An analysis of the uptake of collaborative TB/HIV activities at fourteen TB clinics in Kinshasa, DRC.

by

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Title: An analysis the uptake of collaborative TB/HIV activities at fourteen TB clinics in Kinshasa, DRC.

Objectives: We assessed the uptake of HIV activities when integrated into routine care at 14 TB clinics in Kinshasa, DRC.

Design: Descriptive analysis of prospective data on patients registered with TB between February 2006 and December 2006. Data was collected using modified TB treatment cards to capture both TB and HIV activities.

Results: Among 3521 patients with TB, a high uptake rate of HIV testing was achieved (mean 90.2%), with large variation between clinics (range 65-99%). Almost all patients tested received post-test counseling (mean 95.8%, range 78-99%). The mean HIV prevalence rate was 16.7%, varying by clinic from 8.8 to 33.3%. Cotrimoxazole was initiated in most HIV co-infected patients (81.5%, range 63-91.5%). Referral of HIV-positive patients for psychosocial support increased over time from 32% in the 1st month of operation to 67% in the 10th month, again varying widely by clinic (0 to 85%). Antiretroviral therapy (ART) initiation was sporadic and varied by month and clinic with a mean of 6.9% of patients receiving ART. Among the 39 patients receiving ART, 28 (72%) started ART before TB diagnosis. Only 9 patients gained access to ART following HIV testing at the TB clinic.

Discussion: High uptake of collaborative TB/HIV activities (HIV testing, posttest counseling and cotrimoxazole) was achieved when these activities were integrated into routine TB care. Access to ART was low among newly diagnosed co-infected patients. Quarterly monitoring and evaluation of performance of activities at the clinic level using visual charts of activities demonstrated variable performance between clinics over time.
I. Introduction

Tuberculosis (TB) remains one of the leading causes of infectious disease death worldwide causing 1.6 million deaths in 2005.\(^1\) Twelve of the 15 countries with the highest rates of TB are found in Africa, and 28 percent of TB patients in Africa are estimated to be infected with HIV. Eighty percent of the world’s TB/HIV co-infected patients reside in Africa. The Democratic Republic of the Congo (DRC) is identified as one of the 22 high burden of tuberculosis disease countries in the world with 356 new infections per 100,000 people and 73 deaths per 100,000 people in 2005. While not as affected by HIV as parts of southern Africa, 17 percent of TB patients in the DRC are estimated to be HIV positive and the DRC contains 4 percent of the world’s TB/HIV cases.\(^1\)

Since the 1980’s, TB and HIV have developed a symbiotic relationship. Many patients become latently infected with TB before contracting HIV. As these patients become immune compromised, their systems can no longer contain latent TB infections and, as a result, they progress to active TB. In Africa, TB is often the first sign of HIV infection and is the leading cause of death among HIV-infected patients.\(^2\) A study in the early stages of the TB/HIV co-epidemic in the DRC found that 41 percent of autopsies showed TB as the cause of death in HIV-patients in Kinshasa.\(^3\)

In 2004, WHO recommended the implementation of collaborative TB/HIV activities. In the DRC, tuberculosis clinics are not linked to HIV voluntary counseling and testing centers. Because there was little collaboration between the central TB and HIV efforts in the DRC, a group of UNC researchers provided technical assistance to the National TB and HIV programs to assess the feasibility of collaborative TB/HIV activities. Through their research, they found that incorporating HIV testing activities into routine TB care was the most accepted and successful
way to offer HIV prevention and care to TB patients in the setting specific to Kinshasa. These findings led to new national TB/HIV policy guidelines.

This paper examines the rollout of collaborative TB/HIV activities for TB patients to fourteen clinics in Kinshasa, DRC. We will describe the uptake of collaborative TB/HIV activities both overall and by individual clinics and discuss the process of monitoring and evaluating TB programs. Ultimately, monitoring and evaluation will help to identify clinics that are in need of improvement that can be addressed through clinic interactions and quality improvement activities.

II. Literature review

A. Historical Context

Because of the rapid emergence of the HIV epidemic in resource poor countries where tuberculosis is also present, the health care systems of many countries were not equipped to address patients with TB/HIV co-infections. Tuberculosis control programs are historically vertical programs that take a public health approach to case-finding and treatment of active, smear-positive, pulmonary tuberculosis. Largely because of the stigma that surrounded HIV/AIDS as it emerged in the 1980’s, HIV programs took more of a human rights approach to diagnosing and supporting patients with HIV. Testing was voluntary and on demand of the individual patient. As such, few existing programs integrated HIV activities into routine care and few new clinics initiated collaborative TB/HIV activities.

In 2004, WHO’s Stop TB Department and Department of HIV/AIDS recommended strategies to reduce the burden of suffering caused by TB/HIV co-infections. Their recommendations included a shift toward implementing joint TB/HIV activities and
encompassed three key activities: national oversight of collaborative TB/HIV activities, activities to reduce the burden of TB in HIV patients, and activities to reduce the burden of HIV in TB patients. These recommendations encourage existing TB and HIV programs to expand and consider addressing prevention and treatment of the other half of the co-infection. For tuberculosis programs, WHO identified six specific activities to reduce the burden of suffering caused by HIV in TB patients. It recommended all tuberculosis patients 1) be tested for HIV and 2) receive their HIV test result through post-test counseling. Those patients who are found to be HIV-positive should be 3) started on cotrimoxazole as a preventive therapy (CPT), 4) provided or referred for HIV care and support, and 5) started on antiretroviral treatment (ART). Finally, 6) condoms should be available in TB clinics for all patients.

B. Evidence for collaborative TB/HIV activities

WHO’s recommended collaborative TB/HIV activities were based on limited evidence available at the time of the published recommendation. From that time, the evidence base has grown and is summarized below.

Systematic Review Methods

Identifying literature

Specific research questions of interest were defined for each recommended collaborative activity to reduce the burden of suffering due to HIV in TB patients. They include:

- How effective is counseling and testing for HIV in changing behavior and reducing HIV transmission among newly diagnosed TB patients?
- How does providing CPT to newly diagnosed TB patients found to be HIV-positive affect risk of mortality?
- How does providing referral to HIV care and support to newly diagnosed TB patients found to be HIV-positive affect risk of mortality and/or adherence to treatment?
- How does providing ART to newly diagnosed TB patients found to be HIV-positive affect risk of mortality?
To what extent have collaborative TB/HIV activities been implemented at the national and local or clinic level?

Because TB programs treat patients of all ages, the search included studies of adult and pediatric populations. It included both individual and combined activities as activities may be adopted individually or in a step-wise fashion. Medline was searched collectively for all questions of interest using the following search strategy:

(TB or tuberculosis) AND ((HIV OR (human immunodeficiency virus) OR AIDS OR (acquired immune deficiency syndrome) OR (acquired immunodeficiency syndrome)) AND ((VCT OR testing) OR ("Trimethoprim-Sulfamethoxazole Combination"[MeSH] OR cotrimoxazole preventive therapy OR CPT) OR ("Mental Health"[MeSH] OR "Mental Health Services"[MeSH] OR "Social Support"[MeSH] OR "Counseling"[MeSH] OR "Self-Help Groups"[MeSH]) OR ("Antiretroviral Therapy, Highly Active"[MeSH] OR zidovudine OR lamivudine OR efavirenz OR nevirapine OR stavudine OR ZDV OR 3TC OR EFZ OR NVP OR d4T)).

