antiretroviral drugs in 2000, more people with AIDS are using antiretroviral therapy. Of 370,000 urban residents in India

Figure 2.4 Condom Use in 21 States, as Reported by Female Sex Workers and Their Clients, 2001



Note: Mean condom use was 50.4 percent for female sex workers and 57.5 percent for their clients.
Source: Org-Mark Quest 2002.

being treated for HIV/AIDS, about 12,000 were receiving antiretroviral therapy in October 2002. Most of that therapy is unstructured, and more than half of patients were not adhering to the regimen by the end of the first year, mainly because of the high cost of drugs and tests.

Private Health Care Spending and the Lack of Medical Insurance in India

Private health care spending accounts for more than 80 percent of all health spending in India, and nearly all this spending is out-of-pocket (Ellis and others 2000; Peters and others 2001). Poorer households purchase less curative care from the private sector than do richer households, and they are much less likely to be hospitalized because of lack of ability to pay or lack of any risk-pooling mechanism. A recent calculation based on National Sample Survey data indicates that one-fourth of hospitalized Indians who were not

poor when they entered the hospital become so after hospitalization (Peters and others 2001).

Variation in the quality of health care offered in the public and private sectors has been well documented (Peters and others 2001). The unrestricted growth of private curative care in India has led to questions about its quality. Despite these questions, however, most Indians prefer the private health care sector. For this reason heavy financial burdens are placed on all households, especially poor households, when illness strikes.

India has a multitier health care delivery system, with some elements of insurance involved at various tiers (table 2.4). Public health facilities offer a range of free or reduced-cost services to all Indians. In addition, schemes such as the Central Government Health Scheme and the Employee State Insurance Scheme provide free or subsidized care to central government employees and workers in the formal sector earning less than a certain amount. Public sector institutions such as the railways or defense offer their own health coverage, in the form of employer-managed facilities. A third form of coverage is provided to employees in the as yet small private corporate sector, where firms offer various health insurance schemes to their employees.

The only form of formal insurance in India comes from the General Insurance Company's four subsidiaries, which offer Mediclaim, essentially a reimbursement scheme. Mediclaim represents a small part of the total health coverage offered to Indians, and the recent privatization of insurance has not significantly changed the health insurance scenario. A 1997 study (Ellis and others 2000) indicated that people living in rural areas received the worst health insurance coverage in India, followed by informal sector workers.

Treatment and Care Options for People with HIV/AIDS

Since the launch of Phase II of the NACP in 1999, the government has demonstrated its commitment to providing low-cost care to people with HIV/AIDS to mitigate the impact of HIV–related illnesses. This commitment is evident in the budgetary outlay of 12 percent of the NACP for care and support, including treatment of common opportunistic infections, including tuberculosis, the most common opportunistic infection in India. The government has strengthened the states' capacity by training physicians and technicians, installing flow-cytometers for CD4/CD8 testing at selected medical institutions in 25 large and medium-size states, and allocating Rs. 1,250 ($25) per patient per year for the purchase of drugs to treat common opportunistic infections. The national treatment guidelines also recommend

Table 2.4 Financing of Curative Health Services in India

ITEM	"FREE" PUBLIC HEALTH FACILITIES	CENTRAL, STATE, AND LOCAL GOVERNMENT HEALTH SCHEMES	EMPLOYEE STATE INSURANCE SCHEME	MEDICLAIM	EMPLOYER-MANAGED FACILITIES	EMPLOYER REIMBURSEMENT FOR PRIVATE EXPENSES	NGOS AND OTHER LOCAL OR SPECIALIZED SCHEMES	PRIVATE OUT OF POCKET	NUMBER OF EMPLOYEES (MILLIONS)
Coverage (millions)	All Indians	20	29	1.8	30	20	30	30	n.a.
Type of employee									
Government employees	XX	XXX				X		XXXX	4.6
Military personnel	X				XXXXXXX			XX	9.5
Plantation workers	X				XXXXXX			XXX	1.2
Mine workers	X				XXXXXX			XXX	1.1
Railway workers					XXXXXXX			XX	1.8
Public enterprise employees	X		X	X	XXX	XX		XX	2.1
Private, formal sector									
Large firms	X		X	XXX	X	XX		XX	7.0
Small firms	XX		XX	X		X		XXXX	1.0
Private, informal sector									
Urban	XXX					X	X	XXXXX	128.7
Rural	XXXX							XXXXXX	193.0
Total									350.0
Percent of total health spending	20	1	3	1	5	4	1	65	n.a.

n.a. Not applicable.
Note: Each X represents about 10 percent of all expenditures in a row. All figures in table are approximations, not necessarily based on solid evidence.
Source: Ellis and others 2000.

prophylaxis with cotrimoxazole in people with HIV/AIDS. The care strategy covers 30 percent of the estimated 550,000 people with AIDS who seek treatment at government-run and selected NGO hospitals.

Following the launch of generic antiretroviral drugs by Indian pharmaceutical companies in 2000 and the decline in the cost of these drugs, an increasing number of people with HIV/AIDS have been using antiretroviral therapy. Based on a background study for this report, approximately 90,000 people with HIV/AIDS were being treated by physicians in 60 major cities (Hira 2002). Most of these 60 large cities were in 6 high prevalence states (18 were in Maharashtra). Some cities that revealed unusually high numbers of people with HIV/AIDS were in Gujarat and Uttar Pradesh (see table 2.2).

Using the assumptions described above, these figures suggest that about 555,000 people in India have AIDS, 370,000 of whom live in these cities. Of the 370,000 urban residents with HIV/AIDS under treatment, about 11,700 were receiving antiretroviral therapy from physicians. Although this is probably a larger absolute number of people than in any other poor country, it represents just 13 percent of the 90,000 people with HIV estimated to be receiving treatment and just 2.2 percent of the estimated 555,000 AIDS cases in India.

Physicians prescribing antiretroviral therapy estimated that 36 percent of the patients receiving the therapy were wealthy or middle class, 37 percent were working class, and 27 percent were poor. Although it is difficult to know how the physician's subjective classifications correspond to objective measures of wealth, the results clearly indicate that most patients had moderate or high incomes. Indeed, given that patients were forced to assume the cost of care, it is surprising that 27 percent of patients were believed to be poor.

The study suggests that most antiretroviral therapy is unstructured. Adherence, for example, was reportedly less than 50 percent by the end of the first year of therapy. Reasons for poor adherence included the high cost of drugs and monitoring tests (80 percent), poor counseling and inadequate understanding on the part of patients for proper dosing and continued therapy (40 percent), the stigma and discrimination associated with antiretroviral therapy (45 percent), and intolerance to drugs (30 percent). Anecdotal evidence from local manufacturers of generic antiretroviral drugs reinforced the fact that less than 20 percent of therapy occurred in structured form at a few centers of excellence in the country (that is, in accordance with WHO and NACO guidelines). This is not an unexpected scenario, since physicians need time to become familiar with a new phar-

macology, to learn how to work with and monitor patients, and to update themselves continually on new developments in the field. The study also revealed that physicians who were administering antiretroviral therapy were treating an average of 48 people with HIV/AIDS, 38 of whom were on antiretroviral therapy. This may mean that structured antiretroviral therapy delivery is associated with managing fewer patients, with consequent loss of income.

Of the 639 physicians treating people with HIV/AIDS, 416, or about two-thirds, were providing antiretroviral therapy. Of those providing antiretroviral therapy, three-quarters classified themselves as consultants rather than academic or government employees. Fewer than 10 percent of the 639 respondents were women, most of whom were affiliated with teaching hospitals. Only 17 female physicians in the sample were providing antiretroviral therapy. It is not clear from this study whether the small proportion of female physicians delivering antiretroviral therapy reflects the preference of predominantly male AIDS patients for male physicians, the underrepresentation of female physicians among consultant physicians, or other reasons. The majority of physicians providing care were in the middle of their careers (30–49 years of age). Older physicians were more likely to care for the poorest people with HIV/AIDS.

The study provides overwhelming evidence that a small number of physicians trained in antiretroviral therapy are managing a large number of people with HIV/AIDS. It also reveals that 20 percent of frequent antiretroviral therapy prescribers are managing 80 percent of people with HIV/AIDS. An estimate of 800 antiretroviral therapy prescribers in 60 large cities was obtained from 362 responders who were prescribing antiretroviral therapy, suggesting existing capacity for expanding access to antiretroviral therapy. Another 224 physicians who participated in the study and categorized themselves as nonprescribers are also a potential group among which to expand access.

Government Support. The government's stated policy is "to create an enabling socioeconomic environment so that all sections of the population can protect themselves from the infection and families and communities can provide care and support to people with HIV/AIDS." The NACP has addressed treatment issues in the context of prevention and low-cost care and support components. It is designed to create an enabling socioeconomic environment so that all segments of the population can protect themselves from infection, to help families and communities provide care and support to people with

HIV/AIDS, and to improve services for people with HIV/AIDS in times of sickness, both in hospitals and at home through community healthcare.

Interventions supported by NACO and state AIDS control societies are designed to improve access to sexually transmitted disease services. Public sector sexually transmitted disease specialists and in some states private health care providers are receiving training in quality care. The World Bank credit covers about 9 percent of the cost of medicines to treat sexually transmitted disease.

The government is seeking to exempt antiretroviral drugs from all customs and excise duties in order to reduce prices. Antiretroviral therapy is not covered under the NACP, except for health care providers as post-exposure prophylaxis and through mother-to-child transmission programs cosponsored by UNICEF. However, training programs for doctors highlight the rational use of antiretroviral therapy.

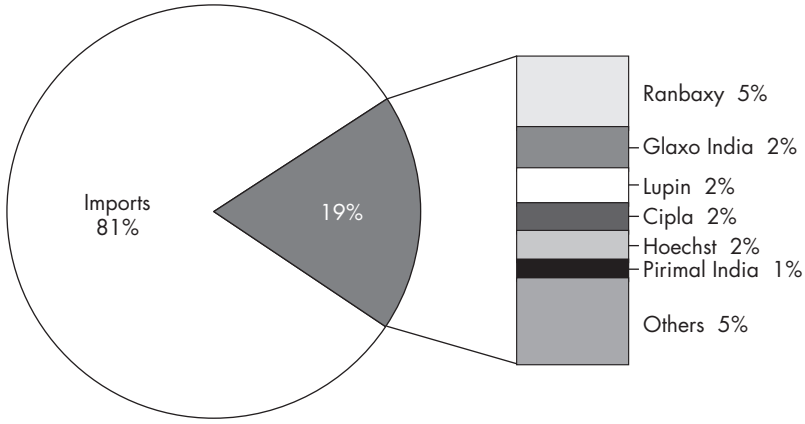
The government has a mandate to provide access to treatment to all employees of central government departments. The Employees State Insurance System covers the costs of antiretroviral drugs and opportunistic infections. The low-cost care and support component of the NACP covers issues related to development of treatment guidelines and appropriate drugs for common opportunistic illnesses. About 12 percent of the World Bank credit is designated for medicines to treat opportunistic infections.

Donor Support. With the exception of UNICEF's support of the program to prevent mother-to-child transmission, official donor organizations have generally avoided financing antiretroviral therapy, focusing instead on strengthening treatment of opportunistic illnesses. At the time of this writing, the situation continues to change.

India's Private Pharmaceutical Sector. Unlike other countries with similar per capita incomes, India has a dynamic domestic pharmaceutical industry that competes vigorously with multinational firms. In 1998 almost a fifth of all wholesale pharmaceutical sales in the country were produced by domestic pharmaceutical manufacturers, up from 16 percent in 1992 (figure 2.5) (Govindaraj and Chellaraj 2002). Competition among domestic firms is fierce, with 10 firms each controlling more than 1 percent of the market and the largest controlling only 5 percent.

At the retail level, most of the population in many states has access to pharmacies. The number of people per pharmacist in Karnataka, Uttar Pradesh, and Tamil Nadu ranges from 1,860 in Karnataka to 5,808 in Tamil Nadu (Govindaraj and Chellaraj 2002). These low numbers suggest that the

Figure 2.5 Market Shares of Domestic Pharmaceutical Manufacturers in India, 1998



Source: Govindaraj and Chellaraj 2002.

Indian population is relatively well supplied with pharmacists. In Tamil Nadu and Uttar Pradash private pharmacies outnumber public pharmacies by a factor of about 10 to 1. All pharmacists, especially private pharmacists, have an incentive to sell new drugs for AIDS as they become available.

India's manufacturing capacity and its laissez-faire attitude toward domestic production of drugs still under patent have dramatically lowered prices to Indians for many patented drugs. Originally focusing on the production of drug ingredients and off-patent drugs in bulk form, the Indian pharmaceutical industry has turned increasingly to the production of generic versions of drugs currently under patent in North America and Europe. In the mid-1990s prices of four typical drugs were 10 times more expensive in Pakistan, 17 times more expensive in the United Kingdom, and 37 times more expensive in the United States than in India (table 2.5) (Lanjouw 1998). None of these comparator countries permitted the production or sale of generic versions of these drugs. The advent of low-priced versions of antiretroviral drugs thus represents the continuation of an established trend.

Treatment-Seeking Behavior and Willingness to Pay for Antiretroviral Therapy

No studies appear to have been conducted on the willingness to pay for antiretroviral therapy in India. This section presents some results from a study

Table 2.5 Prices of Patented Drugs in India and Selected Other Countries, Mid-1990s

DRUG	QUANTITY	PRICE IN INDIA (RUPEES)	MULTIPLE OF INDIAN PRICE IN		
			PAKISTAN	UNITED KINGDOM	UNITED STATES
Ranitidine	300 tablets/ 10 pack	18.53	14.1	26.1	56.7
Famotidine	40 tablets/ 10 pack	18.61	14.0	27.1	54.0
Ciprofloxacin	500 mg/ 4 pack	28.4	8.3	10.3	15.4
Norfloxaciin	400 mg/ 10 pack	39	3.2	6.5	23.2
Average for these four drugs	n.a.	n.a.	9.9	17.5	37.3

n.a. = Not applicable.
Source: Lanjouw 1998.

commissioned for this report to look at treatment-seeking behavior and willingness to pay for antiretroviral therapy (Gupta and Sankar 2003).

A survey was conducted among 269 people with HIV/AIDS in four Indian cities. The study design did not attempt to draw a representative sample, a task that would have required far more time and resources than were available. Instead, the objective was to construct a purposive sample of people diagnosed with HIV and receiving at least some treatment for opportunistic illnesses, if not antiretroviral therapy. Such a sample will not permit conclusions to be drawn about the average person with HIV in India. However, it will reveal how some people with HIV in India are responding to their infection. The study may also reveal the responses of an average HIV–infected person with certain characteristics. For example, since the study collected data on assets, the sample may provide an estimate of what a person with HIV with certain assets would pay for antiretroviral therapy.

A detailed questionnaire was used. The willingness-to-pay questions were formulated based on the emerging consensus on the methodology of contingent valuation methods. The interviews were conducted at settings in which people with HIV/AIDS were being treated or counseled. After informed consent was granted, 218 questionnaires were administered. The survey included questions on initial tests as well as follow-up tests, in addition to drugs. It used two bid structures to measure the willingness to pay for drugs, initial tests, and follow-up tests, each containing two close-ended questions followed by an open-ended question on the maximum willingness to pay. The interviews were conducted face to face.

Slightly less than 19 percent of survey respondents were receiving antiretroviral therapy. About 36 percent of respondents who had ever been on antiretroviral therapy reported stopping and restarting at least once, indicating a fairly high rate of nonadherence. For those currently on antiretroviral therapy, the average expenditures were Rs. 2,498 a month for drugs, Rs. 5,585 for initial tests, and Rs. 5,155 every six months for monitoring tests. By Indian standards these are fairly high expenditures, reinforcing concerns that cost may be a major deterrent to scaling up antiretroviral therapy in India.

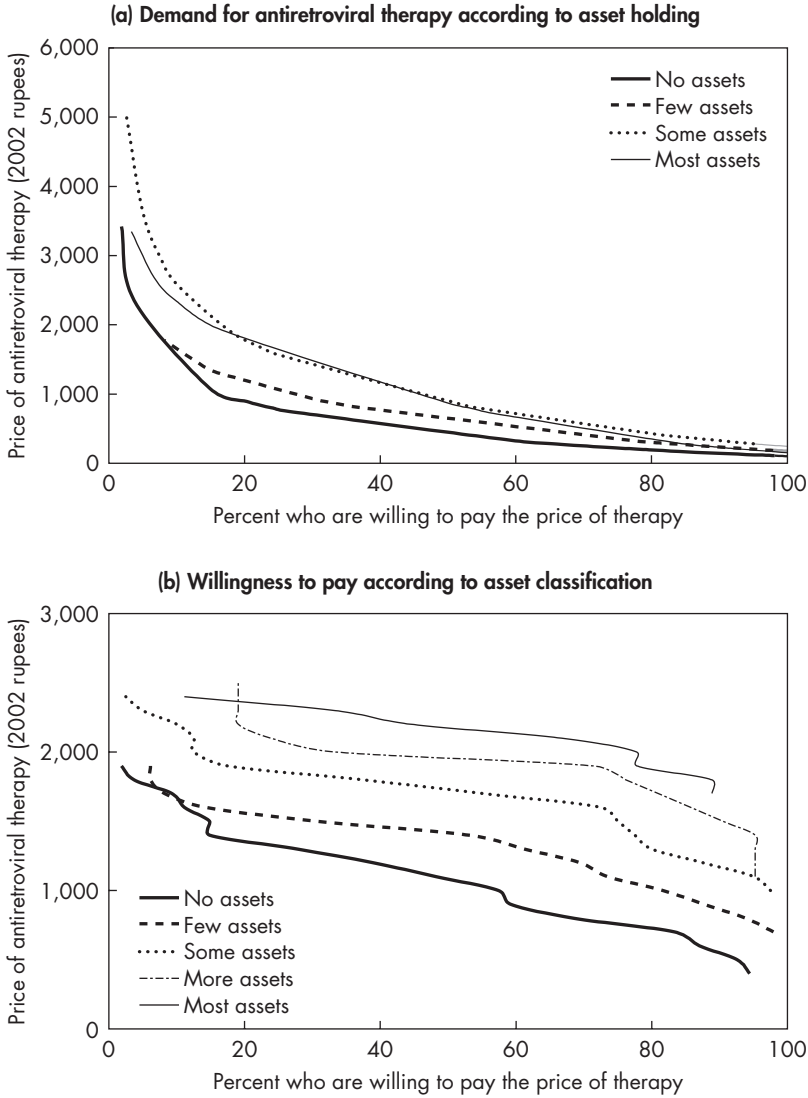
The willingness-to-pay part of the survey (conducted among those not currently on antiretroviral therapy) revealed that about 94 percent of all respondents not on antiretroviral therapy wanted to be on it. However, the willingness to receive treatment did not necessarily translate into willingness to pay. Of those willing to be on antiretroviral therapy, 90 percent were willing to pay for drugs, 74 percent were willing to pay for initial tests, and 83 percent were willing to pay for follow-up tests.

Based on the maximum willingness-to-pay responses, the authors generated demand curves for each of the three components of antiretroviral therapy (figure 2.6, panel a). The double-log specification yielded a very good fit and a standard downward sloping curve, indicating that antiretroviral therapy is a normal good and that price is a key variable affecting its demand.

Econometric analysis of the data confirmed that ownership of assets (as a measure of economic status) was a key variable explaining willingness to pay for all three components of antiretroviral therapy (figure 2.6, panel b). In addition to the pure effect of gender, female ownership of assets plays a key role in explaining variations in willingness to pay. The number of illnesses in the recent past and the belief that there are severe consequences to being HIV–positive are also correlated with willingness to pay. Willingness to pay is lower for initial tests than for drugs and monitoring tests, and willingness to pay for a total packet that includes drugs and monitoring tests is lower than willingness to pay for each of these components separately.

The policy implications of this analysis are straightforward: making antiretroviral therapy more accessible requires lowering the price of all three of its components, especially initial tests. These tests represent the entry point into antiretroviral therapy and can be linked to voluntary testing and counseling mechanisms. Subsidizing initial tests could be one way of stepping up voluntary testing and counseling in any system that offers antiretroviral therapy. Bundling of the components is critical to ensure that patients purchase the testing they need as well as the drugs they want. Making antiretroviral therapy and its components more comprehensible would help patients adopt

Figure 2.6 Demand and Willingness to Pay for Antiretroviral Therapy in India



Source: Gupta and Sankar 2003.

a more rational approach toward their cost. Different pricing structures and subsidy schemes can be devised depending on the cost-sharing mechanism used (public, private-public, or private). Whatever scheme is adopted, however, pricing, the most important constraint to wider adoption of antiretroviral therapy, will continue to play a critical role in determining access. Any subsidy scheme will have to address all three components of antiretroviral therapy as well as equity concerns.

