

**COST AND FINANCING
ASPECTS OF PROVIDING
ANTI-RETROVIRAL
THERAPY:
A BACKGROUND PAPER**

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Introduction

When the HIV/AIDS epidemic was first recognised in the early 1980s, treatment options for HIV-infected people were limited. While prophylaxis was available for some AIDS-associated opportunistic infections such as tuberculosis and pneumocystis carinii pneumonia, therapies which had been demonstrated to affect the behaviour of the virus itself were not available. Following the approval of the drug AZT by the USA's Food and Drug Administration in 1987, however, its prescription to AIDS patients became common medical practice, especially when controlled trials showed it was an effective anti-retroviral agent and that it lengthened life expectancy. More recently, it has also become common medical practice to prescribe AZT (now called zidovudine) to HIV-infected patients who have not yet developed AIDS, both to patients who have HIV-related symptoms and to those who are asymptomatic (Cosler and Lambrinos, 1992). The drug is now widely used in North America, Europe and Australia, along with a number of other anti-retrovirals (ARVs) which have now entered the market.

In contrast, ARVs are not yet widely available to HIV-infected people or AIDS patients in developing countries. While there are notable exceptions such as Thailand, in most countries of Africa, Asia, Latin America and the Caribbean, access to AZT and the newer drugs is only possible through the private sector (Santos et al, 1994). As the HIV epidemic worsens in these regions, policy development in the area of anti-retroviral therapy is increasingly warranted. This is especially so in light of recent suggestions that anti-retroviral combination therapies may not only prolong life but may even, if taken for life, be capable of preventing HIV-infected people from progressing to AIDS at all (Piot 1996); and evidence that provision of AZT to pregnant women reduces transmission to their children (Connor et al, 1994). In addition, with rising rates of infection among hospital patient populations, demand for AZT prophylaxis from health workers exposed to HIV is likely to increase.

The economic aspects of providing ARVs to HIV-infected people and exposed health workers are one of a number of important considerations which can be analysed to help inform policy development. This paper therefore addresses such aspects. It has seven main sections, which are:

- **Cost of providing anti-retroviral therapy (1.)**, in which data on the cost of the drugs is provided and evidence concerning other costs associated with provision of therapy is summarized;
- **Total cost implications of providing anti-retroviral therapy (2.)**, in which the cost data presented in (1.) are used in combination with region-specific data concerning the number of people with AIDS or HIV infection to estimate the total costs for different geographic regions of providing therapy;
- **Total cost implications of providing anti-retroviral therapy in comparison with available resources (3.)**, in which region-specific GDP, health sector expenditures, National AIDS Programme budgets, and official development assistance are compared with the estimates for total costs of anti-retroviral therapy given in 2.;
- **Cost-saving potential and cost-effectiveness of anti-retroviral therapy (4.)**, in which evidence concerning the impact of AZT on health system resource use and life expectancy are used in combination with estimates of the costs of medical care for HIV/AIDS to assess whether, despite the costs associated with their provision, ARVs might be either cost-saving or cost-effective;
- **Cost, cost-saving potential, and cost-effectiveness of providing AZT therapy to pregnant women (5.)**, in which available data concerning the costs associated with providing AZT to pregnant women, the potential for cost-saving due to averted paediatric AIDS cases, and likely cost-effectiveness where therapy may not be cost-saving are discussed;
- **Cost and Cost-effectiveness of Prophylaxis for Health Care Workers (6.)**; and
- **Financing anti-retroviral therapy (7.)**, in which alternative financing options are assessed.

Conclusions (8.) and a bibliography are also included (9.).

1. Cost of providing anti-retroviral therapy

Available data concerning the costs of providing ARV therapy are presented in two separate sections: the first presents the costs of the ARV drugs; the second presents the details on the other costs associated with providing them. A third section highlights other costs which may be important, especially in developing countries.

1.1 Anti-retroviral Drug Costs

The cost of the ARVs themselves are shown in Table 1 below. The most recent figures suggest that, at market prices, AZT costs US\$ 1.5/100mg tablet. Since the standard regimen involves 500mg/day, this means that the daily per patient cost is US\$ 7.5, the average monthly cost per patient is US\$ 228, and the annual cost per patient is US\$ 2 738. This is considerably less than in the late 1980s, when the annual per patient cost of AZT was reported to be US\$ 10 000 (Sabatier et al, 1989).

