Cost and Enrollment Implications of Targeting Different Source Population for an HIV Treatment Program

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Background: Rapid scale-up of antiretroviral therapy (ART) is a worldwide priority, and ambitious targets for numbers on ART have been set. Antenatal clinics (ANCs) and tuberculosis (TB) clinics have been targeted as entry points into HIV care.

Methods: We developed a conditional probability model to evaluate the effects of ANC and TB clinic populations on ART program enrollment.

Results: To start 1 individual on ART, 3 TB patients have to be screened at a crude program cost of US $36 per patient initiated on therapy. By contrast, 48 ANC patients have to be screened at a cost of US $214 per patient on therapy. In an incremental analysis in which ANC HIV testing was borne by a program to prevent mother-to-child transmission, recruitment efficiency increased (8 screened per patient starting ART) and cost decreased (US $114 per patient on therapy). Absolute numbers starting ART, however, remained fixed. If all 60,000 ANC patients seen yearly in the Lusaka District were screened, 1247 would start ART. Approaching the district’s 35,000 annual TB patients would generate 11,947 patients on ART.

Conclusion: In areas with high HIV prevalence, targeting chronically ill populations for HIV treatment may have significant short-term benefits in cost savings and recruitment efficiency.

Key Words: conditional probability model, HIV/AIDS, HIV treatment, antiretroviral therapy, antenatal population, tuberculosis population


At the end of 2003, approximately 39 million people worldwide were infected with HIV. Up to 6 million individuals were in urgent need of antiretroviral therapy (ART), but only an estimated 7% of these had started treatment.1 The World Health Organization (WHO) has set ambitious goals for this global scale-up for ART, calling for the treatment of 3 million people by the end of 2005 in their “3 by 5” initiative.

In 2003, the Zambian government raised its target from 10,000 to 100,000 people on ART in conjunction with the 3 by 5 initiative. Like most countries in sub-Saharan Africa, however, Zambia has experienced slow growth of its national ART program. By December 2004, fewer than 14,000 individuals had been started on therapy.2 Clearly, if these targets are to be met, and an additional 86,000 are to be placed on ART before the end of 2005, an accelerated enrollment rate must be achieved.

As HIV treatment programs look to scale up rapidly, there may be cost and enrollment benefits to focusing on specific source populations. This approach may be particularly useful when program expansion faces significant constraints in human resources, drug availability, and infrastructure. In this study, we evaluated 2 different source populations for recruitment into an HIV treatment program: antenatal clinic (ANC) attendees and outpatient tuberculosis (TB) patients. Using a conditional probability model, we compared the short-term enrollment and cost implications for each group. Outcomes of interest were the efficiency of recruitment (ie, the number that needs to be screened to start 1 patient on ART) and cost per patient started on ART. The model considered 2 hypothetic cohorts based on ANC and TB populations in Lusaka, Zambia to demonstrate the potential effect that strategic recruitment may have on ART program enrollment.

METHODS

To understand how to enroll large numbers of people on a population basis, we first determined the sequence of events that must occur for a single patient to initiate ART in our program (Fig. 1). The patient must (1) agree to HIV testing, (2) be diagnosed with HIV, (3) agree to medical evaluation, (4) meet clinical and/or laboratory criteria for ART, and (5) be ready and willing to start ART. For any individual to start treatment of HIV, he or she must successfully negotiate this screening cascade. These events served as the basis of our conditional probability model.

We chose 2 different outpatient populations for evaluation. Although there are other populations of interest (eg, general outpatient population, those seeking care for sexually transmitted infections, hospitalized inpatients), the ANC and TB groups were selected because they are commonly referenced entry points into HIV care.3–8 They also represent different ends of the spectrum for outpatient care in Lusaka. ANC patients are generally healthier and seek care for health maintenance rather than acute problems. TB clinic attendees...
are, by definition, chronically ill and typically have multiple comorbidities.

Populations described in this report are representative of those in areas of high HIV disease burden and resource constraints. The baseline estimates and costs used are described in the next sections (listed in Tables 1 and 2).

Acceptance of HIV Testing

In Lusaka, a 70% acceptance rate of HIV testing among ANC clients has been consistent since 2001.9 Acceptance rates for HIV testing among TB patients are believed to be similar,10,11 although there are few published data in this regard.

