

The costs and benefits of private sector provision of treatment to HIV-infected employees in Kampala, Uganda

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Objectives: The objective of this study was to determine the financial incentives that companies have to treat HIV-infected employees, in a health care services company in Kampala, Uganda.

Design: Cost-benefit analysis from the company's perspective of three interventions to treat HIV-infected employees.

Methods: The costs and benefits of each intervention were compared with no intervention and with each other: cotrimoxazole prophylaxis (CTX) starting at WHO stage 2; highly active antiretroviral therapy (HAART) plus CTX starting at WHO stage 2; and a 'hybrid' strategy that begins with CTX at WHO stage 2 and later includes HAART. The 5-year health and economic outcomes were calculated using a Markov model. Inputs for disease progression rates and effects of HIV on company costs were derived from published and unpublished data and a survey administered to company officers.

Results: The analysis showed that the 'hybrid' intervention is the most cost-effective. For 100 skilled employees it would save the company US\$ 38 939 and 73 disability adjusted life-years (DALYs). For unskilled workers 'CTX' is the most cost effective and would save US\$ 16 417 and 60 DALYs. 'Hybrid' has an incremental cost-effectiveness ratio of US\$ 45 per DALY for unskilled workers whereas HAART is far less economical at an incremental cost per DALY of US\$ 4118. For 'CTX', net savings are preserved across the full range of input values.

Conclusion: A 'hybrid' intervention combining CTX prophylaxis followed by HAART would generate savings to a Ugandan company. Governments and other donors may find opportunities to share costs with the private sector as part of their phase-in strategy for antiretroviral therapy.

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Introduction

HIV/AIDS incapacitates people in their most productive years. Currently, one in 12 sub-Saharan African workers is infected and in some businesses the rate is one in three [1]. In Cameroon and Kenya, economic growth may be slowed by up to 25% for a period of 20 years [2,3]. In 1999, a Zimbabwean transport company estimated that

HIV-related costs are equivalent to 20% of its profits [4]. Uganda Railways has lost about 5600 employees to AIDS and has an elevated labor turnover rate of 15% annually. The medical and funeral expenses of another Ugandan company doubled in a single year [5]. A well-documented study of laborers at a Kenyan tea plantation found that productivity declined with time before death from AIDS and that in the 12 months prior to death from AIDS,

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absenteeism increased 87%, days on 'light duty' increased 66% and the weight of tea plucked per working day declined by 17% compared with HIV-uninfected workers [6].

The economic consequences of the HIV epidemic is a growing concern, yet access to HIV treatment is below the levels needed in sub-Saharan Africa [7]. Many effective treatments, especially antiretroviral drugs, are perceived to be unaffordable by most payers. However, some companies in southern Africa have implemented policies to treat infected employees [8–10]. According to a 2003 survey of 216 randomly selected large businesses in Uganda, Tanzania, Zambia and Kenya, 17% provide some level of antiretroviral drug therapy to their employees and their family members [11].

Given the important role that employers can play in funding HIV care, it is useful to examine their economic incentives for doing so. In some situations, companies may advance their own financial interests while promoting the public's health, without changes to existing programs or treatment prices. In other situations, subsidies may be needed to encourage participation. This article begins to address the question, 'Can corporations in sub-Saharan Africa save money by providing treatment for HIV/AIDS to their infected employees?' For service sector companies with financial characteristics similar to the one examined here, we find that the answer is 'yes'.

Methods

We used cost-benefit and cost-effectiveness analysis conducted from the perspective of a Ugandan corporation, to estimate net costs for three pharmaceutical regimens: cotrimoxazole prophylaxis (CTX) initiated at the onset of WHO stage 2; highly active antiretroviral therapy (HAART) with CTX at the onset of WHO stage 2, and a hybrid strategy that begins with CTX at WHO stage 2 and later includes HAART. We modeled HIV disease progression and HIV-related incremental costs for each intervention and for no ongoing therapy over 5 years. In 'no ongoing therapy' patients receive neither CTX prophylaxis nor HAART, but may receive episodic, largely symptom-based treatment of opportunistic infections. In order to compare results for low and for high compensation levels, we completed the analysis for hypothetical cohorts of 100 skilled and 100 unskilled workers. The 'base case' used the best estimates of input values derived from published data, unpublished reports, and a survey administered for this study. Sensitivity analyses identified the effect of variations in the values of key base case inputs. We projected base case outcomes over 5 years and discounted at 3% annually [12].

