

**ECONOMIC ANALYSIS OF  
ANTIRETROVIRAL THERAPY  
IN BOTSWANA**

**By**

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## **Conceptual Framework and Priority Setting**

The Botswana AIDS/STD Unit estimates that 14% of the entire population of Botswana and 33% of pregnant women are currently infected with HIV. The economic burden of this overwhelming public health problem has two components. (1) The costs to the health system for caring for those already infected or sick, and for preventing further infections. Economists term these the direct costs. (2) The costs to the economy from lowered output and quality of life due to premature illness and death, termed the indirect costs. These affect both the market economy, such as formal employment, and the household economy, such as the rearing of children. Policy makers are concerned with both the current levels of these components and their future evolution. Public officials are also concerned with the portion of these components, particularly the direct costs, paid by the public sector. Because Botswana has one of Africa's strongest public health systems, much of the direct costs are borne by the public sector.

As serious as the current situation already is, the immediate future is even worse. Because the HIV/AIDS epidemic in Botswana has been sudden and explosive, the number of infected people has grown quickly, while the number of clinical AIDS cases, fortunately, is much lower. Typically, there is an 8-year lag between infection and clinical AIDS. As two recent international reports have concluded, the most critical role of government lies in prevention (World Bank, 1997; Mann et al. 1996). Simulations have shown that raising condom use to 90% in commercial sex, effective treatment of 75% of sexually transmitted diseases, high rates of condom use in casual sex, and serial monogamy, can control the epidemic. The experience of Thailand, which enforces a policy of universal condom use in commercial sex and strongly encourages it in casual sex, shows that concerted government action can have measurable effects.

To help persons already infected and their families, the World Bank (1997:203) recommended that governments should adopt "affordable, humane responses to the epidemic." In previous work with the Ministry of Health, the present author assisted the Botswana Ministry of Health in planning a cost-effective program of home care (Cameron et al, 1996). Applying principles of public finance and equity, the World Bank (1997) recommended that the share of public support for care of HIV/AIDS should be similar to that for other health problems. The remainder of this report sets forth a series of alternatives for developing such responses in regard to anti-retroviral therapy (ARV).

### **Priorities for Anti-Retroviral Therapy in Botswana**

Anti-viral therapy can be used to serve two populations, each with separate objectives. First, it could be offered to pregnant women beginning in last weeks of their pregnancy, and subsequently to their babies, to reduce "vertical" transmission from mother to infant. Second, it could be offered to infected persons, primarily adults, to delay and reduce the development of HIV illness. These two policies differ substantially in costs, benefits, and feasibility.

The first policy, pregnant women, would be targeted at a limited population with treatment of limited duration. Treatment of the mother lasts only four weeks and that of the infant a few days to a few weeks, plus bottle feeding (using current treatment recommendations). The treatment is monotherapy (i.e., a single drug, AZT). This treatment can halve the rate of infections in babies born to HIV-infected mothers. Those babies who are saved can expect a

normal lifespan and no abnormal health expenditures. As will be detailed below, this option is affordable and cost-effective.

By contrast, the second policy would potentially entail treatment of all HIV infected persons who know their status and meet medical eligibility criteria. Each person would be treated for his remaining life and, based on current treatment recommendations, would need triple therapy. As detailed below, this consultant could not find an equitable and affordable approach to HIV anti-retro-viral (ARV) treatment in the public sector for adults generally. There would, however, be feasible options for the private sector.

## **Treatment of Pregnant Women**

On February 24, 1998, the Centers for Disease Control and the Thailand Ministry of Public Health released interim results of a trial of short course zidovudine (AZT). Women in the experimental arm in this trial received 4 weeks of oral AZT (300 mg per day) and oral doses during delivery. Also, all women (both those in the experimental and control treatments) bottle fed their babies. As the full results of the trial have not yet been released, it is not clear what treatment was offered the infants. In another ongoing trial of short course AZT in Thailand, however, infants receive AZT orally (syrup) until their release from the hospital, about three days. The original clinical trial (AIDS Clinical Trial Group 076) provided 6 weeks of oral treatment to the infant. Botswana could potentially use either of these options.

As a recent meeting statement released by UNAIDS (1998) made clear, the greatest reduction in mother-to-child transmission would occur with an integrated program of both zidovudine and safe alternatives to breast feeding. The statement pointed out, however, that it may be impractical to implement both interventions simultaneously in some areas. In these situations, "implementation of one prevention component should not be delayed until the other is feasible."