HIV Prevalence Among Each Population

The ANC HIV prevalence in the Lusaka Urban District is well described.9,12,13 Figures for HIV prevalence among the TB population were less certain. Small studies conducted in Lusaka have found the coinfection rate to be approximately 70%.14 Comparable figures have been found in Malawi (67%),15 South Africa (60%), and Zimbabwe (67%).16

TABLE 1. Baseline Probability Estimates

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Agrees to HIV testing after pretest counseling</td>
<td>0.70 9 10, 11</td>
<td>0.70 10, 11</td>
</tr>
<tr>
<td>Diagnosed with HIV</td>
<td>0.25 9, 12, 13</td>
<td>0.70 14–16</td>
</tr>
<tr>
<td>Agrees to ART evaluation</td>
<td>0.66 See text</td>
<td>0.90 See text</td>
</tr>
<tr>
<td>Medically eligible for ART</td>
<td>0.20 See text</td>
<td>0.86 See text</td>
</tr>
<tr>
<td>Ready and willing to start ART</td>
<td>0.90 See text</td>
<td>0.90 See text</td>
</tr>
</tbody>
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TABLE 2. Baseline Cost Estimates

<table>
<thead>
<tr>
<th>Cost for HIV Screening</th>
<th>US$</th>
<th>Reference No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Determine HIV-1/2, Abbot Diagnostics (screening)</td>
<td>0.80</td>
<td>19</td>
</tr>
<tr>
<td>Genie II HIV-1/HIV-2 (confirmatory test)</td>
<td>2.47</td>
<td>19</td>
</tr>
<tr>
<td>Average supply cost per screening for ANC population (1 in 4 need confirmatory test)</td>
<td>1.42 Calculation</td>
<td></td>
</tr>
<tr>
<td>Average supply cost per screening for TB population (7 in 10 need confirmatory test)</td>
<td>2.53 Calculation</td>
<td></td>
</tr>
<tr>
<td>Cost per patient for counselor’s time</td>
<td>1.00 See text</td>
<td></td>
</tr>
<tr>
<td>Cost of ART evaluation</td>
<td></td>
<td></td>
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<tr>
<td>CD4 cell count via flow cytometry</td>
<td>11.33 See text</td>
<td></td>
</tr>
<tr>
<td>Complete blood cell count, liver function tests, creatinine level</td>
<td>7.80 See text</td>
<td></td>
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<tr>
<td>Cost per visit for staff time (nurses, clinical officer, and physician)</td>
<td>2.10 See text</td>
<td></td>
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Willingness to Access HIV Care

In this model, the proportion of individuals who agree to ART evaluation reflects the willingness among clinic attendees to access HIV care. For the ANC population, the baseline probability of 66% was derived from the 2-clinic Mother-to-Child Transmission (MTCT)-Plus program in Lusaka. Similar data were not available for the TB population. Because TB patients are symptomatic and chronically ill, we reasoned that they would be more likely to undergo ART evaluation (90%).

Medical Eligibility for Antiretroviral Therapy

Medical eligibility for ART was based on the most recent WHO recommendations.17 These include (1) a CD4 count less than 200 cells/mm³, (2) stage IV disease, or (3) stage III disease and a CD4 count less than 350 cells/mm³. For this model, we estimated that 20% of ANC patients medically evaluated meet criteria for ART, based on experience from the Lusaka MTCT-Plus sites. Our TB estimate of 86% was derived from the databases of the Lusaka District HIV Care and Treatment Program (accessed August 3, 2004). Because of our uncertainty about this estimate and the potential effect it could have on our model, we included this parameter in a sensitivity analysis.

Ready and Willing to Start Antiretroviral Therapy

Although an individual may meet medical criteria for ART, other issues of social network and support must be considered.18 It stands to reason that the more stringent these social criteria are, the less likely it is that an individual actually starts treatment. The Lusaka District currently uses minimal social criteria for starting ART, although the patient must demonstrate adherence to a rigorous visit schedule in the months after treatment initiation. In the first 3 months since our program started, 90% of individuals eligible have been ready and willing to start ART (database accessed August 5,
Costs
Supply costs for rapid HIV tests were derived from a price listing published by the United Nations Children’s Fund (UNICEF), United Nations Program on HIV/AIDS (UNAIDS), WHO, and Médecins Sans Frontières. Because the Lusaka District currently uses a serial rapid test algorithm with confirmation of positive results for the diagnosis of HIV, an average per supply cost was calculated based on the HIV seroprevalence among each group. Costs for CD4 cell counts, complete blood cell counts, and liver and renal function tests were adapted from the current laboratory support for the Lusaka District HIV Care and Treatment Program, Central Laboratory, Centre for Infectious Disease Research in Zambia.