Notes

1. India has about three times as many rural adults as urban adults. NACO assumes that infection rates are roughly one-sixth as high in rural as in urban areas on average. The number of people with HIV, and therefore the number of people with AIDS, is thus about half as large in rural as in urban areas.
2. WHO also presents the relative contribution of the different disease categories as measured by disability- adjusted life-years. This breakdown is omitted here because the picture it presents of the relative importance of disease categories is similar to that revealed by the pattern of deaths.
3. A centrally sponsored scheme is a government program funded by the central government (or externally funded) and implemented by state governments. An example in India is International Development Agency support for control programs for HIV/AIDS, tuberculosis, and malaria, for which funds are given to states as grants.
4. The term "social marketing" refers to the use of advertising and marketing techniques developed for the private sector for the distribution of goods and services whose social benefits exceed their private benefits. Social marketing is typically supported by government subsidies.

CHAPTER 3

HIV/AIDS and Antiretroviral Therapy

The risk of transmitting HIV/AIDS depends on the mode of transmission, the infectiousness of the person with HIV, and the susceptibility of the person exposed (table 3.1). Despite these relatively limited modes of transmission, few countries have slowed or reversed the growing HIV/AIDS epidemic.

NACO estimates that 84 percent of new HIV infections occur through heterosexual transmission. Reduction of transmission through vaginal intercourse should therefore have the greatest impact on epidemic dynamics. Strategies to reduce sexual transmission in India would involve:

- Reducing the probability of HIV transmission during each sexual contact by increasing condom use.
- Reducing the number of sexual partners through behavioral interventions for commercial sex workers and the general population.
- Reducing the level and duration of infectiousness through medical interventions, including treatment of sexually transmitted infections and use of antiretroviral therapy.

Infectiousness depends on the concentration of HIV in genital secretions and on the strain of virus a person carries (Dyer and others 1997; Hart and others 1999). Studies of couples in which one partner is infected and the other is not (so-called "discordant" couples) have shown that the risk to the uninfected partner rises dramatically with the concentration of virus in blood plasma (Gray and others 2001). When the plasma viral load is less than 1,500 copies per cubic millimeter, no transmission is observed. The

Table 3.1 Minimum Risk of Contracting HIV through Sexual Contact, Mother-to-Child Transmission, and Blood or Blood Products

MODE OF TRANSMISSION	MINIMUM RISK (PERCENT)	SOURCE
Sexual contact		
Male to female	0.52	Lee and others (1996); Gray and others (2001)
Female to male	0.36	
Mother-to-child transmission		
Delivery Breastfeeding	33	St. Louis and others (1993); Nagelkerke and others (1995); Working Group on mother-to-child transmission of HIV (1995); Mayaux and others (1997); Leroy and others (1998); Lindegren and others (1999); Nduati and others (2000)
Blood products		
Contaminated transfusion	More than 95	McFarland and others (1995)
Needle sharing by injecting drug users	More than 90(?)	
Needlestick injury	0.6	
Occupational exposure	0.3	

Source: Background paper by Manseille (2002).

risk of infection increases to 1 per 10,000 episodes of intercourse at a plasma viral load level of 3,500 copies per cubic millimeter and to 1 per 200 episodes at a plasma viral load greater than 50,000 copies per cubic millimeter. By increasing viral shedding, increasing the number of cells receptive to HIV and the number of HIV receptors per cell, the presence of a classic sexually transmitted disease, such as chancroid or gonorrhea, may increase the risk of HIV transmission for both men and women by a factor of as much as 10, accelerating the spread of the epidemic (Holmes and others 1998; Over and Piot 1993).

Different types of HIV may have different capacities for infection. Subtype C, the subtype most commonly found in India, is believed to be the most infectious. Drug-resistant strains of the virus that are emerging in all parts of the world in response to antiretroviral therapy may be either more or less infectious than strains of the virus that have never been subjected to selection pressure from antiretroviral therapy.

Treating Opportunistic Illnesses with or without Antiretroviral Therapy

Even as the availability of antiretroviral therapy increases in many developing countries, appropriate diagnosis and management of life-threatening opportunistic infections and HIV–associated cancers remain the most important aspects of care of people with HIV/AIDS. Opportunistic infections and cancers usually begin five to seven years after infection and occur progressively as uncontrolled HIV replication destroys the immune system. Clinical or laboratory confirmation of an opportunistic infection or cancer signals the onset of AIDS.

Opportunistic illnesses are caused by organisms that exist in the environment of the body (on the skin, in the lungs, in the gastrointestinal system). These organisms remain latent until they become pathogenic as a result of the impairment of the immune system caused by HIV.

The epidemiology of opportunistic illnesses is complex. Each infection has a unique clinical expression requiring specific diagnostic techniques and treatment related to the severity of the depletion of the immune system. Many opportunistic illnesses can be prevented by judicious use of chemo-prophylaxis, ranging from cotrimoxazole to prevent *Pneumocystis carinii pneumonia*, at a cost of less than $20 a year, to ganciclovir to prevent *cytomegalovirus*, at a cost of more than $2,200 a year (Spector and others 1996; Maynart and others 2001). In Western countries antiretroviral therapy has proven to be so effective in controlling viral replication, thereby stopping destruction of the immune system, that the incidence of opportunistic illnesses and the resultant high death toll have dramatically declined (Palella and others 1998). The emerging problem of poor adherence is now causing HIV resistance to antiretroviral therapy, however, leading to the return of opportunistic illnesses.

Opportunistic illnesses vary markedly across countries (Sengupta and others 1994; Selik and others 1987; Mocroft and others 1998; Morgan and others 2000). Accurate surveillance data do not exist in most countries, because people with HIV/AIDS generally present very late in their illness and usually die without a definitive diagnosis.

The epidemiology of tuberculosis in India closely resembles the pattern of HIV/AIDS, with similar risk groups being infected. Tuberculosis has the greatest cross-country variation of any opportunistic infection. In Australia, Europe, and the United States the prevalence of HIV/AIDS–associated tuberculosis is less than 5 percent; in India, Thailand, and much of Asia, tuberculosis accounts for almost 50 percent of opportunistic illnesses in people with

HIV/AIDS. In India co-infection of HIV/AIDS and tuberculosis is probably the most critical issue to consider. As almost a third of all HIV/AIDS deaths globally are caused by tuberculosis, it is likely that tuberculosis will be the most significant contributor to HIV/AIDS mortality in India.

Treatment of latent tuberculosis to prevent the emergence of infectious clinical tuberculosis in people with HIV/AIDS may be one of the most urgent public health issues facing the Indian healthcare system. Given that more than 60 percent of people with late-stage AIDS in India have tuberculosis, it must be assumed that at least 50 percent of people with HIV/AIDS have latent tuberculosis. HIV infection increases the risk of latent tuberculosis from a 10 percent lifetime risk to a 10 percent annual risk. Co-infection with HIV does not increase the infectiousness of people with active tuberculosis, however, nor does it affect their response to treatment for tuberculosis. Active tuberculosis enhances the viral replication of HIV and causes more rapid disease progression, thus increasing the susceptibility to other opportunistic illnesses. Prophylactic treatment to prevent the development of clinical tuberculosis should be considered in people with HIV/AIDS in many settings in India (Wilkinson and others 1998).

Preventing the onset of opportunistic illnesses is the most cost-effective approach to managing HIV/AIDS where antiretroviral therapy is not widely available (Powederly and others 1992). Almost 20 opportunistic illnesses can be prevented by judicious use of chemo-prophylaxis (U.S. Public Health Service 2001), available to varying extents in India. The pivotal indicator test for initiation of prophylaxis is the CD4 count, an expensive laboratory test that is restricted to major hospital settings. Low-cost, but inadequate, surrogate clinical and laboratory markers for immune depletion are being used in resource-poor and remote settings.

Treating opportunistic illnesses in the absence of antiretroviral therapy does very little to alter the course of HIV/AIDS–related disease. In the absence of antiretroviral therapy, treating opportunistic infections has no lasting impact on the underlying immune deficiency that allowed the infections to manifest. Although in pre-antiretroviral therapy studies in Western countries some survival advantage was observed with early diagnosis, treatment, and prevention of opportunistic illnesses, the effect was not accompanied by restoration of the immune system. Immune function continues to deteriorate, requiring secondary prophylaxis to prevent recurrence of the treated opportunistic infection.

In Western countries common opportunistic illnesses, such as *Pneumocystis carinii pneumonia*, can be diagnosed by clinical history; treated

with low-cost cotrimoxazole, usually for 10 days; and prevented from recurring with daily cotrimoxazole. Less frequently occurring opportunistic illnesses require sophisticated diagnostic equipment and skilled clinicians to confirm a diagnosis from a wide range of pathogenic possibilities before complex and expensive treatment is started. Toxoplasmosis, for example, can be accurately diagnosed only by a lumbar puncture and computerized tomography brain scan; in some cases magnetic resonance imaging is required. Diagnosis of cryptosporidium requires specialized laboratory techniques; diagnosis of *cytomegalovirus* requires viral culture facilities.

In India and many other resource-poor settings, few of these specialized facilities are available for diagnosing opportunistic illnesses. Clinicians have little training in diagnosing or managing complex opportunistic illnesses, and laboratory back-up is either nonexistent or so expensive that it is unaffordable for most patients.

As most late-stage HIV/AIDS patients in India seek medical care for fever, diarrhea, and lymphadenopathy (lymph nodes that are abnormal in size, consistency, or number) without knowing they have HIV/AIDS, it is likely that opportunistic infections will not be suspected, diagnosed, or treated. This situation is of particular concern with regard to tuberculosis. Dr. Subhash Hira and his colleagues in Mumbai note that the most common presenting condition for tuberculosis among their patients with HIV/AIDS is weight loss. Since the tuberculosis program in India focuses on identifying patients with chronic productive cough, attending clinicians often fail to suspect tuberculosis. An additional problem in diagnosis is that as the CD4 count declines, people with active tuberculosis are less likely to produce positive sputum smears than people without HIV/AIDS.

The availability of antiretroviral therapy in Western countries has contributed most to the decline in opportunistic illnesses and the increase in survival of people infected with HIV/AIDS. Effective antiretroviral therapy has reduced the incidence of all opportunistic illnesses by restoring the immune system and obviating the need for continuing primary and secondary chemo-prophylaxis, with their inherent problems of adherence, cost, and toxicity. There is every reason to believe that antiretroviral therapy, if administered in the appropriate context, would have the same effect on opportunistic illnesses in resource-poor settings (Santoro-Lopes and others 2002).

If taken strictly according to directions, antiretroviral therapy can induce a sustained recovery of CD4 T-cell reactivity against opportunistic pathogens

in severely immunosuppressed patients. The effectiveness of antiretroviral therapy is determined by its ability to rapidly reduce viral load and to sustain low levels of viral activity. This viral activity affects susceptibility to opportunistic illnesses.

Initiating antiretroviral therapy in resource-poor settings can have detrimental effects by causing complications from latent or undiagnosed opportunistic illnesses. Patients in resource-poor settings tend to present late in their illness, usually when they have an opportunistic infection that causes them to seek medical care or, in the case of India, buy antiretroviral therapy from a private pharmacy. When antiretroviral therapy is successful in stimulating a patient's immune system, the reinvigorated system often begins to react against pathogens and allergens already present in the patient's body, generating new symptoms which are perceived by the patient as a new illness. These reactions of the immune system may be more serious than the opportunistic infections themselves. Patients in this situation may believe the symptoms are a side effect of their antiretroviral therapy and stop it. It is therefore essential that clinicians be well trained to recognize and treat antiretroviral therapy–related illnesses associated with asymptomatic opportunistic illnesses.

Toxicity, Adherence, and the Development of Resistance as a Result of Antiretroviral Drug Therapy

The advent of antiretroviral drugs in the late 1980s began a revolution in the management of HIV/AIDS, a revolution that may eventually be seen as analogous to the use of penicillin for treating bacterial infections in the 1940s. Antiretroviral treatment strategies seek to suppress viral replication, which leads to restoration of the immune system. The goal is to slow or halt disease progression, prevent drug resistance, and improve quality of life.

Three groups of antiretroviral drugs interrupt viral replication. The use of a single drug or two-drug combinations has been shown to promote rapid development of resistant strains of HIV and consequent ineffectiveness of therapy. In the past five years compelling epidemiological and clinical evidence has shown that with strict adherence, the use of three drugs in combination achieves sustained viral suppression for several years.[1]

Since the introduction of antiretroviral therapy, three issues—toxicity, adherence, and resistance—have tempered initial enthusiasm that HIV/AIDS could be successfully controlled and that people with HIV/AIDS could

look forward to long-term survival with few consequences of treatment. The model used in this report assumes that antiretroviral therapy increases life expectancy by four years.

People with AIDS who have access to high-quality care in rich countries can resort to second- and third-line therapies when first-line treatment fails (box 3.1). The high cost of these therapies, the difficulty and complexity of using them, and enforcement of World Trade Organization stipulations on international property rights will impede widespread use of these drugs in India over the foreseeable future.

Toxicity

Antiretroviral therapy has a range of potential toxicities, ranging from mildly irritating to life threatening. Although individual and class-specific toxicities are known, it is impossible to predict which patients will develop toxicities and when and how they will respond to treatment of these adverse reactions. Drug toxicities compromise the benefits of antiretroviral therapy, both directly, due to the resulting potentially serious health problems, and indirectly, by discouraging strict adherence to therapy (or indeed remaining on therapy at all).

Toxic effects can be classified by their severity and by whether they are acute or chronic. Specific toxicities may be related to the class of drugs. Gastrointestinal problems are common with protease inhibitors; peripheral neuropathy is seen with d4T, ddI, or ddC. Because of the differences in toxicities, one drug from a particular class may be inappropriate while another from the same class may be well tolerated.[2]

Adherence

Well-informed patients and structured HIV/AIDS management conducted by trained and committed healthcare workers improve adherence, leading to delayed development of viral resistance, delayed virological and treatment failure (the point at which drug therapy no longer prevents disease progression), and improved quality and length of life (McNabb and others 2001). With adherence of less than 70 percent, 82 percent of patients developed virological failure; with adherence of more than 95 percent, failure was reduced to 22 percent during about 12 months of observation (Paterson and others 2000). In a study of 139 patients in Mumbai followed for 12 months, 40 percent had an undetectable viral load and 50–60 percent achieved adherence of more than 95 percent (Hira 2002).

Box 3.1 WHO Guidelines on First- and Second-Line Antiretroviral Therapy

The WHO recommends adoption of a public health approach to antiretroviral therapy. This implies that antiretroviral therapy regimens should be standardized and that only a single first-line and a limited number of second-line regimens be made available through the public sector for large-scale use.

A wide variety of considerations must be reflected in the selection of a first-line regimen. These include potency, side effects, ability to keep future treatment options open, ease of adherence, risk during pregnancy, cost, and the potential for primary acquisition of resistant viral strains (WHO 2002).

Taking into account all of these considerations except cost, the WHO recommends the first-line antiretroviral therapy regimens shown in the table below. Each consists of a dual nucleoside component and a potent third drug, either a nonnucleoside agent or a protease inhibitor. No dual-drug regimens are recommended.

WHO Guidelines on First-Line Antiretroviral Therapy Combination Regimens in Adults and Adolescents with HIV/AIDS

REGIMEN	PREGNANCY CONSIDERATIONS	MAJOR TOXICITIES
ZDV/3TC/EFZ or ZDV/3TC/NVP	• Substitute NVP for EFZ in pregnant women or women for whom effective contraception cannot be ensured	• ZDV-related anemia • EFZ-associated CNS symptoms • Possible teratogenicity of EFZ • NVP-associated hepatotoxicity and severe rash
ZDV/3TC/ABC	• ABC safety data limited	• ZDV-related anemia • ABC hypersensitivity
ZDV/3TC/RTV-PI[1] or ZDV/3TC/NPV	• LPV/r safety data limited • NFV: most supportive safety data	• ZDV-related anemia • NFV-associated diarrhea • IDV-related nephrolithiasis • PI-related metabolic side effects

Note: ZDV/3TC is listed as the initial recommendation for dual NsRTI component based on efficacy, toxicity, clinical experience and availability of fixed dose formulation. Other dual NsRTI components can be substituted including d4T/3TC. d4T/ddI and ZDV/ddI depending upon country-specific preferences. ZDV/d4T should never be used together because of proven antagonism.
1. RTV-PI includes IDV/r, LPV/r and SQV/r.
Source: WHO 2002.

Several second-line regimens have been found to be effective in prolonging the benefits of antiretroviral therapy following treatment failure (see the table below). These regimens should ideally include at least three new drugs, with one from at least one new class. This configuration increases the likelihood of treatment success and reduces the risk of cross-resistance.

WHO Guidelines on Second-Line Regimens in Adults and Adolescents with HIV/AIDS

FIRST-LINE REGIMEN	SECOND-LINE REGIMEN FOR TREATMENT FAILURE	ALTERNATIVE SECOND-LINE REGIMEN FOR TREATMENT FAILURE
ZDV/3TC/EFZ or ZDV/3TC/NVP	• RTV-PI[1] + d4T/ddI	• RTV-PI + ABC/ddI • NFV + ABC/ddI or • NFV + d4T/ddI
ZDV/3TC/ABC	• NNRTI[2] + LPV/r +/– d4T or ddI	• RTV-PI + d4T/ddI
ZDV/3TC/RTV-PI or ZDV/3TC/NFV	• NNRTI[2] + d4T/ddI	• NNRTI + ABC/ddI

1. RTV-PI can be either IDV/r, LPV/r or SQV/r.
2. NNRTI can be either EFV or NVP.
Source: WHO 2002.

A 2001 study published in the *New England Journal of Medicine* found that patients starting treatment with average CD4 cell counts of 87 had a life expectancy of only three and a half years with a triple-drug regimen consisting of AZT, 3TC, and the protease inhibitor indinavir (Freedberg and others 2001). Furthermore, each successive switch of regimen appeared to confer a progressively shorter duration of benefit. In a study of some 400 people on various HAART regimens, Sod and colleagues at the University of Alabama found that only about 25 percent of patients were on their original regimen four years after treatment began (Cohen 2002).

In industrial countries, funds are available to pay for second- and third-line therapies. One of the challenges confronting India and other developing countries is that several important second- and third-line therapies, including protease inhibitors, are still under patent. Saquinivir, the first protease inhibitor patent to expire, will not be off patent until 2010.

Manufacturing and pricing of antiretroviral drugs is a highly charged and rapidly shifting area of policy debate, affected by pressure and negotiations involving both multilateral agreements through the WTO and bilateral negotiations. This analysis assumes that India will respect patents on any antiretroviral drugs that it is not already manufacturing generically.

Source: WHO 2002.

This report assumes an adherence rate for structured antiretroviral therapy of at least 80 percent and an adherence rate for unstructured antiretroviral therapy of less than 80 percent, with an average of about 50 percent. This difference in adherence rates would add four years before the onset of AIDS in patients following structured therapy relative to those following unstructured therapy (table 3.2).

Resistance

Because HIV replicates many times each day and each new generation of virus particles contains many slight genetic variations, a drug regime that permits any replication at all will rapidly select for resistant strains of the virus (Perelson and others 1996; Sugiura and others 2002). To date, the only way to prevent development of resistance is to shut down replication altogether, through 90–95 percent adherence to a therapeutic regime containing one of each of the three classes of antiretroviral drugs. European studies indicate that adherence of less than 95 percent leads to annual resistance rates of 4–6 percent (Paterson and others 2000). In India the annual incidence of antiretroviral therapy drug resistance is reported at 8 percent in programs that carefully monitor their patients (Hira and Gold 2002). However, evidence collected for this report shows that few Indian antiretroviral therapy patients are being monitored closely. Preliminary data from a survey of antiretroviral therapy prescribers suggests that only 30 percent of patients who start antiretroviral therapy remain on therapy one year and that adherence is very poor among the majority of patients (Hira 2003).

Table 3.2 Life Expectancy from Structured and Unstructured Antiretroviral Therapy (years)

PERIOD	NO ANTIRETROVIRAL THERAPY	UNSTRUCTURED ANTIRETROVIRAL THERAPY	STRUCTURED ANTIRETROVIRAL THERAPY
Infection to appearance of symptoms	5	5	5
Appearance of symptoms to failure of treatment	n/a	3 / 1	5
Infection to AIDS	4	3	3
AIDS to death	1	1	1
Total	10	12 / 10	14

Note: n/a = not applicable. Patients are assumed to begin antiretroviral therapy when symptoms appear.
Source: Hira and Gold 2002; Marseille 2003. See also Freedberg and others 2001.