Table 1: Anti-Retroviral Drug Costs (US\$) at Market Prices

Drug and dosage required	Unit Cost	Monthly Cost	Annual Cost	Source, Date of Data and Reference
zidovudine (AZT) 250mg twice per day	1.50 per 100mg	228	2 738	USA, 1994, Bozzette et al; Mauskopf et al, 1996
didanosine (DDI) ¹ 200mg twice per day	1.44 per 100mg	175	2 102	USA, 1991, Hellinger 1992
zalcitabine (DDC) 0.75mg three times a day	2.4 per 0.75mg	220	2 640	World wide web page of AIDS Rx, a North Carolina, USA based company, 1997
stavudine (D4T) 40mg twice a day	3.9 per 40mg	232	2 788	As above
lamivudine (3TC) 150mg twice daily	3.6 per 150mg	214	2 572	As above
ritonavir 600mg twice daily	11.5 per 600mg	692	8 308	As above
saquinavir 600mg three times a day	6.1 per 600mg	545	6 540	As above
idinavir 800mg every 8 hours	4.4 per 800mg	533	6 400	As above
nevirapine 100mg twice a day	4.12 per 100mg	272	3 260	As above
Double combination therapies: include ² (a) zidovudine plus either didanosine or zalcitabine or lamivudine or saquinavir or crivivan (b) zalcitabine plus saquinavir (c) stavudine plus didanosine	See above	403 to 773	4 836 to 9 276	Sources quoted above
Triple combination therapies ³ : include: (a) zidovudine plus zalcitabine plus saquinavir (b) zidovudine plus zalcitabine plus lamivudine (c) zidovudine plus lamivudine plus loviride (d) zidovudine plus didanosine plus nevirapine (e) zidovudine plus didanosine plus idinavir	See above	662 to 993	7 944 to 11 916, up to 20 224 if ritonavir is also added	Sources quoted above

Meanwhile, three of the newer “nucleoside reverse transcriptase inhibitors” are slightly cheaper (didanosine costs US\$175 per month, zalcitabine US\$220 per month, and lamivudine US\$214 per month), while a fourth - stavudine - is slightly more expensive at US\$232 per month. The even more recent “protease inhibitors” are considerably more: ritonavir costs US\$692 per month, saquinavir US\$545 per month, and idinavir US\$533 per month. The one “non-nucleoside reverse transcriptase inhibitor” - nevirapine - is at the

¹ approved in 1991 in the USA to treat patients who cannot tolerate AZT (Hellinger 1992)

² see Drug and Therapeutics Bulletin Vol. 35 No. 4 April 1997

³ see Drug and Therapeutics Bulletin Vol. 35 No. 4 April 1997

lower end of the spectrum of costs, at US\$272 per month. Double combination therapies range in costs US\$993, increasing to up to US\$1 465 if ritonavir is added.

These costs are substantial. However, it is important to note that large reductions in these costs may be

have been negotiated in Uruguay on the basis of bulk-purchase (Abreu, personal communication). This shows that annual treatment costs approximately two-thirds of those quoted above have been achieved for

Table 2: Drug Costs (US\$) in Uruguay when Drugs are Purchased in Bulk

Drug		Annual Treatment Cost as % Annual Treatment Cost at market prices
	776	28%
	4 340	66%
	5 528	67%
	2 108	82%

In addition to drug costs, other important costs associated with providing therapy include: HIV tests to establish whether someone is HIV+ and hence eligible for therapy; pre- and post-test counselling; regular

CD4 counts, complete blood counts, viral loads, and chemistry panels to monitor patient health status; and out-patient visits/hospitalizations associated with adverse drug effects. Few data are available concerning

Table 3: Non-Drug Costs Associated with Providing Anti-Retroviral Therapy (US\$)

Cost Item	Cost	Source, Date of Data and Reference
	157 40	USA, 1995, Gable et al JCRC, Uganda, 1997
Viral load test	163	Gotch, 1997, personal communication JCRC, Uganda, 1997
	2 21	USA, 1996, Gorsky et al
Chemistry panel***	35	USA, 1991, Schulman et al
Serum amylase	18	
Transfusion for AZT-induced anaemia	580	
HIV ELISA test	3 6	South Africa, 1996, Wilkinson et al, 1997; USA, 1996, Gorsky et al; JCRC, Uganda, 1997
Rapid HIV Test (Capillus)		South Africa, as above
Rapid HIV Test (Abbot)		South Africa, as above
Pre-test/post-test Counselling Visit for HIV-person		USA, 1994, Mauskopf et al
Pre-test/post-test Counselling Visit for HIV+ person		As above
Test + counselling		Uganda 1992/96, quoted in Mansergh et al
Out-patient visit* therapy-related)	120 17	USA, 1991, Hellinger South Africa, 1996, Floyd et al, 1997
Day in hospital are included here for guidance only. The USA figure is an average for an AIDS patient; costs for Malawi and South Africa are for TB	1 150 2	USA, 1995, Gable et al Malawi, 1995, Sawert 1991, in Bloom

* assumed to be required once/month by Bozette et al and quarterly by Schulman et al ** assumed to be required once/month by

***assumed to be required quarterly by Schulman et al

1.3 Other Costs which may be important, especially in Developing Countries

There are also some additional costs which may be involved in providing ARV therapy, especially in developing countries, and it is worth highlighting these. Many of the costs quoted in Table 3 above are based on US cost data, where the costs of shipping equipment and supplies will be relatively low because they can be domestically produced. In developing countries where these items will probably have to be imported from countries a considerable distance away, costs are likely to be higher.