Personnel costs were based on salary costs per shift for clinical staff (ie, nurses, clinical officers, physicians), counselors, and laboratory technicians in the Lusaka District. No cost provision was made for staff training, counseling room construction and/or renovations, laboratory equipment, laboratory quality control, or other overhead expenses.

Costs incurred for any single individual were modeled to begin at time of entry into the screening cascade. For most, this occurs when the individual agrees to voluntary testing and counseling (VCT) for HIV. Because this is not a formal cost-effectiveness analysis, we did not consider downstream consequences of health care decisions or use discounting of future costs and health effects. Instead, we focused on the immediate cost implications of initiating ART.

Hypothetic Antenatal Clinic and Tuberculosis Cohorts
To demonstrate the population-based effect of strategic recruiting, we based our hypothetic cohorts on ANC and TB populations in Lusaka. To determine the size of these populations, we referenced the yearly averages from 2002 and 2003 from the Zambia Health Management Information Services (N. Kayombo, unpublished data, 2004). Each group was rounded to the nearest 1000.

Sensitivity Analysis
Finally, to explore the robustness of the model’s findings across a range of probabilities, we performed several sensitivity analyses. Because the HIV prevalence among TB patients may vary and because there is some uncertainty regarding the proportion of TB patients who are medically eligible for ART, we determined the relative recruitment efficiencies when both parameters were varied over a wide range.

A second issue we examined was that of previous HIV testing among ANC patients. ANC attendees have been targeted for entry into HIV care because of their relatively high access to and use of VCT services. We studied what incremental effect previous HIV testing may have on enrollment and cost in separate 1-way sensitivity analyses.

RESULTS
We first created hypothetic cohorts of 10,000 patients for the ANC and TB populations and applied them to our model. Using the baseline model assumptions reported in Tables 1 and 2, a total of 208 ANC patients would initiate ART for every 10,000 clinic attendees approached. This would lead to a total screening cost of US $44,461 or US $214 per ART enrollee. For every 10,000 TB patients approached, 3413 would start HIV treatment. The screening cost for this population is estimated at US $121,334 or approximately US $36 per ART enrollee.

Recruitment Efficiency
When VCT was used as the entry point into the cascade, an HIV care program would need to screen 48 ANC patients to start 1 on ART. In this respect, the TB population was more efficient: only 3 patients needed to enter the screening cascade for 1 to start therapy.

This superior recruitment efficiency persisted even when the HIV-TB coinfection rate and proportion of coinfected patients who qualify for ART were varied across a wide range in sensitivity analysis (Fig. 2). Recruiting from ANC populations would be more efficient only in settings in which HIV prevalence among the TB patients is low and most of those infected do not qualify for ART.

Differences in recruitment efficiency remained when we considered that a proportion of ANC patients may have already tested HIV-positive before accessing HIV care. In the most ideal situation, where 100% of ANC women present with previously diagnosed HIV, the recruitment efficiency improved significantly: only 8 women would have to access care in this manner for just 1 to start ART (Fig. 3A).
Cost Per Patient Started on Antiretroviral Therapy

The cost per patient for starting 1 patient on ART was lower than that of ANC population. Using VCT as the entry point, the program cost of starting 1 patient on ART was US $36 for the TB population and US $214 for the ANC population. When a proportion of ANC attendees have previously been tested and access care knowing their HIV status, the cost per patient of starting ART for this population is reduced further (see Fig. 3B). In the situation in which all ANC attendees have been previously tested, a situation that represents the maximal cost savings, the program cost for starting 1 ANC attendee drops to US $114.

Application to Fixed Cohorts

We applied our model to 2 hypothetic cohorts, based on the numbers seeking ANC and TB care in the Lusaka public health system yearly, assuming that an HIV program was being introduced to a treatment-naive population. If we were able to approach all 60,000 pregnant women seeking care in the Lusaka District and initiate them in the screening cascade, 1247 would actually start ART. In contrast, if all 35,000 TB patients seen in the Lusaka District that year were initiated into the screening cascade, 11,947 would commence treatment. Despite large discrepancies in absolute patient numbers in the source populations, nearly 10 times the number of TB patients would start ART as compared with ANC attendees (Fig. 4). The total cost to initiate 11,947 TB patients on ART would be US $442,670. For the 1247 ANC attendees, the total cost would be US $266,764.