Resistant strains of HIV can be spread to others by any of the three modes of transmission. In Mumbai 18 percent of patients newly diagnosed with HIV were already resistant to at least one antiretroviral drug (Hira 2001).[3] The availability of antiretroviral therapy in India is spreading drug-resistant strains in a manner similar to that in unsupported and unstructured tuberculosis treatments in India and many other countries. There are thus public health as well as therapeutic reasons to maximize adherence of patients receiving antiretroviral therapy.

Resistant strains may develop much sooner than treatment failure. Even when phenotypic and genotypic resistance occurs in one or all classes of antiretroviral medication and the viral load rises, it may take months for the CD4 count to fall and symptoms to occur.

The training of the medical personnel administering antiretroviral therapy may affect the time until resistant strains appear or treatment fails. Better-trained physicians, nurses, and counselors are better able to monitor toxicity, sustain adherence, and recognize and treat or prevent HIV/AIDS–related illnesses. International experience indicates that antiretroviral therapy management requires a multidisciplinary team that includes counseling support to back up medical services (Hira and Gold 2002).

Monitoring the Progress of a Patient's HIV/AIDS Disease and the Efficacy of Antiretroviral Therapy

Assessment and monitoring of people with HIV/AIDS is complex. As news about the availability and efficacy of antiretroviral therapy spreads, the possibility of treatment may encourage people to be tested earlier, leading to the monitoring of more people. Monitoring can be used to decide when to begin antiretroviral therapy, when and if to change therapy, and how to respond to toxicities or resistance.

Monitoring requires collaboration among the patient, the physician, and a diagnostic laboratory. Patients must agree to undergo examinations and laboratory tests even when they feel healthy. Physicians must combine information from clinical examination with that from appropriately chosen laboratory tests in order to craft treatment for patients over the course of their illnesses. Laboratories must use proper management procedures to reduce the occurrence of false test results. Since physicians and their staffs are at the crux of this process, the success of antiretroviral therapy depends critically on the training, professional ethics, and incentives of physicians. Creating a

conducive professional environment for Indian physicians monitoring people with HIV/AIDS will not be easy. But recent progress in the development of monitoring and treatment guidelines for resource-poor settings suggests that sophisticated and expensive laboratory studies are no longer critical to the success of therapy.

Monitoring involves four types of laboratory tests:

- Diagnostic tests to determine whether a person is infected with HIV (the ELISA and Western Blot test).
- Tests of the patient's immune system (the CD4 count or the absolute lymphocyte count).
- Tests of the number of virus particles in the blood (the viral load test).
- Tests for the development of toxic side effects (blood biochemistry tests).[4]

Diagnostic testing, often accompanied by counseling, is the essential first step and should be available to any citizen of India who suspects being infected with HIV. Currently, diagnostic testing is available in only a few major cities in India, and less than 10 percent of people with HIV in India know they are infected. Encouragement of testing, in the right circumstances, is critical for individuals and for public health.

The complexity and cost of monitoring and its contribution to therapeutic success depend critically on the way the patient and physician use the other three types of testing. HIV destroys CD4 cells, an important component of the immune system. The number of these cells in the blood is the most useful marker of disease state and provides an indicator of when to start antiretroviral therapy or prophylaxis for opportunistic illnesses (Mellors and others 1997; Sabin and others 1997). However, the CD4 count is a relatively expensive test and is not available in most resource-limited settings. In India, for example, the cost of the test ranges from Rs. 500 in the public sector to Rs. 1,000 in the private sector. An increasingly acceptable alternative to the CD4 count is a count of the lymphocytes, or white blood cells, in the blood. This test is much more widely available, and at Rs. 60 it is much more affordable than the CD4 count (van der Ryst and others 1998).

Both the CD4 count and the lymphocyte count track the state of the immune system. In contrast, the HIV viral load test goes directly to the source of the problem by counting the number of virus particles in the blood. The viral load test is the best marker of disease progression and the most

accurate predictor of CD4 decline (Mellors and others 1995, 1996). However, the cost of continuous viral load monitoring is Rs. 6,000–8,000 per test for two tests a year, or Rs. 12,000–Rs. 16,000 annually. Viral load tests also require more technical equipment and training and are less accurate than CD4 or lymphocyte tests. Experience is accumulating that good patient monitoring can be performed in resource-poor settings without viral load tests.

The last category of tests—those that monitor liver and kidney function and the effects of the protease inhibitors stavudine and didanosine—become important when treatment begins to fail (Richman and others 1987; Saves and others 2000; Reisler 2001). These tests can help the physician treat the adverse effects of ongoing antiretroviral therapy and alter the drug combination in order to avoid certain toxic reactions. Proper use of this category of tests is a complex and subjective skill, for which guidelines are not fully developed. Furthermore, some of the treatment responses called for in guidelines addressing treatment failure will require pharmaceutical products that are too expensive for all but the wealthiest Indians. Guidelines for the use of this category of tests in resource-poor settings are urgently needed. This report focuses on the costs of the first three types of tests, assuming that India cannot yet afford to increase public financing of the fourth category of testing.

Biological and Behavioral Effects of Antiretroviral Therapy on Transmission

Public policymakers need to consider not only the direct effects of policy on patients receiving antiretroviral therapy but also the indirect effects policy has on new cases of HIV infection. Economists classify the impact of antiretroviral therapy on transmission of HIV as an "externality." Because these externalities are not experienced directly by patients, they are not fully reflected by current market demand. The presence of positive externalities indicates that the unregulated market will produce too little of the commodity, because the price does not reflect the commodity's true societal benefit. It is one of the strongest rationales for government intervention. In theory, consumption of such commodities should be subsidized or otherwise encouraged by governments, just as commodities with negative externalities should be taxed or otherwise discouraged.[5]

Assessing the externalities associated with antiretroviral therapy is therefore an indispensable part of designing policy. All else equal, if antiretroviral

therapy generates net negative externalities, its availability should be limited or targeted specifically to subgroups among which these externalities do not exist. Conversely, the presence of significant positive externalities suggests that financial and other barriers to antiretroviral therapy access should be reduced.

Antiretroviral therapy can have various biological and behavioral effects on transmission (table 3.3). It can slow the transmission of the virus by reducing infectiousness and encouraging prevention. It can speed transmission by selecting resistant strains of the virus; by increasing the longevity of people with HIV/AIDS, thereby increasing the period during which they can transmit the virus; and by "disinhibiting" risky behaviors.

Reduction in Infectiousness

Discussions of the potential benefits of providing antiretroviral therapy in resource-poor countries focus on the ability of antiretroviral therapy to reduce the quantity of HIV in bodily fluids, thereby reducing the risk of transmission (Vernazza and others 1999). Based on the observed reduction in viral load in blood plasma, experts estimate that antiretroviral therapy reduces infectiousness by a factor of two to eight (Chakraborty and others 2001).

Table 3.3 Possible Beneficial and Adverse Effects of Antiretroviral Therapy on HIV Transmission

TYPE EFFECT	BENEFICIAL	ADVERSE
Biological	*Reduces infectiousness.* Therapy may lower viral loads, lowering the risk of transmission per sexual contact.	*Leads to development of resistant strains of HIV.* Imperfect adherence selects for resistant strains of the virus, which can then be transmitted. *Increases duration of infectiousness.* Increased longevity increases the period during which people with HIV/AIDS can transmit the virus.
Behavioral	*Encourages prevention, especially diagnostic testing.* Therapy may increase participation in prevention activities, particularly voluntary counseling and testing.	*"Disinhibits" risk behaviors.* People receiving antiretroviral therapy and both HIV–positive and HIV–negative people may engage in more risky behaviors than they would if the therapy were not available.

Source: Authors' construction.

Much less evidence links reduced viral load in the plasma to reduced transmission. Indeed, some studies have shown that active virus can be isolated from the genital tract even when the virus in the blood plasma is controlled (Zhang and others 1998; Taylor and others 1999; Vernazza 2001), because the plasma and genital tract are separate biological compartments (Zhu and others 1996). A cross-sectional study of 311 HIV–positive women found that the concentration of plasma RNA was a good predictor of HIV shedding in the genital tract (Kovacs and others 2001). Nevertheless, a third of the 27 women who had viral loads of less than 500 copies per millimeter, most of whom were receiving antiretroviral therapy, also had detectable genital tract HIV–RNA. Of these, six had a genital viral load of 10,000–100,000 copies per millimeter.

The concentration of antiretroviral therapy can vary substantially between plasma and genital compartments (Moss and others 1995). For example, less than 5 percent of some protease inhibitor levels (ritonavir and saquinavir) in blood plasma are found in genital secretions. This finding is important because it indicates that transmission may be occurring even though viral load seems to be well controlled. Further research is needed to examine the relation between therapeutic drug levels, plasma, and genital viral loads, especially in men, in whom the separation between the plasma and genital compartments is more distinct than in women.

Antiretroviral therapy–induced reductions in infectiousness depend on how early therapy begins. Recent evidence suggests that transmission occurs disproportionately during the first weeks following infection, when most people are unaware they are infected (Pilcher and others 2001). Antiretroviral therapy is almost always initiated during the latter stages of the disease, as recommended by WHO guidelines on scaling up of antiretroviral drug therapy in resource-limited settings (WHO 2002). The fact that residual virus remains in the genital compartments and that transmissibility may be greatest early in the disease, before antiretroviral therapy is initiated, could limit the preventive benefits of antiretroviral therapy.

Increase in Preventive Activities, Especially Diagnostic Testing

Antiretroviral therapy may increase incentives to use preventive services by motivating people to come forward for voluntary counseling and testing. Greater voluntary counseling and testing in turns means that more people receive prevention counseling. This argument is often cited as part of the

rationale for extending availability of antiretroviral therapy in developing countries; it frequently accompanies the argument that treatment and prevention should be advanced in tandem.

Little evidence is available on the importance of this effect. The magnitude of any prevention effect will be highly context specific and will depend on how many people seek testing and counseling; the proportion of discordance in couples receiving counseling (that is, the proportion of couples in which one partner is HIV–positive and the other is not); and the risk characteristics of both couples and single people receiving counseling and testing. A small beneficial effect of antiretroviral therapy on voluntary counseling and testing might be overwhelmed by the much larger negative effects described below. Policy actions based on the notion that greater availability of antiretroviral therapy will lead to increased voluntary counseling and testing should not be made before the validity of the claim is confirmed through monitoring and evaluation.

Development of Resistant Strains of HIV

Overwhelming evidence from industrial countries reveals that even modest departures from adherence to antiretroviral therapy regimens foster the development of drug-resistant strains of HIV (Miller and Larder 2001), including strains resistant to regimens containing protease inhibitors (Vergne and others 2002).

The presence of these drug-resistant strains limits treatment options and can lead to treatment failure. At the population level, transmission of resistant strains may reduce the benefits of an antiretroviral therapy distribution program. A study of 99 people with HIV/AIDS in the United States documented treatment failure in 22 percent of patients with adherence of at least 95 percent, in 61 percent of patients with 80–94.9 percent adherence, and in 80 percent of patients with less than 80 percent adherence (Paterson and others 2000).

In Mumbai 18 percent of people recently diagnosed with HIV had resistance to at least one antiretroviral drug. Although India has had access to antiretroviral therapy only since 2001 this figure is already higher than the 14 percent of newly infected people estimated to carry resistant strains of HIV in North America in 2001 (Marseille 2002; Little and others 1999). As the percentage of recently diagnosed people with resistant strains grows over time, the inexpensive generic brands of antiretroviral therapy drugs currently available in India will cease to be effective. Unless Indian pharmaceutical manufacturers are able to produce generic versions of all these newer drugs,

people with HIV/AIDS will have no choice but to buy imported drugs, at prices that will be beyond the reach of all but a tiny minority.

Increased Duration of Infectiousness

The increased longevity associated with antiretroviral therapy increases the period during which people with HIV can transmit the virus. The magnitude of the effect depends on how much additional longevity antiretroviral therapy provides. The WHO Commission on Macroeconomics and Health estimates that antiretroviral therapy adds four years to the lives of people with HIV/AIDS (Marseille 2003). This estimate falls between the 10 years that may be achievable under clinical trial conditions and the 2.5 years before treatment failure that has been observed in some settings. Other estimates are available from industrial countries, but they may not be relevant in India.

Disinhibition of Risky Behavior

Government interventions and individual decisions have reduced the frequency of sexual partner change, increased condom use, improved treatment for sexually transmitted disease, and reduced needle sharing in Australia, Europe, North America, Senegal, Thailand, Uganda, and parts of Kenya. In all of these places people have curtailed their risky sexual and drug-using behavior, partly because of worry about AIDS (Stigum and others 1997), and the rate of new HIV infections has declined. Tamil Nadu has documented similar gains (figure 2.3).

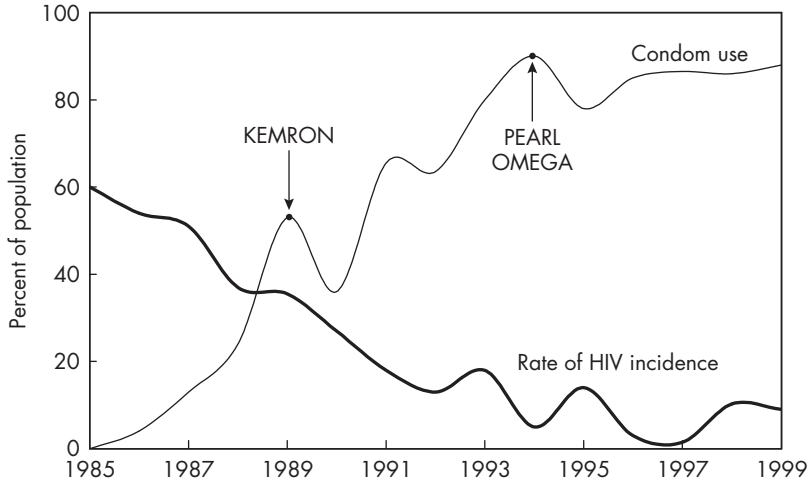
Evidence is mounting that antiretroviral therapy may reverse these trends. Aware that treatment exists, people may be less inclined to avoid risky behavior (Van de Ven and others 1999, 2002; Stolte and others 2001; Suarez and others 2001; Stephenson and others 2003). This potential relaxation of preventive behavior as a result of the availability of treatment is known as "disinhibition."[6]

Studies of men who have sex with men in Europe and the United States have shown that the presence of potent antiretroviral therapy may induce both HIV–positive and HIV–negative men to engage in riskier behavior than they would in the absence of such therapies (Marseille 2002). A cross-sectional interview-based study of men in San Francisco who have sex with men found that the percentage who reported both unprotected anal intercourse and multiple sexual partners increased from 24 percent in 1994 to 45 percent in 1999, the period during which antiretroviral therapy became widely available (Katz and others 2002; Page-Shafer and others 1999).

Evidence on disinhibition in developing countries and among heterosexuals is scant, although there is some indication that similar dynamics may operate in developing countries. The Brazilian Ministry of Health attributed the recent 3.7 percent rise in the national incidence of HIV/AIDS to decreased condom use in young men who have sex with men, noting that the decline seemed to have begun after the introduction of antiretroviral drug therapy, which Brazil provides free to all Brazilians with AIDS (*Washington Times*).

The most remarkable data on this point come from a long-term study of condom use in Kenya during a period in which two reported "cures" for AIDS, Kemron and Pearl Omega, were announced and widely touted by government leaders (figure 3.1). After each announcement condom use dropped substantially during encounters with a sample of sex workers. After the advertisement of Pearl Omega, the incidence of HIV infection increased. Eventually the ineffectiveness of these drugs against AIDS became apparent. In both episodes it took more than a year to reestablish previous levels of condom use. Whether the drop in condom use was caused by the public announcements cannot be established, but the association is sufficiently striking to serve as a warning to

Figure 3.1 Reduction in Condom Use in Kenya Following Announcements of "Cures" for AIDS



Source: Jha and others 2001.

India and other countries of the possibility of substantial disinhibition of risky behavior as a result of expanding access to antiretroviral therapy.

Notes

1. The practice of combining a drug from each of three classes is referred to as highly active antiretroviral therapy (HAART).
2. A background paper provides guidelines for the management of selected adverse effects of antiretroviral drugs that usually do not require drug discontinuation (Hira and Gold 2002).
3. "Primary resistance" is defined as the presence of a resistant strain of virus in a newly infected person. The development of resistance during antiretroviral therapy is known as "secondary resistance."
4. A fifth category of tests measures infectiousness by counting the virus particles in the patient's bodily fluids. This type of testing, while potentially important, is difficult and is found only in research settings.
5. Immunization to prevent the transmission of an infectious disease is an example of a product with positive externalities, since the vaccine not only protects the person receiving it but also protects others who otherwise might have contracted the disease. Immunization should therefore be priced lower than supply and demand in a free market would dictate. Industrial pollution is a classic example of a negative externality. The health problems and dirty environment resulting from the pollution are not experienced directly by the firm that pollutes. In an unregulated market, it will therefore produce more pollution than is socially optimal. Social welfare is increased if governments induce firms to internalize these costs—for example, by taxing pollution.
6. People whose houses are insured against fire are more likely to experience house fires. That people relax efforts to prevent a mishap when they know that some of the consequences of the mishap will be mitigated by insurance is a well-known obstacle to the market provision of inexpensive insurance. In some cases, this problem can be so severe as to render such insurance unaffordable. In the economics and insurance literature this entirely rational feature of human behavior is known by the infelicitous term "moral hazard."

CHAPTER 4

Projecting the Course of India's HIV/AIDS Epidemic without Policy Change

The impact of a policy change can be assessed only relative to what would have happened in the absence of that change. This chapter describes current AIDS treatment in India and projects the future course of India's AIDS epidemic in the absence of policy change. It first proposes a general framework for assessing AIDS treatment policy and its effects that could be applied to any country. It then describes the epidemiological model and presents projections in the absence of policy change. Box 4.2 at the end of the chapter summarizes the experience of other countries with government-financed antiretroviral therapy.

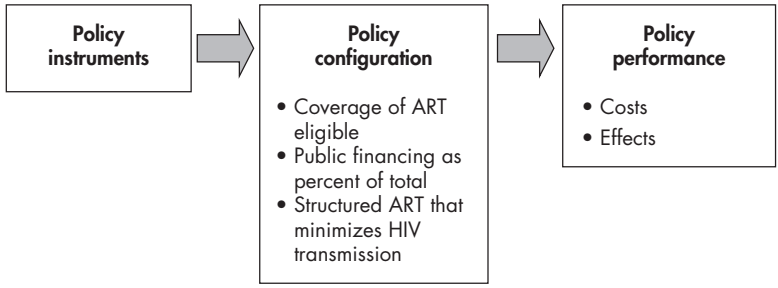
A Framework for Analyzing Antiretroviral Therapy Policy

The performance of an antiretroviral therapy policy can be measured by the difference between the economic costs and epidemiological consequences incurred by that policy and the costs and consequences that would occur in the absence of any policy change. The costs and consequences are determined by the manner in which antiretroviral therapy is provided, or the "configuration" of antiretroviral therapy provision in the society (figure 4.1). This configuration is in turn determined by government policy and by features of the environment beyond the government's control.

Configuration of Antiretroviral Therapy Provision

Fully describing the delivery of antiretroviral therapy in a country would require detailed data. For the purposes of policy design, it may be sufficient

Figure 4.1 Policy Framework for Antiretroviral Therapy



Source: Authors' construction.

to focus on three attributes: coverage, the public-private mix, and the transmission-minimizing structure.

"Coverage" refers to the percentage of people receiving antiretroviral therapy as a percentage of those whose disease progression makes them eligible for such therapy. The fact that a person is covered does not necessarily imply that he or she is receiving high-quality care; the person may be self-medicating with antiretroviral therapy drugs purchased from a pharmacy. Coverage refers merely to the consumption of antiretroviral therapy drugs. About 11,700 people in India are currently receiving antiretroviral therapy. Assuming that 400,000–500,000 people in India are eligible for such therapy, coverage is about 2.4–3.0 percent.

The "public-private mix" refers to the proportion of public sector spending in total spending. Overall, India's public sector finances and provides about 10–20 percent of total health care spending. The proportion of public spending on antiretroviral therapy costs is much smaller. Given that people with AIDS are often refused treatment at public hospitals, the percentage of public spending on antiretroviral therapy is probably about 5 percent.