In order to project the cost and impact of a program of screening and treatment of pregnant women, it was first necessary to determine the unit costs of ambulatory visits and inpatient hospital days. To do this, the costs of the Botswana Ministry of Health were allocated between these two services. First, based on the 1998-98 budget, costs were divided between "health services" and "administration and support," as shown in Table 1. It turned out that administration and support were equivalent to an overhead cost of 61% over the direct expenses of health services. Then, administration and support were allocated between the two types of health services in proportion to their direct costs.

Table 1. Allocation of Administration and Support Expenditures

Part	MOH Budget for 1998-99, Million Pula				Total Cost
	Total MOH	Health Services	Admin. & Support	Allocated Support	
1 Headquarters (Admin.)	81.92	-	37.20	-	
Transfers, memberships			-	27.24	71.95
2 Health Manpower	24.14	-	24.14	-	
3 Hospital Services	129.09	129.09	-	78.64	207.73
4 Primary Health Care Services	64.85	64.85	-	39.51	104.36
5 Technical Support Services	84.05	-	84.05	-	
TOTAL	384.05	238.66	145.39	-	384.05

Finally, unit costs were calculated by dividing the total costs of each of the two types of health services by their volume from the most recent annual statistical report (Republic of Botswana, 1997). The resulting unit costs, shown in Table 2, were \$65 or P250 for one hospital day, and P35 or \$9 for one outpatient visit. These are all-inclusive costs, for services, laboratory tests, and drugs.

Table 2. Derivation of unit costs

Part	Total Cost (Pula)	Quantity	Unit	Unit Costs	
				P	US\$ 3.85
3 Hospital Services	207,729,158	830,562	Inpatient days	250.11	64.96
4 Primary Health Care Services	104,361,797	2,989,390	OPD Visits	34.91	9.07
TOTAL	384,045,060				

Next, it was necessary to determine the cost of the proposed drug protocol for AZT for pregnant women. The recommended pre-natal dose is 300 mg. per day for the last four weeks of pregnancy. During labor, there is a "loading dose" of 300 mg. at the start of labor, and an additional 300 mg. dose after 6 hours if labor is still continuing. For the infant, on the recommendation of Dr. G. Anabwani, it was assumed that 6 mg. per kg. of weight would be given daily for 28 days. As the average weight in Botswana is 3.1 kg, the average daily dose would be 19 mg. The infant dose is given as syrup, a more expensive formulation.

The price of AZT tablets was derived from the US wholesale price. The price of AZT syrup was based on the cost in the Ontario Drug Program (Toronto Hospital, 1998), converted from Canadian to US dollars. Each of these amounts were reduced by 50 percent based on the press release by Glaxo-Wellcome to discount the price of AZT by 65 to 75 percent to "public health agencies" compared to the standard wholesale price. It estimated that the resulting cost would be about \$70 per pregnant woman (CNN, 1998). This analysis assumed 50 percent, with the remaining margin of 15 to 25 percent covering shipping and distribution costs. Table 3 shows that the cost of the resulting drug protocol is \$113. Alternative, less expensive protocols would also be possible. In the Northern Thailand Perinatal Prevention Trial, the

infants were given AZT only for the 3 days that they remained in the hospital. In the Bangkok trial of AZT, it appeared that no AZT was given to the infant. As the syrup formation is expensive, these changes would reduce the cost by about a third. The cost of treating only the mother, which would provide most of the benefit, would be \$71.

Table 3. Cost of proposed drug protocol for one pregnant woman

Component	Dose	Daily		Total	Unit	Total
		100 mg	Days	100 mg	Cost	Cost
		Doses		Doses	\$	\$
Daily	300 mg	3	28	84		
Loading	300 mg	3	1	3		
After 6 hrs	300 mg	3	1	3		
Subtotal, prenatal				90	0.80	71.55
Newborn						
ZDV Syrup	6mg/kg	0.19	28	5.32	7.80	41.48
Total				95.32		113.03

To determine the cost of a national program of treatment of pregnant women, the most comprehensive treatment scenario (28 days) for the infant was retained, but two alternative policies about breast feeding were considered. The more limited policy assumed that breast feeding would continue. This approach ensures that infants continue to receive maternal protection against diarrheal diseases and other infections, do not face the risks of nonsterile formula and bottles, and does not undermine the important public health message about the importance of breast feeding. This policy might be applied in rural areas, or in the initial stages of a program for mothers.

Table 4 sets forth the assumptions and resulting calculations from this policy. For each step, there are three components. First is the rate, generally indicating the percentage of women from a previous step who would reach that step. Second is the number of women who would reach the step. Third is the unit cost, in dollars and Pula, per woman at each step.