In addition, in developing countries laboratories may have to be strengthened considerably if they are to be capable of providing the diagnostic and monitoring support necessary for provision of ARV therapy. This could include installation of air-conditioners and back-up generators to cope with electricity cuts, and proper maintenance contracts. Developing such capacity may have large costs attached to it.

2. Total cost implications of providing anti-retroviral therapy

The unit costs presented in 1. can be used to estimate what the annual per patient cost of providing ARVs might be. While the drug costs are fairly uniform among countries and will only differ according to freight/customs charges, the costs of the non-drug components are likely to vary substantially - as the costs for a day in hospital shown above indicate. Since most of the non-drug cost data are from the USA, this means that cost estimates cannot be very precise. This problem is aggravated by the fact that approaches to case management are not well defined for many countries - for example the frequency and type of laboratory tests which would be appropriate, how often monitoring visits would be required, etc. This makes costing difficult, since the required resource inputs cannot be clearly identified.

Moreover, a portion - perhaps even a majority - of patients will not be able to tolerate the drugs and will suffer adverse effects (Hay et al, 1988), or will decline to take them at all (Alcorn 1995). This means that the average annual cost of ARV therapy per HIV infected person may be either more or less than the average annual cost for a patient who tolerates the therapy without any problems. It will be more if the costs of patients suffering adverse effects in a given year exceeds the cost of those patients continuing with therapy for that year; it will be less if the cost of adverse effects is less than the costs which would be incurred were those patients suffering from adverse effects to continue therapy.

Due to these difficulties, a simplified cost analysis is given here. The annual cost for a patient receiving ARV is assumed to be the cost of the drugs, the cost of four outpatient visits (with a range from 1 to 120), the cost of four complete blood cell counts (with a range of 2 to 21), four CD4 counts (with a range from 30 to 157), four viral load tests (a frequency suggested in the minutes of the February 26th 1997 meeting of the "HIV physicians forum for the North West Region in the UK") at US\$163 each, and four chemistry panels (with a range from 12 to 35). The range in costs for the final three components reflects the range shown in the Table 3 cost data. The range in outpatient costs uses the highest figure for the USA shown in Table 3 as an upper estimate, but US\$1 is used as a lower estimate since the day in hospital cost for Malawi suggests that in very poor countries this may be a realistic figure. Counselling costs and HIV test costs are ignored since these are one-off costs and are minor in comparison with other cost components. The cost impact of adverse effects is also ignored since there are so few data which can provide guidance. However, it is worth noting that in the USA it has been suggested that adverse effects will substantially increase ARV therapy costs (Bozette et al, 1994). It has also been suggested that outpatient costs for HIV-infected people are higher than those for non-infected patients (McDermott et al, 1991), and both the minimum and maximum estimates used here may therefore underestimate the cost of an OPD visit for patients receiving ARV which would be incurred in practice.

Using the above assumptions, the per patient annual cost for ARV therapy would range from US\$ 3 570 to US\$ 4 722 for AZT therapy, and from US\$ 8 776 to US\$ 13 902 for triple-combination therapy (excluding a regimen which includes ritonavir). It is noteworthy that *the drugs constitute between 58% and 77% of total per patient annual costs with AZT therapy, and between 86% and 91% of total per patient annual costs with triple combination therapy.* This illustrates that if drug costs can be reduced, as has already happened with AZT, and as has been demonstrated to be possible in Uruguay, a substantial

impact will be made on the affordability of therapy. Partnerships among international agencies, individual governments and drug companies may also have potential to have a large impact on the cost of drugs. However, at present, at market prices, even the cost of AZT therapy is higher than average incomes in most countries.

To estimate the total annual cost which would be incurred if ARV therapy were to be provided in different geographic regions, these figures are then used in combination with 1996 data concerning the number of people with HIV infection but not AIDS, and the number of people with AIDS (taken from figures quoted in Mann and Tarantola, Chapter 1, 1996). Two scenarios are presented. In the first, everyone receives ARV therapy - though unrealistic, it is useful in providing an upper total cost estimate; in the second, 50% or those eligible are assumed to receive therapy. The results are shown in Table 4 below. When considering these figures, it is worth bearing in mind that it has been calculated that implementation of six major prevention strategies in developing countries would in total cost between US\$ 1.5 and US\$ 2.9 billion (Broomberg and Schopper, 1996).

