

## DRAFT MEMO

**To: Uganda ARV Finance Sub-Committee**

**March 26, 2003**

**Subject: Preliminary results from ATC in Uganda**

This memo provides preliminary results from a study of the costs of providing ARVs in Uganda, using the *AIDSTreatCost* software model. It updates an earlier version presented by Marty Makinen to the Uganda ARV Finance Sub-Committee on March 11<sup>th</sup>. A more comprehensive report covering more topics will be issued at a later date. There are four sections to this memo, with each one covering a different HIV/AIDS related service: HAART, OIs, MTCT, and VCT.<sup>1</sup>

The emphasis in this memo will be on the per-patient costs of providing different HIV/AIDS related services, since the actual number of patients who will receive these services has yet to be determined. Of course, this is precisely one of the areas where cost information can be useful – to help understand what levels of population coverage are feasible given existing resource constraints.

### **I. Highly-Active Anti-Retroviral Therapy (HAART)**

The costs shown in the scenarios in this section include ARV drugs, monitoring tests, and training, but not VCT, MTCT, or OIs, which are dealt with in later sections. Note that on a per-patient basis, training costs never account for more than 2% of costs, since one trained health worker can provide services to a large number of patients. Building and staff costs are excluded, since generally these will not be incremental – that is, they are already part of Uganda’s existing health budget allocation. The capital costs that are being incurred to purchase laboratory equipment will be discussed at the end of this section.

All drug costs presented in this section represent the lowest (landed) price currently available in Uganda, whether brand or generic, based on data from four entities: JCRC, Mildmay, MSF, and Medical Access. Note that in all scenarios, 10% has been added to drug and test costs to account for logistical inputs (storage and distribution) as well as wastage. It is important to emphasize that drug costs are changing rapidly. It is very possible that when Uganda negotiates for large-scale purchases of ARV drugs, prices will be lower than the currently prevailing costs listed here (which were the outcome of negotiations for much smaller quantities). But it is difficult to predict how much cheaper. As a further note, the rapid changes in drug prices means that it should not be automatically assumed that if regimen A is cheaper than regimen B based on current prices, that this would necessarily remain the case when large-scale purchases are negotiated.

#### *A. Benchmark case*

The following table presents a ‘benchmark’ case for annual per patient costs that uses the most common drug cocktail and a moderate level of monitoring tests. Alternative drug and testing regimens will be considered shortly.

ARV drugs (triomune)	\$393.00
AIDS tests	\$86.18

<sup>1</sup> The exchange rate assumed throughout this memo is 1850 Ush = 1 USD. A weaker dollar would lower costs, but it is unlikely that any such changes would be substantial.

Total (also includes training)	<b>\$483.18</b> per patient per year
--------------------------------	--------------------------------------

The ARV drug regimen here is triomune (3TC/d4T/NVP). In the case of children aged 5-14 on triomune, the cost for drugs is \$198 instead of \$393. The number of annual monitoring tests in this scenario are as follows: three haemoglobin tests, three blood count + differential, two liver function tests, two renal function tests, two CD4 counts, and zero viral loads.

*B. Benchmark case but with minimal testing*

An important issue to be addressed in clinical care guidelines for providing ARVs in Uganda is the number and frequency of monitoring tests to be carried out on patients. The scenario presented below uses triomune as in the benchmark, but offers less monitoring than in the benchmark case above. Specifically, it includes two haemoglobin tests, two blood count + differential, one each for liver and renal function tests, and one CD4 count annually. The cost per patient per year is thus about \$43 less than in the benchmark.

ARV drugs	\$393.00
AIDS tests	\$43.98
Total (also includes training)	<b>\$440.98</b> per patient per year

For reference, per unit test costs (based on information provided by Mildmay) are presented in the table below. These include the variable costs of testing (e.g., reagents, etc.), but not the fixed cost of purchasing equipment, which will be discussed later. As noted earlier, an additional 10% has been added to account for logistics costs and wastage.