Table 4. Projected effect of a hypothetical national policy of AZT and breast feeding

Number	3000	Rate	Number	Unit Cost, \$	Annual cost for country		
					US \$	Pula, at 3.85	%
Population (pregnant women)			49,717				
Receiving ante-natal care		83%	41,265				
Offered testing and counseling		100%	41,265				
Accept testing and counseling		90%	37,139	21	779,911	3,002,656	35%
Prevalence, HIV+		33%	12,256				
Receive confirmatory test		100%	12,256	5	61,279	235,923	3%
Accept ARV		90%	11,030	113	1,246,716	4,799,855	56%
Bonus (P50) to nurse for ARV counseling		100%	11,030	13	143,249	551,508	6%
Baby infected without AZT to mother		35%	3,861				
HIV infections averted from AZT and bottle		50%	1,930				
Subtotal					2,231,154	8,589,942	100%
Infected babies who would have been hospitalized		50%	965				
Hospitalizations averted		6	5,791	-600	-3,474,502	-13,376,831	-156%
Net cost (savings)					-1,243,348	-4,786,890	-56%
Disability-adjusted life years (DALYs) gained		34	65,629				
Gross cost-effect.					34	131	
Cost-effectiveness					(19)	(73)	

This more limited policy would have a gross cost of \$2.2 million of P 8 million. It would more than pay for itself, however, in savings in hospital costs for affected babies. Thus, the net cost to the health system would actually be negative. The cost-effectiveness ratio based on gross costs would be \$34 per DALY gained. This low ratio would make this one of the most cost-effective public health interventions, comparable to childhood vaccinations. The net cost-effectiveness ratio is even more favorable, a negative ratio.

The broader policy about ARV for pregnant women assumed that all women who received AZT also were offered bottle feeding. This approach entails an additional cost for bottle feeding, some potential risks from bottle feeding, but added protection against HIV transmission through breast milk. Table 5 shows the corresponding calculations for the policy with bottle feeding.

Table 5. Projected effect of a hypothetical national policy of AZT and bottle feeding

Number	3000	Rate	Number	Annual cost for country			%
				Unit Cost, \$	US \$	Pula, at 3.85	
Population (pregnant women)			49,717				
Receiving ante-natal care		83%	41,265				
Offered testing and counseling		100%	41,265				
Accept testing and counseling		90%	37,139	21	779,911	3,002,656	16%
Prevalence, HIV+		33%	12,256				
Receive confirmatory test		100%	12,256	5	61,279	235,923	1%
Accept ARV		90%	11,030	113	1,246,716	4,799,855	26%
Bonus (P50) to nurse for ARV counseling		100%	11,030	13	143,249	551,508	3%
Accept bottle feeding		100%	11,030	182	2,005,484	7,721,115	42%
Attend follow up visits		90%	9,927	45	446,722	1,719,878	9%
Bonus (P50) to nurse for monitoring bottle feeding		100%	9,927	13	128,924	496,357	3%
Baby infected without AZT to mother		35%	3,861				
HIV infections averted from AZT and bottle		55%	2,123				
Subtotal					4,812,284	18,527,292	100%
Infected babies who would have been hospitalized		50%	1,062				
Hospitalizations averted		6	6,370	-600	-3,821,952	-14,714,514	-79%
Net cost (savings)					990,332	3,812,778	21%
Disability-adjusted life years (DALYs) gained		34	72,192				
Gross cost-effect.					67	257	
Cost-effectiveness					14	53	

Under this policy, the gross costs would be \$5 million (P19 million). The gross cost per HIV infected woman is \$393 for testing (including the testing of women who prove negative), drug treatment, and infant formula. Most (79%) of the costs would be offset, however, by lower hospital costs. Here the cost of formula (P700 per infant of \$182) is based on the retail price in Gaborone. If international generic prices were used, this cost would drop to \$88 (44 kgs at \$2 per kg). Although the net costs are positive, the cost-effectiveness ratios are still extremely favorable, at \$67 per DALY gross, or \$14 per DALY net (counting savings in hospitalization).

An incremental analysis compares these two policies, as shown in Table 6. The calculations show that the addition of formula adds substantially to costs, but only moderately to

effectiveness. Thus, the policy with AZT alone is actually more cost-effective than the policy with AZT and bottle feeding. The incremental cost-effectiveness ratio is still reasonable, however. The actual policy that this analysis suggests is consistent with the recommendation of UNAIDS (1998). AZT should be extended, as rapidly as practicable, to all pregnant women in the country. In areas where bottle feeding could be safely conducted, it should be offered, with government subsidy (or provision of formula) to mothers unable to purchase it. In the remaining areas, just AZT should be offered.