"Structure" refers to the set of resource utilization patterns, decision rules, and counseling practices that guide the service delivery process for people with HIV/AIDS. Because antiretroviral therapy is a rigorous therapy requiring precise actions by both the physician and the patient, the concept of "structured" antiretroviral therapy treatment has been developed to define model clinical practice. The elements of structured treatment vary somewhat from country to country and are in the process of being defined in India. For

the purposes of this report, structured treatment consists of the following elements:

- Standardized training of physicians to a mandated level of competence in antiretroviral therapy management.
- Prescription of a standard combination drug regimen, as recommended by national guidelines.
- Access to support from a multidisciplinary team, including a counselor and a nutritionist.
- Access to a good-quality laboratory for immunological testing.
- Regular clinical and laboratory-based monitoring of patients' treatment status.
- Provision of counseling to prevent transmission.

Structured treatment is the touchstone of quality antiretroviral therapy care. Either the public or the private sector could deliver structured treatment, provided care adheres to the above criteria. To the extent that structured treatment maximizes adherence and thereby minimizes the transmission of resistant strains of the virus, this model also addresses the public health imperative to slow transmission. However, as typically described and practiced, structured treatment does little to address the risk behavior of people not under treatment.

As chapter 3 suggests, disinhibition of the risk behavior of people who engage in the riskiest activities could easily negate the beneficial effects of antiretroviral therapy. This report therefore proposes a mechanism for delivering antiretroviral therapy that could facilitate safe behavior by groups within which the virus is spreading most rapidly. "Transmission-minimizing antiretroviral therapy" consists of structured antiretroviral therapy treatment, incentives to state and local government and community leaders to improve prevention programs, and monitoring and evaluation of the effectiveness of both treatment and prevention programs. In a well-functioning transmission-minimizing antiretroviral therapy program, these three elements work together to achieve public health goals.

Several features of prevention programs in India suggest that it may be possible to link incentives for prevention among high-risk groups to an antiretroviral therapy treatment program. First, as in most countries, physicians

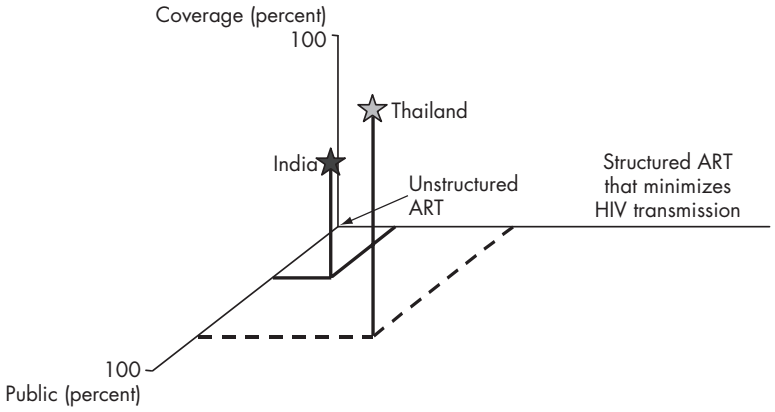
who are most engaged in treating AIDS patients have little direct interaction with AIDS prevention programs, which are operated by NGOs and typically do not perceive the need for highly qualified, and therefore expensive, medical personnel. If India begins to finance antiretroviral therapy, even on a limited basis, the danger of disinhibition is that some people at greatest risk of AIDS may believe that they no longer need to worry about the health consequences of risky sexual behavior. They will need to hear the messages "antiretroviral therapy is not a cure for AIDS" and "even with antiretroviral therapy you will be very sorry to have contracted AIDS." Prevention-oriented NGOs may lack credibility with their target groups. The target populations with whom NGOs work may suspect, for example, that condom manufacturers and retailers have an interest in scaring people into using condoms. Physicians who are treating patients with antiretroviral therapy, together with patients who volunteer, will be the most persuasive bearers of these messages. It is thus critical to find mechanisms to engage the leading antiretroviral therapy treatment physicians in prevention programs in their states.

Second, the success of state-level AIDS control programs varies a great deal from state to state. Condom use during high-risk contacts, while close to 75 percent in a few states, is as low as 25 percent in others. Coupling aspects of antiretroviral therapy financing with prevention performance at the state level could motivate less aggressive states to improve their efforts, efforts that would prevent hundreds of thousands of HIV infections.

The opposite of transmission-minimizing antiretroviral therapy is transmission-maximizing antiretroviral therapy. Antiretroviral therapy that is unstructured and therefore permits or even encourages intermittent monotherapy rather than regular and sustained triple-therapy maximizes the creation and spread of resistant viral strains. In the absence of incentives to improve prevention as well as monitoring and evaluation to measure the development of resistance and the reemergence of risky behavior, financing antiretroviral therapy is likely to cause a public health disaster for India.

Individual countries will want to compare their policy choices with those of other countries. Figure 4.2 illustrates the three dimensions of a country's antiretroviral therapy policy configuration, situating India and Thailand with respect to all three dimensions. Thailand is currently planning to expand its antiretroviral therapy policy by offering a form of structured antiretroviral therapy in its public health facilities. It is not clear how it will monitor the quality of care. There has been no discussion of coupling antiretroviral therapy financing with prevention incentives in order to achieve transmission-minimizing antiretroviral therapy. As information on the coverage, pub-

Figure 4.2 Antiretroviral Therapy Policy Configurations in India and Thailand



Note: Structured ART could be public or private, but must adhere to the criteria listed in the text. Unstructured ART is more haphazard and more likely to generate viral resistance.

lic-private mix, and prevention effects of other countries' treatment policies becomes available, it will be possible to add them to this figure, easily identifying clusters of countries with similar policy configurations.

Policy Instruments Affecting the Configuration of Antiretroviral Therapy

How can the Indian government affect the three dimensions of the policy configuration? An increase in antiretroviral therapy financing would increase coverage and the percentage of public spending, but the effect on transmission reduction is not clear.

Structured antiretroviral therapy includes voluntary counseling and testing, tests to determine the stage of infection, triple-drug antiretroviral medications, physician visits, and public information campaigns about the advantages and limitations of antiretroviral therapy. The government could finance all or some of these components, or it could subsidize them at different rates. Various forms of nonprice rationing, such as eligibility criteria or waiting lines, could be used to steer patients toward structured treatment. Eligibility criteria could be used both to improve the structuring of treatment and to achieve equity objectives.

Box 4.1 Performance-Based Fiscal Mechanisms in India

The government is currently using a variety of policy instruments to provide incentives to state governments to undertake economic reforms. One class of performance-based policy instruments is intergovernmental fiscal transfers (Bardhan 1996, 2002; Jin and others 1999; Zhuravskaya 2000). Some of these transfers seek to promote broad policy changes at the state level; others target specific sectors or local governments. In some schemes the fiscal resources are disbursed as budgetary support; in others they finance sector-specific investments.

Performance-based schemes in India include the Fiscal Reform Facility (general fiscal reform), APDRP (power sector), RGDWM (drinking water), and PMGSY (rural roads). These performance-based schemes have also been proposed in the urban sector, but details have yet to be worked out. These schemes are new and the lessons of experience are only now becoming apparent.

Experience with the operation of these schemes and with the design of schemes proposed for the urban sector indicates that the following features are essential:

- A clear policy framework within which the scheme operates.
- A clear and agreed on mechanism for independent evaluation of state proposals for funding.
- Effective project implementation and monitoring and evaluation capacity.
- Focused Memoranda of Agreement that specify the performance-based mechanism.
- Project monitoring and evaluation by an independent third party.
- Willingness by both the national and state governments to make disbursements conditional on monitoring and evaluation results.
- Where necessary, capacity building as an integral part of the program. Both multilateral and bilateral donors can contribute by supporting the development of capacity for performance-based mechanisms at both the national and state levels of government.

Antiretroviral therapy involves patients, physicians, state and local government officials, AIDS organizations, and prevention-oriented NGOs. Instruments that could affect the behavior of these participants include national funding of a medical center of excellence for structured antiretroviral therapy treatment, creation of a brand name signifying high-quality AIDS treatment and franchising of the brand to private sector physicians, and provision of state and local block grants for structured antiretroviral therapy, which are conditional on prevention performance. Box 4.1 gives examples of existing performance-based fiscal mechanisms in India on which transmission-minimizing antiretroviral therapy could be modeled.

As an alternative to providing incentives to state governments, a transmission-minimizing antiretroviral therapy program could couple structured treatment with prevention incentives aimed at consortia of treatment and prevention institutions. For example, the national government could solicit joint proposals from medical centers applying for antiretroviral therapy treatment funds and NGOs responsible for HIV prevention in the same city. To encourage transmission-minimizing antiretroviral therapy, the government could channel funding to those consortia that best manage the twin tasks of treatment and prevention.

Measuring the Effects of Antiretroviral Therapy Policy

Antiretroviral therapy will have both immediate effects and effects that will be felt only in the future. Expanded use of antiretroviral therapy could reduce the number of AIDS orphans, for example. Children who lose their mother at age one will suffer 14 years of under-15 orphanhood, a welfare loss that can never be reversed. Assuming that the average child is seven years old when orphaned, government policy slows HIV infection rates in the current year will have most of its impact on orphanhood 7–15 years later. Since orphanhood is one of the most important consequences of an HIV/AIDS epidemic and its avoidance one of the most important benefits of intervention, these long-term consequences must be considered in setting policy.

Because these effects cumulate over time, analyses of impact that adopt a 5- or even a 10-year time horizon fail to provide policymakers with a full view of the legacy they are passing on to the next generation. A medium-term analysis would ignore any costs or benefits, such as unavoidable future years of orphanhood, that occur beyond the chosen horizon.

If a longer perspective is adopted, future costs and benefits must be discounted by a social discount rate. This report presents results for two discount rates, 10 percent and 0, the upper and lower bounds on rates an Indian decisionmaker might select.[1]

The model examines 4 years of historical data and projects 31 years into the future, a period long enough to observe temporary trends reverse themselves due to longer-run influences. A longer period is not necessary, because at a 10 percent discount rate, $1 saved at the end of a 31-year projection period is equivalent to just $0.05 today and one life-year saved at the end of the period is equivalent to just 19 days saved in 2002.[2]

Many alternatives exist for measuring the health effects of interventions. These include using deaths prevented, quality-adjusted life-years saved, and dollar values of these quantities. This report uses three measures of health impact: HIV/AIDS cases prevented, life-years saved, and years of orphanhood prevented. Assuming that the average HIV–infected person dies at age 32 and that life expectancy would otherwise have been 60, every HIV infection prevented adds 28 years of life. The model does not attempt to adjust the saved life-years for the disability experienced by a symptomatic person with HIV/AIDS or by a person on antiretroviral therapy who suffers from the toxic side effects of treatment.

Measuring the Costs of Antiretroviral Therapy Policy

To an individual making a decision about antiretroviral therapy, what matters is the projected health benefit from the therapy compared with the cost the individual and his or her family must incur. To the decisionmaker at the Ministry of Finance, what matters is the opportunity cost of budget allocations to antiretroviral therapy in terms of alternative uses (building bridges, paying the salaries of schoolteachers or judges). This report focuses on the perspective of the Ministry of Health official who has been allocated a certain budget for AIDS and must decide how to allocate it between treatment and prevention.

This decisionmaker is interested in both the budgetary costs of antiretroviral therapy and the opportunity costs of that therapy in terms of forgone health-improving activities, including HIV prevention. Budgetary costs can be estimated using simple unit cost assumptions about the cost of antiretroviral therapy per patient-year. These assumptions allow for neither economies nor diseconomies of scale. Cost studies currently underway in India may improve these estimates and allow for adjustments in the estimated costs used in this report.

Antiretroviral therapy helps postpone the cost of treating opportunistic illnesses in people with AIDS who otherwise would have sought and received treatment in public facilities. In the United States and Brazil the cost savings associated with these treatments has been cited as sufficient economic justification for government financing of AIDS treatment. These potential benefits are limited in India because, in contrast to the United States and Brazil, only 10–20 percent of AIDS patients receive government-subsidized treatment for their opportunistic illnesses. Furthermore, depending on the design of a government subsidy, resources saved by the improved health of people receiving subsidized antiretroviral therapy may be consumed by other poor AIDS patients, thereby eliminating any cost savings. The health benefits of treating opportunistic illnesses are also thought to be small at best.

This report assumes that one out of every five patients whose antiretroviral therapy is subsidized by a government program would have otherwise received government-subsidized treatment for his or her opportunistic illnesses. The cost per patient to the government of such treatment is estimated at $100 a year for three years and $800 during the year before death

Table 4.1 Cost and Timing of Treating Opportunistic Illnesses of Average Indian with HIV under Different Antiretroviral Treatment Regimens (circa 2002)

ITEM	NO ANTIRETROVIRAL TREATMENT	UNSTRUCTURED ANTIRETROVIRAL TREATMENT	STRUCTURED ANTIRETROVIRAL TREATMENT
Infection to symptoms	5 years @ $0	5 years @ $0	5 years @ $0
Symptoms to treatment failure		3 years → 1 year @ $25	5 years @ $0
Time to AIDS	4 years @ $100/year	3 years @ $100/year	3 years @ $100/year
AIDS to death	1 year @ $800	1 year @ $800	1 year @ $800
Lifetime costs			
Discounted at 0 percent	$1,200	$1,175	$1,100
Discounted at 10 percent at time of treatment	$814	$660	$494
Discounted at 10 percent at time of infection	$505	$410	$307

Note: These cost estimates were used as the basis for estimating benefits of the second World Bank–supported Indian National AIDS Control Project. See table 3.2 for timing assumptions.
Source: World Bank estimates

(table 4.1). If the patient receives antiretroviral therapy, these costs are postponed until after treatment failure.[3] In addition to the health benefits of antiretroviral therapy, there is thus a budgetary benefit for each person started on structured antiretroviral therapy. If no value is placed on postponing costs (that is, the discount rate is zero), the cost savings are small: $25 for unstructured antiretroviral therapy and $100 for structured antiretroviral therapy. At a discount rate of 10 percent, unstructured antiretroviral therapy reduces costs from $814 to $660, for a savings of $154, or about 19 percent of the cost of treating opportunistic infections per patient. Structured antiretroviral therapy saves $320, or about 39 percent of the cost of treating opportunistic infections.

Policymakers need to compare life-years saved from antiretroviral therapy with life-years saved from other interventions at the same cost. Because such data are not available for India, data from Africa are used as a proxy for the costs of saving lives through various interventions in India.

Studies in Africa estimate the cost per disability life-year saved at $1 for condom distribution and $19 for prevention of mother-to-child transmission (Marseille 2002). Assuming that these prevention options form part of an integrated program with the mix as shown in table 4.2, the cost of saving one life-year would be about $12.50. In the absence of research from India indicating much higher costs per saved life-year, policymakers should assume that increased expenditure on these typically underfunded classic interventions could purchase life-years at these low prices.

Table 4.2 Opportunity Cost of Antiretroviral Therapy in Terms of Forgone HIV/AIDS Prevention

HIV PREVENTION INTERVENTION	COST PER DALY (DOLLARS)	BUDGET ALLOCATION (PERCENT)
Mother-to-child transmission prevention	19.00	20
Female condoms for child sex workers	1.00	10
Sexually transmitted disease control for child sex workers	1.00	10
Sexually transmitted disease control (general)	13.00	25
VCT	17.78	25
Blood supply safety	8.00	10
Weighted average cost per DALY	**12.50**	

Note: Cost per DALY for hypothetical national HIV prevention program using cost-effectiveness estimates based on African studies.
Source: Marseille 2004.

The Challenge Facing Policymakers

The challenge facing Indian policymakers is to understand how the policies they establish—and the intensity with which those policies are implemented—will affect the antiretroviral therapy policy configuration, especially as it affects HIV transmission, and what costs and health consequences for Indian society will be created by their choices. Because the epidemic is slow and has strong momentum, guiding it is like navigating an ocean liner: current changes in direction take a long time to change the course of the epidemic. Decisions on the speed and direction of the ship must be made now in order to affect its trajectory in the future, keeping it out of danger in the years ahead.

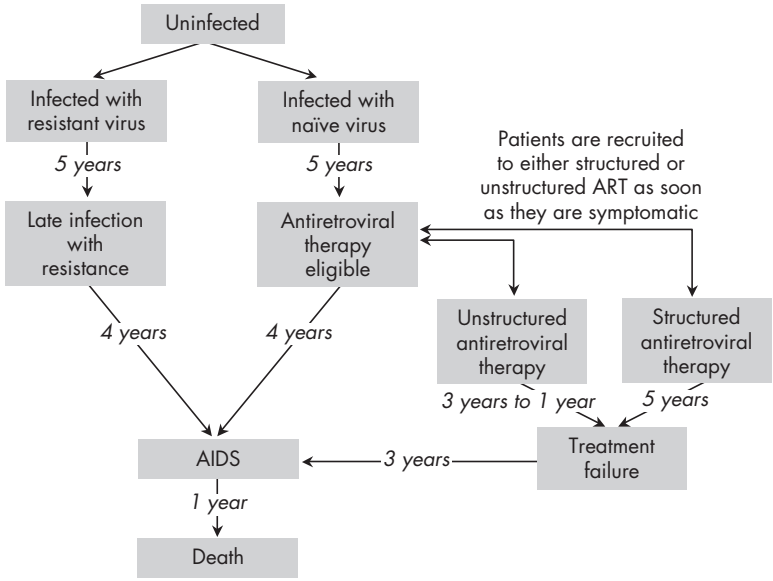
Structure of the Epidemiological Projection Model

An epidemiological projection model developed by Nagelkerke, Plummer, and Jha (2001) was modified to estimate the health consequences of alternative government policies. The structure of the model is designed to capture the stages of HIV disease.

The model draws on the international AIDS literature to set biological parameters for the progression of transmission and disease. The pathways an infected person follows from infection to death depend on whether the person is infected with a resistant or naive virus and whether he or she has access to antiretroviral therapy at the onset of symptoms (figure 4.3).

The model assumes that the probability of transmission of HIV from a male to a female on a single sexual contact is 0.0052 and the probability of female to male transmission is 0.0036. These transmission probabilities apply to untreated infected people over the duration of their infection. Infectiousness is assumed to be 24 percent lower than average during the five-year period before symptoms emerge and, in the absence of treatment, 30 percent higher than average during the symptomatic period.[4] Unstructured antiretroviral therapy treatment is assumed to reduce infectiousness by 50 percent, while structured antiretroviral therapy eliminates transmission altogether. After treatment failure these effects are vitiated and infection can occur. People for whom treatment has failed as well as people whose primary infection is with a resistant virus will transmit resistant viruses.

Figure 4.3 Structure of Treatment Portion of Epidemiological Projection Model

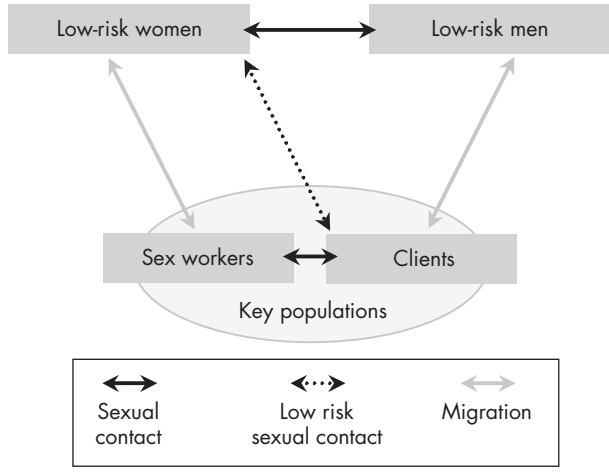


Note: Structured ART could be public or private, but must adhere to the criteria listed in the text. Unstructured ART is more haphazard and more likely to generate viral resistance.
Source: Authors' construction.

The model of transmission divides the population into four groups based on their sexual behavior: low-risk men, low-risk women, male clients of sex workers, and female sex workers (figure 4.4). Each of these groups is divided into a small subgroup of people infected with HIV and the majority, who are not infected and are therefore susceptible to infection, making a total of eight subgroups. (The split into infected and uninfected subgroups is shown in figure 4.3 but not in figure 4.4.)

At the beginning of a simulation, the proportion of adults in each of the eight groups is fixed. When the model is run, the numbers of people in each category change as a result of births and deaths (not shown in figure 4.4) and "migration" of individuals between high- and low-risk categories (solid grey arrows). Rates of sexual contact between low-risk men and women and between sex workers and clients are based on the assumptions

Figure 4.4 Model of Sexual Transmission of HIV



Source: Author's construction.

described below. These sexual contact rates (shown as solid black arrows in figure 4.4), in combination with the assumptions described above, determine the rate of growth of HIV/AIDS prevalence, the demand for antiretroviral therapy, and the costs and consequences of any antiretroviral therapy policy.