Table 4: Estimated Total Annual Costs (US\$) for ARV therapy by Geographic Region under Alternative Assumptions in 1996

Geographic Region ⁴	Estimated Number of People with AIDS in 1996	Estimated Number of People with HIV infection but not AIDS in 1996	Estimated Total Cost for AZT therapy if 50% of those eligible receive it	Estimated Total Cost for triple-combination therapy if 50% of those eligible receive it	Estimated Total Cost for AZT therapy if 100% of those eligible receive it	Estimated Total Cost for triple-combination therapy if 100% of those eligible receive it
North America	91 000	837 000	1.65 billion to 2.2 billion	4.1 billion to 6.5 billion	3.3 billion to 4.4 billion	8.1 billion to 12.9 billion
Western Europe	52 000	642 000	1.25 billion to 1.65 billion	3 billion to 4.8 billion	2.5 billion to 3.3 billion	6.1 billion to 9.6 billion
Oceania	2 000	23 000	0.04 billion to 0.06 billion	0.1 billion to 0.2 billion	0.09 billion to 0.1 billion	0.2 billion to 0.35 billion
Latin America	61 000	976 000	1.85 billion to 2.45 billion	4.6 billion to 7.2 billion	3.7 billion to 4.9 billion	9.1 billion to 14.4 billion
Sub-Saharan Africa	803 000	10 809 000	20.7 billion to 27.4 billion	50.9 billion to 80.7 billion	41.5 billion to 54.8 billion	101.9 billion to 161.4 billion
Caribbean	19 000	343 000	0.65 billion to 0.85 billion	1.6 billion to 2.5 billion	1.3 billion to 1.7 billion	3.2 billion to 5 billion
Eastern Europe	2 000	30 000	0.06 billion to 0.08 billion	0.15 billion to 0.2 billion	0.1 billion to 0.15 billion	0.3 billion to 0.4 billion
SE Mediterranean	4 000	65 000	0.12 billion to 0.15 billion	0.3 billion to 0.5 billion	0.25 billion to 0.3 billion	0.6 billion to 1 billion
Northeast Asia	6 000	169 000	0.3 billion to 0.4 billion	0.75 billion to 1.2 billion	0.6 billion to 0.8 billion	1.5 billion to 2.4 billion
Southeast Asia	112 000	6 378 000	11.6 billion to 15.3 billion	28.5 billion to 45.1 billion	23.2 billion to 30.6 billion	57 billion to 90.2 billion

⁴ see Appendix 1 for a list of the countries included in each geographic region

3. Total cost implications of providing anti-retroviral therapy in comparison with available resources

The total costs associated with providing ARVs would be substantial in absolute terms (Table 4). However, it is important to consider these costs in the context of available resources. Table 5 below illustrates how the total costs derived in 2. compare with GDP, health sector expenditure, and National AIDS Budgets in the different geographic regions⁵. The lower estimate represents the situation illustrated in Table 4 in which 50% of those eligible receive AZT therapy at the lowest estimated annual cost of AZT therapy (US\$3 570 per patient); the higher estimate represents the situation illustrated above in which 100% of those eligible receive triple-combination therapy at the highest estimated annual cost for such therapy (US\$13 902 per patient).

Table 5: Estimated Total Annual Cost for ARV Therapy as a percentage of GDP, Health Sector Expenditures, and National AIDS Budgets by Geographic Region

Geographic Region	Estimated Annual Cost of ARV Therapy as % 1991 GDP	Estimated Annual Cost of ARV Therapy as % 1990 Total Health Expenditures	Estimated Annual Cost of ARV Therapy as % National AIDS Budgets
North America	0.03 to 0.2	0.2 to 1.8	31 to 243
Western Europe	0.02 to 0.1	0.2 to 1.9	1 136 to 8 727
Oceania	0.01 to 0.1	0.15 to 1.3	57 to 500
Latin America	0.1 to 1	3.1 to 23.9	93 to 720
Sub-Saharan Africa	8.6 to 66.9	215 to 1 673	258 750 to 2 017 500
Caribbean	1.9 to 14.8	48.1 to 370	92 857 to 714 286
Eastern Europe	0.006 to 0.04	0.15 to 1	750 to 5 000
SE Mediterranean	0.02 to 0.1	0.4 to 3.5	2 400 to 20 000
Northeast Asia	0.007 to 0.06	0.2 to 1.5	300 to 2 400
Southeast Asia	1.9 to 14.6	46.8 to 364	16 571 to 128 857

These figures suggest that ARV therapy would be unaffordable in sub-Saharan Africa, South-East Asia, the Caribbean, and Latin America, but could be considered in other regions where total costs would be less than 1% of GDP and less than 4% of health sector expenditure even for the very expensive combination therapies. Overseas Development Assistance for HIV/AIDS, estimated at US\$ 257 million in 1993 (Laws, 1996), is also too small to change this conclusion.