Haemoglobin	\$0.89
Blood count + differential	\$0.89
Liver function tests	\$4.16
Renal function tests	\$3.56
CD4 count	\$32.70
Viral load	\$92.16

*C. Benchmark case but with extensive testing*

This scenario shows the implications of pursuing a more extensive monitoring test protocol. Annual per patient costs are about \$135 higher than in the benchmark, and \$177 more than if minimal testing is undertaken.

ARV drugs	\$393.00
AIDS tests	\$220.54
Total (also includes training)	<b>\$617.54</b> per patient per year

Once again, triomune is the drug regimen used in this scenario. Extensive testing here means four haemoglobin tests, four blood count + differential, three each of liver and renal function tests, three CD4 counts, and one viral load annually.

*D. Benchmark case but with Efavirenz instead of Nevirapine*

The clinical care subcommittee has proposed alternative first-line regimens for adults that use efavirenz instead of nevirapine as the NNRTI drug. This is particularly aimed at those patients who are taking treatment for a tuberculosis co-infection. Up to now efavirenz has been a relatively expensive drug: a yearly supply of efavirenz *alone* has cost about \$618 (including 10% for wastage and logistics costs), so when combined in a regimen with either d4t/3tc or azt/3tc (combivir) the per-patient drug cost would be about \$787 or \$898, respectively. This is at least twice as expensive as the triomune regimen in the benchmark case.

However, the Logistics sub-committee has recently learned of a 600mg dose of efavirenz being marketed by Merck that would cost just \$130 per patient per year, so that when combined in a regimen with either d4t/3tc or azt/3tc (combivir), annual per patient drug costs would be \$299 or \$410, respectively. This new dosage is presently in the process of being registered in Uganda. This new development should be followed closely.

Lastly, if another of the clinical care committee’s proposed 1<sup>st</sup> line regimens were to be used, combivir (zdv/3tc) plus nevirapine, drug costs would be \$514 per patient.

*E. Benchmark but with second line regimens*

The clinical care subcommittee has recommended alternative 2<sup>nd</sup> line regimens in the event of treatment failure. These regimens are much more expensive, as shown in the table below. If special monitoring tests will be given to those on 2<sup>nd</sup> line drugs, treatment would be even more expensive (the scenario here offers the same tests as those given to 1<sup>st</sup> line patients).

ARV drugs	\$1168.00
AIDS tests	\$86.18
<b>Total (also includes training)</b>	<b>\$1258.18</b>

The regimen here is azt/ddI + kaletra. If an alternative 2<sup>nd</sup> line regimen of d4t/ddI + kaletra is applied, the overall cost would be about \$1104. Clearly this raises some difficult issues about the trade-off between providing expensive 2<sup>nd</sup> line treatment to those patients who do not respond to first-line therapy, or providing 1<sup>st</sup> line treatment to as many patients as possible. This issue is taken up in the next section.

*F. Scaling up to wider population coverage*

The following table takes the per-patient costs discussed above and considers the overall annual costs of ARV provision (but still excluding OI, MTCT, and VCT) under various scenarios of the number of people treated.

	10,000 treated	20,000 treated	50,000 treated
Benchmark case	\$4,831,300	\$9,662,600	\$24,156,500
Benchmark, minimal testing	\$4,409,800	\$8,819,600	\$22,049,000
Benchmark, extensive testing	\$6,175,400	\$12,350,800	\$30,877,000
90% on benchmark and 10% on 2 <sup>nd</sup> line	\$5,606,350	\$11,212,700	\$28,031,750

The results demonstrate some of the difficult trade-offs inherent in the selection of a monitoring test protocol for patients on ARVs. A comprehensive approach to testing is critical for treatment success, but with a limited budget for ARV provision, more testing of those on ARVs will mean fewer patients receiving ARVs in the first place. Specifically, the table indicates that 28% more patients could be treated with the moderate level of testing compared to extensive testing; and 40% more patients could be treated with minimal testing compared to extensive testing (refer to the earlier sections for definitions of minimal, moderate, and extensive testing).