DISCUSSION

With large-scale commitments for HIV care and treatment, a heightened sense of urgency has developed regarding access to ART. Unfortunately, countries hit hardest by the HIV/AIDS epidemic are also among those with the least developed health care infrastructure, creating a major impediment to the rapid deployment of ART services. Although the
inflow of funding undoubtedly expedites implementation, resources such as trained medical personnel, technologic infrastructure, and adequate clinical facilities may not be immediately available.

Two key populations that have been targeted as entry points for HIV treatment have been ANC and TB clinic attendees. Many facets of ANCs lend themselves to integration with long-term care. Availability of services to prevent mother-to-child transmission of HIV (PMTCT) can be a strong incentive for interventions such as HIV testing and behavior modification. Large proportions of this population may already know their HIV status through prior PMTCT testing or through other VCT programs. Provision of ART among pregnant women may help to preserve the family unit. Recent work has shown that children orphaned by HIV-positive mothers have increased mortality rates within the first 5 years of life. Participating in maternal HIV care may also improve access to newborn and infant medical care.

There may be numerous advantages in using TB programs as an entry point for HIV care as well. Benefits include typically high coinfection rates among the 2 populations and the use of complicated drug regimens to treat both diseases. The infrastructure surrounding TB care is usually well established, with programs for directly observed therapy and community outreach already in place. ART has also been shown to increase survival among TB patients, an important consideration in areas with high disease prevalence.

In this analysis, we focus on some of the enrollment and cost ramifications of recruiting ANC and TB patients into HIV treatment programs. Because HIV-infected antenatal patients are relatively healthy, our model demonstrates that TB outpatients may be more suitable for focused recruitment when the goal is rapid large-volume ART provision. The TB population was found to have far greater recruitment efficiency when compared with the ANC population. The differences were most dramatic when VCT was provided by the ART program and the starting antenatal population had not yet undergone testing. More than 15 times as many ANC patients need to be screened to start 1 person on ART. Although these differences may diminish in settings in which PMTCT services can offset the demand and cost for HIV testing, it does not change the absolute number that can be enrolled.

Beyond the relative narrow comparison of ANC and TB populations, one can use these results to demonstrate how the relative healthiness of a population may affect ART program enrollment. Other chronically ill populations are likely to have recruitment efficiency and cost characteristics similar to our modeled TB population. For example, the HIV prevalence among medical admissions in Lusaka’s University Teaching Hospital has been estimated at 62% (I. Zulu, MD, MPH, unpublished data, 2004). Palliative care facilities such as hospices may have even higher rates. High proportions of these example populations are likely to have advanced HIV disease by virtue of their decreased functional status and need for inpatient medical care.

We believe that focused recruitment from these types of clinic populations is important, particularly in settings of severe resource constraint. Enrollment and long-term care of healthy populations, whose members may require multiple clinical visits over time before initiating ART, may divert valuable resources away from groups at higher risk for advanced disease. The ratio of clinic attendees to trained health care workers is already as high as 45:1 in the Lusaka District, more than 3 times the limit recommended by the WHO. Focusing on relatively healthy groups may thus come at a large opportunity cost, possibly at the expense of those who need ART the most.

Although models are commonly used to aid in decision making, by nature, the simplifications required in their construction can lead to variable findings. This analysis has some limitations that should be considered in any critical evaluation. The baseline estimates used are specific to settings in which HIV prevalence and TB coinfection are high; however, globally, these rates vary greatly. Although recruitment from a TB population is likely to be more efficient over a wide range of conditions, for an HIV treatment program, these differences may be marginal or even insignificant at certain baseline rates. The single-event conditional probability model that we have used may not take into account the complexities of health care access, where a certain proportion of individuals who initially decline services may later change their mind. That this phenomenon may differentially affect these 2 groups is probable, because those who are chronically ill may have a greater motivation to use health care services early on. Unfortunately, there is little evidence to support this notion. In addition, the end point used in this analysis, the number of individuals who would start ART, is a short-term surrogate marker for programmatic success and does not consider long-term outcomes such as life expectancy and quality of life. Because our immediate interest is in the rapid scale-up of an HIV treatment program, however, we believe that its use is justified.

Lastly, although we have demonstrated significant differences among specific source populations, cost and recruitment efficiency alone should not dictate accessibility to any HIV treatment program. Policy makers must also take into consideration various other factors such as gender, race, socioeconomic status, and geography. When HIV disease burden is high and resources are limited, however, enrollment of a large proportion of healthy individuals may not be a luxury that can easily be afforded. ART programs looking to scale up rapidly should give special consideration to populations with high HIV prevalence and high proportions of advanced HIV disease.

REFERENCES