4. Cost-saving potential and cost-effectiveness of anti-retroviral therapy

4.1 Cost-Saving Potential

Despite the large costs associated with ARVs, it is possible that their provision would actually deliver overall cost-savings through reducing costs associated with HIV-related illnesses. It has been suggested that annual medical care costs for AIDS care per case are in the region of 1 to 4.6 times per capita GNP for any given country (Martin, 1996). Data on costs prior to development of AIDS are scarce and published data are confined to the USA, Australia and South Africa (Hurley et al, 1995; Hellinger, 1992; Kinghorn et al, 1996; Karstaedt et al, 1996). One study has suggested costs/year of approximately 25% those for the cost/year for a person with AIDS.

⁵ GDP figures from 1991 were used, since these were readily available. Health expenditure data were not readily available, and therefore calculations assumed that, on average, developing countries spend approximately 4% of their GDP on health (World Development Report 1993). Calculations for North America, Western Europe and Oceania were based on 1990 country-specific data reported in the World Development Report 1993. National AIDS Budgets data taken from "AIDS in the World II", eds. Mann and Tarantola 1996, and come from 1992 or 1993. See Appendix 1 for full details of GDP, Actual or Estimated Total Health Expenditure, and National AIDS Budgets.

4.1.1 Triple-combination therapies

This means that if triple combination therapies were to succeed in preventing HIV-related illnesses, costs saved in any year would be a maximum of 4.6 times per capita income. They would then be cost-saving for the health system over the expected period of HIV/AIDS illness in any country with a per capita income of US\$ 1 908 (if the annual per patient cost was US 8 776) to US\$ 3 022 (if the annual per patient cost was US\$ 13 902 per year). The majority of countries do not have such high incomes - for example Thailand, a relatively wealthy newly industrializing country, had an average per capita income of US\$ 1 570 in 1991 (World Development Report, 1993); and most African countries have average per capita incomes of less than US\$1 000, with many below US\$ 500 (World Development Report, 1993).

If annual costs for care of HIV/AIDS related illnesses were *equivalent* to per capita incomes (most cost data suggest this to be a more realistic figure even for AIDS care, with pre-AIDS care having a much lower cost where it has been measured: the higher estimates were from the early years of the epidemic when more care was provided in tertiary facilities and doctors were less familiar with HIV/AIDS-related health problems), therapies would only be cost-saving over the expected period of HIV/AIDS illness, from the health system's perspective, in countries with average per capita incomes of at least US\$ 8 776. Moreover, cost-savings would be unlikely in the long-run, since therapy costs might have to be incurred for many years or even for life, while medical care costs for illness would extend for only the more limited period from infection to death. Very few countries have incomes as high as US\$ 8 776 per capita, although in those that do, the cost-saving potential of therapies would be enhanced if a societal perspective is taken, since this takes the indirect costs associated with lost income due to illness/early death into account.

In the vast majority of countries where incomes are considerably less than US\$8 776 to US\$13 902 per year, therapy is very unlikely to be cost-saving even when this wider perspective is taken. For example, even in a relatively high-income developing country such as South Africa, where annual per capita incomes are in the region of US\$ 2 000, medical care costs saved are likely to be approximately US\$2 000 per year for AIDS care (and less for care pre-AIDS). Prevented income losses would be worth US\$ 2 000 per year. Triple combination therapy would not be cost saving even at the lower cost estimate of US \$8 776 per year. In a very poor country such as Malawi, with a per capita income of US\$ 230 in 1991 (World Development Report, 1993) costs saved over the lifetime of HIV/AIDS illness for a given person would be unlikely to match the cost of even one month's supply of combination therapy drugs.

4.1.2 AZT Therapy

Meanwhile, the limited evidence available indicates that AZT mono-therapy may initially result in reduced health care costs in comparison with HIV+ individuals not receiving the drug, but that these cost-savings are not sustained for long (Cosler and Lambrinos, 1992; Montaner et al, 1989). One study found similar lifetime costs for AIDS patients (Schitovsky et al, 1990), while others have suggested that both patients with symptomatic HIV illness and AIDS patients receiving AZT incur higher costs than those not receiving the drug over the course of their infection, due to lengthened survival time (Cosler and Lambrinos, 1992; Moore et al, 1994).

4.2 Cost-Effectiveness

While ARV therapy may not be cost-saving, this is true of most health care interventions. The important issue then becomes whether their provision would represent a cost-effective use of resources, for example in terms of the cost per year of healthy life gained, or the cost per quality adjusted life year gained.

