CHAPTER 6

Sensitivity of the Policy Rankings to Key Assumptions

The preceding chapters construct a model of the economics and epidemiology of antiretroviral therapy (ART) in order to arrive at concrete estimates of the cost-effectiveness of the NAPHA (National Access to Antiretrovirals Program for People Living with AIDS) policy and of three alternative enhancements to it. The empirical support for the many assumptions behind the model varies from substantial for some assumptions—such as the survival patterns for people with HIV/AIDS who do not receive treatment—to weak for others—such as the responsiveness of the demand for voluntary counseling and testing (VCT) to price and distance by risk group. Other assumptions pertain to the evolution of technology and prices, matters on which we can only make informed guesses.

One approach to the existing uncertainty on all these matters is to make policy by instinct, without reference to any explicit model. Frequently policy makers are forced to enact policy in exactly this way. However, to the extent that policies have any logic, they are based on an implicit model and its assumptions. Because they are not explicitly discussed, these implicit models may contain internal inconsistencies or depend critically on unstated assumptions. They may therefore lead policy makers and their constituents into making mistakes that could have been avoided using an explicit model.

The advantage of using an explicit model, as we have done here, is that the assumptions can be made explicit and their influence on the results can be studied using sensitivity analysis.

Sensitivity to Alternative Biological and Price Assumptions

In this chapter, we perform sensitivity analysis for two groups of assumptions:

- First, we study the effect of alternative assumptions regarding key biological features of antiretroviral medicine and the prices at which ART drugs can be purchased.
- Second, we analyze the effects of alternative behavioral assumptions.

All analyses are performed in comparison with the projections of NAPHA including second-line therapy that are presented in chapter 4.

Key Biological Parameters

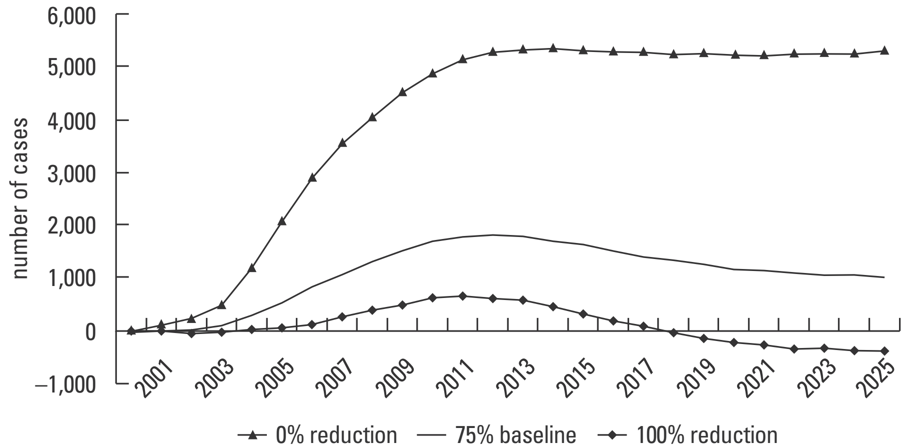
Several biological assumptions affect the results. We report sensitivity analysis regarding two: infectivity and resistance.

Infectivity

In our baseline model, we assume that the infectivity of people on ART is reduced by 75 percent. To measure the sensitivity of the results to this assumption, we run both optimistic and pessimistic scenarios (100 percent reduction versus no reduction). Figure 6.1 reports the effect of the infectivity assumption on a key indicator of epidemic growth: the number of new HIV infections in any given year. The central curve, which peaks at 1,823 in 2012 and then declines asymptotically to 1,000, presents the number of additional new HIV infections transmitted under NAPHA by the people who remain healthy because of ART. Because the trend toward safer behavior is assumed to be unchanged by ART, these additional HIV infections are caused solely by the increased longevity of AIDS patients.