Description of interventions and their effectiveness

Cotrimoxazole prophylaxis

CTX prophylaxis is recommended by UNAIDS for wide administration to symptomatic HIV-infected adults and children in Africa [13]. Standard dosing consists of two single-strength or one double-strength daily dose where a single-strength dose is trimethoprim-sulphamethoxazole 800 mg/160 mg.

A double-blind, randomized trial of CTX prophylaxis provided to 454 stage 2 and 3 HIV-infected patients in Abidjan, Cote d'Ivoire found that the treatment group had 43% [95% confidence interval (CI), 25–57%], lower incidence of severe clinical events than did a placebo group [14]. A recent trial from Uganda found a mortality reduction of 46% over 1.5 years of follow-up [15]. Combining data on reported efficacy by CD4 strata in the Cote d'Ivoire study and on the joint distribution of CD4 cell count levels and WHO stages, we estimated CTX efficacy defined as the proportionate reduction in progression to more severe WHO stages of 54.0, 37.5 and 25% for stages 2, 3 and 4, respectively.

Highly active antiretroviral therapy

We define this intervention as HAART and CTX, both started at stage '2A'. We previously reviewed the effect of HAART on the progression of HIV disease in the developed world. Based on 21 studies published between 1996 and 1998, we estimated a 95% reduction in progression from HIV to AIDS, estimated from viral load suppression data, and an 85–90% reduction in progression to death, from clinical endpoint data [16]. This is in general agreement with results from the more recent EuroSIDA study group, which found a 94% reduction in deaths (range, 88–98%) [17]. In extrapolating to Africa, we use a conservative value of 85% reduction in progression to AIDS and to death. We assume that each year 15% of individuals remaining on HAART need to change to a second-line regimen, due to virologic failure, or adverse reactions. This is comparable with clinical trials, but not verified in clinical practice in Africa [18–21].

'Hybrid' strategy

We also defined an intervention strategy that combines CTX early in disease and adds HAART as symptoms worsen. Specifically, CTX is started at the beginning of stage '2A' (i.e., mild symptoms) and HAART is started at the beginning of stage '2B' (i.e., moderate symptoms, with 1–2 lost days of work per month). The justification for this strategy is threefold. First, it is consistent with recommendations for earlier initiation of CTX than HAART in resource-poor settings [22]. Second, it delays HAART to a stage of illness when it is likely to yield significant clinical benefits. Third, HAART initiation is early enough to prevent work disability (which occurs with onset of stage 3 due to such symptoms as weight loss,

prolonged fever, severe bacterial infection, chronic diarrhea or being bedridden up to 50% of the day) [23]

Description of model

We calculated health and economic outcomes using a Markov transition state model programmed in Excel (Microsoft Corporation, Redmond, Washington, USA) by the authors. The model uses monthly cycles over a 60-month period. Natural history data from seropositive individuals in a survey in rural southwest Uganda beginning in 1989–1990 served as benchmarks to calibrate our model [24]. We assumed that of 100 HIV-positive employees at program onset, 90 are asymptomatic (WHO stage 1) and 10 are symptomatic (WHO stage 2). Therapy, consisting of CTX prophylaxis in the CTX and 'hybrid' interventions, and HAART for the HAART intervention, is initiated at the onset of symptoms, namely in stage '2A'. In the base case, the company provides therapy only until the patient is disabled and the costs of treatment following disability are borne by another entity such as the government or a non-governmental organization. For untreated patients, disability occurs in WHO stage 3 since at this stage patients experience moderate symptoms and may be in bed for up to 50% of daytime hours. We subdivided WHO stages 2 and 3 to portray the timing of disability onset and of treatment strategies more flexibly. The new stages (e.g., 2A and 2B) have characteristics in the aggregate consistent with the original stage (e.g., 2); there are lower medical costs, absenteeism, and disutility in the 'A' than in the 'B' sub-stage. Monthly transition probabilities used in our model generated outcomes that fell within the 95% confidence intervals for all benchmarks. (A Technical Appendix that is available on request from the corresponding author provides details).