Table 6. Incremental cost-effectiveness analysis comparing breast and bottle feeding

Feeding	Cost	DALYs	Cost-Effectiveness
<u>Amounts in dollars</u>			
Breast	\$ 2,231,154	65,629	34
Bottle	\$ 4,812,284	72,192	67
Increment	\$ 2,581,130	6,563	393
<u>Amounts in Pula</u>			
Breast	8,589,942	65,629	131
Bottle	18,527,292	72,192	257
Increment	9,937,350	6,563	1,514

To integrate this program with Botswana's excellent program of prenatal care, it is suggested that the program be phased in by districts. Education about AZT, prenatal administration of AZT, bottle feeding (if indicated), and treatment of the newborn with AZT (if included) should be offered by the same team and in the same clinic as currently conducts prenatal care. The delivery dose should be offered in the same location as deliveries currently take place.

The most rational phasing of districts would be based on the estimated prevalence among pregnant women in the district. The districts with the highest prevalence have the greatest need, and will also be most cost-effective (as all women need to be screened). In districts with sentinel surveillance, this sero-prevalence rate can be estimated from anonymous sites in the district. In other districts, the prevalence can be estimated based on the number of reported cases of AIDS from the district in relation to the population of the district.

One of the concerns with treatment of pregnant women is that the program benefits the child, but not the mother directly. This theoretical concern can be responsibly addressed in Botswana. First, surveys organized by Dr. G. Anabwani in Molepolole District showed that all women surveyed would, in fact, agree to be screened if they knew that a treatment to benefit their babies might be available. Second, infected women could also be offered preventive treatment against tuberculosis (if TB positive), discussed in a subsequent section below. Screening and preventive treatment, where indicated, could also be offered to any interested HIV-infected sexual partners of the pregnant women.

## **Treatment of Infected Adults**

In the late 1980s, zidovudine (AZT) was the first anti-retroviral therapy (ART) to prove clinically useful. As its benefit was limited and drug resistance developed, this single drug is no longer recommended for treatment of infected adults generally. In the United States, a

panel convened by the U. S. Centers for Disease Control (CDC) published treatment guidelines in 1998 for ARV, based on current knowledge. The panel recommended “triple therapy,” that is, treatment that combines three anti-retroviral drugs. One of these drugs should be a protease inhibitor. The other two should be a compatible pair of Nucleoside Reverse Transcriptase Inhibitors (NRTI). In addition, after stabilization, the patient requires monitoring with a visit and a series of laboratory tests once every four months, equivalent to 0.008333 per day.

Table 7 below shows the cost for one patient for one year of maintenance ARV. The total annual cost is US \$16,016, or P 61,662. This amount is not the total cost of HIV medical care. In addition, the patient would require more frequent visits and tests for initiating treatment, and concurrent treatment of complications of HIV related illness, both inpatient and outpatient.

Table 7. Annual Costs of Maintenance Plan of ARV for One Adult Patient

Component	Daily	Package		Unit Cost, \$	Daily cost	
	Fre- Quency	Cost	Quan- tity		US \$	Pula at 3.85
<u>Monitoring lab tests and visits</u>						
Viral Load	0.0083	150	1	150	1.25	4.81
CD4 Count	0.0083	30				
CBC	0.0083	5	1		0.04	0.16
Chem12	0.0083	20	1		0.17	0.64
Urinalysis	0.0083	5	1		0.04	0.16
Visit	0.0333	54	1	54.05	1.80	6.94
<u>Protease inhibitor:</u>						
Indinavir, 400 mg	6	450	180	2.50	15.00	57.75
Nelfinavir, 250 mg tab	9	557.28	270	2.06	18.58	71.52
Ritonavir, 100 mg caps	12	155.82	84	1.86	22.26	85.70
Average protease inhibitor	9				18.61	71.66
<u>Nucleoside Reverse Transcriptase Inhibitors (NRTI)</u>						
Zidovudine (ZDV) 100 mg	6	159.29	100	1.59	9.56	36.80
Didanosine (ddI), 100 mg	4	101.56	60	1.69	6.77	26.07
First pair	10				16.33	62.86
Stavudine (d4T), 40 mg	2	255.53	60	4.26	8.52	32.79
Didanosine (ddI), 100 mg	4	101.56	60	1.69	6.77	26.07
Second pair	6				15.29	58.86
Zidovudine (ZDV) 100 mg	6	159.29	100	1.59	9.56	36.80
Dideoxycytidine (ddC), 0.75 mg	3	235.67	60	3.93	11.78	45.37
Third pair	9				21.34	82.16
Average NRTI	8				17.65	67.96
Overall triple drug ingredients	17				36.26	139.62
Mark up (10%)					3.63	13.96
Daily total					39.89	153.58
Days per year					365	365
Annual total					16,016	61,662