4.2.1 AZT Therapy

AZT therapy has been reported to prolong life in a variety of studies. For example, it has been reported to increase survival of AIDS patients from a median of 9.6 months to a median of 21.2 months (Elhaggar 1993), from a median of 235 to 605 days (Moore et al, 1994), by an average of between one and two years (Anderson and May, 1992), by eight months (Hay et al, 1988), by 227 days (Santos et al, 1994), between 0.3 and 3.3 discounted life years (Schulman et al, 1991), and by two months (Oddone et al, 1993). The cost per healthy life year gained has been variously estimated at US\$ 48 000 (Moore et al, 1994), between US\$ 15 043 and US\$ 30 641 (Bozzette et al, 1994), between US\$ 6 653 and US\$ 70 526 (Schulman et al, 1991), and US\$ 129 000 (Oddone et al, 1993). At the lower cost range this may represent a cost-effective use of resources in North America or Western Europe, but is unlikely to do so in many other contexts. For comparison, the cost/year of healthy life gained has been estimated to be US\$ 46 249 for renal dialysis and US\$ 113 087 for coronary artery bypass surgery in the USA (Schulman et al, 1991). In developing countries, the cost/disability-adjusted life year (DALY) has been estimated at US\$ 3-5 for short-course tuberculosis chemotherapy, US\$ 30-50 for prenatal and delivery care, US\$ 1-3 for STD treatment, and US\$ 25-30 for the expanded programme of immunization (EPI).

Meanwhile, the European multicentre Concorde trial involving 1 749 people followed over a three year period found no difference in time progression to AIDS or survival in the AZT vs placebo group. This would suggest the drug is not cost-effective at all.

4.2.2 Triple-combination Therapies

The cost/year of healthy life gained would be only US\$8 776 to US\$13 902 for triple combination therapies if they worked, even before cost-savings due to prevented income losses and avoided medical costs are considered. This would appear to make the intervention relatively cost-effective in developed countries, where many accepted health care interventions cost substantially more than this. They would be unlikely to be cost-effective in many other countries, however, as the above figures for STDs, prenatal and delivery care, immunization, and tuberculosis indicate.

5. Cost, cost-saving potential, and cost-effectiveness of AZT therapy for pregnant women

5.1 Cost

While anti-retroviral therapy appears prohibitively expensive in many regions, therapy for HIV infected pregnant women over a relatively very short time-period may be more affordable. It may also be cost-effective: in the USA, treating pregnant women with AZT has been shown to reduce maternal-child transmission from a rate of 25.5% to 8.3% (Connor et al, 1994).

In the USA, treatment consisted of 500mg AZT per day on an out-patient basis, starting treatment between weeks 14 and 34 of gestation and continuing until the onset of labour. During labour, a loading dose of 2mg/kg was given, followed by continuous infusion of 1mg/kg of bodyweight per hour during delivery. In the final phase, new-born infants were treated orally with AZT syrup at 2mg/kg bodyweight every six hours, beginning 8 to 12 hours after birth and continuing for six weeks. The cost for such treatment per pregnant woman has been estimated at US\$ 895 for drugs and US\$ 150 for laboratory tests, US\$ 1 045 in total (Mauskopf et al, 1996). In addition, there are costs associated with testing and counselling all

pregnant women, since this is necessary for identification of pregnant women who should receive the AZT treatment. This was estimated to cost US\$ 60 for a women testing negative and US\$ 163 for those who test positive. On the assumption of a prevalence rate among pregnant women of 1.71%, testing would on average cost US\$ 61.8 per pregnant woman. AZT treatment for HIV+ pregnant women would on average cost US\$ 79.6 per pregnant woman. With around 4 million births per year (World Development Report, 1993), this equates to an annual cost of approximately US\$ 318 million or US\$ 0.3 billion. In the context of health expenditures in the region of US\$ 690 billion per year, this appears affordable. For other high income countries with usually lower prevalence rates than those found in the USA, such treatment also appears affordable.

In poorer countries with higher prevalence rates, these costs appear very high. For example, in Uganda there are an estimated 884 000 births per year (World Development Report, 1993). Drug costs alone would be US\$ 79.1 millions, even assuming only 10% of women were HIV+. Total health expenditure in 1990 was only US\$ 95 millions (ibid.). It is therefore not surprising that the one published article concerning AZT for pregnant women in Sub-Saharan Africa has concluded that the treatment regimen used in the USA trial is too expensive for developing countries (Mansergh et al, 1996). Instead, a shorter regimen, of as yet unproven efficacy, has been suggested to be more realistic. Trials currently underway in Thailand and sub-Saharan Africa will, when completed, demonstrate whether shorter and cheaper regimens are as effective.