Medical costs, absenteeism, and disutility are a function of treatment regimen and stage. These three outcomes are reduced in parallel, since they are functionally inter-related and we could find no empirical basis otherwise. For HAART, the reduction in non-HAART medical costs and other outcomes is 85%, which is the efficacy of HAART in reducing disease progression. For CTX, the reductions are larger late in disease, due to the higher risks of opportunistic infections. For the 'hybrid' strategy, reduction depends on which of the two treatments is in place.

Treatment both slows progression to later stages and reduces symptoms and disability within each stage. For CTX, disability is delayed from the onset of stage 3 to the onset of stage 3B. For HAART, disability is delayed until the onset of stage 4.

Costs

Costs are assigned to each month that an employee resides in one of the possible disease stages. All costs are given in 2005 US dollars.

Cost of CTX: drug and monitoring. A single-strength dose of CTX costs US\$ 0.0714 [25]. For the recommended regimen consisting of two daily doses, the cost is US\$ 5.21 per patient-year. In accordance with UNAIDS guidelines, we assume follow-up once a month for the first 3 months [26]. However, rather than quarterly visits thereafter as recommended by UNAIDS, we calculated costs assuming biannual visits as this is in keeping with the Médecins Sans Frontières monitoring regimen for HAART.

Cost of HAART: drugs and monitoring. Due to its low cost and clinical appropriateness we modeled the WHO pre-qualified regimen containing nevirapine 200 mg at US\$ 77 per patient-year (Hetero, Hyderabad, India), and zidovudine 300 mg plus lamivudine 150 mg in a fixed-dose combination pill at US\$ 182 per patient-year (Cipla, Mumbai, India), for a total annual cost of US\$ 259 [27]. Second-line HAART-protease inhibitor (PI) therapy consists of nelfinavir 250 mg at US\$ 978 per patient-year (Roche, Basel, Switzerland), stavudine 30 mg at US\$ 21 (Hetero), and didanosine 100 mg at US\$ 310 (BMS, New York, New York, USA), for a total of US\$ 1309 per patient-year [27]. In the revised 2004 guidelines, WHO does not include regular CD4+ or viral load tests as recommendations [28]. This analysis adopts the monitoring regimen evaluated by Médecins Sans Frontières, Khayelitsha, South Africa [29]. In this trial, efficacy was monitored by viral load (HIV RNA) and CD4+ T-cell tests every 6 months. These tests cost US\$ 30.00 and US\$ 5.00 per test respectively [30–32].

HIV-related medical care costs. The increase in annual medical care costs due to HIV was US\$ 1020 per infected employee. We assume that medical care costs unrelated to the provision of HAART for those on HAART would be 15% of the amount spent on those in standard care for employees in the same stage of illness because of the 85% lower incidence of opportunistic infections in the treated group. For CTX-only we assigned a cost reduction of 39–54%, varying by stage of illness, and also echoing its clinical effectiveness. (See the Technical Appendix for details.)

Annual days of absenteeism due to HIV. Absenteeism contributes to lost productivity by disrupting work processes, under-utilizing equipment, and requiring the use of temporary staff [33]. We assume that the number of absent days for employees receiving HAART is 15% of the number for those receiving no ongoing therapy and reduced by 39–54% for those on CTX, the same difference as we used for medical costs for those in the same disease stage. Upon entering stage 3B, employees receiving CTX only are disabled, and absenteeism is no longer a factor. (See Technical Appendix for details.) The company reported a range of absenteeism of from 5 to 20 days per year for all employees and we adopted a mid-range base-case estimate of 12.5 days per year. A study of a cohort of male sugar cane workers in South Africa

suggested 28 days absent per year and we used this estimate for the upper end of our estimate range [34]

Funeral expenses and death benefit payments. The company pays US\$ 303 as reimbursement for funeral costs and US\$ 1515 and US\$ 2517 for unskilled and skilled workers, respectively, as a lump-sum death benefit.

Outcome measures

The analysis focused on six outcome measures, projected to 5 years.

Health outcomes

- (1) Deaths averted. Decrease in the number of HIV-related deaths due to program implementation (not discounted).
- (2) Disability-adjusted life-years (DALYs) saved. Net present value of the DALYs generated by the program. A DALY is defined as a year of life adjusted for age-related productivity and for the quality of life (also referred to as the 'utility') experienced during that year [35]. It is a standard and widely-used measure of health benefits [12].