To determine the national costs of ARV treatment for Botswana under alternative scenarios, one must estimate the total number of infected persons, and the share that might obtain ARV if it were available at little or no cost. The number of cases was based on the model EPI Model, an epidemiological projection model, initially developed by the World Health Organization's Global Programme on AIDS (now UNAIDS). The model was calibrated by the AIDS/STD Unit to the 1997 situation, in which 14% of the Botswana population, or

200,000 people, were thought to be infected with HIV (Table 8). It was assumed that 50% of positive persons would know their status with widespread screening and treatment. This is about the share that exists in the United States. Because of two counterbalancing factors this assumption seemed plausible for Botswana. On the one hand, testing might be less available and would be more expensive. On the other, the much greater prevalence in Botswana would make HIV infection even more salient.

Table 8. National Cost of Maintenance Treatment with ARV in Botswana

	1997	1998	1999	2000
Number of epidemiologically projected HIV+ persons in Botswana	200,000	225,824	250,631	273,967
Share of positive persons who would know their status with widespread screening and treatment	50%	50%	50%	50%
Projected number of HIV+ persons with known status	100,000	112,912	125,316	136,984
Annual cost per patient (US \$)	16,016	16,016	16,016	16,016
Annual cost per patient (P)	61,662	61,662	61,662	61,662
Assumed fraction of known HIV+ persons receiving ARV	<u>Cost in billions of Pula</u>			
0%	0.00	0.00	0.00	0.00
25%	1.54	1.74	1.93	2.11
50%	3.08	3.48	3.86	4.22
75%	4.62	5.22	5.80	6.34
100%	6.17	6.96	7.73	8.45

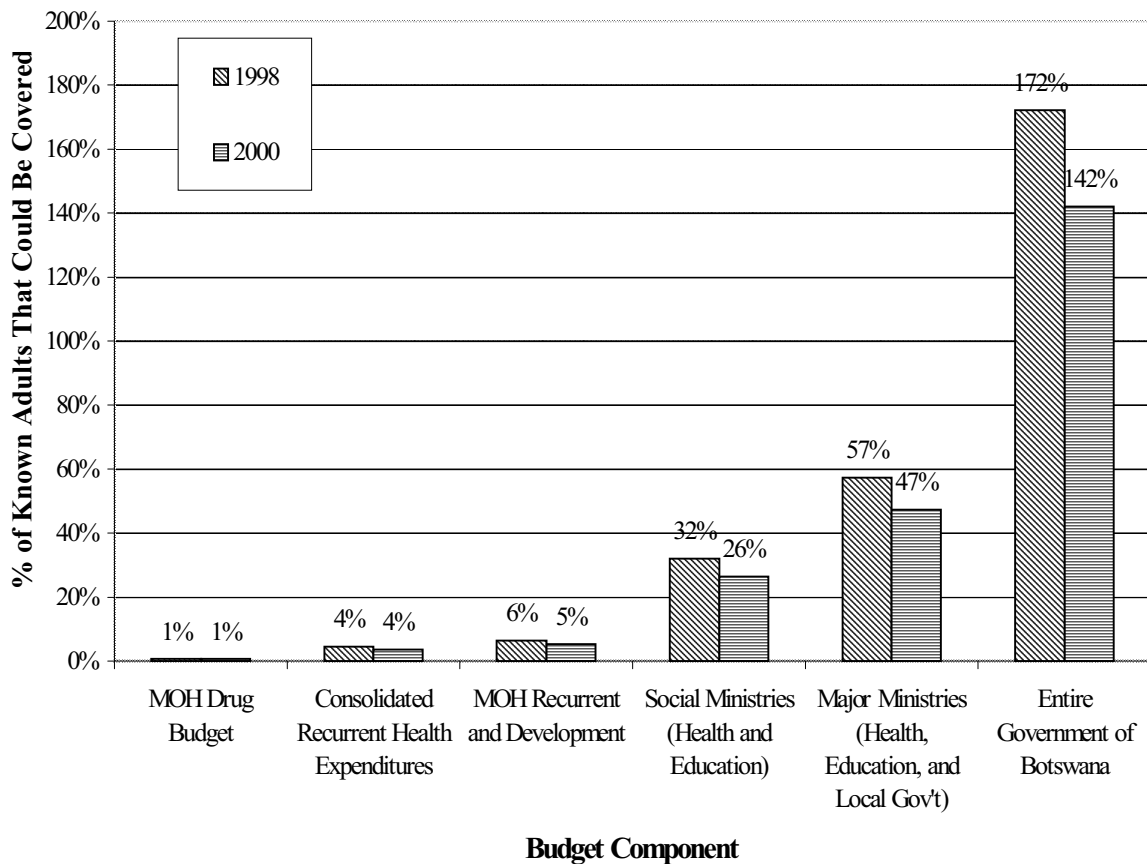
To appreciate the magnitudes of the costs that would be involved, it is useful to compare the projected costs for 1998 with selected budget components for the same year (Table 9). The fiscal year 1998 drug budget of P 50 million (P 0.05 billion) would support only 1% of the potential ARV patients.