Similar trade-offs are faced with regard to the provision of expensive second-line regimens. This table implies that the number of patients who could be treated would be 16% greater if a policy of *only* providing triomune as a first line was adopted, instead of trying to treat 10% of patients with a second line regimen. In other words, the cost of providing first-line therapy to 116 patients is the same as providing first-line treatment to 90 patients *and* second-line treatment to a further 10 patients.

Finally, the discussion in this section has overlooked the important cost of equipping laboratories to undertake monitoring tests. Information provided by the AIDS control project at the Ministry of Health indicated plans to purchase 11 flow cytometers, 11 viral load analyzers, 11 haematology analyzers, 11 chemistry analyzers, and 117 microscopes in order to equip regional hospitals. When amortized over a period of 5 years, the total *annual* cost associated with this equipment (plus one vehicle for each regional hospital) is approximately \$890,000. This sum should therefore be added to *all* scenarios noted in the table above.

## II. Opportunistic Infections (OIs)

The treatment of opportunistic infections is an important component of a comprehensive ARV policy. However, estimating the number of people eligible for OI treatment can be difficult. It is true that patients receiving ARV therapy will have fewer OIs (and thus in theory the cost of ARV provision will be partially offset by cost savings in terms of fewer OIs). However, these patients will also live longer, and if ARV therapy merely delays the onset of OIs, rather than eliminates them altogether, then ultimately they still need to be treated. In addition, in the early stages of ARV provision resource constraints mean that it will not be possible to treat all those who are clinically eligible, and thus significant numbers of patients not receiving ARVs will still require OI care. Lastly, there is some uncertainty surrounding the average co-infection rates of OIs among HIV+ individuals (e.g., what percent of HIV+ individuals develop oral candidiasis each year).

Nevertheless, unit costs for OI treatment still offer valuable information for resource planning. The following table provides unit costs for drugs and tests only (i.e., the cost of admissions is excluded, as the associated labour and capital costs are generally not incremental). The costs are based on the JCRC price list.

OI	Total
Pneumonia (PCP)	\$27.35
Cryptococcal meningitis*	\$136.47
Tuberculosis**	\$28.32
Oral Candidiasis	\$9.50

\*=the cryptococcal meningitis cost includes giving sets and cannulars associated with IV delivery

\*\*=the TB cost is a preliminary estimate

The costs reported here are for first-line treatment only, as second-line treatment is rare. Certain OIs, such as toxoplasmosis and cytomegalovirus, are not included, as they are less common and/or very seldom treated.

### III. Prevention of mother-to-child transmission (pMTCT)

The prevention of mother-to-child transmission is one of the most cost-effective HIV/AIDS interventions. Per-unit costs (for treating both mother and child) for pMTCT drugs in Uganda is about \$1.30 if nevirapine is used, possibly considerably less. Nevirapine is the regimen of choice for pMTCT in Uganda, as there are only a small number of (donor-funded) facilities providing AZT.

Each year there are about 1.2 million births in Uganda, of which about 110,000 are to HIV+ mothers. This is the potential annual target group for pMTCT. Research at Mulago hospital has found a 27% MTCT rate if the mother is untreated, so about 30,000 HIV+ babies are born each year. Providing MTCT treatment lowers the transmission rate to perhaps 10%, meaning there would be about 11,000 HIV+ births if all HIV+ mothers were treated (so 19,000 could be averted).

However, since only 35-40% of deliveries in Uganda are assisted, it would be very difficult to come close to complete coverage (although sometimes nevirapine is given to expectant mothers who do not have an assisted delivery, by providing it when they attend an ante-natal clinic earlier in their pregnancy). In addition, some expectant mothers may refuse or not have access to VCT services. But even considering the absolute maximum target group of 110,000, given the unit cost of just \$1.30, the MTCT programme is not costly compared to ARVs. The more significant burden imposed by an MTCT programme would be on human resources due to the need for counselors to advise HIV+ mothers about breast-feeding, etc. Training costs would also be considerable. More work will be done on these issues for the final report.