MeSH terms were not used for TB or HIV search terms as using them greatly reduced citations returned. First-line antiretroviral medications as identified by WHO were used to complement the ART search. Search dates were from 1980 to April 2007, and the search was restricted to human studies published in English. Additional citations were identified from relevant review articles. The grey literature was not reviewed. Titles and abstracts were reviewed to include efficacy studies and reports on the uptake or cost-effectiveness of each intervention, individually or in combination. Because of the lack of randomized-controlled trials, non-controlled trials, observational studies, and decision analyses were included. Case reports and case-series of less than ten patients were excluded. Outcomes of interest included death, CD4 count or viral load, treatment harms, collaborative activity uptake, and cost-effectiveness.
Validity assessment/data abstraction

Full texts of selected articles were independently reviewed to extract key findings into a summary comparison table and to determine study quality. Because of the small number of studies identified, this review includes all studies with mention of study limitations where appropriate.

Systematic Review Results

Initial searching yielded 1173 citations. After review of titles and abstracts, eight comparative trials were identified that provided information on the efficacy of recommended interventions using patient-centered outcomes. They are summarized in table 1. Five trials examined the efficacy of CPT (with or without HIV testing) while three addressed ART. No trials independently assessed HIV counseling and testing or the effectiveness of referring patients for HIV care and support in TB/HIV co-infected populations. The effectiveness of HIV counseling and testing and referral for HIV care and support have been reported in HIV-positive populations. Such studies are briefly reviewed below and give insight into the effectiveness of such interventions among patients co-infected with TB and HIV.

Cotrimoxazole preventive therapy

Of the citations addressing CPT, only Wiktor, et al. (1999) was a randomized-controlled trial of the effectiveness of CPT in HIV-positive patients. In this study of adult patients in Cote d’Ivoire, those taking CPT had a hazard ratio of death of 0.54 (95% CI: 0.38-0.77) compared to those in the intervention group\(^5\). This result was seen despite the study being stopped early as an unrelated trial of CPT in HIV patients (not specific to TB patients) was published showing net benefit of CPT\(^14\). Side effects and adverse effects necessitating stopping treatment were equal
<table>
<thead>
<tr>
<th>Citation</th>
<th>Year</th>
<th>Location</th>
<th>Study type</th>
<th>Intervention</th>
<th>Number of pts</th>
<th>Patient characteristics</th>
<th>Outcome</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wiktor, et al. 5</td>
<td>1999</td>
<td>Cote d'Ivoire</td>
<td>RCT</td>
<td>Randomized CPT for HIV-positive patients</td>
<td>771</td>
<td>18+yo HIV-1+</td>
<td>Death among TB/HIV co-infected (10 mo medial follow-up)</td>
<td>Hazard ratio: 0.54 (95% CI: 0.38-0.77)</td>
</tr>
<tr>
<td>Grimwade, et al. 6</td>
<td>2005</td>
<td>South Africa</td>
<td>cohort with historical controls</td>
<td>CPT for all TB patients</td>
<td>3325</td>
<td>13yo+ no HIV test</td>
<td>Death among all TB pts (6 mo)</td>
<td>14.5% control, 10.3% CPT (p&lt;0.001)</td>
</tr>
<tr>
<td>Mwaungulu, et al. 7</td>
<td>2004</td>
<td>Malawi, Karonga District</td>
<td>cohort with historical controls</td>
<td>CPT for HIV-positive members of intervention cohort</td>
<td>712</td>
<td>2mo+ 70% HIV positive</td>
<td>Death among all TB pts (18 mo)</td>
<td>Hazard ratio: 0.72 (95% CI: 0.50-1.02)</td>
</tr>
<tr>
<td>Chimzizi, et al. 8</td>
<td>2004</td>
<td>Malawi</td>
<td>cohort with neighboring district controls</td>
<td>HIV-testing for intervention cohort and CPT for those HIV-positive</td>
<td>2342</td>
<td>1yo+ 78% HIV positive</td>
<td>Death among all TB pts (12 mo)</td>
<td>RR: 0.84 (95% CI: 0.78-0.91)</td>
</tr>
<tr>
<td>Zachariah, et al. 9</td>
<td>2003</td>
<td>Malawi, Thyolo District</td>
<td>cohort with historical controls</td>
<td>HIV-testing for intervention cohort and CPT for those HIV-positive</td>
<td>1986</td>
<td>&gt;2 yo 77% HIV-positive</td>
<td>Death among all TB pts (12 mo)</td>
<td>Hazard ratio: 0.76 (95% CI: 0.69-0.83)</td>
</tr>
<tr>
<td>Dheda, et al. 10</td>
<td>2004</td>
<td>UK</td>
<td>cohort with historical control</td>
<td>Those treated during HAART era versus those treated before HAART era. No mention of CPT.</td>
<td>96</td>
<td>23-62 yo all HIV-positive</td>
<td>Death in HAART era vs. pre-HAART era</td>
<td>Hazard Ratio: 0.18 (95%CI: 0.06-0.52)</td>
</tr>
</tbody>
</table>
| Dean, et al. 11   | 2002 | UK           | retrospective cohort                  | Thos who received HAART vs. those who did not. Number of patients on CPT not reported. | 188           | median age 34 yo (range 21-70) all HIV-positive | 1) AIDS-defining illness in HAART recipients vs. non-HAART recipients 2) Death in HAART recipients vs. non-HAART recipients | 1) Risk ratio: 0.14 (p<0.001) 2) Unadjusted risk ratio: 0.27
| Garcia, et al. 12 | 2002 | Spain        | retrospective cohort                  | Patients diagnosed before and after HAART initiation (31 Dec 1996). | 549           | All HIV-positive        | Death in HAART era vs. pre-HAART era                | Hazard Ratio: 0.37 (95% CI: 0.21-0.64)         |
| Schiffer, et al. 13| 2007 | US           | Decision analysis                     | Early vs. late vs. no ART                              | -             | All cause mortality     | 33 vs. 47 vs. 147 deaths per 1000 patients, respectively | Author’s unadjusted calculation from figures reported in article |
between the two groups. In their analysis, they confirmed the results seen in HIV-positive non-TB patients supporting the use of CPT for patients with TB/HIV co-infections.

Since further placebo controlled trials of CPT for TB/HIV co-infected patients would have received ethical criticism, the subsequent four studies were cohort studies completed in Africa that used historical or neighboring district control groups that did not receive CPT. They enrolled children and adults of varying ages, and at least 70 percent of TB patients enrolled were HIV-positive. Results include a risk ratio of death of 0.84 (95% CI: 0.78-0.91), a hazard ratio of 0.72 (95% CI: 0.78-0.91), and in the smallest trial (n= 712), a hazard ratio of 0.84 (95% CI: 0.50-1.02). The fourth trial reported a statistically significant absolute risk reduction of 4.2 percent for those taking CPT. Only two of these observational trials reported adverse events. In the largest trial of over 3,000 patients, 23 people stopped CPT because of perceived adverse events including two serious dermatological reactions. In the other trial to report side effects, 2 percent of the study participants reported minor skin rashes that resolved upon stopping CPT. As these were all cohort studies with non-randomized control groups, each is likely subject to confounding. Most notably, the implementation of CPT requires additional training and resource input that increases overall quality of care. This could affect a study outcome that would make CPT appear more beneficial than it would be alone. The district that received treatment had a long history of working with the sponsoring NGO, likely altering medical norms in the community. Despite these limitations, these trials taken together support the use of CPT in patients with TB/HIV co-infections.

Anti-retroviral therapy

Three citations investigated the role of ART in TB/HIV co-infected patients. As was seen for CPT, ART has been shown highly effective at preventing opportunistic infections and
death in HIV-positive patients. ART has just started to become available in parts of resource poor countries. As a consequence, very few studies have reported outcomes of ART in TB/HIV co-infected patients. In this review, four were identified. The first two are retrospective cohort studies from patients in the United Kingdom. They both enrolled adult TB patients, many of whom had known their HIV status for several years. Dean, et al., report a risk ratio of 0.14 (p<0.001) for AIDS-defining illness in TB patients on HAART therapy versus those not on therapy. An unadjusted risk ratio of 0.27 for death between the two groups was calculated from figures reported in the article. Dheda, et al., reports a hazard ratio for death of 0.18 (95% CI: 0.06-0.52) between those taking and those not taking HAART. As is common in retrospective, observational studies, baseline populations differed in these studies and unaccounted for factors, such as health systems improvement prompted by the implementation of HAART, likely confound the true relationship between treatment and outcome. Nevertheless, the demonstrated benefit is great enough that ART is likely beneficial in these populations.