Table 9. Cost of ARV in Relation to Selected Budget Items

Budget Component	1998 Budget Billion Pula	Coverage That Could Be <u>Financed</u>	
		1998	2000
MOH Drug Budget	0.05	1%	1%
Consolidated Recurrent Health Expenditures	0.31	4%	4%
MOH Recurrent and Development	0.44	6%	5%
Social Ministries (Health and Education)	2.22	32%	26%
Major Ministries (Health, Education, and Local Gov't)	3.99	57%	47%
Entire Government of Botswana (Recurrent and Development)	11.99	172%	142%
Projected cost of ARV, 1998	6.96		
Projected cost of ARV, 2000	8.45		

The figure below graphically shows the percentage of known infected adults who could be maintained on ARV if the entirety of selected budget components were used to finance that item. As the number of infected persons is growing rapidly, the percentage of people who could be covered in the year 2000 is substantially less than that in 1998. The costs of maintenance ARV therapy are formidable. The entire consolidated recurrent budget of the Ministry of Health would suffice to treat only 4% of the infected population in 1998. In fact, the development and recurrent budgets of three major ministries (Health, Education, and Local Government) would suffice to treat only 57% of the infected population in 1998 or only 47% in the year 2000. The budget of the entire government of Botswana would suffice to treat 172% of the known population in 1998, or 142% in 2000. Recalling that only half of infected people would be assumed to know their status, however, even the entire government budget would be treating only half of this percentage, or 71%, of the total number of infected people in the year 2000.

## Budget Components Required to Finance ARV, Years 1998 and 2000



The funding equivalent to the major ministries (Health, Education, and Local Government) would have to be in addition to the present funding, as the existing functions of these ministries would still need to be supported. Thus, to treat all known HIV positive patients in 1998 would require a 58% increase in government expenditures, and a 70% increase in the year 2000.

### Prevention of Tuberculosis

Throughout Africa, tuberculosis is one of the major complications of HIV. Because of their compromised immune systems, HIV-infected persons are more likely to develop tuberculosis and the tuberculosis, in turn, may accelerate the progression of other HIV-related illness. A recent trial in Uganda (Whalen et al, 1997) demonstrated the efficacy several preventive regimens. The most effective, and also the most affordable, was 300 mg of isoniazid (INH) daily for six months. A trial in Haiti (Halsey et al, 1998) showed that an even shorter (two month) regimen based on a combination of pyrazinamide and rifampicin.

Based on prices in Canada under the public Ontario Drug Benefit, the recommended dose of isoniazid would cost only \$0.06 per day, of \$10.80 (P42) for 180 days. Assuming that each visit cost P40, the cost of the preventive program would be P 280 for seven visits plus P 42 for INH, or P322 in total. Botswana might be able to buy the drug generically from international sources at an even lower price.

In the Ugandan trial, INH lowered the risk of tuberculosis by a highly significant 67% compared to placebo, from about 10% to 3.3% per person year. Following the six months of treatment, the benefits persisted over the two-year period of follow up. Whalen et al. Estimated that the case fatality rate from tuberculosis in HIV infected patients was about 20%, so important mortality benefits could be anticipated. In 100 patients, 2.7 deaths might be averted over 2 years by INH prevention. In the Ugandan trial, the INH patients did have somewhat lower mortality than the placebo patients, but the study was not designed to test the significance of the mortality effect. Each of these deaths averted might add an additional 5 Disability Adjusted Life Years (DALYs), as the patients are HIV infected, but not AIDS cases.