Cost and cost-effectiveness outcomes

- (3) Intervention costs. Net present value of the cost of the drugs and the cost of patient monitoring.
- (4) HIV-related costs to the employer. For each intervention, the net present value of medical care costs,

HIV-related productivity and training losses, disability payments, and death and funeral benefits.

- (5) Net discounted costs (savings). The difference between HIV-related expenses and program costs that is, (3) plus (4), for each of the three interventions.
- (6) Net cost per DALY. This is defined as (5) divided by (2).

Company financial data

We developed a survey instrument with 25 questions pertaining to wages and other compensation, absenteeism and disability rates in HIV-infected individuals, re-hire rates, training costs, funeral expenses, death benefits, and companies' current outlays for treatment of HIV-infected employees. We administered the survey to seven companies based in Kampala, to the personnel manager or human resource officer, who consulted files as necessary. We selected companies exceeding 50 employees that were willing to respond to questions regarding HIV. To encourage full disclosure, anonymity was offered to all respondents. Six companies had insufficient records on HIV-related expenditures and lost productivity. Thus, we concentrated our efforts on a single medical services company with annual revenues of US\$ 5.7 million referred to here as 'Health Care Company'.

All model input values and ranges and data sources, are displayed in Table 1. All costs represent incremental resources occasioned by the interventions.

Table 1. Base-case and ranges of model inputs.

| Parameter | Base case estimate | Range in input values | Data sources |
|---|--|-----------------------------|-----------------------|
| Intervention effectiveness | | | |
| Effectiveness of CTX prophylaxis | Stage 2: 54% Stage 3: 37% Stage 4: 25% | 65–135% of base-case values | [14,15] |
| Effectiveness of HAART | 85% | 75–95% | [20,21] |
| Treatment failure rate (annual rate of switch to second-line HAART regimen) | 15% | 10–20% | [18,19,36,37] |
| Intervention costs | | | |
| Cost of first-line HAART (per patient-year) (US\$) | 259 | 130–389 | [38] |
| Cost of second-line HAART(per patient-year) (US\$) | 1309 | 655–1964 | [38] |
| Cost of CTX (per patient-year) (US\$) | 5.21 | 2.60–7.82 | [25] |
| Cost of HIV counseling and testing (one time) (US\$) | 15.20 | – | [39] |
| Cost of monitoring CTX (per monitoring session; two per year in base case) (US\$) | 6.23 | 3.11–9.34 | ^{a,b} |
| Cost of monitoring HAART per monitoring session; (2 per year in base case) (US\$) | 35 | 17.50–52.50 | [30–32] |
| Non-medical economic variables | | | |
| Number in WHO stage 2 HIV at start of program | 10 | 0–20 | NA |
| Wages per year including benefits for (skilled/unskilled) (US\$) | 4178/2507 | – | Survey |
| Discount rate: | 3% | 1–5% | [12] |
| Absenteeism (days/person-year) with no ongoing therapy | 12.5 | 5–28 | Survey; [34] |
| Days between disability and hiring of replacement (skilled/unskilled) | 75 / 50 | 38–113 / 25–75 | Survey |
| Disability compensation; one-time (skilled/unskilled) (US\$) | 482 / 289 | 241–723 / 144–433 | Survey |
| Funeral and death benefit payments; one-time (skilled/unskilled) (US\$) | 2820 / 1818 | 1410–4230 / 909–2727 | Survey |
| Medical care costs | | | |
| Incremental medical care expenditures for HIV infected (annual) (US\$) | 1020 | 510–1530 | Survey |
| Variation in medical care costs, absenteeism and disutility with intervention efficacy (where '1' signifies base-case values) | 1.0 | 0.50–1.50 | Authors' construction |

^aPersonal communication to S.M. from physician for employees of 'Health Care Company', Kampala, 2001.

^bPersonal communication to S.M. from Dr Raymond Mwebaza, Medical Officer Nsambya Hospital, Kampala, 2001. Ranges are used in sensitivity analyses. Numbers before a '/' pertain to skilled workers; those after a '/' to unskilled. All local costs are converted to US dollars at the rate of Sh. 1595 per dollar and inflated to mid-2005 costs using the US consumer price index. Source: US Bureau of Labor Statistics, 2005. <http://www.bls.gov/infoCenter/Topics/Economy/USinflation.html>. HAART, highly active antiretroviral therapy; CTX, cotrimoxazole; NA, not available.