A third, cohort study retrospectively studied 549 cases of extra-pulmonary TB who were HIV-positive. This analysis compared cohorts before and after 31 December 1996 when HAART became available in the country of study. The hazard ratio of death for those taking HAART was 0.37 (95% CI 0.21-0.64). The study has several potential shortcomings in that there were no baseline characteristics of the groups presented, 82 percent of patients were in the no HAART group, and DOTS was implemented around the same time as HAART. Despite the strong potential for confounding, the results are consistent with the figures reported in other trials.

Schiffer and Sterling used a decision analysis to model the effect of ART in TB patients. They report 33, 47, and 147 deaths per 1000 people in groups initiating HAART

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1 Calculation of unadjusted RR (# of patients who died while taking HAART/total patients taking HAART divided by # of patients who died while not taking HAART/total # of patients not taking HAART) = (3/85)/(13/98) = 0.27
early (during the first two months of TB treatment), initiating HAART late (after the first two months of TB treatment), and not starting HAART. In their model, the majority of deaths in the late and no HAART groups were secondary to tuberculosis or HIV. However, a significant number of deaths in the early HAART group are due to immune reconstitution inflammatory syndrome (IRIS). Nevertheless, the decision analysis clearly favors starting HAART over not, and also supports starting HAART early after TB diagnosis rather than waiting until patients are stable on their anti-tuberculosis regimen.

In addition to the three citations evaluating ART in TB patients above, one larger (n=439) retrospective cohort study from Malawi and six additional small, cohort studies (n=20 to 92) were identified. The retrospective study from Malawi examined survival at 6 and 12 months between children under age 12 taking ART who had current TB diagnoses, a TB diagnosis in the past two years, and non-TB diagnoses. Researchers found no difference in death rates between these groups with the probability of survival being 0.86, 0.86, and 0.88, respectively. Because this was a retrospective cohort study drawing on routine, clinic-collected data and the difficulty of diagnosing TB in HIV-positive children, a substantial portion of patients may have been misclassified regarding their TB status. However, the results suggest that children given ART have a high likelihood of survival irregardless of TB status.

The other six studies that were conducted in Spain, South Africa, Thailand, and Brazil report undetectable HIV viral load rates of 62.5 to 94.1% in TB/HIV patients on ART. In these studies, very few, if any, patients died over a maximum follow-up of four years. This low death rate supports ART efficacy in TB/HIV co-infected patients. Up to 35 percent of patients experienced minor side effects of treatment, and some required stopping or changing treatments regimens.
Referral for HIV care and support

The literature search returned no citations that quantified the effect of referring patients for HIV care and support among TB/HIV co-infected patients. Such programs are diverse and good evaluation measures are lacking. The only studies identified were descriptions of the role that community HIV care and support have played in parts of Malawi.\textsuperscript{23} In their community, volunteer resources play an integral part in caring for TB/HIV co-infected patients including operating community gardens, providing child/orphan care, monitoring side-effects, providing nutritional support, and directly caring for patients in their homes. Authors were also clear to emphasize the importance of including community members in the development and initiation of community HIV care and support activities and the importance that community resource groups do not duplicate activities that should be the responsibility of clinic staff. The importance of HIV care and support activities is hard to measure, but such reports emphasize the importance of providing community support for patients with TB, HIV, or both.

Voluntary counseling and testing for HIV

While no studies meeting inclusion criteria addressed the effectiveness of VCT in reducing the burden of HIV in patients with TB, more research is available on the usefulness of VCT in HIV-positive populations. One RCT and several meta-analyses of smaller studies suggest that VCT may reduce high-risk behaviors. The RCT compared patients who received VCT to patients receiving routine health information in Kenya, Tanzania, and Trinidad.\textsuperscript{24} It found that those receiving VCT had lower rates of unprotected intercourse and intercourse with non-primary partners than the control group. When the group receiving routine health information was provided VCT, their rates of high-risk behaviors were reduced to a similar rate as the initial VCT group. In post-hoc analysis among those who received VCT, HIV-positive
individuals had lower rates of high-risk behaviors compared to HIV-negative patients. This suggests that being diagnosed with HIV may change high-risk behaviors more than if one undergoes VCT but tests negative.

Two meta-analyses show similar trends toward effectiveness of VCT in reducing high-risk behavior, at least in HIV-positive populations.\textsuperscript{25,26} The first included 27 studies from the US, Africa, and Europe and reported that HIV-positive patients and discordant couples were significantly more likely to use condoms and less likely to have unprotected intercourse than untested patients. The rate of high-risk behavior for HIV-negative patients was not statistically different, but also not higher, than untested patients.\textsuperscript{25} The second meta-analysis included 11 trials from the US. It reported that HIV-positive patients who underwent VCT had 53 percent less unprotected anal or vaginal intercourse than HIV-negative patients after VCT (95\% CI 45 to 60 percent).\textsuperscript{26}

Such studies suggest that VCT may be effective at reducing high-risk behaviors among HIV-positive patients and do not show an increase in high-risk behavior among HIV-negative patients. The applicability of such trial data to the widespread rollout of VCT has been questioned, however. One of the hurdles to these studies’ generalizability is the concern that people who volunteer for VCT effectiveness trials are often at high risk for HIV.\textsuperscript{27} Patients who know they are at high risk for HIV may change their behavior after VCT in a different way than those who are at low risk for HIV. When such VCT programs are scaled up to population levels, patients on the whole are likely to be at lower risk and have lower rates of HIV. The effectiveness of VCT in changing behavior may be more limited than the studies suggest.

Patients presenting to TB clinics in sub-Saharan Africa are generally at high risk for HIV. In many places, up to 72 percent of TB patients are HIV-positive.\textsuperscript{28,29} Such a population with a
high risk of HIV infection may be more similar to some of the VCT trial populations than the general public. As a result, trial outcomes may be more generalizable to this group with high risk for HIV than the population at large. In such instances it seems reasonable to extrapolate the results of the VCT effectiveness trials to such populations, especially for those who test HIV-positive. To truly measure effectiveness in TB populations, however, separate trials would have to be completed, but completing such trials would not be ethical under the current guidelines to screen all TB-positive patients for HIV.

C. Monitoring, evaluation, and uptake of collaborative TB/HIV activities

Monitoring and evaluation of activities are integral to all interventions. WHO has published guidelines to guide the monitoring and evaluation process of collaborative TB/HIV activities. As described in WHO recommendations, there are two parts to program evaluation. Monitoring refers to routine analysis of clinic performance using regularly gathered information to evaluate the extent to which a program is achieving its stated goals. Evaluation is an episodic process of evaluating the extent to which results that can be attributed to an intervention or program and can include results of program monitoring in addition to other specially collected data. Often evaluation of a program is subdivided into evaluating the processes involved in implementing the program and evaluating the outcome of the program. While this present analysis is at its core an outcome evaluation, it can contribute to the understanding of the collaborative activity rollout process and the process of clinic evaluation.