The baseline projection in the absence of NAPHA (scenario A1) predicts that the number of new HIV infections would decline from 17,000 in 2003 to about 3,600 in 2015 and then to about 2,400 in 2025. In comparison with these baseline numbers, the central curve in figure 6.1 shows that NAPHA will substantially increase the number of new infections, especially in the later years. In percentage terms, NAPHA increases the number of new HIV infections by about 40 percent in each year between 2012 through 2025. The bottom curve

Figure 6.1 New HIV Cases by Infectivity Rates among People on ART: NAPHA Scenario



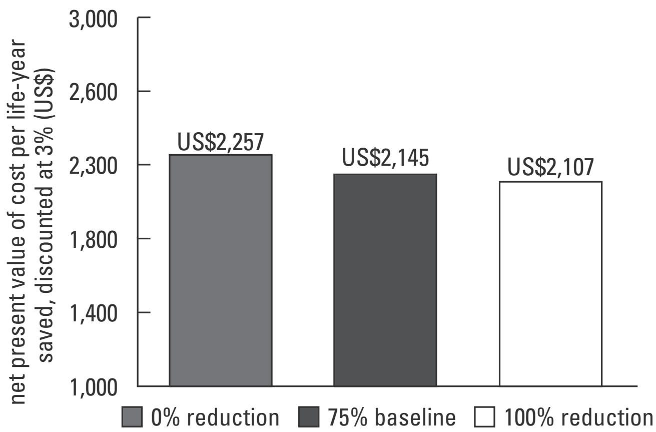
Source: Authors.

in figure 6.1 shows that the number of new infections is reduced if ART is assumed to completely eliminate transmission by the infected person (100 percent reduction). In this case, the only increase in new infections attributable to NAPHA is the result of treatment failure, when ART can no longer sustain health or impede transmission.

The top curve in figure 6.1 shows that the spillover effect from greater longevity would be far greater if, as argued by Auvert and others (2004), ART had no biological impact on infectivity. By increasing the number of new infections by about 5,000 in every year after 2011, NAPHA would more than double the new infections in every year after 2012 and would triple the number of new infections in the last four years of the projection, from about 2,500 per year to about 7,500 per year.

Despite its sizable effect on the number of new HIV cases, a change in the infectivity rate has a relatively minor effect on the cost-effectiveness results, as shown in figure 6.2. Under the worst-case scenario of zero reduction in infectivity for ART patients, the cost per life-year saved of NAPHA rises by only 5 percent, from US$2,145 (B 85,800) for the basic program to US$2,257 (B 90,280). This result follows directly from our adoption of a finite planning horizon of 2025. Because progression from HIV infection to a need for treatment takes a median time of seven years and first-line therapy will sustain people from that point for several more years, few of those infected by AIDS patients in any of these scenarios will progress to expensive second-line therapy before the end of the planning period.

Figure 6.2 Net Present Value of Cost per Life-Year Saved by Infectivity Scenario



Source: Authors.

Resistance

The second key assumption used in the analysis is a rate of resistance among the ART patients for whom first-line ART therapy failed. The model uses the assumption that 80 percent of people on ART develop resistance strains when first-line ART therapy fails for them. In Thailand, we assume that because of the lack of physicians experienced with ART treatment and the limited availability of viral-load testing at district level facilities, some 20 percent of ART patients are switched to second-line ART without having any resistant strains. However, more trained physicians and wider availability of viral-load testing throughout the country would reduce this proportion and allow only patients with resistant virus to switch to second-line ART therapy.

We conducted sensitivity analysis by using resistance assumptions of 50 and 100 percent. The results indicate that with 100 percent resistance approximately 23 percent more HIV-positive people carry resistant strains by 2025 than do under our starting assumption of 80 percent resistance. When a 50 percent resistance rate is used instead, the prevalence of resistant strains is reduced by 14 percent. However, again because of the 20-year planning horizon, these changes make almost no difference in the number of new HIV cases or the cost per life-year saved.

Price of First- and Second-Line ART Therapy

Chapter 3 presented the estimated unit cost for both first- and second-line therapy based on current drug regimens and using the current prices of both generic and branded drugs in Thailand. If current efforts by multinational pharmaceutical manufacturers to extend patent protection to second-line drugs are successful, the prices of second-line drugs are likely to remain high. However, if such efforts fail, the prices of second-line drugs could fall by as much as we have seen the prices of first-line drugs decline in recent years. However, recent legislative changes in India to comply with the World Trade Organization's Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)[1] raise concern that the costs of the raw materials that Thailand imports from India to make its GPO-vir will rise in price, forcing cost increases in GPO-vir, which is used in first-line therapy.