The demographic indicators on HIV+ mothers also gives an indication of the potential target group for “MTCT+” – that is, providing HAART to mothers who receive pMTCT. The key variables for this calculation are presented in the following table. They suggest that the total potential annual target group for MTCT+ could be fewer than 2,000 patients per year. Of course, if the treatment is successful and the mothers stay healthy, the number of mothers on this programme would grow each year.

Annual # of HIV+ pregnant mothers	110,000
Of which: 38% of deliveries are assisted	41,800
Of which: VCT uptake of maybe 75%	31,400
Of which: MTCT uptake of maybe 75%	23,500
Of which: 10-20% are clinically eligible for HAART	2,350-4,700
Of which: maybe 33% have access to HAART before full scale-up	800-1,600

### IV. Voluntary Counseling and Testing (VCT)

The entry point for the HIV/AIDS services discussed in other sections is voluntary counseling and testing to determine HIV status. The most common algorithm currently being used in

Uganda for HIV testing is a series of three rapid tests – Capillus (about \$2.20) for screening<sup>2</sup>, Serocard (\$1.10) for confirmation, and if necessary Multispot (\$3.30) for a tie-breaker. This is the algorithm provided by the AIDS Information Centre (AIC); it should be noted that the specific tests to be used nationwide in the future have not yet been decided upon, and rapid tests are available elsewhere for under \$1.

Per-person testing costs will depend on the percentage of all samples that will require confirmation and tie-breaker testing. If 20% require confirmation, and 20% of these require a tie-breaker, then per-person VCT costs for the test kits alone would be \$2.55. (Note that rates of positive diagnosis through VCT are typically higher than population-wide prevalence rates due to self-selection among those who come for testing). Training costs per patient for VCT is about 47 cents (of which about 20 cents is for counselors). Therefore, overall variable costs for VCT are approximately \$3.00 per patient (this excludes labour and capital costs which generally would not be incremental).

A very uncertain variable in the cost and human resource calculations for an ARV programme is the uptake rate for VCT. According to the 2000 DHS for Uganda, about 10% of adults have been tested for HIV, while 60% have said they would like to be tested. A potentially large benefit of an ARV drug provision programme would be higher rates of testing, so that even if people could not access ARV right away, they would know their status. But with about 12 million adults in Uganda, even a testing uptake rate of 5% would entail testing 600,000 people, which is about five times the number of individuals tested by AIC in 2002. If per patient VCT costs are about \$3.00, then overall VCT costs would be \$1.8 million – similar to the cost of providing ARVs to nearly 4,000 patients under the benchmark case discussed in Section I above.

The human resource implications of VCT are also very large. Assuming 30 minutes of counselor time per patient (AIC counseling averages about 35-40 minutes per patient) and a six-hour work day (in terms of time spent with patients), even a 5% uptake rate for VCT services would require 200 counselors. AIC, by far the largest provider of VCT in Uganda, has only about 55 counselors at present. Counselors required for those actually taking ARVs – an important component of an ARV programme – would be additional.

A similar calculation can be done for laboratory personnel. A 5% VCT uptake rate and 15 minutes of lab time to conduct tests would require 100 lab technicians for VCT alone (this excludes the considerable lab time required for the ARV monitoring tests discussed in the first section). According to the Ministry of Health's March 2000 Inventory of Health Institutions, there are a total of about 500 laboratory personnel in Uganda (assistants, technicians, and technologists) in the public and private/mission sectors combined.

---

<sup>2</sup> Apparently Capillus tests are being contributed free of charge, but how many and for how long is not yet known. This memo focuses on total costs regardless of who pays (e.g., the MoH, donors, patients), since this is the essential first step before resource mobilization (i.e., exactly *who* will pay) can be considered.

**ANNEX:****DATA SOURCES FOR USE OF AIDS TREATCOST MODEL IN UGANDA**

Note that in general epidemiological data will not have an impact on the costs of HAART as long as ARVs are only provided to a subset of those eligible. Certain epidemiological assumptions will be revisited in the final report.