WHO identified seven key indicators to measure collaborative TB/HIV activities. They are listed in table 2. Six of these are based upon the six activities listed above. The seventh is the proportion of HIV-tested patients who are found to be HIV-positive.
Table 2. Indicators of uptake of activities to reduce the burden of HIV/AIDS in TB patients

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Numerator</th>
<th>Denominator</th>
<th>Periodicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of registered TB patients tested for HIV</td>
<td># of registered TB patients tested for HIV</td>
<td># of total TB patients registered</td>
<td>Quarterly</td>
</tr>
<tr>
<td>Proportion of registered TB patients who are HIV-positive</td>
<td># of registered HIV-positive TB patients</td>
<td># of total TB patients registered</td>
<td>Quarterly</td>
</tr>
<tr>
<td>Proportion of HIV-tested patients who receive post-test counseling</td>
<td># of patient who are tested for HIV and receive post-test counseling</td>
<td># of total TB patients tested for HIV</td>
<td>Quarterly</td>
</tr>
<tr>
<td>Availability of free condoms at TB services</td>
<td># of TB facilities where condoms are distributed</td>
<td># of total TB facilities</td>
<td>Annually</td>
</tr>
<tr>
<td>Proportion of HIV-positive TB patients who receive CPT</td>
<td># of HIV-positive patients who receive at least one dose of CPT during their TB treatment</td>
<td># of total HIV-positive TB patients</td>
<td>Quarterly</td>
</tr>
<tr>
<td>Proportion of HIV-positive TB patients who receive HIV care and support services</td>
<td># of HIV-positive patients who are referred to HIV care and support during their TB treatment</td>
<td># of total HIV-positive TB patients</td>
<td>Quarterly</td>
</tr>
<tr>
<td>Proportion of HIV-positive TB patients who receive ART</td>
<td># of HIV-positive patients who start ART or continue previously initiated ART during their TB treatment</td>
<td># of total HIV-positive TB patients</td>
<td>Quarterly</td>
</tr>
</tbody>
</table>

Since WHO recommended the implementation of collaborative TB/HIV activities, uptake has varied widely by country. In its 2007 report, WHO reports the worldwide uptake of collaborative TB/HIV activities. Reported figures are based on those submitted by national tuberculosis programs and their clinics, and, unfortunately, the reporting practices and rigor may vary widely by country. WHO specifically reports on the activities of 63 high-burden countries: 58 countries with >1 percent of the population HIV-positive plus 5 countries with a high percentage of TB patients with HIV. While rates of testing and reporting of testing have been increasing since 2002 (see Figure 1), globally only 6.7 percent of TB patients are tested for HIV and it is estimated that only 13 percent of patients with TB/HIV co-infections have been identified. Twenty-three percent of tested TB patients worldwide are HIV positive. Among
TB/HIV co-infected patients, it is estimated that between 0.5-18 and 1-55 percent are started on CPT and ART, respectively.

Africa contains 37 of the world’s 63 high burden of TB countries (see Figure 2). Of these 37 countries, only 21 reported the percentage of TB patients who had been tested for HIV in 2005. Uptake of collaborative TB/HIV activities in Africa as reported by countries to WHO is summarized in table 3. Overall in the Africa region in 2005, an estimated 11 percent of TB patients were tested for HIV, and 51 percent of those tested were HIV-positive. Of those who were TB/HIV co-infected, 82 and 29 percent of the HIV-positive patients were reported to have started CPT and ART, respectively.¹

Several authors have reported uptake rates of collaborative TB/HIV activities on a local or regional level to provide an idea of the acceptability and feasibility of such activities in resource poor settings and in settings of high TB/HIV co-infection rates. One of the first reports
For each country or region, the number of incident TB cases arising in people with HIV is shown as a percentage of the global total of such cases. AFR* is all countries in WHO African Region except those shown separately; AMR* excludes Brazil; EUR* excludes the Russian Federation; SEAR* excludes India.

Initial testing rates in local programs in Malawi varied in their success. Zachariah, et al. (2006) report on collaborative TB/HIV activities in a rural district in Malawi between January and December 2000. In two local hospitals, 91% of TB patients accepted referral to the hospitals’ VCT unit. Eighty-seven percent received post-test counseling where 77 percent learned they were HIV-positive. Ninety-four percent started CPT. When broader activities were initiated in Malawi, Chimzizi, et al. (2004) report testing rates of 59 percent in 15 diverse hospitals throughout the country. These rates varied widely by district (range 40 to 96 percent).
Table 3. Collaborative TB/HIV activities in 2005 in Africa as reported by WHO\textsuperscript{1}

<table>
<thead>
<tr>
<th>Country</th>
<th>% of world TB/HIV cases\textsuperscript{b}</th>
<th>Estimated new TB cases\textsuperscript{c} (n)</th>
<th>Total TB cases identified (n)</th>
<th>TB patients tested for HIV (n)</th>
<th>Tested TB patients HIV-positive (n)</th>
<th>Identified TB/HIV co-infected patients started on CPT (n)</th>
<th>Identified TB/HIV co-infected patients started on ART (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>19</td>
<td>284538</td>
<td>302467</td>
<td>67998</td>
<td>35299</td>
<td>35299 100</td>
<td>11654 33</td>
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<td>371642</td>
<td>66848</td>
<td>7013</td>
<td>10 1230 18 0 0 0</td>
<td></td>
<td></td>
</tr>
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<td>Kenya</td>
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<td>219582</td>
<td>108401</td>
<td>15494</td>
<td>14 8899 57 7119 80 1779 20</td>
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<td></td>
</tr>
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<td>Zimbabwe</td>
<td>5</td>
<td>78187</td>
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<td>Zambia</td>
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<td>70026</td>
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\textsuperscript{a}Not equal to total due to rounding.
\textsuperscript{b}From Figure 6, pg. 27. 2007 WHO TB Report.
\textsuperscript{c}From Table A2.1, pg.174. 2007 WHO TB Report.
\textsuperscript{d}From Table A2.2 pg.175. 2007 WHO TB Report.
Of the patients who tested positive 97 percent started CPT (range 64 to 100 percent). Factors that the authors cite as reasons for higher testing rates include well organized and enthusiastic staff, no stockouts of supplies, full time counselors, and dedicated counseling and testing rooms in the facility.  

The feasibility of collaborative TB/HIV activities has also been reported at the national level. Several African countries have made substantial efforts to implement collaborative TB/HIV activities; four of which have been highlighted by WHO tuberculosis reports. In 2002 and 2003, Malawi tested 8 and 15 percent of its TB patients, respectively, and in 2003 provided CPT to 87 percent of the patients who tested positive. As a complement to its rollout of antiretroviral programs, Malawi started nationwide HIV screening of TB patients in 2004. Initially 24 percent of TB patients were tested for HIV, and 72 percent were found to be HIV-positive. By the third quarter of 2005, at least 43 percent of TB/HIV co-infected patients started ART. In 2005, 44 percent of TB patients nationwide were tested for HIV, and nearly half of TB/HIV co-infected patients start ART.

In March 2005, Kenya implemented a nationwide program to rapid test TB patients. By the third quarter of 2005, 32% of TB patients were tested in the country. This doubled to 64% one year later (3rd quarter 2006). Of the 54% of patients found to be co-infected, 80% were given CPT and 30% started ART.  

Rwanda rolled out nationwide program starting in 2004 when 46% of patients were tested. By the third quarter of 2006, 81% were tested. Of the 38% of TB patients who tested HIV positive in 2006, 43% were given CPT and 31% started ART.
Finally, Zambia implemented collaborative TB/HIV activities in 2006 and testing increased from 2 to 52% by the third quarter. Of the 56% of TB patients who were co-infected with HIV, 29% were given CPT and 33% started ART.¹

## III. Methods

*Clinic profiles and integrated TB/HIV activities*

Data were collected from all patients at 14 tuberculosis clinics in Kinshasa, Democratic Republic of Congo. Of these clinics, 1 is public (a hospital) and 13 affiliated with religious institutions or denominations. They were chosen among the 92 TB clinics present in the city of 6.5 million people because they had a significant patient population, enthusiasm for expanding patient care, and the space needed to implement collaborative TB/HIV activities.