In this section, we keep the technical specification of ART unchanged (for second- as well as first-line therapy) in order to compute the cost-effectiveness of the following:

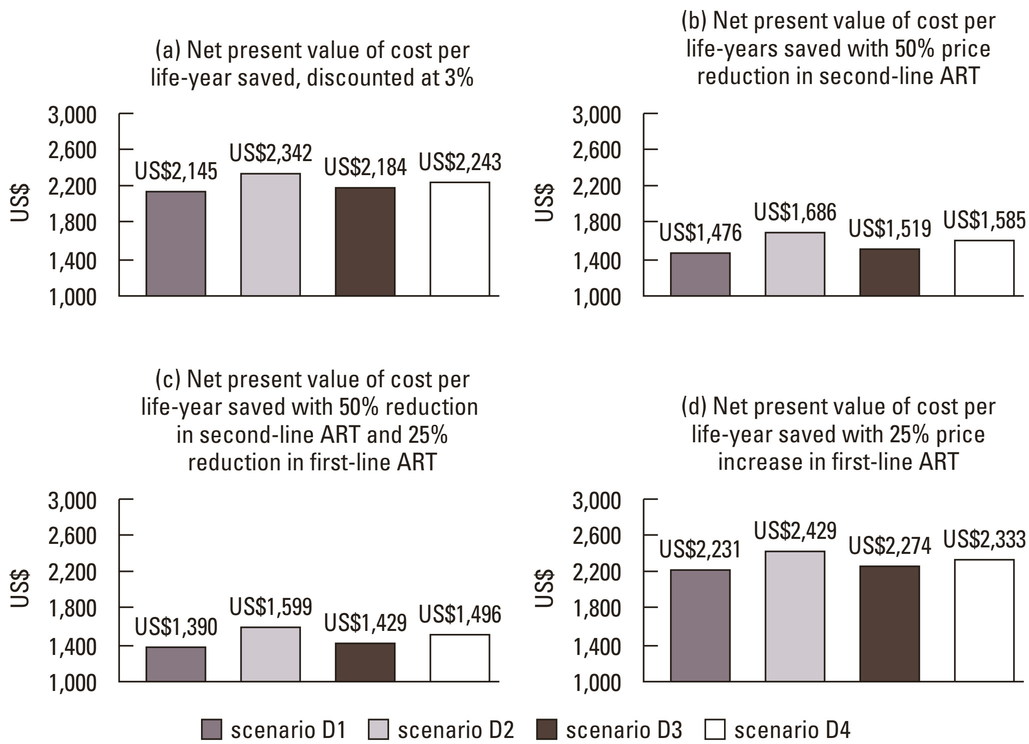
- 50 percent reduction in the price of second-line ART therapy
- 25 percent reduction in the price of first-line therapy and a 50 percent reduction in the price of second-line therapy
- 25 percent increase in the price of first-line therapy.

In all simulations, we assume that the price to the patient remains unchanged, so that patient behavior does not change and the government absorbs all the cost savings from the reduction.[2]

The results of these alternative price assumptions regarding the prices of first- and second-line therapies are displayed in the four panels of figure 6.3. Panel (a) repeats the findings of chapter 5, which showed that NAPHA is the most cost-effective option, followed by augmented care. The other three panels present the cost-effectiveness results of varying the first- and second-line drug prices as specified above.

Panels (b) and (c) show that if the price of second-line therapy were reduced by 50 percent, the cost-effectiveness of all policy scenarios would greatly improve. Unlike the "no second-line" option simulated at the end of chapter 5, these simulations retain the health benefits of second-line therapy but pay less for them. They suggest the potential benefits to Thailand of negotiating much better prices on second-line drugs from multinational corporations or, alternatively, of compulsory licensing of these pharmaceuticals.

Figure 6.3 Sensitivity of the Cost-Effectiveness Analysis to Prices of First- and Second-Line ART



Source: Authors.

Panel (d) shows the result of higher prices for first-line therapy (perhaps caused by the new legislation in India) with unchanged prices for second-line therapy. This set of simulations shows that in a context where many people receive expensive second-line care, a small increase in the cost of first-line drugs could be absorbed relatively easily. However, if second-line drugs were unavailable, the same increase in the cost of first-line drugs would be larger in percentage terms and might cause a political reaction.