5.2 Cost-saving potential and Cost-effectiveness

In the USA, it has been suggested that AZT therapy for pregnant women is not only affordable but also cost-saving, due to averted paediatric HIV/AIDS treatment costs, which are very large (Mauskopf et al, 1996; Gorsky et al, 1996). In the first study, a child infected by its mother was estimated to incur HIV/AIDS-related health care costs of US\$ 98 915. In developing countries, paediatric HIV/AIDS costs are much lower and are unlikely to offset the costs associated with AZT therapy - even when the indirect costs associated with lost productivity are considered (Mansergh et al, 1996). Furthermore, even assuming a less costly treatment regimen than the one shown to be effective in the USA, and making assumptions concerning its likely effectiveness, the cost/HIV infection averted in the baseline analysis was US\$ 1 115 (ibid). The authors commented that "This figure would be considered highly cost-effective from a developed country perspective; in a developing country setting in which health care expenditures are much more limited, one might question the cost-effectiveness of this program". Again, more definitive answers concerning the cost-effectiveness of AZT therapy in developing countries will be available when trials now underway in Thailand and Sub-Saharan Africa are completed.

6. Cost and cost-effectiveness of prophylaxis for health care workers

With rising rates of HIV infection among patients, health care workers (HCWs) are increasingly at risk of contracting HIV through, for example, needlestick injuries. There are two prophylaxis options, which have different implications for both cost and cost-effectiveness. These are AZT prophylaxis and triple-combination therapy prophylaxis.

6.1 Prophylaxis with AZT

AZT prophylaxis involves taking 1000mg per day for four weeks after exposure. At US\$ 15/day, the total cost is US\$ 420. In addition, at least two HIV tests would be required - one to establish the patient's HIV status and one to test the HCW's status after prophylaxis. Counselling may also be considered necessary, and this will incur additional costs.

It has been estimated that there is a 0.3% risk of seroconversion after exposure, although study estimates range from 0 to 1.82% (Allen et al 1992). It has also been recently estimated that prophylaxis reduces this risk by 80% (MMWR June 7, 1996 p468) i.e. to 0.06%. Assuming a 0.3% risk of sero-conversion, this means that for every 10 000 health workers who are exposed to HIV but not given prophylaxis, 30 will be

infected. With prophylaxis, for every 10 000 health workers exposed to HIV and given prophylaxis, 6 will be infected. Thus for every 10 000 health workers given prophylaxis, 24 infections will be prevented. The cost per prevented infection will be US\$ 175 000⁶. This figure suggests that prophylaxis may only be cost-effective in high-income countries. Moreover, cost-effectiveness in terms of years of life prevented will be further affected by the frequency with which HCWs are exposed to HIV infection: the more the exposures, the higher the chance that a given HCW will become infected and the lower the likely cost-effectiveness of prophylaxis.

6.2 Prophylaxis with triple-combination therapy

Prophylaxis with triple-combination therapy consists of 200mg of AZT three times a day, 150mg of lamivudine twice a day, and 800mg of indinavir three times a day (MMWR June 7 1996 p471) for four weeks. The cost of this regimen is US\$26.4 per day, and US\$792 for one month. If it is assumed that this regimen would be 100% effective, the cost would be US\$264 000 per infection averted, making it less cost-effective than AZT prophylaxis.

7. Financing anti-retroviral therapy

The high costs associated with anti-retroviral therapy mean that traditional approaches to financing care may not be sufficient. The main approaches to health care financing at present include taxation, social insurance systems, private insurance, user fees and community financing schemes. Of these, the high costs at an individual level make cost-recovery through user fees unrealistic. Experience with community financing schemes also tends to indicate that their revenue potential is not large, and mobilizing finance for medical treatment that does not realize individual benefits for everyone would be a significant challenge. Private insurance companies, meanwhile, are in business to make money and as a consequence try to eliminate bad risks. For example, in the USA insurance companies have turned to HIV testing in order to eliminate poor risks from pay pools (Oppenheimer and Padgug, 1986). In South Africa, it has been commented that individual companies are offering lower premiums to people with low HIV/AIDS risk features (Klopper et al, 1993), and in doing so they are likely to force other companies to do the same in order to remain competitive. This means HIV+ patients find it hard, if not impossible, to obtain coverage; and policies increasingly specifically exclude cover for HIV/AIDS-related health problems. There is even evidence that some cost-conscious employers in the USA have tried to exclude AIDS patients from group insurance policies (Oppenheimer and Padgug, 1986).

It is therefore not surprising that even in the USA, where private insurance is most extensive, HIV/AIDS care is largely financed through the public sector. In Maryland, for example, 65% of AIDS patients' care was financed by the programme Medicaid by the time they died (Moore et al, 1994) such that "Medicaid has become the dominant financier of the health care costs of HIV disease". This reliance on Medicaid is supported by other evidence suggesting that 40% of AIDS patients receive care through Medicaid support (Roper and Winkenwerder, 1988). Moreover, in a review of financing policy options by staff at the Harvard AIDS Institute, the major suggestions included mandated workplace insurance, extension of Medicaid eligibility to all those with incomes below the federal poverty level, an opportunity for individuals with incomes to 200% of the poverty level to purchase Medicaid coverage, mechanisms to encourage public and private agencies to pay for continued health insurance after loss of employment, and a shortened waiting period for Medicare disability (Makadon et al, 1990).