The model assumes that in 1998, at the start of the simulation run, 15 percent of the adult male population (37.5 million men) were clients of sex workers, with each client purchasing 50 sexual contacts a year. The model also assumes that 1.1 percent of the adult female population (or 2.8 million women) were sex workers, so that the average sex worker had about 675 commercial sex transactions a year.[5] Condoms were used during half of these commercial sex transactions, reducing the probability of infection to zero in those cases. These assumptions are based on the sketchy information available on numbers of sex workers and on a survey of sexual behavior.[6]

What Would Happen without Policy Change?

The estimated impact of a policy change depends critically on what one believes would happen in the absence of the change. A key question in this regard is how fast the Indian population would adopt antiretroviral therapy

in the absence of policy. Panel a of figure 4.5 shows the rate of adoption of a key component of antiretroviral therapy, and the associated decline in mortality, in a cohort of patients in Europe. The proportion of patients using a protease inhibitor in combination with other antiretroviral therapy drugs rose from 0 to 80 percent within two years, with most of the change taking place in a single year. Deaths among these patients declined by two-thirds, from 30 per patient-year to about 10 per patient-year over the same period, presumably as a consequence of the therapy.

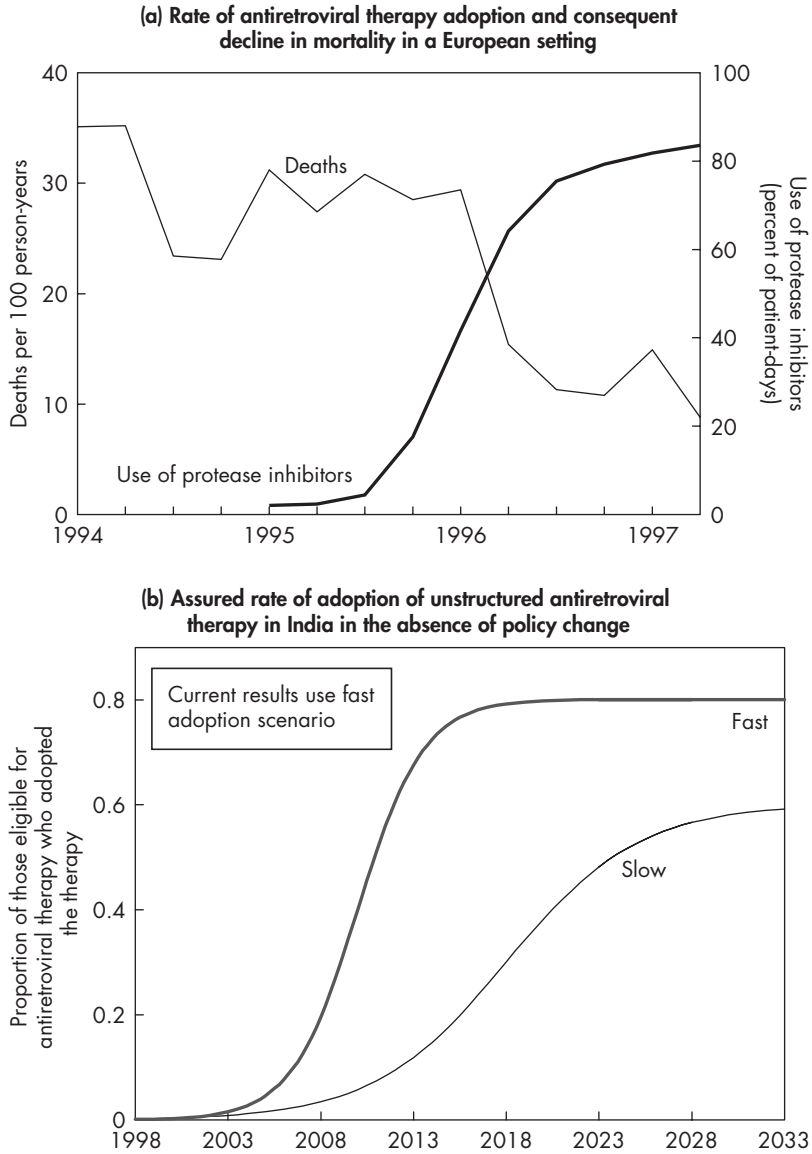
This dramatic change occurred in a wealthy country in which insurance coverage was available for the thousands of dollars of drugs and clinic time consumed by these patients. Given that insurance coverage is almost nonexistent in India, in the absence of government intervention, the growth of structured antiretroviral therapy programs is likely to be slow, perhaps 2 percent a year. Growth will be constrained by both the limited capacity to raise funds from private sources and the need to reallocate and train healthcare workers.

The baseline model assumes that the unstructured use of antiretroviral therapy will grow steadily, until half of symptomatic HIV–infected Indians are under some kind of antiretroviral therapy by 2013 and 80 percent are under treatment by 2018. A slower pattern of adoption could occur if the government decided to retard the growth of unstructured antiretroviral therapy on the grounds that it is less effective than structured therapy (figure 4.5, panel b). This option seems unlikely, however, in view of India's tradition of unfettered private sector health care and of the potential lobbying strength of the growing numbers of people with HIV infection.

Unstructured therapy is assumed to yield lower rates of patient compliance than structured care and therefore to yield a smaller health benefit for patients. Because treatment failure generates resistant viruses, the steady growth of unstructured care is likely to facilitate the spread of strains of AIDS virus that cannot be treated with first-line therapies. In the absence of government policy, the quality of unstructured care will decline as it spreads.

The baseline scenario thus assumes that if India adopts no AIDS policy, an increasing proportion of Indians with AIDS will achieve modest health gains by accessing antiretroviral therapy in the private sector. However, these gains will be eroded by the decline in the quality of unstructured antiretroviral therapy and by the spread of resistant strains. Relative to this baseline, what could India gain from financing a portion of antiretroviral therapy—and at what cost?

Figure 4.5 Adoption of Antiretroviral Therapy in Europe and India



Source: Panel a is from Palella and others 1998. Panel b was constructed by the authors.

Baseline Epidemiologic Projections

The model projects the course of the Indian AIDS epidemic (figure 4.6).[7] The engine of the epidemic is the prevalence rate among the key populations most at risk of contracting and transmitting HIV/AIDS. Under the baseline assumption of 50 percent condom use during high-risk sexual contacts, prevalence among sex workers is projected to increase from its current level of about 15 percent to about 44 percent in 2033. Prevalence among clients of sex workers will increase from the current rate of about 4 percent to about 15 percent by 2033. Because both of these groups have contacts with low-risk categories, these high rates of infection will gradually spill over into the general adult population.

Within the general population, prevalence is projected to rise from the current level of less than 1 percent to almost 4 percent. In contrast to epidemiologic projections in other parts of the developing world, these projections indicate higher rates of infection among men than among women.

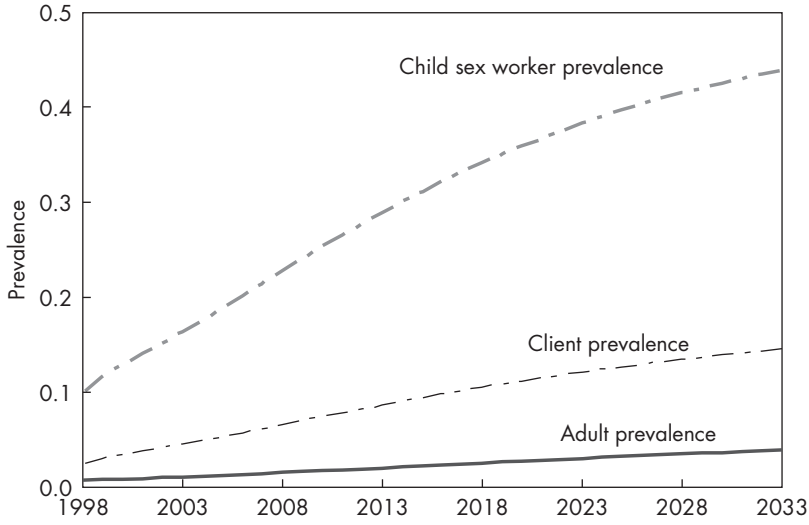
As a result of increasing access to unstructured therapy, the number of people with resistant strains is projected to grow faster than the number of people with nonresistant strains. By the end of the period, more than half of people with HIV/AIDS will be untreatable with generic medications currently available in India.

India has signed international agreements on intellectual property rights and must begin to enforce compliance among generic drug manufacturers. As a result of these agreements, Indian generic manufacturers will not be permitted to copy the newest antiretroviral therapy drugs and produce them at low prices. Thus Indians infected with resistant strains of the virus will not be able to benefit from inexpensive versions of second line drugs now available. Given that first-line therapies will fail immediately, produce side effects, and be costly, the model assumes that people with resistant strains of HIV will not seek antiretroviral therapy and that the government will allocate no resources for antiretroviral therapy in people with resistant strains of the virus. The progression of their disease will thus pass from early stage infection directly to late stage infection and then to AIDS and death.

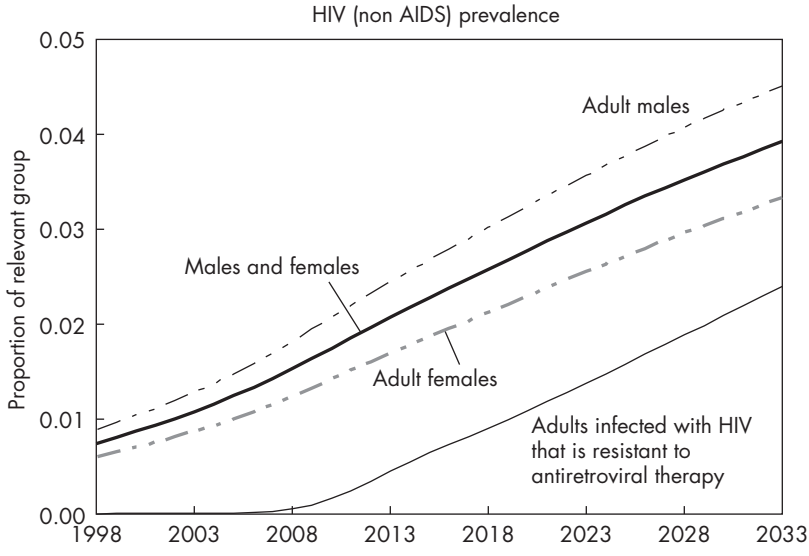
The model also projects the growth of structured and unstructured antiretroviral therapy (figure 4.7). (Because the number of people in structured treatment is very small relative to the projected growth of unstructured treatment, the figure's vertical axis uses a logarithmic scale.) The number of people in structured treatment is projected to rise from the current level of about 2,000 to about 10,000 by 2033. The number of people using unstructured

Figure 4.6 Projected HIV Prevalence Rates in Baseline Scenario

(a) Projected HIV prevalence rates among high-risk adults in India, 1998–2033

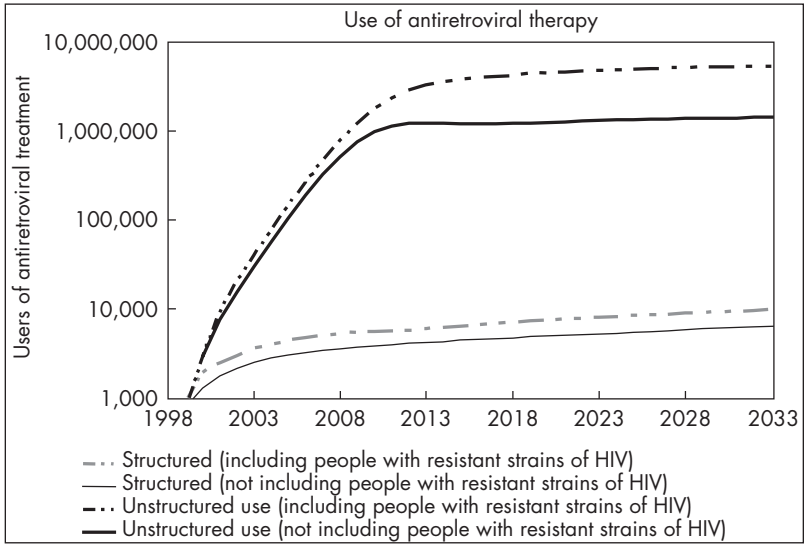


(b) Projected HIV prevalence rates among entire adult population in India, 1998–2033



Source: Authors' calculations.

Figure 4.7 Projected Growth of Antiretroviral Treatment in the Absence of Policy, 1998–2033



Note: Structured ART could be public or private, but must adhere to the criteria listed in the text. Unstructured ART is more haphazard and more likely to generate viral resistance.
Source: Authors' construction.

treatment is projected to rise from the current level of about 10,000 to about 3 million people in 10 years, when it will begin to be constrained by the size of the epidemic. By 2033 the number of people in unstructured treatment programs will reach 5.3 million, 3.9 million of whom will be infected with resistant strains.

Treatment is assumed to postpone disease progression, with a three-year delay from treatment onset until treatment failure for unstructured treatment and a five-year delay for structured treatment. Patients continue to receive treatment during the three years before the onset of AIDS and the year between the onset of AIDS and death. The gaps between the dashed lines and the corresponding solid lines in figure 4.7 represent the projected number of patients who develop resistant strains of the virus and can potentially transmit those strains until they contract AIDS and cease sexual activity, usually because they are too ill. This gap remains small and constant for people on structured treatment (the bottom pair of lines), but it grows for people on unstructured treatment (the top pair). By 2033, 1.4 million of the

5.3 million people on unstructured treatment are projected to have resistant strains of the virus.

In this baseline scenario, HIV/AIDS will become the dominant cause of death in India, accounting for 17 percent of all deaths and 40 percent of all infectious deaths, as illustrated in figure 2.2. This baseline assumes no change in antiretroviral therapy policy and stagnation in prevention policy, with condom use during high-risk sexual contacts remaining at 50 percent.

Box 4.2 International Experience with Government-Financed Antiretroviral Therapy

Developing countries have introduced antiretroviral therapy through a variety of mechanisms, including the first phase of the UNAIDS–sponsored Drug Access Initiative in Chile, Côte d'Ivoire, Vietnam, and Uganda. Perhaps the boldest and certainly the largest-scale program is that in Brazil, which in 1996 enacted universal free access to antiretroviral therapy for all Brazilians in need. Government agencies, NGOs, and academic institutions in Haiti, Senegal, South Africa, Thailand, and elsewhere have undertaken smaller initiatives.

Most experience with antiretroviral therapy in developing countries is from Latin America and Sub-Saharan Africa, regions that differ from India in terms of culture, demographics, health systems, and epidemiology. Even within Africa and Latin America there is a substantial range in reported outcomes of antiretroviral therapy (see table). Lessons for India must therefore be drawn cautiously.

Clinical Benefits

A substantial body of evidence indicates that antiretroviral therapy can provide the same level of clinical benefits in resource-poor settings as in industrial countries. These benefits include dramatic increases in CD4 cell counts, reduction of viral loads to or close to undetectable levels, reductions in AIDS–related death rates, and the recovery of high levels of functioning and well-being. In some settings, however, results have been less encouraging. Only 58 percent of those enrolled in the Uganda Drug Access Initiative remained alive and in treatment after two and a half years (UNAIDS 2000). This high mortality rate may partly reflect the late stage of disease at which these patients entered treatment. Evidence from other studies is equivocal and may reflect differences in adherence.

(continued)

Box 4.2 continued

Adherence

Experience strongly suggests that antiretroviral therapy programs put sufficient resources into supporting high levels of adherence counseling and monitoring. Review of cross-cultural studies indicates that high levels can be achieved but that the range of adherence levels is wide. Data from India and Uganda indicate that drug cost can be a significant barrier to adherence. A program of operations research to identify effective adherence techniques specific to India may be useful.

Higher levels of adherence can be attained with less complex regimens, such as those consisting of two nucleoside analog reverse transcriptase inhibitors (Gold and Hira 2003). However, studies in Sub-Saharan Africa found these regimens to be less effective than triple-drug antiretroviral therapy. In one study viral load and CD4 counts reverted back to their baseline levels within one year in the majority of patients. It appears that the substitution of less intensive regimens will rarely, if ever, be an appropriate solution.

Effects on Prevention

Evidence on changes in risk behavior and increases in voluntary counseling and testing and other prevention options as a result of antiretroviral therapy is scarce and poorly documented. Evidence from industrial countries indicates that disinhibition can be a significant problem. The epidemiological model presented in chapter 5 suggests that even a small increase in disinhibition can overwhelm the public health benefits of antiretroviral therapy distribution. It is therefore critically important that changes in risk behavior following the introduction of antiretroviral therapy be carefully monitored. Information, education, and communication for the general population and risk-reduction counseling for those receiving antiretroviral therapy should accompany the initiation of any antiretroviral therapy program to help mitigate potential disinhibition and encourage voluntary counseling and testing.

Effects on Medical Care Utilization and Costs

The evidence on reductions in medical care utilization from delayed or prevented opportunistic infections is minimal and of dubious relevance to India.

(continued)

Box 4.2 continued

Some of the short-term costs of antiretroviral therapy will be offset by reduced medical care costs, but since most health care costs in India are paid for by individuals, the public sector will realize few of these savings. The extent of any savings depends critically on the levels of adherence and on how antiretroviral therapy affects prevention behaviors. Furthermore, reductions in medical care utilization in the short-term may be partially or completely offset by medical care costs following treatment failure. The extent to which costs are merely delayed rather than eliminated depends on the levels of adherence attained and the availability of second-line and salvage antiretroviral therapy regimens.

The table showing the cross-cultural results on effects of antiretroviral therapy begins on page 74.

Cross-Cultural Results on Effects of Antiretroviral Therapy

COUNTRY	*CLINICAL BENEFITS*	*EFFECTS ON PREVENTION*	*IMPACT ON MEDICAL CARE UTILIZATION AND EXPENDITURE*	*ADHERENCE/RESISTANCE*
Brazil	Results similar to those obtained in richer countries. Mortality reduced 60–80 percent, notable reduction in number of main opportunistic infections (Teixeira and others 2002).		Average hospitalization time fell from 20 days in 1998 to 16 days in 1999 (Casseb and others 2001).	69 percent of 1,000 patients surveyed achieved 80 percent adherence (Rosenberg 2001).
			Hospital admissions per AIDS patient fell from 1.65 in 1996, the year antiretroviral therapy was introduced, to 0.24 in 2001 (Laurence 2001).	Not sufficient to control the virus but comparable to U.S. rates (Laurence 2001).
			Cost of antiretroviral therapy in 2001 was $235 million; treatment costs 50 percent less than in 1997. Significant growth in demand for outpatient services and decrease for home and day-care services (Teixeira and others 2002).	

Brazil		Access to universal antiretroviral therapy led to savings on medicines for treating opportunistic illnesses and direct costs of hospital admissions. During 1997–2001, 358,000 admissions were avoided, saving $1 billion (Teixeira and others 2002). Drug cost for 85,000 people was $339 million, or about $4,000 per person per year, in 1999. Costs offset by $200 million savings in prevented AIDS–related hospitalizations (UNAIDS 2000; Willbond 2001).	"Regular" or "quasi-regular" adherence reported in 60 percent of 182 HIV–infected outpatients at University of São Paolo teaching hospital (Brigido and others 2001).
Côte d'Ivoire	700 patients in Côte d'Ivoire accessed antiretroviral therapy through Drug Access Initiative. Therapy recipients were more		In study of 68 patients with history of earlier antiretroviral treatment enrolled in Drug Access Initiative in Abidjan, 57 percent had resistance to one or more antiretroviral agents (Adje and others 2001).