All fourteen study clinics treated TB patients. In preparation for collaborative TB/HIV activities, TB clinic staff underwent a four-day training on HIV testing and counseling and opportunistic infections. Clinics initiated collaborative TB/HIV activities between January 18 and February 27, 2006. Monthly meetings were held with program and clinic staff to discuss concerns and hurdles to implementation and care.

*Study design and data collection*

Descriptive analysis of uptake of collaborative TB/HIV activities is reported from analyzing routine clinic data collected by TB clinic staff on modified TB treatment cards included in Appendix A. This information includes routine TB data but also date of pre-test counseling, HIV testing, post-test counseling, initiation of CPT and ART, and referral to HIV support programs. These data, with patient identification removed, were collected from clinic registers and transferred to an electronic database by research staff. For acceptance of HIV
testing, HIV test results and referral for HIV care and support, TB treatment cards included boxes to check for accepting or denying an HIV test, for HIV-positive, negative, or indeterminate status, and for being referred or not. For the remaining uptake indicators, the activity was considered completed if a date was entered on the TB treatment card for each activity.

Study population and clinic procedures

All patients presenting to the study clinics were screened for tuberculosis using sputum microscopy, and physician clinical judgment if smear negative. If found to have TB, clinic staff entered patients into the TB registry and started them on TB treatment according to the national DOTS program guidelines. They were offered HIV counseling and testing by the TB nurse at the time of diagnosis, and if they initially refused, the offer was repeated after one and two months of TB treatment or the patient was tested upon his or her request. All testing was done using Determine HIV-1/HIV-2 (Abbott Laboratories, Tokyo, Japan) and Uni-Gold™ HIV-1/HIV-2 (Trinity Biotech, Wicklow, Ireland), according to WHO strategy II for antibody HIV testing {P1-#9}. HIV-positive TB patients were offered cotrimoxazole, 480 mg twice daily for adults and 6-8 mg/kg for children, unless contraindications were present. Infected patients were referred to a local HIV care and support program if available, offered ART at the clinic if available, or referred to a local HIV clinic. If patients obtained ART, the HIV clinic also managed their CPT.

Outcome measures

This study measured six of the seven WHO indicators for collaborative TB/HIV activities:
1) the acceptance of HIV testing over all TB patients, 2) the percent of tested patients who are
HIV-positive, 3) the percent of tested patients who received post-test counseling, 4) the percent of HIV-positive patients who started cotrimoxazole preventive therapy, 5) the percent of HIV-positive patients referred for HIV care and support, and 6) the percent of HIV-positive patients who started anti-retroviral therapy. Per WHO recommendations, these six indicators are to be recorded continuously, extracted at the end of TB treatment, and reported to the national TB program quarterly with routine TB data. This allows for patients who are tested for HIV any time during their treatment to be measured. Following WHO recommendations, patient data were extracted at the conclusion of TB treatment, with patients divided into quarterly groups based on their registration date. WHO recommends that the seventh indicator, the availability of free condoms at tuberculosis services, be measured annually, and was therefore not included in this analysis.

**Statistical analysis**

Descriptive statistics were performed to assess WHO indicators. Patients were categorized by registration date into three month blocks indicating in which quarter of the program they were registered. WHO indicator performance collectively and for individual clinics was plotted by quarter after program implementation and a line of best fit was drawn using a linear prediction model. One way analysis of variance tested for significant changes in indicators by clinic over time using a two sided alpha of 0.05. Analysis was performed using Stata 9.2 (College Station, TX).
IV. Results

Study population

Between January 2006 and January 2007, the fourteen TB clinics registered 3,521 tuberculosis patients for an average of 252 patients per clinic (range 80 to 450). Over seventy-five percent of patients were adults with visible BCG scars and new cases of pulmonary tuberculosis, of which seventy-three percent were smear positive (Table 4). The average age was 33 years with 84.2 percent of patients being older than eighteen and 2.8 percent under age 2. Slightly more men than women were enrolled: 52.2 and 47.4 percent, respectively.

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Uptake of HIV counseling and testing

Overall 3,173 (97.6 percent) of the 3,521 registered tuberculosis patients were offered an HIV test and 93.3 percent of all registered patients accepted an HIV test (Figure 3). While consistently over 90 percent of patients were tested for HIV, rates trended upwards over time (Figure 4) from 92.8 percent in the first quarter of clinic operation to 96.9 in the final quarter (p=0.29). 98.8 percent of those who accepted testing did so at the initial offer of testing during tuberculosis clinic registration. Of the patients who accepted an HIV test, 95.8 percent returned
for post-test counseling. Unlike testing rates, return for post-test counseling rates decreased over time from 96.6 percent in the first quarter to 92.3 percent in the final quarter (p=0.031).

When viewed by clinic, the percentage of patients who accepted HIV testing and post-test counseling varied substantially and trends in rates of testing and counseling differed between clinics. All clinics tested more than 90 percent of patients except four which tested 65.0, 82.4, 86.1, and 86.2 percent. Eight clinics had initial testing rates over 90 percent and sustained them over the year. One clinic increased its testing rate from 76.9 percent in the first quarter to 95.6 percent by the third (p=0.0024). Two clinics had statistically significant declines in testing rates over time from 100 to 71.4 percent (p=0.018) and from 97.2 to 87.5 percent (p=0.048). Two

Figure 3. Number of patients participating in each TB/HIV collaborative activity

* Values for rates of initiation of CPT and ART and referral for HIV care and support are calculated for the proportion of patients who are HIV-positive
additional clinics had rates that trended downward from 96.7 to 88.0 percent (p=0.072) and from 72.7 to 60.7 percent (p=0.27).

Thirteen clinics had more than 90 percent of patients tested for HIV return for post-test counseling. One of these clinics saw a decline in counseling rate to 41.2 percent by the third quarter (p<0.001). Another’s counseling rate trended downward to 80.0 percent by the third quarter (p=0.22). Both of these clinics still counseled over 90 percent of patients during the study period. The final clinic’s counseling rate trended downward from 84.6 to 73.3 percent between the first and third quarter (p=0.59).
**HIV positive rate**

Overall, 525 TB patients tested positive for HIV (16.7 percent; 95% CI: 15.4-18.0). This rate had a slight, non-significant decrease over time from 17.6 percent in the first quarter to 14.5 percent in the fourth (p=0.31). The range of HIV-positive rates in TB patients tested by clinic was 8.8 to 33.3 percent. Two clinics showed substantial, but not statistically significant, increases in their HIV-positive rates over time. The rate in the clinic with the most HIV-positive patients trended upward over time from 28.0 percent in the first quarter to 40.0 percent in the third quarter (p=0.74) as did the rate of the clinic with the second highest percent of HIV-positive patients from 18.7 percent initially to 50.0 percent in the third quarter (p=0.071). However, in the third quarter this clinic had only 10 patients compared to 90 in each of the previous two quarters. Three clinics saw trends toward decreases of about ten percent in their HIV-positive rates between the first and third quarters from rates around to 20 percent to around 10 percent (p=0.16 to 0.39).

**Care for TB/HIV co-infected patients**

Of the 525 patients co-infected with TB and HIV, 81.5 percent started CPT, 41.2 percent were referred for HIV care and support, and 6.9 percent started or continued ART. Overall, rates of CPT initiation trended downward from 85.6 percent the first quarter to 72.0 percent the fourth quarter (p=0.062). Ten clinics achieved an average CPT initiation rate greater than 80 percent, and the remaining four averaged over 60 percent. Only five clinics maintained rates of over 80 percent over time while one increased from 77.8 percent in the first quarter to 100.0 percent in the third quarter (p=0.43). Two clinics had significant decreases in CPT initiation from 100 to 50 percent (p=0.041) and 88.9 to 42.9 percent (p=0.010). Five clinics showed declining trends from initial rates near or above 80 percent to rates ranging from 42.9 to 68.8 percent by the third
quarter (p=0.13-0.65). The final clinic had consistent average near 70 percent. Of the 92 patients who did not begin CPT, 28 were already taking ART and would thus be prescribed CPT by their HIV clinics, three refused treatment, two had contraindications, and four were followed elsewhere. Data was missing for the remaining 55, 10.5 percent of co-infected patients.