In none of the four panels does the ranking of policy options change. In all four, the pure NAPHA policy (scenario D1) remains the most cost-effective. In all four, the increase in cost per life-year saved of the both option (scenario D4) over the NAPHA-only option is small, given that the both option saves many more lives. Accordingly, in all four cases the recommendation would be to choose the both scenario, which enhances public ART delivery with both early recruitment (using VCT) and adherence support (using groups of people living with HIV/AIDS).[3]

Sensitivity to Changes in Risk Behavior

The simulation modeling performed in chapters 4 and 5 assumes that treatment policy does not affect risk behavior. This assumption may not be the case. As pointed out in chapter 2 and in the bottom row of table 3.8 in chapter 3, risk behavior may respond either positively or negatively to the availability of effective low-cost ART. We model a positive effect of ART availability on the demand for VCT (through responsiveness to lower price and distance to ART). However, in the basic policy and epidemiological models used in chapters 4 and 5, we permit no direct effect of VCT on risk behavior. In the baseline scenario and in the four policy scenarios, risk behavior continues to improve gradually following the trend of the past 15 years, when ART was neither very effective nor easily available. This section presents the results of sensitivity analysis with respect to risk behavior. Using the NAPHA policy (scenario D1) from chapter 4 as the benchmark, this section shows how the cost per life-year saved would be affected by either "beneficial" or "adverse" behavioral reactions of different groups of the population.

Table 6.1 presents the alternative assumptions about risk behavior for which sensitivity analysis is performed. The first column of the table presents the central assumptions under which all of the simulations of scenarios A, D1, D2, D3, and D4 are computed in chapters 4 and 5. The second and third data columns present, respectively, the beneficial assumptions and the adverse assumptions regarding behavioral response to treatment availability.

The sensitivity analysis compares the NAPHA cost-effectiveness result under the unchanged central behavioral assumptions—US$2,145 (B 85,800) per life-year saved—with the cost-effectiveness of NAPHA when behavior changes in response to treatment. Four types of behavioral response are considered:

- baseline behavior using central assumptions
- beneficial
- adverse
- extremely adverse

A beneficial behavioral response associates improved treatment availability with improved condom use in all risk groups. Condom use is assumed to increase from the central assumptions used in all previous scenarios to the beneficial assumptions listed in table 6.1. The result: the number of life-years saved is greater at the same or lower treatment cost. Cost-effectiveness is improved. According to the simulations, the results of which are depicted in figure 6.4, the cost per life-year saved drops from US$2,145 to US$1,952, an improvement of about 9 percent.

An adverse behavioral response is simulated by assuming that condom use in all risk groups declines from the central levels previously assumed to the lower levels presented in the "adverse" column of table 6.1. In this case, as figure 6.4 shows, the cost-effectiveness of the NAPHA policy deteriorates, from US$2,145 to US$2,487 (B 85,800 to B 99,480) per life-year saved.

We also simulated a mixed beneficial-adverse scenario by assuming that risk behavior among those on ART improves, while risk behavior among those not on ART deteriorates. The result of this combination of behavioral responses falls naturally between the adverse and beneficial results. However, since the groups whose behavior deteriorates are larger and include the major drivers of the epidemic, the result is closer to the adverse scenario than to the beneficial one. These results are omitted from the discussion and the figures.

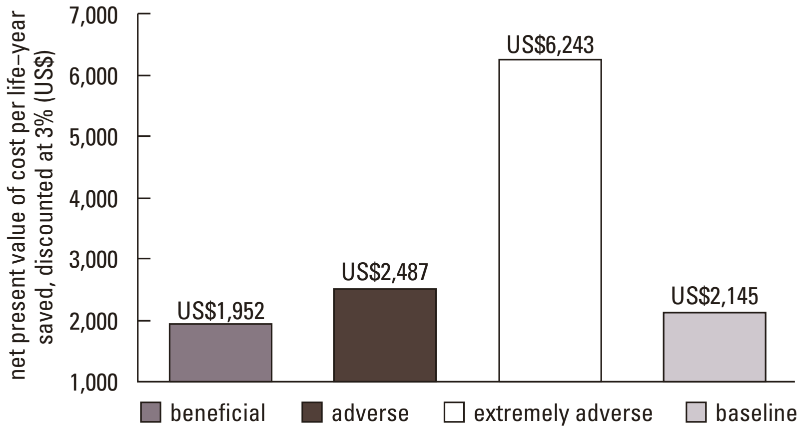
Finally, we examined the behavior of the model under a set of extremely adverse assumptions. Here, we adopt the pessimistic