(continued)

Cross-Cultural Results on Effects of Antiretroviral Therapy (continued)

COUNTRY	CLINICAL BENEFITS	EFFECTS ON PREVENTION	IMPACT ON MEDICAL CARE UTILIZATION AND EXPENDITURE	ADHERENCE/RESISTANCE
Côte d'Ivoire		likely to maintain sexual activity but declared more frequent condom use than untreated people with HIV/AIDS (Kazatchkine and Moatti 2001). No quantitative results reported.		
Gabon				Major mutation-inducing viruses found in 11 out of 19 drug-naïve people with HIV/AIDS in Libreville with mean 17.7 months of antiretroviral drug therapy (Vergne and others 2002).
Haiti	Response by a cohort of 60 rural patients was reportedly dramatic and positive; no data on viral loads or CD4 cell	Demand for HIV testing and opportunity for counseling rose since antiretroviral	Study of 60 patients revealed that patients receiving HAART were far less likely to require hospital	

Haiti	counts reported. Side effects were minor and readily managed; six patients required a change in regimen (Farmer and others 2001).	therapy made available (Farmer and others 2001). No information on possible disinhibition effects of antiretroviral drug therapy.	admission than patients with untreated HIV disease (Farmer and others 2001).	
Senegal	59 percent of 58 patients receiving antiretroviral therapy in a government-sponsored initiative achieved almost undetectable viral loads. CD4 count rose markedly (to about 180 per cubic millimeter). Cumulative probability of remaining alive or free of new AIDS–defining events was 94.8 percent after 6 months of follow-up, 85.0 percent after 12 months, and 82.3 percent after 18 months (Laurent and others 2002); staff medical writer 2002.			Good adherence to antiretroviral therapy regimen administered under government cohort study of 58 patients, as measured by patients' self-reporting and corroborated by excellent virological response to antiretroviral therapy and rarity of drug resistance. Adherence of at least 80 percent reported by 87.9 percent of patients, although adherence declined over time (Laurent and others 2002).

(continued)

Cross-Cultural Results on Effects of Antiretroviral Therapy (continued)

COUNTRY	CLINICAL BENEFITS	EFFECTS ON PREVENTION	IMPACT ON MEDICAL CARE UTILIZATION AND EXPENDITURE	ADHERENCE/RESISTANCE
South Africa	In MSF–sponsored program treating 220 patients in Khayelitsha township near Capetown, average CD4 levels increased 128 points, bringing average to about 200 per cubic millimeter. Average weight gain was 8.2 kilograms; 91 percent of patients had undetectable viral loads (Médecins Sans Frontières 2002).			Patients' inability to contribute to cost of treatment did not hinder adherence (staff medical writer 2002).

Uganda	905 patients in advanced disease stage received antiretroviral therapy as part of Drug Access Initiative. Two and a half years after program initiation, only 58 percent were alive and remained in care (UNAIDS 2000).	Resistance to one or more drugs found in 65 percent of 94 patients for whom results were available (UNAIDS 2000). Study of adherence among 577 patients registered at Joint Clinical Research Center in Kampala found that of 39 percent who returned at least once, 56 were classified as adhering to therapy regime at every follow-up visit. Two-thirds were classified as adhering to therapy on at least 80 percent of return visits (Kityo and others 2002).

Source: Authors' construction.

Notes

1. The appropriate discount rate is open to debate. A 10 percent rate is often used for government investment projects outside the health sector. For the health sector the cost-effectiveness guidelines developed for the United States by Gold and others (1996) recommend that a discount rate of 3 percent be applied to both health gains and costs. The World Bank's 1993 *World Development Report* made the same recommendation for developing countries. Here the choice of discount rate does not affect the ranking of policy options.
2. Some argue that a long planning horizon is not necessary because technical improvement will inevitably produce a vaccine and more effective antiretroviral therapy. There are several problems with this view. First, it ignores the fact that some consequences, such as orphanhood, are not reversible. Second, almost two decades of optimism about a vaccine and a cure have yet to produce either. Third, India has not yet succeeded in distributing existing vaccines to large percentages of those eligible. Fourth, distribution of either a vaccine or improved antiretroviral therapy would divert resources away from other urgent health and development needs. For these reasons, it would be imprudent for the government to ignore the long term. Comparison of the analysis with and without a substantial discount rate allows decisionmakers to gauge the relative importance of short- and long-term costs and consequences of alternative policies.
3. The annual cost of treating opportunistic infections after treatment failure may be higher than the annual cost of treating patients who never receive antiretroviral therapy. This report assumes that the costs of treating opportunistic infections borne by the government would not exceed those incurred for patients who never receive antiretroviral therapy.
4. According to the "bathtub" model of viremia, the virus count in the bloodstream of a person with HIV is extremely high during the first few days after initial infection. It rises again when the patient becomes symptomatic and when treatment fails. The initial period of high infectiousness is ignored here; weights of 0.76 and 1.30 are used to capture the onset of symptoms and treatment failure. In view of the posited period of nine years from infection to AIDS, the weights reflect the assumptions that onset of symptoms occurs on average five years after infection and that treatment failure occurs four years later (that is, $w_1*(5/9) + w_2*(4/9) = 1$).
5. Child sex workers are omitted from the model because of lack of information.
6. Venkataramana and Sarada (2001) survey the evidence on the number of female sex workers. The Tata Institute of Social Science estimates that there were 2 million female sex workers in India in 1994. The National Commission on Women puts the figure at 5 million in 1998. The *Calcutta Telegraph* estimates that there were 16.2 million female sex workers in 1992. This report uses the most conservative of these estimates, that from the Tata Institute, increasing the figure by the rate of population growth between 1994 and 1998.
7. Model calculations and the graphs of the results were computed using version 4 of the ModelMaker software package, available at http://www.modelkinetix.com.

CHAPTER 5

Evaluating the Costs and Consequences of Alternative Government Policies

India's current ability to treat HIV/AIDS with inexpensive and effective locally produced antiretroviral medications can be thought of as an exhaustible resource. Over time the efficacy of these inexpensive drugs will be used up, just as the resources of a gold mine are eventually exhausted. The speed with which the efficacy of India's inexpensive antiretroviral therapy drugs is eroded depends on both the extent of their use and the quality of care with which they are managed. Failure to adhere to therapy hurts not only the current patient but also future patients, whose disease will be more resistant to treatment. For this reason the public sector has an interest in helping private sector physicians and their patients attain the highest possible level of adherence to an appropriate triple-drug regimen.

This chapter examines three different policy options for providing antiretroviral therapy. ADHERE is a national capacity-building program that helps patients in unstructured and structured care adhere to therapy. It would provide information, education, and communication; training; laboratory strengthening; and subsidies for patient monitoring in private and public sectors. MTCT+ is a government-financed structured antiretroviral therapy for HIV–positive mothers and their partners who are eligible for therapy based on national treatment guidelines. It would build on the existing MTCT (Mother-to-Child Transmission) program, which aims to reduce mother-to-child transmission but does not offer treatment. A third policy would finance structured antiretroviral therapy for people living below the poverty line.

Comparison of Policy Options Assuming Antiretroviral Therapy Has No Effect on Risk Behavior

Antiretroviral therapy is expected to have behavioral as well as biological impacts on the epidemic. Since little is known and no studies are available to suggest how the availability of antiretroviral therapy will affect the risk behavior of key populations in India, the model first assumes that antiretroviral therapy can be implemented without changing risk behavior. (An alternative interpretation of this assumption is that the positive and negative effects of antiretroviral therapy on risk behavior cancel each other out.)

ADHERE: National Antiretroviral Therapy Capacity Building

In view of India's large and active private health sector and the projected growth in private sector access to antiretroviral therapy, the first policy is designed to address the market failure resulting from suboptimal adherence by patients receiving unstructured care. It is the least interventionist of the four policies analyzed.

To prevent erosion in the quality of unstructured care projected in the baseline scenario, ADHERE would provide government-financed training of both public and private sector physicians and laboratories in the basic techniques of antiretroviral therapy and diagnostic testing. The policy would subsidize laboratory tests, for which patients are less willing to pay than for medications or clinic visits.

Estimating the costs of ADHERE is a complex exercise that is beyond the scope of this report. Instead, the costs are modeled by assuming that the government finances $100 a year of physician and laboratory training and laboratory tests for each HIV–infected person in India. Patients would continue to pay for their own medications. Five years of payments would be provided for patients in structured treatment and three years for patients in unstructured treatment.

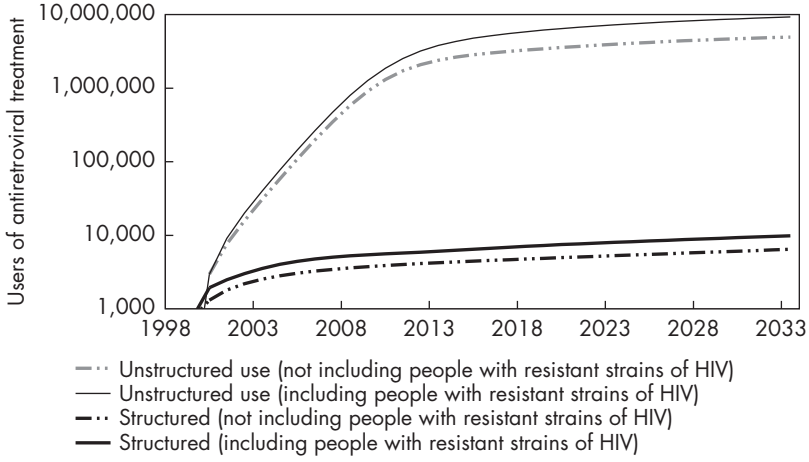
In the baseline scenario, patients self-financing structured treatment are presumed to pay for all testing and clinic visits necessary to sustain maximum possible adherence. Government financing for these people would thus constitute a simple transfer.

The effects of ADHERE on the epidemic are modeled to maintain the quality of unstructured care at its current quality level. Thus instead of declining from three years to one year, as described in table 4.1 and figure 4.3, the period of time between the beginning of treatment and treatment

failure remains constant at three years. This period is still two years shorter than the five years until treatment failure that fully structured treatment provides. In people receiving unstructured treatment, this policy reduces the number of people carrying resistant strains, represented by the gap between the upper dotted and solid lines.

Because ADHERE maintains the quality of unstructured treatment, patients receiving such treatment in the private sector live longer. Furthermore, in each year a smaller proportion of patients is able to transmit a resistant virus to sex partners. Projections for structured antiretroviral therapy (figure 5.1) are unchanged from those shown as the bottom two curves in figures 4.7 and 4.8. However, the number of patients under unstructured treatment is considerably larger. Starting at the current level of 10,000, the number of people receiving unstructured treatment would rise to 3.8 million by 2013 and 9.3 million by 2033. These numbers reflect a 25 percent increase by 2013 and a 75 percent increase by 2033 relative to the baseline. The number of people in unstructured treatment who are infected with resistant viruses (the gap between the top two curves) would increase from 1.4 million in 2013 to 4.4 million in 2033. This figure is

Figure 5.1 Projected Reduction in Resistant Virus Associated with ADHERE Policy, 1998–2033



Note: Structured ART could be public or private, but must adhere to the criteria listed in the text. Unstructured ART is more haphazard and more likely to generate viral resistance.
Source: Authors' construction.

larger than the baseline scenario in absolute terms but much smaller in relative terms. In the baseline 91 percent of people on unstructured treatment carry resistant strains by 2033. In the ADHERE scenario 47 percent carry resistant strains at the end of the period.

ADHERE has two effects on transmission. It reduces the proportion of patients who have and can transmit resistant strains, and it increases the opportunity to infect others (by increasing the period of time before HIV progresses to AIDS). The total effect of the epidemic on health is the net result of these two offsetting effects.

Three measures are used to measure health impact: HIV infections prevented, life-years saved, and years of orphanhood prevented. Based on any of these measures, ADHERE is estimated to have a small impact on the epidemic (table 5.1). The policy actually increases the number of people with HIV/AIDS, because the beneficial effect of lengthening the period during which transmission is reduced is more than offset by the increase in the opportunity to infect others. The net increase in HIV/AIDS cases from 101.7 million to 103.7 million over the projection period represents an increase of 2 percent. When future cases are discounted at 10 percent, the present value of the future stream of cases is 22 million under the baseline and 22.1 million under the ADHERE policy, an increase of 0.4 percent. The impact of the ADHERE policy is smaller for the discounted measure because the increased number of cases is concentrated in the outer years.

In terms of lost years of life, extended patient survival offsets the larger number of people with AIDS, leading to a net benefit of 0.6 percent. Because

Table 5.1 Projected Impact of ADHERE Policy in India, 1998–2033

IMPACT	BASELINE POLICY	ADHERE POLICY	DIFFERENCE	PERCENTAGE IMPROVEMENT
Cases of HIV				
Millions of cases	101.7	103.7	–2.0	–2.0
Millions of discounted cases	22.0	22.1	–0.1	–0.4
Lost years of life				
Millions of years	2,845.3	2,829.2	+16.1	0.6
Millions of discounted years	202.6	191.1	+11.5	5.7
Years of orphanhood				
Millions of years	249.3	229.2	+20.1	8.1
Millions of discounted years	44.3	41.2	+3.1	7.0

Note: Discount rate is 10 percent.
Source: Authors' computations.

the extra life-years are gained early in the epidemic, discounting increases the benefit of the policy to 5.7 percent. The net effect of the substantial government effort required to implement ADHERE will be to purchase additional life-years of health beginning immediately at the expense of additional cases of HIV infection, especially in the outer years. The combined effects of more successful unstructured care and more new HIV infections is the increase by the end of the projection period in the number of people receiving unstructured therapy, as illustrated by the upward shift of the dashed line in figure 5.1 relative to figure 4.7.

ADHERE has the largest beneficial effect on orphanhood, reducing the burden by 7–8 percent. The percentage impact of ADHERE on orphanhood is larger than the effects on the other two measures of health benefit, reducing the burden by 7–8 percent. The large impact occurs because it improves the quality of unstructured care, which is increases very rapidly in this scenario.

MTCT+: Government-Financed Antiretroviral Therapy for Mothers

Of the 21 million women who delivered babies in India in 2002, 150,000–300,000 were HIV–positive. As a result, 50,000–100,000 infants were probably born with HIV. The model estimates that 54,000 babies were born with HIV in India in 2002.

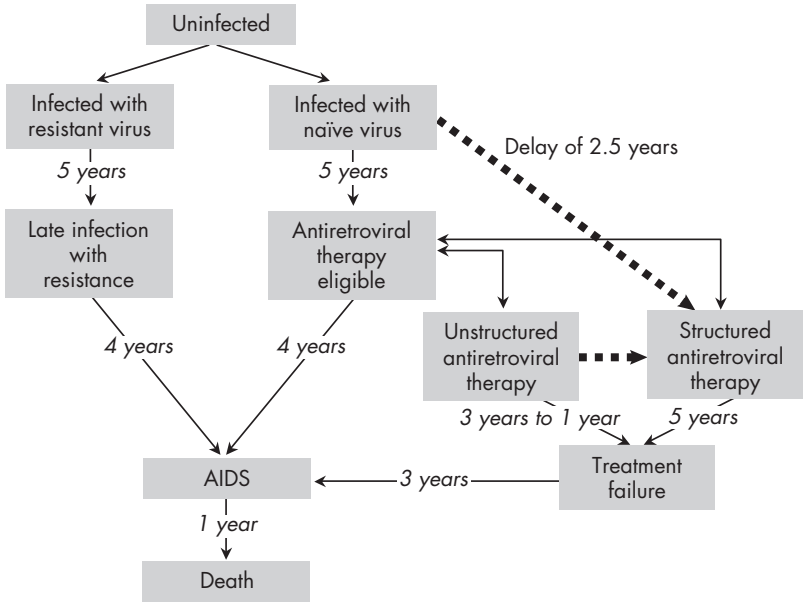
In response to this problem, the government has introduced a program to prevent mother-to-child transmission of HIV, which it is currently scaling up to eventually cover all pregnant women who receive antenatal care in the public sector. The program conducts HIV testing on all women who present at government-owned antenatal clinics and implements a nevirapine-based preventive strategy to reduce mother-to-child transmission for those who test positive. Few of the women testing positive will have symptoms of AIDS or be eligible for antiretroviral therapy. The current program does not attempt to remain in contact with or treat women found to be infected with HIV, and it pays little attention to the male partners of these women, an estimated 85–90 percent of whom may also be infected.

The MTCT program is offered through the public sector, which screens about half of all pregnant women.[1] Test results at a few pilot sites found that 1.7 percent of women tested positive for HIV (NACO 2002). Since these sites were chosen because they offer more opportunities to prevent infected births, the expanded program is expected to encounter lower infection rates, perhaps half those observed in the pilot.

Projecting the effects of the MTCT+ program requires modifying the model to incorporate antenatal screening as an avenue to treatment (figure 5.2). Women can be identified as HIV–positive at any stage of infection. The model assumes that the average woman identified at an early stage would not be eligible for antiretroviral therapy until two and a half years later. Women already in unstructured antiretroviral therapy would be recruited to begin structured antiretroviral therapy immediately. Women with resistant viruses would not be recruited. The model assumes that the program would succeed in recruiting 25 percent of HIV–positive women and about half of their husbands.

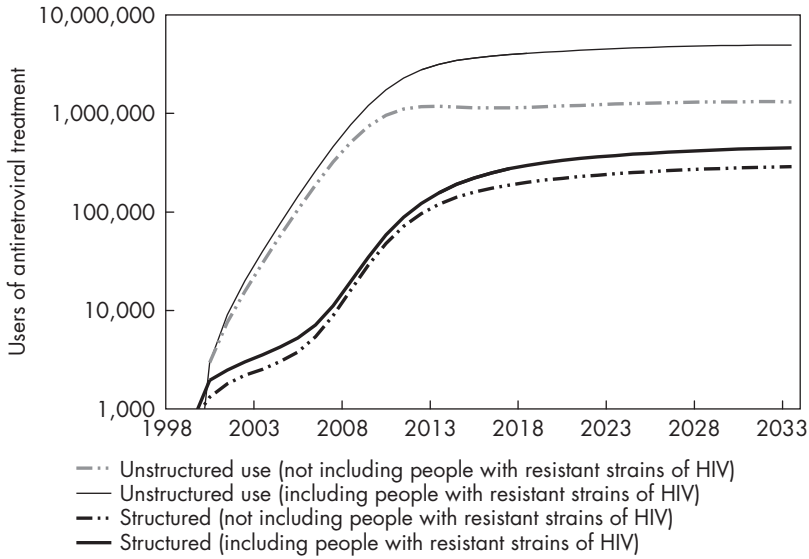
Under MTCT+ recruitment rises from 2,000 the first year to 183,000 in 2013 and 750,000 in 2033 (figure 5.3). Somewhat fewer people receive unstructured care under MTCT+ than under ADHERE, because some of

Figure 5.2 MTCT+ Treatment Model



Note: Bold dashed arrows represent recruitment into the MTCT+ treatment program. Structured ART could be public or private, but must adhere to the criteria listed in the text. Unstructured ART is more haphazard and more likely to generate viral resistance.
Source: Authors' construction.

Figure 5.3 Estimated Participation in Structured and Unstructured Treatment under MTCT+ Policy



Source: Authors' construction.

the 750,000 women who eventually receive structured care under MTCT+ would otherwise have received unstructured care.

In contrast to the ADHERE policy, the MTCT+ policy improves health in terms of all four measures (table 5.2). The health impacts are substantial in absolute terms, with the policy preventing 1.6 million undiscounted or 200,000 discounted cases of HIV/AIDS and saving 50 million undiscounted or 3 million discounted years of life. However, the MTCT+ policy has only a small beneficial effect on the national epidemic, with no effect exceeding 2 percent of its total anticipated burden.

An additional benefit of any antiretroviral therapy policy is that it postpones orphanhood. Because it targets pregnant women, MTCT+ will prevent more years of orphanhood per adult in publicly financed structured treatment than any of the other policies considered here. In the absence of antiretroviral therapy, the average HIV–positive pregnant woman could be expected to die five years after she gives birth. Unstructured antiretroviral therapy would add 3 years to her lifespan, while structured antiretroviral therapy would add 5 years, so that the child would be 8 or 10 before the

Table 5.2 Projected Impact of MTCT+ Policy in India, 1998–2033

IMPACT	BASELINE POLICY	MTCT+ POLICY	DIFFERENCE	PERCENTAGE IMPROVEMENT
Cases of HIV				
Millions of cases	101.7	100.1	1.6	2.0
Millions of discounted cases	22.0	21.7	0.3	1.3
Lost years of life				
Millions of years	2,845.3	2,794.7	50.5	1.8
Millions of discounted years	202.6	199.6	3.0	1.5
Years of orphanhood				
Millions of years	249.3	243.7	5.7	2.3
Millions of discounted years	44.3	43.4	0.9	2.0

Note: Discount rate is 10 percent.
Source: Authors' computations.

mother dies. This benefit is offset by the fact that during these extra years of life, the mother could have more children, who would become orphaned at an even earlier age. The total impact of MTCT+ on years of orphanhood would be the net result of these two offsetting impacts. The estimates of orphanhood impacts presented here are admittedly crude, and the subject deserves more detailed examination. However, the large orphanhood benefits of this program are expected to be robust to alternative modeling approaches.