Referral of TB/HIV co-infected patients for HIV care and support occurred in 41.2 percent of patients. This number consistently increased over time from 32.3 percent of patients being referred the first quarter to 68.0 percent being referred the fourth quarter (p=0.001). Four clinics averaged referring over half of their patients, three of which showed increases in referral rate from between 23 to 40 percent (p<0.001, 0.018, and 0.065, respectively). The remaining ten clinics referred patients much more sporadically, with one clinic never making a referral.

Thirty-nine patients (6.9 percent) received ART after TB registration. Of these, 28 (72 percent) had initiated ART before entering TB treatment. Ten patients from one of six clinics received ART as a consequence of HIV testing by TB clinics. Initiation of ART did not change over time (p=0.57), and when viewed by clinic was sporadic with only one clinic having a non-significantly increasing rate over time from 7.1 the first quarter to 42.9 the third quarter (p=0.15). All of this clinic’s patients started ART before enrolling in TB treatment.

Rates of collaborative TB/HIV activity uptake by clinic

Examining individual clinics with regards to rates of uptake of collaborative TB/HIV activities demonstrated variation among clinics. Three clinics performed well, consistently providing HIV testing and post-test counseling to over 90 percent of their patients and starting more than 80 percent of the HIV-positive patients on CPT. Two of these clinics substantially increased their referrals for HIV care and support over time as well from 21.4 to 56.5 and 72.7 to 93.4 percent (p=0.0001 and 0.064, respectively). One clinic had substandard performance. Its
rate of HIV testing, post-test counseling, and CPT initiation all decreased or trended downward from 100 to 71.4 percent (p=0.017), 85.7 to 50 percent (p=0.41), and 100 to 50 percent (p=0.041), respectively, between the first and third quarters. One clinic improved in some indicators but worsened in others. It showed an increase between the first and third quarter in its rate of HIV testing (76.9 to 95.6 percent, p=0.002) and a higher trend in the number of patients who were taking ART (7.1 to 42.9 percent, p=0.14). Even though the rate of HIV positive patients trended down from 20.3 to 10.8 percent (p=0.32), the percent of patients starting CPT also trended downward from 78.6 in the first quarter to 42.? in the third (p=0.26). The remaining clinics showed varied improvements or declines in performance of up to two indicators over time. An example of summary graphs of selected indicators for an individual clinic is shown in Figure 5.

V. Discussion

This study was the first to examine uptake of collaborative TB/HIV activities in the DRC under routine clinic conditions. The results demonstrate that rollout of collaborative activity at TB clinics in Kinshasa, DRC, can be successful. Over ninety percent of newly enrolled TB patients accepted an HIV test and returned for post-test counseling. The HIV positive rate among TB patients was similar to WHO estimates. Over eighty percent of HIV positive patients initiated CPT. Rates for referral for HIV care and support were lower, but increased over time. Only initiation rates of ART remained low throughout the study period.

Such rates are comparable to those in other areas of Africa with higher rates of HIV infection among TB patients (greater than 40 percent). This study demonstrates that high rates of collaborative activities can be achieved in areas with relatively low HIV prevalence in the general population where the perceived importance of testing for HIV may be lower.
**Figure 5.** Example graphs detailing uptake of collaborative TB/HIV activities at one TB clinic, overall and with selected indicators by quarter.
addition, during the study period, these fourteen clinics tested more patients than were tested in the whole of the DRC during the previous year. In 2005, the national TB program reported that 1,885 TB patients were tested for HIV (1.9 percent of TB patients in the DRC). Of them, 386 tested HIV-positive (20 percent), 284 initiated CPT (74 percent) and 3 started ART (1 percent).¹

There are several potential reasons for the high uptake of collaborative activities in these clinics. First, from the patient perspective, counseling and testing for HIV was convenient because it occurred at the start of TB treatment and was done in the TB facility by TB staff. The immediate availability of the HIV test simplified the testing process for the patient by eliminating the cost for transportation to another facility and preventing a second clinic visit to a separate facility with different medical staff.

Second, the clinics chosen to participate in the program were selected based on enthusiasm and infrastructure. Motivated staff likely contributed to the acceptance of new clinic procedures and responsibilities and subsequent testing and treatment of patients. Presence of space for the increased workload of pre- and post-test counseling facilitate program implementation. While this study shows that rollout of collaborative TB/HIV activities in TB clinics is feasible, not all TB clinics nationwide might have the motivated staff or available infrastructure to expand their services to the same degree. As a result, one would expect expanded rollout performance to be less successful in other settings.

Third, the rollout of these programs occurred with international assistance and guidance. As is often the case in low resource settings, material and staff resources are often of limited supply due to limited financial resources. Rollout of collaborative activities was done in a variety of established public and private TB clinics that report to the DRC’s national tuberculosis program. These clinics rely on private agencies or the government for their funding. For the
rollout of collaborative TB/HIV activities, no additional clinic staff were hired but outside funding contributed to the program. International aid provided funding for supervision of activity rollout, training, cotrimoxazole, monitoring and evaluation of the rollout, and support for formation of support groups. In January 2007, just as the last data in this analysis were becoming available, responsibility for the program was shifted to the national tuberculosis program. Unfortunately, in the subsequent months, some clinics experienced stockouts of HIV tests and cotrimoxazole, contributing to observed decreased rates of CPT initiation.

International assistance also contributed to the development of HIV care and support referral services. Upon implementation of collaborative TB/HIV activities, few agencies existed to which patients could be referred for HIV care and support. Often the ones in existence already had a full patient load and were reluctant to take on additional patients. Only one clinic initially referred over half of its patients for HIV care and support. During the implementation of collaborative activities at the TB clinics, HIV support groups were organized by TB clinics, increasing the possibility for referral of patients for care and support. Such local group formation significantly increased referral rates at three of the TB clinics. Unfortunately, the referral activities at the remaining clinics were sporadic and suboptimal and are a point of further attention, study, and improvement.

Finally, political unrest did not impact the uptake of collaborative TB/HIV activities as was feared. The DRC is a country that has had a long history of civil war and political unrest. When this program began in January 2006, the population had just approved a new constitution that allowed for the first presidential elections in 40 years to occur in July during the second quarter of collaborative activities. After the elections there were periods of sporadic violence between rival political parties in Kinshasa. A run-off election in October 2006 declared a winner,
which was also followed by occasional political violence until March 2007. During such times, it is conceivable that collaborative activities may decrease as patients may be nervous about leaving their homes or being in public, supply lines for HIV tests or cotrimoxazole may be interrupted, or clinics may have to close for security reasons. During the time of the study, no clinics closed because of violence. Numbers of people presenting to TB clinics were constant. While rates of CPT initiation did decrease slightly over time, there is no direct evidence that political unrest significantly contributed to this decline.

In this analysis, uptake measures for all clinics were first analyzed collectively. Uptake trends were stable with a slight increase in acceptance of HIV testing and slight decreases in post-test counseling and initiation of CPT. Referral for HIV care and support substantially increased over time. As can be expected, when clinics were looked at individually, differences among clinics became apparent. The fourteen clinics selected for implementation of collaborative activities were a diverse group. Several clinics performed well on all indicators except initiating ART while others performed below average in their HIV testing rates, post-test counseling, and CPT initiation. The referral for HIV care and support between clinics was very variable. Five clinics consistently referred substantially more patients for care and support than the remaining nine clinics. Some clinics’ performance improved over time while others’ performance declined.