Table 6.1 Proportion of Risky Sexual Acts Protected by Condoms: Alternative Behavioral Responses to Treatment Availability
percentage

		Assumptions for behavioral change			
Risk groups		***Central***	***Beneficial***	***Adverse***	***Very adverse***
High	CSW	85	95	75	60
	Clients	85	95	75	60
	MSM	85	95	75	60
	IDU	20	30	10	10
Low	General male	35	45	25	25
	General female	35	45	25	25
Risk groups		***Central***	***Beneficial***	***Adverse***	***Very adverse***
Percentage of men who visit					
Direct sex workers		10	5	20	20
Indirect sex workers		10	5	20	20
STI prevalence (among CSWs)		1.8	0.6	3.4	10.1

Source: Authors.
Note: CSW = commercial sex worker, MSM = men who have sex with men, IDU = injecting drug user, STI = sexually transmitted infection.

Figure 6.4 Sensitivity of the Cost Effectiveness of NAPHA Policy to Risk Behavior



Source: Authors.
Note: Beneficial = beneficial effects (reduced risk behavior) of those who are on ART and those who are not on ART. Adverse = adverse effects (increased risk behavior) of those who are on ART and those who are not on ART. Extremely adverse = adverse effects (increased risk behavior) of those who are on ART and those who are not on ART, with the risk behavior at the same level as in 1980.

hypothesis that condom use in high-risk contacts, needle exchange among drug users, and the rates of prevalence of other sexually transmitted infections all return to levels not seen since the early to mid-1990s. In contrast to the "adverse" scenario described above, this "extremely adverse" scenario produces a dramatic acceleration in new HIV infections: 85,000 new infections per year by 2015, instead of only 5,000 under the NAPHA scenario with no change in risk behavior. By 2025, the annual number of new HIV infections rises to more than 180,000, as compared with less than 3,000 new infections under our baseline projection. Despite the 20-year planning horizon, which excludes most of the cost of treating these thousands of new infections, the cost per life-year saved for NAPHA would almost triple to US$6,243 (B 249,720).[4]

One lesson of this sensitivity analysis is that where effective prevention has already greatly limited the growth of the epidemic and condom use is quite high among almost all groups, the cost-effectiveness of ART is less sensitive to behavior than it would be in an epidemic like that in India, where infections are spreading rapidly from a core of high-risk populations into an unprotected general population. Nevertheless, the Thai government must guard against the possibility that extreme complacency would decrease condom use even more than we have assumed in our "adverse" scenario. Dramatic reductions in condom use would indeed reignite the epidemic. A second lesson from this section is that policies that use ART to effectively leverage improved prevention efforts might improve the cost-effectiveness of ART in Thailand by as much as 10 percent.

Notes

1. Before 2005, Indian patent law differed from patent law elsewhere in granting patents exclusively on processes rather than on products. Under that law, Indian pharmaceutical manufacturers were able to legally produce copies of internationally patented drugs by developing novel processes for their production. To conform with World Trade Organization provisions on intellectual property rights, the Indian parliament passed a new Patents Act on March 23, 2005, which abolishes process patents in favor of product patents and recognizes international product patents. Under the new law, Indian pharmaceutical firms may be able to produce and sell internationally patented drugs, if those drugs were patented before 2004. However, they will be required to negotiate licensing agreements in order to copy and sell newer drugs, such as the second-line AIDS therapies. It is not yet clear whether Indian firms will pay royalties for the first time on the older drugs used in first-line therapy.

2. We also computed the costs and cost-effectiveness of treatment if second-line therapy were reduced in price by 90 percent.

3. If second-line therapy falls to 10 percent of its current price, the cost per life-year saved falls to US$940 (B 37,600) per life-year saved under the NAPHA scenario, only slightly more than the cost per year of saving fewer life-years with only first-line therapy. The present value of future ART spending drops from US$5.7 billion (B 228 billion) through 2025 to only US$2.5 billion (B 100 billion) a saving over the entire period of US$3.2 billion discounted dollars (B 128 billion).

4. This result is in contrast to the results of simulation modeling in India, where a reduction of condom use from 50 percent to 40 percent was enough to completely offset all the health gains from ART (Over and others 2004, p. 101). The projected impact of adverse behavioral change or “disinhibition” was worse in India because the epidemic is at an earlier stage and because the authors used a longer time horizon.