Below the Poverty Line: Government-Financed Antiretroviral Therapy for the Very Poor

An alternative to targeting HIV–positive mothers is to target the poorest HIV–positive adults, a policy referred to here as the Below the Poverty Line policy. The baseline scenario implicitly assumes that the poorest people eligible for antiretroviral therapy will be the last to adopt or among the 20 percent who never adopt. To project the effect of adoption of the Below the Poverty Line policy, the model assumes that a mechanism could be designed to identify the poorest people with symptomatic HIV infection and finance their access to structured antiretroviral therapy. No broad-based attempt has yet been made to estimate the socioeconomic status of HIV–infected people in India. In the absence of such data, the model assumes that the Below the Poverty Line policy would provide subsidized access to structured antiretroviral therapy to 40 percent of those people with HIV/AIDS who carry a susceptible virus.

The model projects that the number of people receiving government-financed structured antiretroviral therapy would rise to equal the number

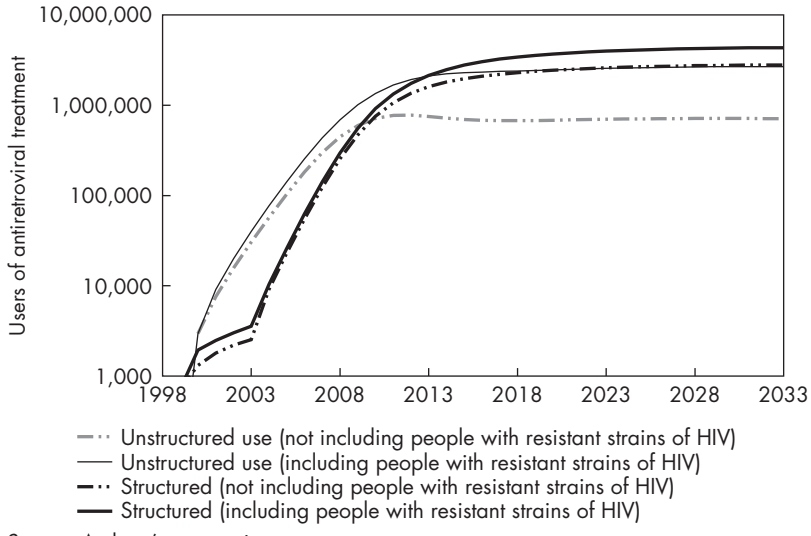
using privately financed unstructured antiretroviral therapy by 2013, when 2.1 million people would be using each type of therapy (figure 5.4). By 2033, 7 million people would be using antiretroviral therapy, of which 4.3 million would be receiving structured care financed by the government and 2.7 million would be receiving self-financed unstructured care.

While the total number of people under treatment is similar to that achieved by other policies, the quality of treatment is assumed to be higher in structured care, which accounts for the higher health benefits. The impact of this much larger government effort is therefore much greater than that of the other policies, reducing the discounted burden of the AIDS epidemic by about 8–13 percent (table 5.3). The undiscounted effect would be about 12–16 percent, depending on the measure.

Comparing the Benefits of the Three Policies

Each of the three antiretroviral therapy policies yields a different path for the epidemic in terms of the annual number of new HIV infections and the number of AIDS orphans (figure 5.5). None of the policies has a dramatic impact on either of these measures. The most ambitious program, the Below the

Figure 5.4 Projected Effects of Below the Poverty Line Policy, 1998–2033



Source: Authors' construction.

Table 5.3 Projected Impact of Below the Poverty Line Policy in India, 1998–2033

IMPACT	BASELINE POLICY	BELOW THE POVERTY LINE POLICY	DIFFERENCE	PERCENTAGE IMPROVEMENT
Cases of HIV				
Millions of cases	101.7	89.9	11.9	11.7
Millions of discounted cases	22.0	20.3	1.7	7.7
Lost years of life				
Millions of years	2,845.2	2,452.3	392.9	13.8
Millions of discounted years	202.6	177.4	25.2	12.4
Years of orphanhood				
Millions of years	249.3	209.4	39.9	16.0
Millions of discounted years	44.3	38.7	5.6	12.6

Note: Discount rate is 10 percent.
Source: Authors' computations.

Poverty Line policy, has the largest impact. The MTCT+ program is barely distinguishable from the baseline scenario, perhaps because it reaches fewer people than the other two programs.

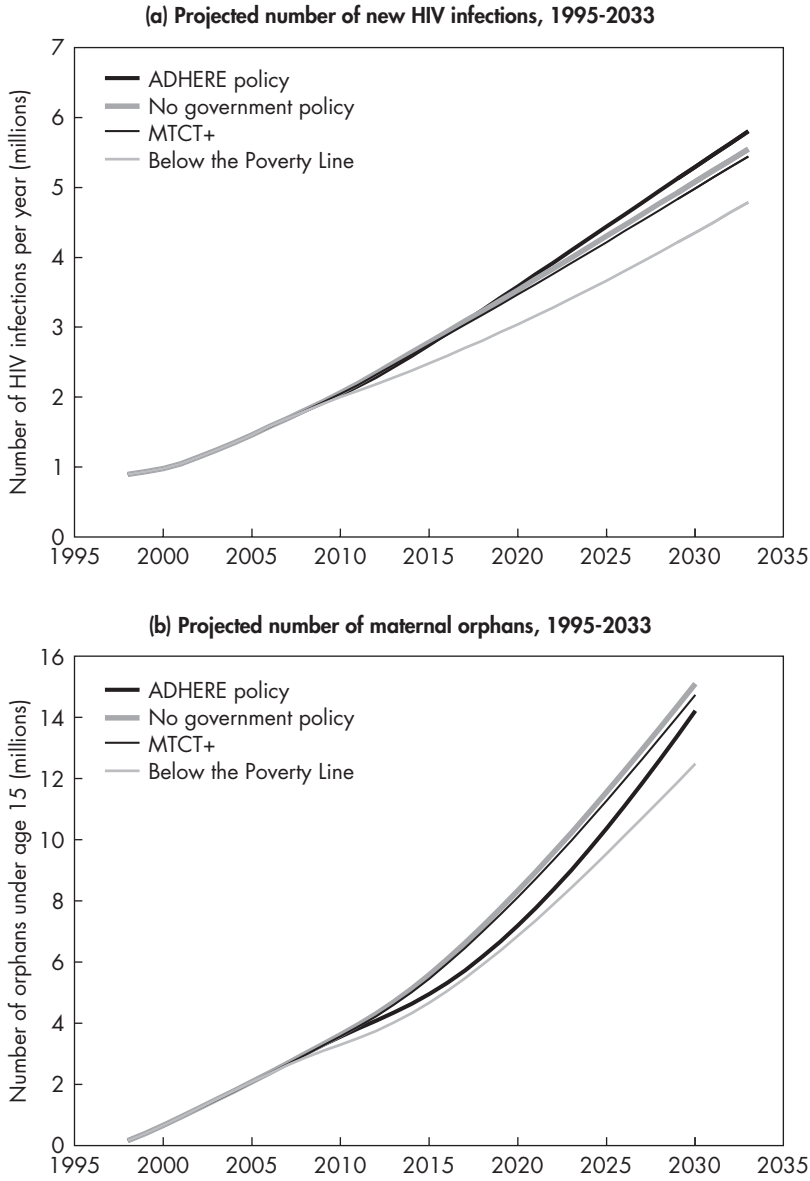
Only the ADHERE policy has a qualitatively different effect on the two measures shown in figure 5.5. After temporarily reducing the number of HIV infections between 2007 and 2015, ADHERE increases the number of new infections relative to the baseline scenario. This effect occurs because by 2015 the life-lengthening effect of ADHERE eventually leads to more infections than are prevented by the modest reduction in infectiousness. In contrast, ADHERE reduces the years of orphanhood, having almost as great an effect as the much more ambitious Below the Poverty Line policy between 2010 and 2020.

Each of the three policies has both direct and indirect effects on the number of life-years lost to the epidemic. The direct effects are the longer lives of patients receiving subsidized testing or structured care who would otherwise not have received it. The indirect effects are the reduced transmission of HIV infection.

The net impact of each policy can be estimated by comparing the differences between each policy trajectory and the baseline. A full economic analysis would assign a dollar value to the benefits of each of these policies and compare the benefits with the costs of each policy. Such analysis is eschewed here in favor of cost-effectiveness analysis.

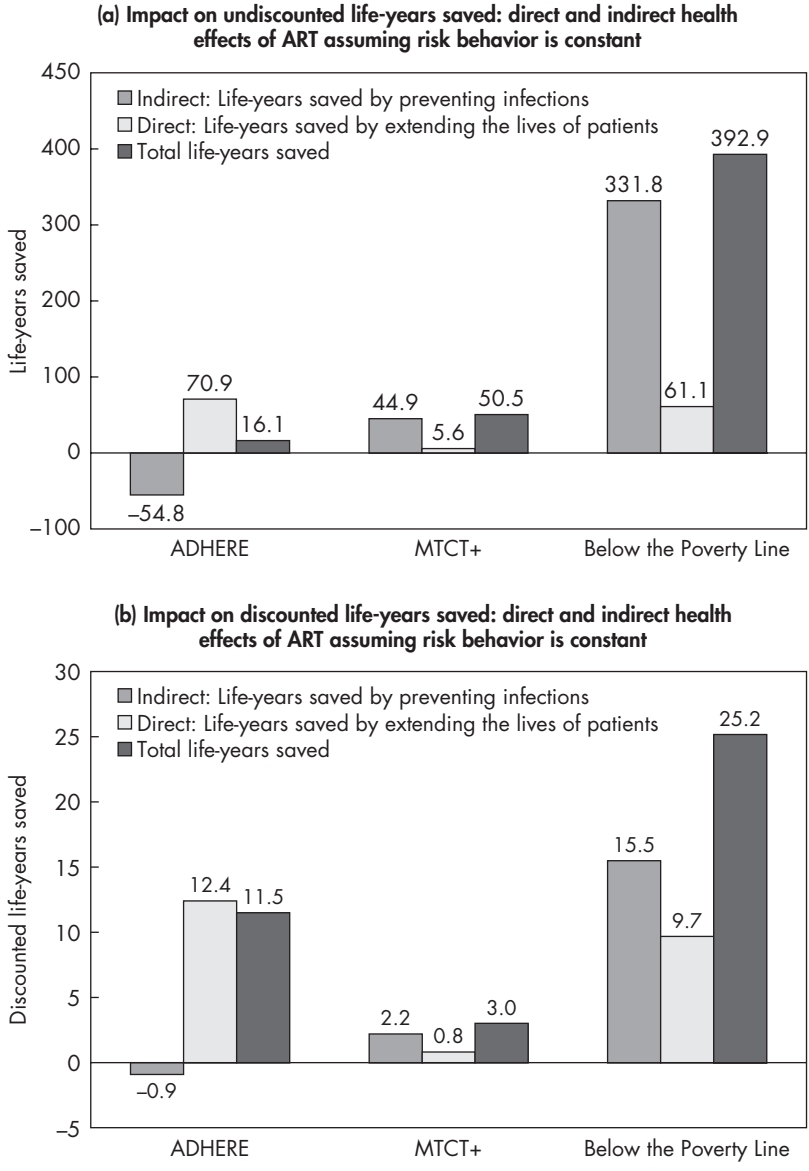
The benefits of the ADHERE policy accrue almost exclusively to those receiving subsidized treatment monitoring (figure 5.6), with the negative

Figure 5.5 Sensitivity of Epidemic to Alternative Antiretroviral Therapy Financing Policies



Source: Authors' construction.

Figure 5.6 Indirect and Direct Components of Health Benefits of Alternative Antiretroviral Therapy Financing Policies



Note: Discount rate is 10 percent.
Source: Authors' construction.

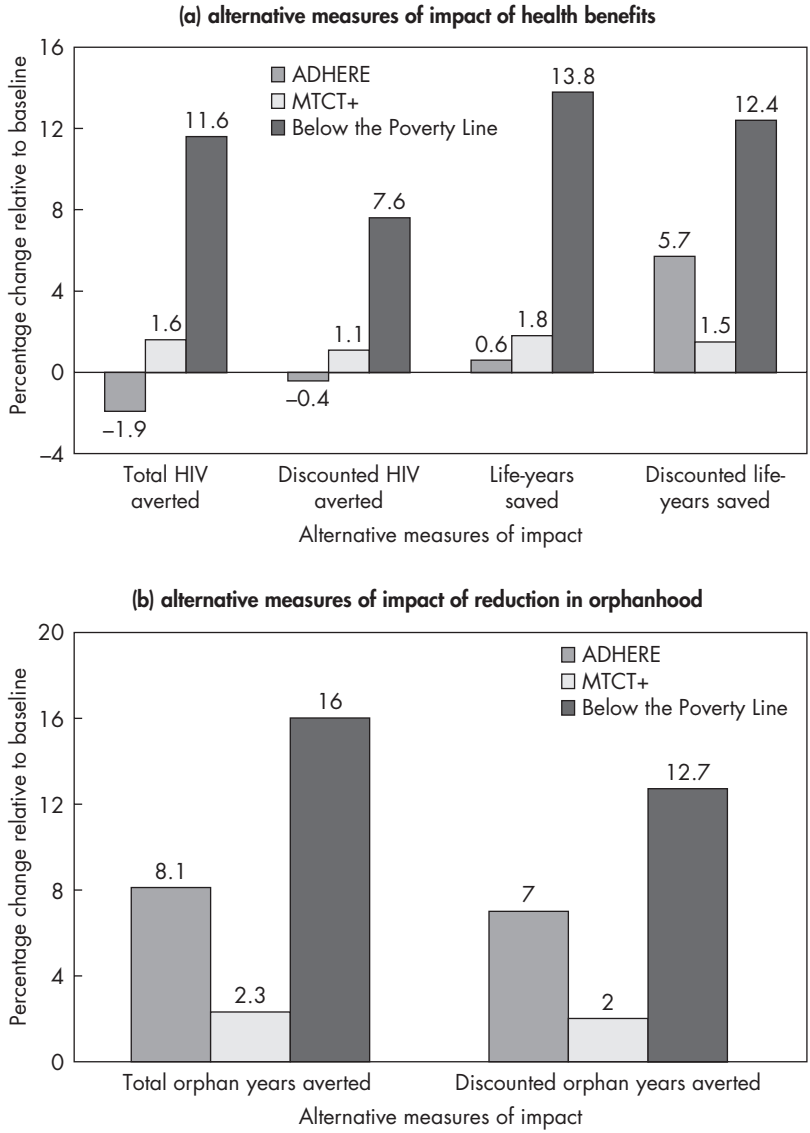
indirect effects of the policy offsetting the positive direct effects. For both the MTCT+ and the Below the Poverty Line policies, most of the estimated benefit stems from indirect rather than direct effects, namely, the reduced infectiousness of people receiving high-quality structured care. This result is counterintuitive. By subsidizing laboratory tests, the component of antiretroviral therapy that patients in unstructured care are least likely to demand, ADHERE reduces the spread of resistant viruses, thereby slowing the spread of the epidemic. This beneficial effect seems to be more than offset by the greater infectiousness of patients in unstructured care compared with those in structured care, however. Thus in the absence of a disinhibiting behavioral response, the MTCT+ and Below the Poverty Line policies have more positive externalities than ADHERE.

The relative weight of the indirect component depends on the discount rate. Without discounting, 89 percent of the health benefit of MTCT+ and 84 percent of the benefit of Below the Poverty Line are due to indirect effects. Because reducing the infectiousness of antiretroviral therapy patients slows the growth rate of the epidemic, the number of prevented cases of infection increases, first slowly and then more rapidly as time goes on. Discounting reduces the importance of these future benefits relative to those that accrue earlier, reducing the relative contribution of the indirect component of the MTCT+ to 73 percent and the contribution of the Below the Poverty Line Policy to 62 percent. The same mechanism causes the ADHERE policy to yield stronger results when effects are discounted.

Comparison of the net impacts of the three policies reveals, not surprisingly, that publicly subsidized antiretroviral therapy has the largest impact on the epidemic when it directly supports structured treatment for the largest number of people, as in the Below the Poverty Line program (figure 5.7). That program could reduce the epidemic's burden by 6–14 percent. MTCT+ reduces the burden of the epidemic by a modest 1–2 percent. Without discounting, the policy has a larger impact on the number of people with HIV/AIDS than the ADHERE policy. When saved life-years are discounted at 10 percent, the ADHERE policy's immediate health benefit to people receiving unstructured care yields five times the health gains of MTCT+.

Both with and without discounting, all three programs reduce the orphanhood burden of AIDS by more than they improve either measure of health. ADHERE is particularly effective in this regard, performing almost as well as the much more ambitious and expensive Below the Poverty Line program. In contrast, the MTCT+ program has a smaller effect on orphanhood. Although it targets mothers, MTCT+ does not provide treatment to enough

Figure 5.7 Improvement in Health and Reduction in Orphanhood Associated with Alternative Antiretroviral Therapy Policies



Note: Discount rate is 10 percent. Figures assume that antiretroviral therapy policy induces no change in risk behavior.
Source: Authors' construction.

people to provide the benefits associated with either of the other two programs in terms of reducing orphanhood.

Comparing the Costs of the Three Policies

This report uses only rudimentary cost assumptions to estimate the costs—and cost-effectiveness—of the alternative antiretroviral therapy policies. It assumes that the ADHERE policy will cost $100 for every patient-year of structured or unstructured treatment. The costs of the MTCT+ and the Below the Poverty Line program are assumed to be $500 per patient-year for drugs and clinic visits and $100 for laboratory tests, with the government financing only structured programs.

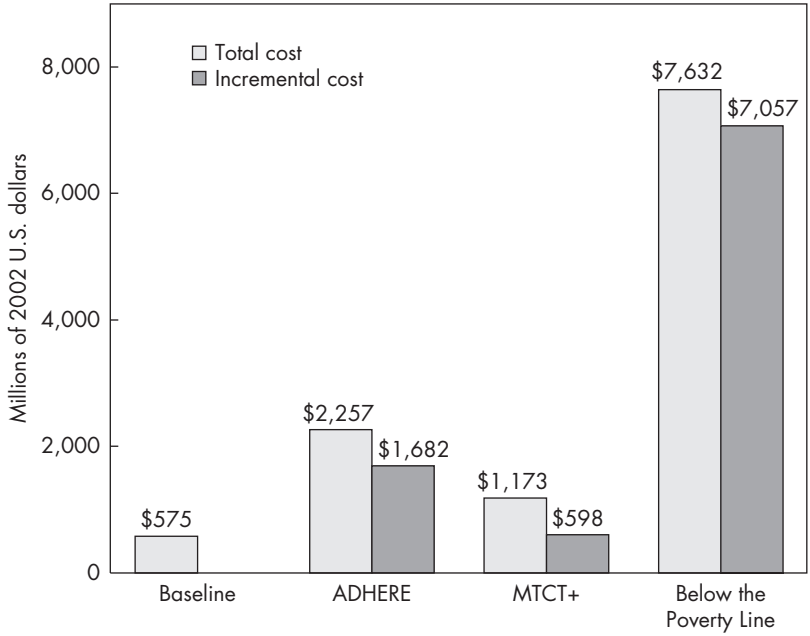
In the absence of information on the potential economies or diseconomies of scale of large government-supported structured antiretroviral therapy programs, the report assumes that the same average cost of $500 applies to all people treated by a program. These assumptions are heroic in the extreme but so would be any alternative assumptions (Over 1986).

Over the 31-year period, the present value of the cost to the government of continuing its policy of financing only the cost of treating opportunistic illnesses for 20 percent of the population amounts to $575 million in 2002 dollars (figure 5.8). Adding the MTCT+ policy would cost an additional $598 million, adding ADHERE would cost $1.7 billion, and financing the Below the Poverty Line program would cost $7.1 billion. These amounts are equivalent to a constant annual budget over that period of $63–$744 million.

The costs of these programs include the cost of treating opportunistic infections, conducting testing, and providing antiretroviral therapy (figure 5.9). Each of the three policies would somewhat reduce the cost of treating opportunistic infections. The ADHERE policy reduces expenditures on opportunistic infections by $60 million, MTCT+ reduces these expenditures by $23 million, and the Below the Poverty Line policy reduces these expenditures by $186 million. These reductions are dwarfed, however, by the cost of providing antiretroviral therapy. Under the ADHERE policy the $60 million in saved opportunistic infection treatment costs does little to offset the $1.7 billion of testing costs. The Below the Poverty Line policy achieves the largest reductions in the costs of treating opportunistic infections, but the $186 million reduction does little to offset the $7.2 billion of testing and antiretroviral therapy treatment costs.