<b>Data Item</b>	<b>Data</b>	<b>Sources/notes</b>
Additional AIDS mortality rate	0.5	Assumed that once a person develops full blown AIDS (and is not taking ARVs), life expectancy is 2 years, so there is a 50% chance they will die in a given year
AIDS symptoms development rate	0.125	Assumed that once a person is HIV+, typically they spend 8 years in that state before developing full blown AIDS. If there are equal numbers in years 1 through 8 nationwide, on average there will be a 1/8 (0.125) chance that a person will develop AIDS in a given year
AIDS test availability by facility	All are available at national and regional hospitals, all except CD4 and viral load at district hospital, none at HC IV	Based on ARV implementation guidelines: i.e., scale-up only to regional hospitals in first year
AIDS tests	Haemoglobin WBC + differential Liver function tests Renal function tests CD4 Viral load	Drawn from clinical care guidelines test list, excludes those special tests for people on PIs (i.e., 2 <sup>nd</sup> line). Cost per test from Mildmay. Viral load added because equipment for this is being purchased.
ARV-ARV conflicts	None listed.	
ARV drug type	NRTI, NNRTI, PI	Standard everywhere
ARV drugs – NNRTI	Nevirapine Efavirenz	Clinical care guidelines, recommended regimens. Costs from cheapest available in Uganda among JCRC, Mildmay, MSF, and Medical Access
ARV drugs – NRTI	Zidovudine Lamivudine Stavudine Didanosine	Clinical care guidelines, recommended regimens. Costs from cheapest available in Uganda among JCRC, Mildmay, MSF, and Medical Access
ARV drugs – PI	Kaletra (lopinavir-ritonavir)	Clinical care guidelines, recommended regimens.

		Costs from cheapest available in Uganda among JCRC, Mildmay, MSF, and Medical Access
ARV protocols	2 NRTI + 1 NNRTI 3 NRTI 2 NRTI + 1 PI	Clinical care guidelines
Building requirements	2 national hospitals 11 regional hospitals 44 district hospitals 214 HC IVs	“Inventory of Health Institutions in Uganda”. MoH, March 2000. Not relevant when doing incremental costs.
Capital item costs – buildings	Nothing yet.	Will draw from MoH health financing tables. Not relevant when doing incremental costs.
Capital item costs – equipment	Flow cytometer, chemistry analysers, viral load analysers, haematology analysers, microscopes	Costs for these were provided by procurement officer at Uganda AIDS control project
Capital item costs – vehicles	\$20,000	Estimate. Assumed one vehicle for each regional hospital. Hasn’t been addressed in any policy documents.
Eligible populations		User-defined.
Equipment requirements	11 of each kind of lab equipment (1 per regional hospital) and 110 microscopes (10 per regional hospital).	Accords with # purchased (information provided by procurement officer at AIDS control project).
Fertility rate time trend	0%	2000 DHS
Health facility types	All hospitals and HC IVs. Assumed ARV only at national and regional hospitals, OI and MTCT at all hospitals and some HC IV’s.	Various implementation and policy documents.
HIV confirmation tests	Not yet officially chosen. Used AIC. Serocard, \$1.10 Multispot, \$3.30	Dr. Hitimana, AIC
HIV infection rate		Assumed 100,000 new adult infections and 10,000 new child infections per year (drawn from MoH surveillance document, June 2002). Assigned these to age/gender groups using actual AIDS case reporting as weights.
HIV screening tests	Not yet officially chosen. At AIC, use Capillus, \$2.20	Dr. Hitimana, AIC