The poorer uptake of collaborative TB/HIV activities in two clinics and the high HIV positive rate in an additional clinic stood out. The first of these TB clinics was located in one of the larger referral hospitals in the area. As such, it had the highest HIV-positive rate among any of the clinics. This clinic also happened to have the smallest number of TB patients of any in the study (n=80). Most likely, the low rates of uptake in this study were due to the added
responsibilities of the clinic staff in the referral hospital setting. They likely were not as motivated about implementing collaborative TB/HIV activities to the same degree as many health care clinics that treat patients from a single community. Study staff also found it hard to motivate the nurses at a second clinic to routinely offer and test TB patients for HIV. As a result, that clinic had the lowest rates of HIV testing of all of the clinics. A third clinic had the second highest HIV-positive rate at 23.6 percent which increased from 18.7 percent in the first quarter to 50 percent in the third (p=0.07). The explanation for this increase is unclear, but clinic staff suggested it may be due to the clinic’s proximity to a major rail station and the anonymity that such a setting might provide.

Only one other group has published data examining uptake of activities by clinic.\textsuperscript{33} They reported an evaluation of collaborative activities in one quarter after rollout. The fifteen clinics they evaluated also had heterogeneous clinic characteristics, sized and affiliations. They had lower and variable rates of HIV testing by clinic (59 percent tested, range 40 to 96 percent), but high rates of CPT initiation across clinics (97 percent started CPT, range 64 to 100 percent).

Periodic monitoring provides crucial information to programs. The above findings highlight the importance of monitoring and evaluating programs but also evaluating the performance of individual clinics. Analyzing data on the individual clinic levels allows for tailoring of interventions and education to specific clinic situations. In this study, most clinics had very high rates of HIV testing, counseling, and CPT initiation. A large part of this success was likely due to the motivation of clinic staff. Showing them outcomes of their hard work can help to perpetuate future success in those clinics. All clinics regardless of performance can benefit from such attention and motivation. For example, as seen in the clinic demonstrated in
Figure 3, rates of HIV testing and referral for HIV care and support trended upwards over time, and the clinic staff should be congratulated for their efforts.

Periodic assessment also provides an opportunity to discover clinics that are deficient in their performance and intervene to improve rates of uptake activities. It is a springboard for discussion of ways to improve and can be used as the background or baseline information in quality improvement activities (e.g. Plan, Do, Study, Act cycles). However, rates of CPT initiation trended downward. Knowing this trend, clinic staff can hypothesize the reason for the decline, and quality improvement measures can be taken to reverse the trend in CPT initiation.

As another example, the rates of CPT initiation in the clinic shown in figure three trended downward. Knowing this trend, clinic staff can hypothesize the reason for the decline, and quality improvement measures can be taken to reverse the trend in CPT initiation. Such clinic examination can also provide comparative data to demonstrate what other clinics are achieving and to identify nearby clinics that can be used as models, training sites, or sites with which a clinic could swap staff to promote improvement.

Data obtained by individual clinic monitoring can also be used to target training resources and motivational activities. Clinics that perpetually perform well during routine monitoring and periodic evaluations likely do not need frequent oversight, motivation, and intense contact with the oversight body. Rather, the oversight body’s limited resources can be more effectively spent with poorer performing clinics. Targeted exploration of the reasons behind low performance and collaboration on ways to improve performance in these clinics will benefit a larger number of patients than equal distribution among all clinics irrespective of performance.
Finally, the quarterly timeframe for routine monitoring used in this analysis is also conducive to performance improvement. WHO recommends quarterly reporting of collaborative TB/HIV activities because that coincides with the reporting of outcomes of TB treatment by clinics to national programs. We found quarterly measurements to be an appropriate interval in which to analyze our data by clinic. It allowed significant number of patients to be enrolled in each clinic to provide stable trends in data. Because of low numbers of HIV positive patients in many of the clinics, uptake rates differed substantially in some clinics by month due to small sample sizes. In these instances, more frequent analysis could lead to a misleading picture of clinic performance. Compiling uptake rates over three months provided adequate sample size in most cases to obtain a more realistic picture of collaborative activities. Quarterly monitoring was also frequent enough to address performance concerns and is consistent with reporting of other TB clinic data to national tuberculosis programs. If clinics or programs implement specific programs to improve performance, more frequent monitoring may be justified, but in routine clinic management quarterly assessment provides the needed guidance.

**Strengths and weaknesses**

Several strengths and limitations for this study exist. One of the biggest strengths was that there were few missing data in this study. Only 0.2, 1, and 3.3 percent of data for referral for HIV care and support, HIV status, and accepting HIV testing were missing, respectively. Observed results provide an accurate assessment of these three variables. The rates of three variables, post-test counseling, initiating CPT, and initiating or continuing ART, were recorded as occurring if a date of the activity was listed on the clinic TB treatment card. All those without dates were considered not having received the counseling or commenced the prescription. This
provides a conservative estimate of uptake activity rates as occasionally staff may have neglected to enter the date of a completed activity on a treatment card. A second strength was that this was an effectiveness study, with collaborative activities being integrated as part of routine activities in established TB clinic settings without the hiring of additional staff. Activities were implemented over a wide range of clinical presentations seen routinely in TB clinics.

The true value of this effectiveness study in establishing HIV prevalence rates and measuring uptake activities may be limited by the difficulty of diagnosing TB in resource poor settings. Study clinics used microscopy of sputum samples to diagnose smear positive TB, which has a low sensitivity. Smear negative pulmonary TB cases and extra-pulmonary TB cases are diagnosed on clinical grounds by a physician, which has a low specificity. With such uncertain diagnostic instruments, not all pulmonary TB patients are likely to be identified and subsequently tested for HIV, and a number of extra-pulmonary patients tested for HIV are likely to not have TB. This could provide an underestimate or overestimate of the true TB/HIV co-infection rate.

Two other limitations involve the data collection and analysis. First, despite a narrative field to record the reason for not initiating CPT existing on the TB treatment cards, this field was blank for the majority of patients. If these data were provided it would assist clinics in identifying the hurdles to increasing CPT initiation rates. Second, for this evaluation, data were extracted as individual observations into a central database by study staff. This is a resource intensive process that is too complex for sustainable performance monitoring. Because routine performance monitoring for clinics not in this study will occur using simpler WHO reporting forms, the degree of concordance between the two methods is unknown.
Finally, these clinics were selected for participation in the rollout of collaborative TB/HIV activities based on their location in the capital city, their enthusiasm, and preexisting infrastructure. While most of the studied clinics succeeded in implementing collaborative activities, such success may not be generalizable to all other clinic settings. However, even if other settings may be more difficult, the experience gained by program staff in such settings may be useful in addressing the needs and limitations that other sites present as activities continue to be rolled out in other settings.

Recommendations for TB clinics

This evaluation of uptake of collaborative TB/HIV activities has implications for TB clinics, both those in this study and others in similar and diverse environments, in regards to each of the recommended TB/HIV collaborative activities. First, WHO recommended model for testing and counseling moved away from traditional, voluntary, opt-in, patient-initiated testing to a provider-initiated, opt-out approach. Opt-out testing emphasizes the importance of HIV testing to patients and actively recruits patients for testing while still providing patient autonomy to consider the benefits and risks of testing in their particular situation. In this study, provider-initiated testing appeared well accepted and led to high HIV-testing rates. In theory, the approach also required patients to provide informed consent allowing them to decline testing. In this study, there was one clinic that reported 100 percent testing rates for several consecutive quarters. In other words, out of several hundred patients, none refused testing. While this is possible, it begs the question to what extent patients were provided with knowledge of testing and had informed consent obtained from them. The testing routine at this clinic should be examined to ensure that patients are provided with the autonomy to decline testing. Allowing
patients to opt-out of testing may require slightly more clinic time and resources to properly educate patients but is essential for protection of patient autonomy. This perfect testing rate could also come from clinic staff reporting the completion of activities that did not occur. The importance of truthfully recording figures should be routinely emphasized to all clinic staff in order to obtain the most accurate data possible.