The cost of treating 100 patients would be P 32,200 (\$8363). The cost effectiveness is P11,925 (\$3098) per death averted, or P2385 (\$620) per DALY. This would be a relatively cost-effective intervention. It compares particularly favorably to adult ARV. Assuming, optimistically, that one year of ARV achieves one DALY, the cost effectiveness of ARV is P61,000 (\$16,000). Thus, tuberculosis prevention is at least 30 times more cost effective than adult ARV. The population benefits of reducing secondary tuberculosis cases would further strengthen the rationale for encouraging tuberculosis prevention with INH.

The constraint on tuberculosis prevention is not cost, but compliance. A patient must remember to take INH daily for six months, and must report monthly to a clinic for follow up and prescription renewals. Nevertheless, the potential benefits to the individual patient and to the public overall argue for seriously considering this intervention.

### **Privately Funded ARV**

Limited privately funded ARV for adults already occurs in Botswana. Government should encourage the clinicians involved to set clinical guidelines to ensure that his treatment is of maximal benefit to the patients involved, and to the broader population of Botswana. These guidelines should consider the following principles:

1. To minimize the problem of drug resistance, patients should not start treatment unless it is likely that they will be able to continue with treatment (they have adequate financial and social support).
2. ARV should encourage the open discussion about preventing HIV, and accepting those who are infected. It should not give the mistaken impression that HIV is curable and the problem is passed. Thus, patients receiving ARV should be encouraged to serve as peer educators and counselors, and consideration should be given to offering both financial and emotional support for their efforts. This service might be affected through the patient volunteering for one day per week of unpaid service in an AIDS-related non-governmental organization approved by the AIDS/STD Unit in Gaborone.
3. Privately funded treatment should provide a source of data for government to revisit policy about ARV in the future. Thus, the clinical committee should define a registry of ARV. Data on the drug regimens, compliance, and outcomes (both laboratory and clinical) should be maintained for each patient on ARV. Funding for the maintenance and analysis of this registry should come from government and the pharmaceutical sector, with confidential reports sent to each physician who supplies data. Preferred drug prices would be extended to each patient for whom data are accurately recorded.

4. Privately funded ARV should not use scarce public resources. Thus, the laboratory tests and professional visits needed to initiate and monitor ARV should also be privately financed.
5. Privately funded ARV should include self-pay, payments through private insurance and medical aid schemes, and the public system for civil servants, the Botswana Officers Public Medical Assistance Scheme (BOPMAS). It should be limited to the high option plan under BOPMAS, however, with most of the added cost of ARV being paid by the officers choosing that option, rather than the government generally.
6. Coverage under private insurance must balance the needs of those seeking treatment and the employers and other subscribers who pay premiums. Thus, coverage for ARV cannot be allowed to bankrupt private insurance, nor to make it so expensive that it becomes unaffordable. To achieve this balance, consideration should be given to requiring that coverage for anti-retroviral drugs should be subject to a deductible (about 4 months usage), coinsurance (50%) and an annual ceiling (US \$20,000, or P 80,000 per year).
7. To minimize the problem of adverse selection, all insurers should follow the same criteria regarding eligibility and level of reimbursement on their high option plans.
8. To ensure that therapy is effective and the patient is compliant, the physician must submit a viral load test showing very low viral load before the insurance takes effect.

### **Additional Funding Prospects**

Macro-economic data compiled by the World Bank (1996) indicate the difficulties of major tax increases to support large expansions in government expenditures for ARV. As of 1994, central government expenditures represented 32.8% of GNP for current expenditures, and an additional 7.4% of GNP for capital expenditures, or 40.2% overall. These shares were already higher overall than those of Botswana's southern neighbor, South Africa, which devoted 34.4%, 1.6%, and 36.0% of its GNP to current, capital, and total government expenditures. Similarly, Botswana's tax and non-tax revenues, 30.5% and 25.6% of GNP, respectively, are also higher than those of South Africa or of most other middle countries. As the government revenue structure is already relatively comprehensive, there would seem to be few large untapped sources of revenue.

Finally, it is worth examining the possibility of reallocations of government expenditures. The share of central government expenditures devoted to social services, 36.0%, is appreciable, but not as high as that in some other middle income countries, such as Costa Rica (61.3%). Some of the differences may be artifacts, rather than real. In Botswana, many health services are delivered through the Ministry of Local Government, but these expenditures may not be counted under social services in the World Bank's international comparisons.