This suggests that unless the public sector can afford to provide ARVs, it is unlikely that their provision to anything but a small minority of patients will be financed through other means. Creative, innovative ways of financing care are not in evidence even in North America.

⁶ i.e. $(10\,000 \times 420) \div 24 = 175\,000$

8. Conclusions

The analysis indicates that high costs are associated with the provision of ARV therapy. The drugs themselves are easily the most important cost component. The large costs associated with therapy, in combination with the number of people eligible for such therapy, appear to make provision of ARVs unaffordable in many parts of the world at present. However, ARV therapy does appear affordable and cost-effective in high-income countries, where it may also be cost-saving when given as prophylaxis to HIV-infected pregnant women. ARV therapy does not appear to be either cost-saving or cost-effective in a developing country context, and this is true for prophylaxis to pregnant women as well as more general provision to HIV-infected individuals. Prophylaxis for health workers does not appear particularly cost-effective in any region. For all except the wealthiest individuals, financing of therapy is likely to depend on public sector provision.

A few notes of caution concerning these conclusions are, however, warranted. It is possible that ARV therapy may become much more affordable in time, as bulk-purchase arrangements become more commonplace, and as partnerships are established among international agencies, governments and drug companies. It is also conceivable that lower drug dosages may be discovered to be as effective as those currently recommended, and that drug companies may be able to reduce their prices once the costs of drug development have been recouped. Nevertheless, the framework of analysis developed above should be useful for informing current policy development, for enabling individual countries to analyse their own current situation *vis a vis* ARV therapy, and for the generation of cost analyses under different assumptions concerning drug costs.

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Appendix 1: Countries included in Geographic Regions shown in Tables 4 and 5

North America: Canada, USA

Western Europe: Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, U.K.

Oceania: Australia, Fiji, New Zealand, Papua New Guinea

Latin America: Argentina, Belize, Bolivia, Brazil, Chile, Columbia, Costa Rica, Ecuador, El Salvador, Guatemala, Guyana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname, Uruguay, Venezuela

Sub-Saharan Africa: Angola, Benin, Botswana, Burkino Faso, Burundi, Cameroon, Central African Republic, Chad, Comoros, Congo, Ivory Coast, Djibouti, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Mozambique, Namibia, Niger, Nigeria, Réunion, Rwanda, Senegal, Sierre Leone, Somalia, South Africa, Sudan, Swaziland, Togo, Uganda, Tanzania, Zaire (Democratic Republic of Congo), Zambia, Zimbabwe

Eastern Europe: Albania, Armenia, Azerbaijan, Belarus, Bosnia, Bulgaria, Croatia, Czech Republic, Estonia, Georgia, Hungary, Kazakhstan, Kyrgyztan, Latvia, Lithuania, Poland, Moldova, Romania, Russia, Slovakia, Slovenia, Tajikistan, Macedonia, Turkmenistan, Ukraine, Uzbekistan, Yugoslavia

Caribbean: Bahamas, Barbados, Cuba, Dominican Republic, Haiti, Jamaica, Trinidad and Tobago

North-East Asia: Bhutan, Cambodia, China, North Korea, South Korea, Hong Kong, Japan, Laos, Mongolia, Vietnam

South-East Asia: Bangladesh, Brunei, India, Indonesia, Malaysia, Maldives, Myanmar, Nepal, Philippines, Singapore, Sri Lanka, Thailand

South-East Mediterranean: Afghanistan, Algeria, Bahrain, Egypt, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Qatar, Saudi Arabia, Syria, Tunisia, Turkey, United Arab Emirates, Yemen

GDP, Actual or Estimated Total National Health Expenditure, and National AIDS Budgets by Geographic Region (US\$ billions)

Geographic Region	GDP in 1991	1990 Actual* or 1991 Estimated** National Health Expenditure	National AIDS Budgets 1992/3
North America*	6 121.6	700	5.3
Western Europe*	6 934.9	515	0.11
Oceania*	347.8	26.3	0.07
Latin America**	1 503.8	60.2	2
Sub-Saharan Africa**	241.2	9.7	0.008
Caribbean**	33.7	1.4	0.0007
Eastern Europe**	1 000	40	0.008
SE Mediterranean**	720	28.8	0.005
Northeast Asia**	4 100	164	0.1
Southeast Asia**	619.7	24.8	0.07