For those patients who do initially decline testing, TB treatment requires repeated encounters with medical services providing numerous opportunities for further education and examination of a patient’s reasons for refusal. In the studied clinics, 98.8 percent of patients who accepted an HIV test did so at the initial offer of testing. Such a high rates suggests that repeated offering of HIV testing may unnecessary and could instead lead to patients being coerced into testing against their will.

Several authors have also discussed using TB clinics as a springboard for further HIV case finding. Current WHO recommendations call for testing only TB positive patients. Two studies have examined testing of all patients who present to TB clinics. In one hospital in Uganda, a country without routine HIV-testing of HIV positive patients and limited access to ART, 39 percent of TB-positive patients were found to be HIV-positive while 49 percent of TB suspects not diagnosed with TB were HIV positive (p= 0.06). Over 35 percent of the HIV-positive patients identified would not have been diagnosed if only TB-positive patients received HIV testing. In a smaller cross-sectional study in Malawi, a country with expanding testing of HIV in TB clinics and increasing availability of ART, 56 percent of patients diagnosed with something other than TB in four TB clinics were found to be HIV-positive. Both of these studies examined rates in areas of high HIV-prevalence and demonstrated that, as might be expected, patients who present with respiratory symptoms may be at higher risk of having HIV
than the general public. In such settings, expanded provider-initiated, opt-out testing of all patients who present to HIV clinics may significantly increase case finding of HIV. However, the benefit of testing all patients presenting to TB clinics in setting with a lower HIV prevalence is less clear.

A second way to increase HIV case finding is by testing close contacts and family members of TB/HIV co-infected patients. In a small, retrospective, cohort study done in the US, 16 of 30 close contacts of TB/HIV co-infected patients (e.g. family members, houseguests, or friends) who had been tested for HIV were found to be HIV-positive.\(^{43}\) In a cross-sectional study of TB/HIV infected patients in Thailand, 13.8 percent of contacts and 48.6 percent of spouses of TB/HIV co-infected patients were HIV-positive.\(^{44}\) In these studies, contacts of HIV negative patients were also found to be positive but at much lower rates. These studies suggest that offering counseling and testing to close contacts of TB/HIV co-infected patients could identify substantial numbers of HIV-positive patients. Testing such contacts may prove even more useful in higher prevalence settings like the DRC or other countries in Africa. Even if TB clinics lack the resources to test all patients presenting to TB clinics or the contacts of TB/HIV co-infected patients, they could refer such populations to local VCT programs.

Third, clinics should strive to identify HIV care and support resources in the community. Especially in areas with high rates of TB/HIV co-infection, testing TB patients will increase the number of patient needing HIV support services. The most efficient way to provide services is through collaborative efforts with already established local resources. If such resources do not exist within a community, TB clinics should explore promoting or developing such support services, with the help of VCT centers or other groups involved with HIV/AIDS care. In the setting such as the one in this study, clinics with higher percentages of patient referred for HIV
care and support could provide assistance in identifying barriers to referral and guidance for the
formation of support groups and activities. By taking advantage of, strengthening, or building
community support for co-infected patients, TB clinics help reduce the burden of suffering
caused by TB/HIV and facilitate effective treatment.

Anti-retroviral therapy has been shown to significantly reduce mortality among people
living with HIV/AIDS. While randomized trials of the effect of ART on the mortality of TB
patients would be considered unethical, cohort studies demonstrated high rates of TB patients
achieving undetectable viral loads and very few to no deaths while on therapy. According to
the DRC’s 2005 UNAIDS progress report, just over 9,000 of the estimated 338,700
eligible HIV-positive patients in the DRC have access to ART. A total of 73 prescribing sites
exist in 53 of the country’s 515 health districts. The few patients that received treatment
during this study were fortunate enough to be treated by one of these few clinics, and most of
those on ART were diagnosed with HIV and taking ART prior to TB clinic enrollment. For
effective uptake of ART to occur, the number of HIV prescribing clinics must be dramatically
increased and the availability of anti-retroviral medications must be consistent. Malawi has
devised such a system that is thus far operating well. Ideally, such clinics would be found in or
alongside each TB clinic in urban and rural areas to maximize availability and minimize the
burden placed on patients who need to regularly obtain services from both TB and HIV
services.

TB reporting materials should be tailored to collecting information on collaborative
TB/HIV activities. In these study clinics, patient TB cards and clinic registers were altered to
allow for centralized data gathering. Other groups have proposed similar alterations. In
September 2006, WHO also published revised TB reporting forms and registers that guide clinics
in implementing collaborative activities. One addition that does not appear on the new WHO treatment cards is a narrative field identifying the reason for not implementing CPT. While contraindications to CPT are not common events, they occur frequent enough that a significant portion of the 18.5 percent of patients who did not initiate CPT in this study may have been ineligible. Such information can help to address barriers to treatment and motivate clinic staff. With such revisions, reporting of such figures can be done by clinic staff and become normal parts of TB clinic duties.

Finally, questions remain about the optimal way to rollout collaborative TB/HIV activities logistically and to ensure sustainability. Two clinical questions concerning ART have been debated in the literature: the best treatment regimen and the correct time in relation to TB treatment for its implementation. Other operational issues also exist, especially when considering implementation of ART. While TB clinic staff were successfully trained in this study to provide HIV testing, post-test counseling, and CPT initiation, initiating ART requires determination of CD4 counts and management of an additional set of complex drug regimens. If resources are available, integrating ART into TB clinics would be the most convenient for the patient as distance and cost of travel have been shown to significantly affect initiation of ART among TB patients. However, few clinics are likely to have the resources for such programs and referral to HIV specific programs will likely be necessary. Currently, patients are recommended to continue CPT and ART indefinitely beyond the completion of TB treatment, and TB clinics are unlikely to be able to support such patients indefinitely. This again requires referral to additional facilities. The best way to effectively organize responsibilities and optimize patient flow between facilities will need to be addressed in every location where collaborative activities are implemented. Organizations must be adapted to local institutions, traditions, and
resources, with an emphasis on reducing the effort required for patient to obtain treatment, and in all settings, medical staff must work to minimize risk of nosocomial transmission, especially of TB to susceptible HIV-positive patients.

When considering expanding collaborative TB/HIV activities, program sustainability must be addressed from inception. While the demand for such activities is high, implementing programs without planning for their long-term success has high potential for wasting resources. To the highest degree possible, the expertise of local leaders and professionals should be utilized and collaboration with existing programs should be explored and secured. Local people should be hired and trained as program staff. By obtaining local buy in and, if possible, local financing, programs are less likely to require outside support to be sustainable.

Conclusion

Most collaborative TB/HIV activities were successfully implemented in 14 TB clinics in Kinshasa, DRC. HIV testing, post-test counseling, and CPT initiation were acceptable in this setting with moderate rates of TB/HIV co-infection, while referral for HIV care and support and ART initiation were more sporadic. Examining the uptake quarterly rates by individual clinics highlighted clinics with substandard performance in a timely way while maintaining adequate sample sizes. In general, uptake was aided by including HIV testing and CPT initiation within TB clinics where staff was motivated to expand clinic scope. Being a resource poor setting, availability of referral site for HIV care and support and ART were not readily available. Routine monitoring and evaluation can help to clarify the strengths and limitation of TB care on the clinic and system level in order to guide program implementation to address the large burden of suffering caused by TB/HIV co-infection.
REFERENCES