Limited taxes might be possible to support activities related to HIV. For example, in the state of Massachusetts in the U.S., voters approved an increase in the state excise tax on cigarettes of \$0.25 per pack. Most of the funds are awarded competitively by the state health department to local governments for non-smoking initiatives. The increase in expenditures to control smoking (such as vigorous enforcement of laws prohibiting sales to minors) and in their impact, have been substantial. With about a quarter of the adult population smoking, the tax generates revenues of about \$20 per capita. In Botswana, a comparable tax would generate about \$28 million, or P 108 million. While these sums would do little to fund ARV

in adults, they could be major contributors to ARV for pregnant women, or for strengthened AIDS prevention programs generally.

## **Operational Research Opportunities**

Once effective and affordable approaches to ARV have been identified, it is important to optimize their utilization and quality. The need and opportunities for operations research in ARV are analogous to the situation in a closely allied field, tuberculosis. While Directly Observed Therapy, Short-course (DOTS) is efficacious, only 12% of patients worldwide receive the treatment. Recognizing this need, international officials met in Geneva from March 3 to 5, 1998 to set priorities (McConnell, 1998). The World Health Organization (WHO) officials stressed the importance of “developing operational-research capacity...and of coordinating research with the routine functions of national tuberculosis programs.” Operational research is needed to become more glamorous, to attract more funding and the best scientists. While strategic research on new basic science is also valuable, it may take decades to have impact. Thus, WHO committee recommended that the short run emphasis should be on operational research.

In ARV, operational research can strengthen services to pregnant women and to adults through the following opportunities.

### Pregnant Women

1. How to integrate AZT into pre-natal care. How can Family Welfare Educators, nurses, and midwives be trained and encouraged to motivate pregnant women to seek prenatal care early, to accept testing for HIV when offered, and to accept AZT if found to be sero-positive.
2. How to support HIV-infected pregnant women in making informed and humane choices about breast feeding. This will include developing counseling approaches for them and their family so that they can accept their HIV status and, if necessary, publicly acknowledge it.
3. How to integrate safe bottle feeding into newborn care. This includes identifying sterile ways of cleaning bottles, safe water for preparing formula, financial means tests for subsidized formula for mothers unable to pay, and developing government distribution channels for subsidized formula.
4. Testing innovative motivation systems for clinic staff. Recognizing the extra time involved in counseling, a payment system of P 100 per women who completes a course of therapy with AZT from four weeks prior to delivery through delivery. An additional payment of P 50 would be offered for completion of an alternative to bottle feeding without major complications. These payments would compensate for the additional hours, often outside of working hours, in talking with pregnant women, earning their confidence. Each could be divided among all the clinic staff (Family Welfare Educators, nurses, and midwives) based on their share of involvement. As all of these staff are busy and have many competing demands, the additional payments should help ensure that both existing responsibilities and added services to pregnant women are addressed.

### Infected Adults

1. Analyze the Anti-retroviral Registry Data base to determine the degree of compliance, costs, and outcomes of patients receive ARV in the private sector.
2. Use the results to consider future government policies if such treatment becomes less expensive or more efficacious.

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## **References**

- Cameron, C., Shepard, D.S., Mulwa, J. Caring for persons with AIDS (PWA) in Botswana: is home-based care the answer? In: AIDS in the World II, Mann, J., Tarantola, D.J.M., eds. New York: Oxford University Press, 1996, pp. 405-407.
- Cable News Network (CNN). Press release from Peter Young, Spokesman, Glaxo-Wellcome PLC about AZT. Atlanta, March, 1998.
- Halsey N et al. The Lancet, March 14, 1998.
- Mann, J., Tarantola, D.J.M., eds. AIDS in the World II, New York: Oxford University Press, 1996.
- McConnell J. WHO's tuberculosis research initiative. The Lancet. 351:852, 1998.
- Republic of Botswana. Health Statistics 1996. Gaborone: Central Statistics Office, 1997.
- Toronto Hospital. Opportunistic Infections, TB (Web site), May 30, 1998.
- US Centers for Disease Control, National Center for HIV, STD and TB Prevention. Short Course Regimen of AZT Proven Effective in Reducing Perinatal HIV Transmission: Offers Hope for Reducing Mother-to-Child HIV Transmission in Developing World, Atlanta, GA: CDC, Office of Communication, Wednesday, February 18, 1998.
- Whalen CC, Johnson JL, Okwera A, Hom DL, Huebner R, Mugenyi P, Mugerwa RD, Ellner JJ. A trial of three regimens to prevent tuberculosis in Uganda adults infected with the Human Immunodeficiency Virus. N Engl J Med 337:301-308, 1997.

World Bank. World Development Report 1996: From Plan to Market. Oxford: Oxford University Press, 1996.

World Bank. Confronting AIDS: Public Priorities in a Global Epidemic. Oxford: Oxford University Press, 1997.