Initial fertility rate	Age-specific births per 1000 women.	2000 DHS
Initial non-AIDS mortality rate	Age-specific	Calculated using US Census Bureau projections from 2000 to 2005.
Initial population	Age-specific.	Used US Census Bureau projection for 2003. Assigned to HIV+ using prevalence rates, divided between symp and asymp using 1:4 ratio (ie, 20% symptomatic; will redo with lower estimate later).
Interest rate	0.10	EIU country report
Mortality rate time trend	0%	2000 DHS
MTCT rate	0.27	MTCT policy document, based on a test at Mulago hospital.
MTCT regimens	Nevirapine, \$1.30	MTCT policy document and discussion with Dr. Ojera, AIDS control programme. Includes extra 10% for wastage and logistics.
OI-ARV conflicts	None listed.	
OI protocols – cryptococcosis	DELIVER paper for protocol; JCRC for drug costs; Mildmay for test costs	
OI protocols – oral candidiasis	MoH 2003 clinical care guidelines for protocol; JCRC for drug costs; Mildmay for test costs	
OI protocols – pneumocystis pneumonia	MoH 2003 clinical care guidelines for protocol; JCRC for drug costs; Mildmay for test costs	
OI protocols – tuberculosis	DELIVER paper for protocol; JCRC for drug costs; Mildmay for test costs	
OIs	TB, cryptococcal meningitis, PCP, oral candidiasis are included. Excluded toxoplasmosis and cytomegalovirus, as these are less commonly treated.	Discussion with Dr. Bahendeka, Nsambya hospital.
Pregnancy test – MTCT only	2.25 per test	Mildmay Since MTCT programme uses nevirapine, pregnancy tests are not included.

Staff wages	Hourly wages for several staff types.	MoH health financing tables provided by MoH planning dept. Excluded from costs since they're not incremental (except for new counselors, etc., which will be addressed later).
Training requirements	5 days training for all staff except 2 days for record keepers	Training guidelines of clinical care committee. Cost of \$100 per person per day is 50% of estimated typical Mildmay course costs (which are probably more sophisticated than a public sector training).
Vehicle requirements	13	Assumed 1 AIDS programme vehicle for each national and regional hospital. Not yet spelled out anywhere in policy documents.

## SCENARIO ASSUMPTIONS

Data Item	Data	Sources/notes
Access rate	60%	Reportedly 40-45% of Uganda's population lives within 5km of a health facility; assume higher for HIV patients since prevalence is somewhat higher in urban areas
Screening uptake rate	Varied by scenario. This is a difficult variable to estimate. A 5% uptake rate among adults would mean screening 600,000 people.	2000 DHS said 10% have been tested, 65% haven't but would like to. A July 2002 WHO document set the goal of 4% VCT uptake per year among adults.
Confirmation uptake rate	Assumed all those who get screened and require a confirmation test do get one.	
ARV uptake rate	This will be supply-side determined (rationing) because can't afford to treat everyone.	
MTCT uptake rate	Assumed 75%.	
Staff time for pre-test counseling	20 minutes for counselor	Discussions with Dr.Hitimana (AIC) and Dr. Akol (MoH)
Staff time for post-test counseling	15 minutes for counselor	Dr. Hitimana and Dr. Akol
Staff time for screening	10 minutes for both nurse and lab tech	Dr. Hitimana and Dr. Akol Varies a lot on whether doing several specimens at once.
Staff time for confirmation	15 minutes for both nurse and lab tech	Dr. Hitimana and Dr. Akol Varies a lot on whether doing several specimens at once.
Annual visits for ARV	10 visits	Nearly monthly, at least for drug dispensation, is common among existing programmes
Staff time for ARV	10 min for dr. 10 min for nurse 15 min for lab tech 15 min for counselor 10 min for pharmac't	Not every visit will be the same; many will just be to collect drugs. So 10 minutes per visit for 10 visits per year is equivalent to 20 minutes per visit for 5 visits per year. One doctor said typical visit is 30 minutes (for both dr and nurse time) if clinical exam included.
Number of times per year for each AIDS test	Varies across scenarios.	Clinical care guidelines leave this ambiguous.
Number of lines of treatment	Either 1 or 2. Varies across scenarios.	Clinical care guidelines

Drug protocol for ARVs	Varies across scenarios.	Clinical care guidelines
Attrition rate		
Drug protocol for OIs	Used first line only	DELIVER paper and Uganda clinical guidelines booklet 2003
Drug protocol for MTCT	Nevirapine	Discussion with Dr. Ojera, AIDS control project
AIDS mortality rate among those taking ARVs	15%	Still a very uncertain statistic in developing country context.