How affordable are annual expenditures of this magnitude? Assuming that the national implications of funding antiretroviral therapy would justify federal spending, these amounts can be compared with the current budgets of

Figure 5.8 Impact of Alternative Antiretroviral Therapy Policies on Present Value of Future Government Expenditures

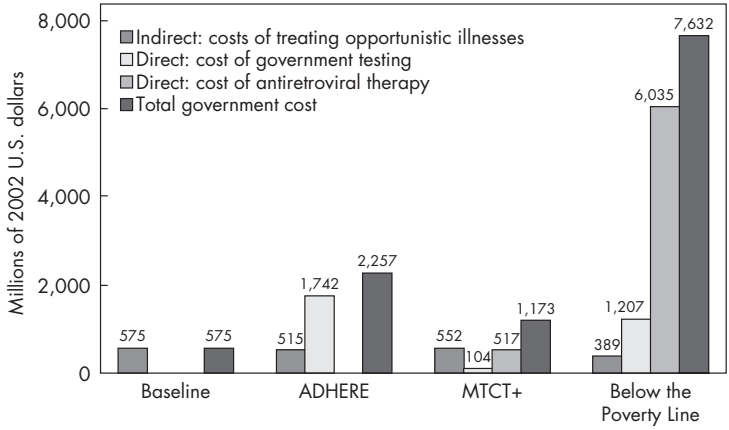


Note: Discount rate is 10 percent.
Source: Authors' construction.

relevant government departments. The health department's annual budget is currently about $300 million. The $60 million annual budget required to fund the MTCT+ program would thus represent an increase of 20 percent, an amount that might be affordable with the help of generous outside donor support and a major national effort. The $774 million annual expenditure required to support the Below the Poverty Line policy is about three times the annual health budget and represents more than 70 percent of all central health and social welfare expenditures.

Whether such expenditures are affordable is essentially a political question. Affordability of any expenditure depends on the other purposes to which such funds could be put and the lobbying power of the constituencies for those other uses. At least in part, the argument will turn on what antiretroviral therapies India will be able to buy with its resources and on the value it will receive.

Figure 5.9 Components of Present Value of Future Government Expenditures on Treating People with HIV/AIDS through 2033



Note: Discount rate is 10 percent.
Source: Authors' construction.

Comparison of Baseline and Below the Poverty Line Policy Assuming Antiretroviral Therapy Affects Risk Behavior

The projected health impacts of the three policies analyzed were based on the assumption that antiretroviral therapy has no impact on risk behavior. In particular, the scenarios assume that condom use during sexual contacts between male clients and female sex workers remains constant at 50 percent. But the availability of antiretroviral therapy may have positive or negative effects on risk behavior. Some observers argue that the availability of antiretroviral therapy will lead people to seek voluntary counseling and testing and then practice safer sex or needle-injecting habits. Others point to evidence that the availability of antiretroviral therapy has led to the return to risky sexual behavior and hence to higher rates of new HIV infections.

This section examines the sensitivity of the estimates of the costs and consequences of the most ambitious of the three treatment policies, the Below the Poverty Line policy, to the assumption that the policy has no impact on risk behavior. It examines the effect of different rates of condom use (40 percent, 50 percent, 70 percent, and 90 percent) during high-risk contacts. The

40 percent value captures the possibility that risky behavior might be mildly disinhibited by the availability of antiretroviral therapy; the 70 percent and 90 percent scenarios capture the possibility that antiretroviral therapy increases prevention (figure 5.10).[2]

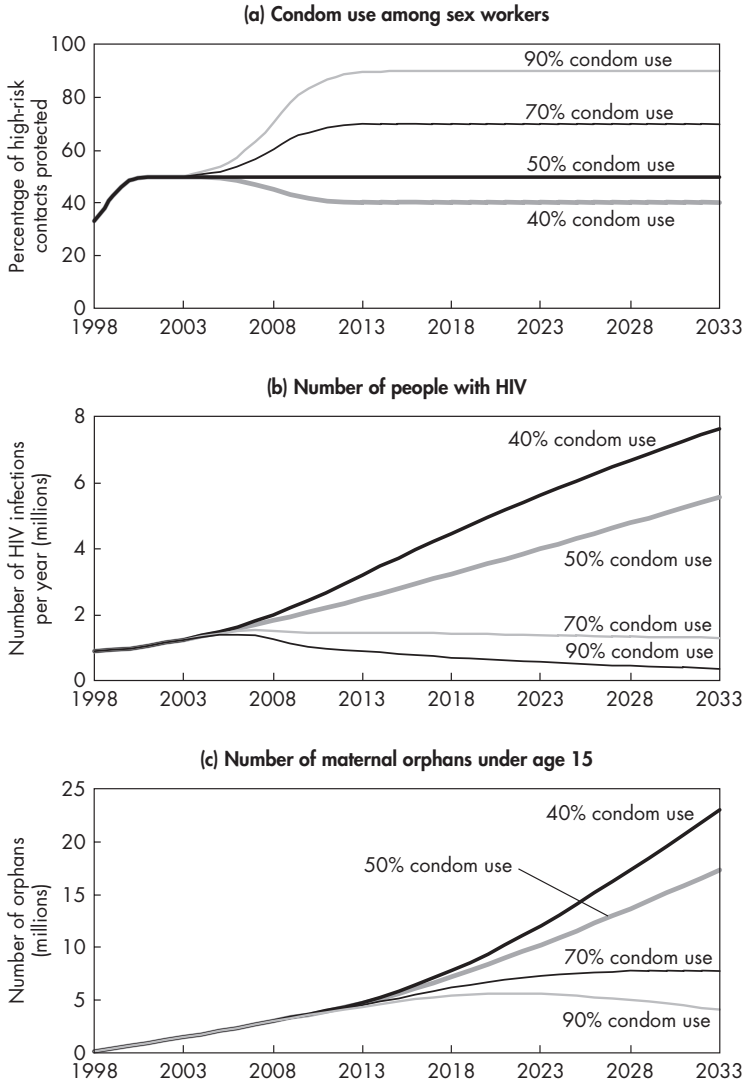
How much difference does condom use during high-risk contacts make to the future of the Indian epidemic and to the costs of an antiretroviral therapy program? The epidemic is much more sensitive to condom use during high-risk contacts than it is to the choice among the three antiretroviral therapy policies. Increasing the current rate of condom use during high-risk contacts by 20 percentage points to 70 percent would be enough to change the direction of the epidemic, preventing many millions of cases of HIV infection and years of orphanhood. Raising condom use to 90 percent would have an even greater effect, preventing 2 million new infections a year by 2013 and 2 million years of orphanhood in 2025. Conversely, reducing condom use to 40 percent would add 1 million new infections a year by 2013 and create more than 2 million orphans in 2025.[3]

With condom use among high-risk groups stalled at 50 percent nationally, how realistic is it to hope that rates could improve to 70 or 90 percent? Some parts of India have already attained rates of condom use exceeding 70 percent (See Figure 2.4). Thailand's success in increasing condom use to 90 percent during high-risk contacts suggests that vigorously targeting those at highest risk can achieve very high rates of condom use and markedly decrease the incidence of sexually transmitted infections (figure 5.11).

How sensitive are the estimates of health benefits and costs to alternative assumptions about risk behavior? Depending on the rate of condom use, the discounted number of prevented HIV infections ranges from –18.1 million (a net increase in the burden of the epidemic) to 120.1 million (almost five times the 25.2 million under the baseline assumption) (figure 5.12). The discounted number of prevented orphan years ranges from 2.1 million to 14.3 million. The cost of the program ranges from $4.1 billion to $9.2 billion.

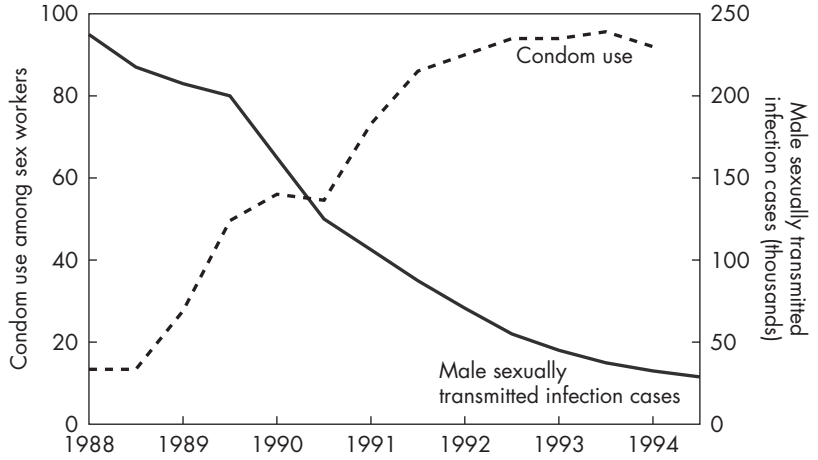
This analysis reveals the extreme sensitivity of the costs and consequences of antiretroviral therapy policy to prevention. Better prevention will make any of the antiretroviral therapy policies more affordable. Without careful attention to prevention, however, provision of free structured antiretroviral therapy may reduce condom use by disinhibiting risky behavior. In the worst case, the financing of antiretroviral therapy could *reduce* the health status of the country while greatly increasing the costs to the government. Alternatively, antiretroviral therapy policy could enhance the effectiveness of prevention efforts.

Figure 5.10 Sensitivity of Epidemic to Rate of Condom Use During High-Risk Contacts, 1998–2033



Source: Authors' construction.

Figure 5.11 Sexually Transmitted Infections and Condom Use During High-Risk Contacts in Thailand, 1988–1994



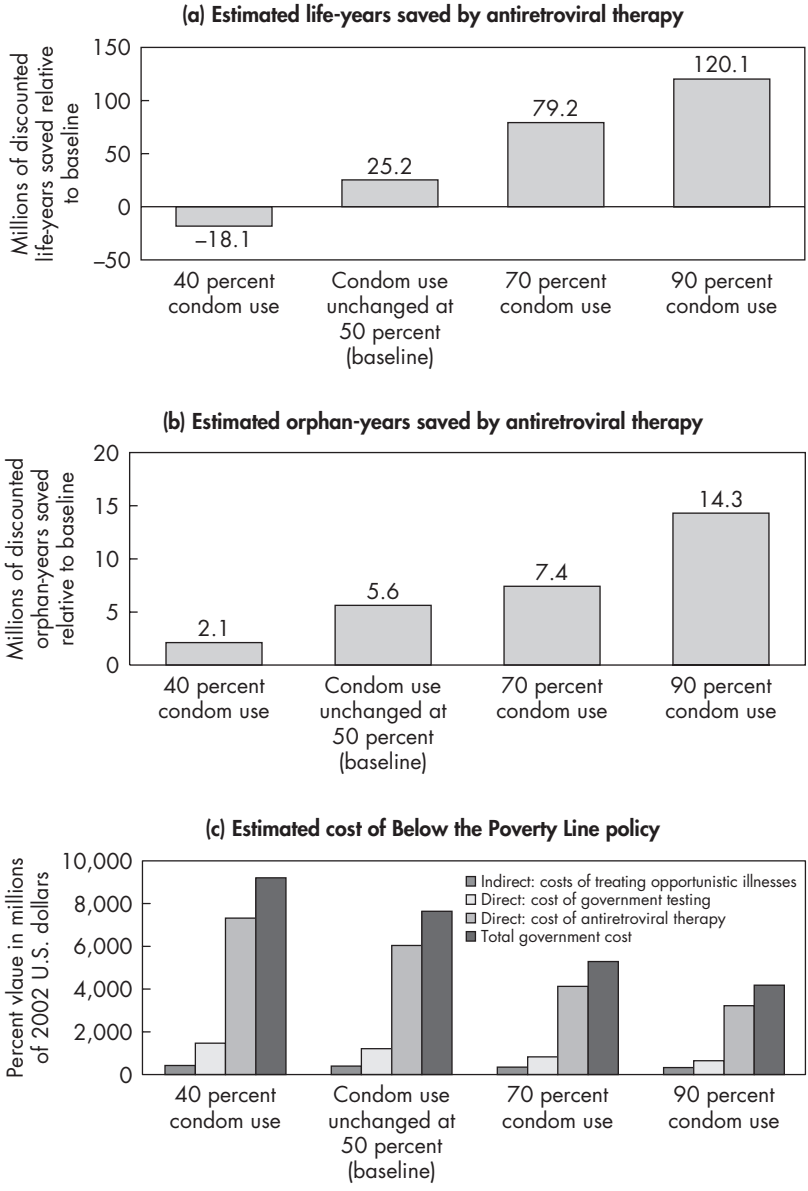
Source: World Bank 1997.

Cost-Effectiveness of Alternative Antiretroviral Therapy Policies

The cost-effectiveness of alternative policies can be computed from several different perspectives. Individual patients are interested in knowing the health benefits they could expect to achieve per rupee of their own expenditure. Taxpayers or their representatives are interested in the social benefits of antiretroviral therapy relative to its social costs. This report adopts the perspective of the government health sector decisionmaker with a fixed budget who is allocating that budget among alternative programs in an attempt to maximize the health impact of those resources. It thus considers only government costs, not private or social costs.

Any change in the health impact of the epidemic is assumed to be attributable to the antiretroviral therapy program. Since the more ambitious antiretroviral therapy programs provide subsidized care for some people who would have paid for their therapy themselves, the net health effect is less than the sum of the beneficial effects on the total number of people subsidized. Subsidies to people who would otherwise have paid for care themselves are transfers. Although such transfers would not be

Figure 5.12 Sensitivity of Costs and Benefits of Below the Poverty Line Policy to Condom Use



Note: Discount rate of 10 percent.
Source: Authors' construction.

included as benefits in a conventional cost-benefit analysis, they have important equity implications, as they may help these people and their families avoid poverty. These effects are not, however, included in the calculations presented here.

Assuming no behavioral change, the cost per life-year saved from the three antiretroviral therapy policies ranges from $146 to $280 (figure 5.13). These estimates are much lower than those in the literature, which estimates costs 8–20 times higher (World Bank 1997). These figures are also much smaller than the $600 per year cost the model assumes the government would spend for each patient-year of structured treatment.

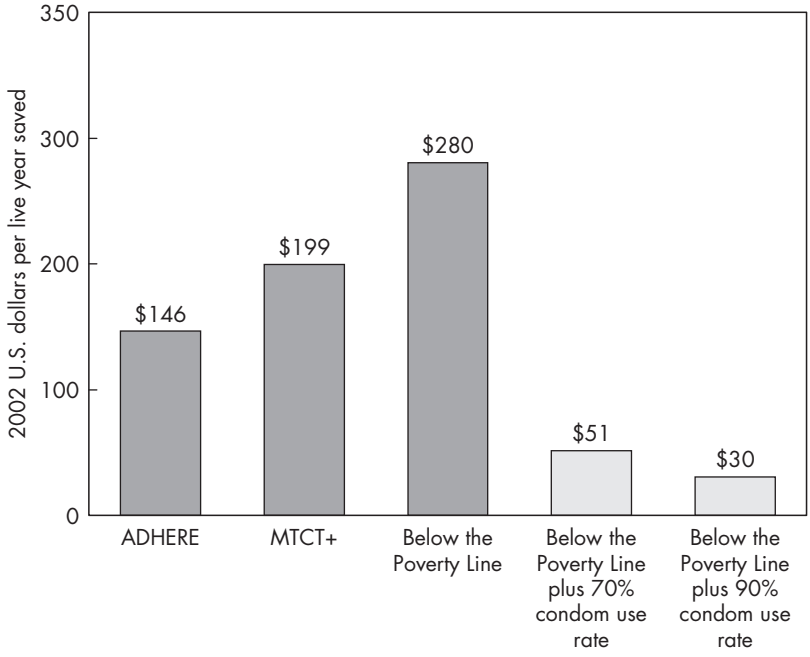
Two features of the Indian environment contribute to the relatively low cost per unit of health benefit of these subsidized antiretroviral therapy programs. First, medications cost much less than they did even five years ago. Second, antiretroviral therapy reduces infectiousness. The transmission-reducing effects of antiretroviral therapy, which operate independently of any behavioral change, account for most of the life-years saved under the MTCT+ and Below the Poverty Line policies. These costs per life-year saved are still much higher than the estimated cost of saving life-years through HIV prevention or through tuberculosis or malaria control.

The story is very different if antiretroviral therapy increases risk behavior. If antiretroviral therapy has a disinhibiting effect on condom use, the negative effects of riskier behavior could easily outweigh the positive effects of even the most generous program. This disinhibition possibility is illustrated by the steeply rising curves in panels b and c of figure 5.10 and by 40 percent condom use figures in figure 5.12.

If the government takes seriously the need to use antiretroviral therapy to enhance prevention, it might be able to design a transmission-minimizing antiretroviral therapy policy. In that case attributing the success of the prevention program to the antiretroviral therapy program might be justifiable, thus dramatically increasing the benefits of such therapy.

The estimated cost per life-year saved from a transmission-minimizing antiretroviral therapy policy would be $30 or $51, depending on the rate of condom use—higher than but of the same order of magnitude as estimates for the cost of saving life-years through HIV prevention or other less than fully exploited public health interventions. Unlike HIV prevention programs, which have been shown to be cost-effective in a variety of settings, and disinhibition, which has been observed in several parts of the

Figure 5.13 Cost-Effectiveness of Alternative Antiretroviral Therapy Policies (lower cost is better).



Note: Discount rate is 10 percent. Changes in condom usage rate are assumed to be entirely attributable to government expenditures on the Below the Poverty Line policy.
Source: Authors' calculations.

world, transmission-minimizing antiretroviral therapy has not yet been demonstrated. Where antiretroviral therapy programs have attempted to influence behavior, they have focused on the behavior of those under treatment, not on the behavior of the epidemiologically more important high-risk groups. The low cost per life-year saved of antiretroviral therapy policy displayed in figure 5.13 is thus more of a hypothesis than a result. If India could design and implement a structured antiretroviral therapy program that would motivate prevention efforts, it would be able to use antiretroviral therapy in a way that would benefit the country at large for decades to come.

Notes

1. The proportion of pregnant women screened could increase if the program attracts pregnant women who suspect they are HIV–positive. The existence of the program could also induce women who believe they are at high risk of HIV infection to become pregnant in order to qualify for treatment. The model does not explore either of these possible behavioral responses.
2. Allowing condom use to vary between 40 and 90 percent is similar to varying the proportion of high-risk groups protected from infection in some other way, such as by a partially effective vaccine or a vaccine with less than complete coverage of targeted groups (Stover and others 2002; Nagelkerke and Sake 2003).
3. The effect of safer behavior is apparent relatively quickly in the path of new infections but only with a lag in the path of orphans. These calculations suggest that the impact of the AIDS epidemic on future orphanhood is largely immutable for the next 10 years.

CHAPTER 6

Recommendations and Conclusions

Even at very low prevailing prices for generic antiretroviral therapy medications in India, government financing of antiretroviral therapy is very expensive and reduces the burden of the AIDS epidemic only marginally. While more cost-effective than ever before, antiretroviral therapy still costs more than $100 per life-year saved and thus would not rank high in comparison to many other life-saving interventions.

In view of the relatively high costs and potentially dangerous spillover effects of financing antiretroviral therapy, this report recommends that the government proceed cautiously. It recommends that the government:

- Collect better statistics on the current prevalence and incidence of HIV infection in India in order to improve the accuracy of planning exercises like the present one.
- Support improvements in the quality of unstructured antiretroviral therapy provided by the private sector in order to minimize its negative spillover effects at the lowest possible cost to the government. Under the assumptions made here, such a policy is the most cost-effective approach to antiretroviral therapy.
- Evaluate both the costs and the effects of prevention programs. If the government finds that prevention programs are stalled and can no longer be extended at a cost of $10–$20 per life-year saved, the case for antiretroviral therapy, especially transmission-minimizing antiretroviral therapy, would be strengthened.
- Evaluate the costs and effects of alternative antiretroviral therapy programs. It would be useful to know what modes of treatment maximize patient adherence to a drug regimen in India.

- Support measurement of the prevalence of resistant strains of the virus in people with HIV.
- To ensure that condom use increases rather than declines, monitor the behavioral effects of awareness of improved access to antiretroviral treatment on risk behavior of people not under treatment, especially high-risk groups.
- In consultation with all state and national stakeholders, design and implement an institutional arrangement that rewards effective prevention programs, thereby ensuring that the availability of treatment has beneficial (rather than perverse) spillover effects.

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BACKGROUND PAPERS AND NOTES

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20 March 2000

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