Sensitivity analyses

Using Crystal Ball software (version 7.2; Decisioneering, Denver, Colorado, USA), we conducted univariate and multivariate sensitivity analyses to assess the impact of input value uncertainty on results. Input parameters were assigned symmetrical beta distributions and plausible ranges, in most cases from 50 to 150% of base-case values. We conducted a Monte Carlo simulation using 100 000 trials to account for the aggregate uncertainty from all varied inputs, thus estimating the overall probability that results fall within specified ranges.

The Technical Appendix (available on request from the corresponding author) provides additional details on model design, company costs, and methods for estimating intervention costs and effectiveness.

Role of the funding source and conflict of interest statement

Employees of Axios, one of the funding sources, participated in the design, data collection and interpretation for this report. All authors had full access to the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. We declare that we have no conflict of interest.

Results

Base-case outcomes

Health outcomes

Over 5 years, the CTX, 'hybrid' and HAART interventions would avert 15, 36 and 37 deaths, respectively, compared with no ongoing therapy. CTX would add 60 discounted DALYs. 'hybrid' and HAART would add 133 and 138 discounted DALYs respectively (Table 2).

Costs

At US\$ 5537, CTX would be less costly than either 'hybrid' at US\$ 93 113 or HAART at US\$ 136 026. 'Hybrid' would be the least costly at US\$ 227 732 over 5 years for skilled workers. For unskilled workers, CTX at US\$ 189 073 would be the least costly (Table 2).

Table 3 displays the HIV-related costs for each intervention. In comparison with no ongoing therapy, CTX would increase overall absenteeism and medical care costs for both skilled and unskilled workers (by extending life with ongoing morbidity) while substantially reducing other productivity losses and death benefit payments. 'Hybrid' and HAART would reduce company costs for all categories of HIV-related expenses.

Cost-benefit and cost-effectiveness outcomes

Using 'no ongoing therapy' as the first comparator, Table 4 shows the incremental costs and benefits of each intervention arrayed by increasing effectiveness. For skilled workers 'hybrid' would be the most cost-effective option. It was superior to CTX as the latter was found to be both US\$ 38 939 higher in net costs compared with 'hybrid' and to generate 73 fewer DALYs. In comparison with 'hybrid' HAART would add about 5 DALYs, at an added cost of US\$ 14 037 or US\$ 3008 per DALY.

For unskilled workers CTX would generate savings of US\$ 16 417 and 60 additional DALYs. 'hybrid' would be the next most cost-effective, at an incremental cost of US\$ 45 per DALY. HAART would be the least cost-effective option, at US\$ 4118 per DALY gained.

Sensitivity analyses

Univariate sensitivity analyses

'Hybrid' for skilled workers was found to be most sensitive to the level of HAART and CTX efficacy and the cost of second-line antiretroviral drugs. It would be

Table 2. Five-year health outcomes and incremental costs for three employer-provided HIV/AIDS treatment regimens.

| | No ongoing therapy | CTX | 'hybrid' | HAART |
|--|--------------------|--------|----------|--------|
| Health outcomes | | | | |
| AIDS mortality | 47.5 | 32 | 11 | 10 |
| Deaths averted | 0 | 15 | 36 | 37 |
| DALYs | 472 | 532 | 605 | 610 |
| DALYs saved | 0 | 60 | 133 | 138 |
| Costs | | | | |
| Skilled workers | | | | |
| Intervention costs (US\$) | 0 | 5537 | 93113 | 136026 |
| Other company HIV-related costs (US\$) | 312797 | 261134 | 134619 | 105743 |
| Company HIV-related costs plus intervention costs (US\$) | 312797 | 266671 | 227732 | 241769 |
| Unskilled workers | | | | |
| Intervention costs (US\$) | 0 | 5537 | 93113 | 136026 |
| Other company HIV-related costs (US\$) | 205490 | 183536 | 99214 | 75518 |
| Company HIV-related costs plus intervention costs (US\$) | 205490 | 189073 | 192327 | 211544 |

Deaths, disability adjusted life-years (DALYs) and costs are adjusted to 2005 US dollars and discounted at 3% annually. The interventions and 'No ongoing therapy' groups each consist of 100 employees. HAART, highly active antiretroviral therapy; CTX, cotrimoxazole.

including private enterprises, since there are potential opportunities for cost-sharing. This implies a coordinated approach including business, government, and donors.

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