Implementation Issues in Tuberculosis/HIV Program Collaboration and Integration: 3 Case Studies

Gerald Friedland, Anthony Harries, and David Coetzee

The many interactions between tuberculosis (TB) and human immunodeficiency virus (HIV) infection influence the design and implementation of programs to address the needs of patients living with or at risk for both diseases. Collaboration between national TB and HIV programs and some degree of integration of services at a local level have been advocated by the World Health Organization and other international bodies and are recognized as essential in areas where the 2 diseases are prevalent. However, in most settings, strategies to accomplish this are only beginning to reach the field where their impact will be made and the expectation of improving the outcome of both diseases realized. In this article, 3 such strategies, offering varying degrees of collaboration and integration, are described, 1 at a national level in Malawi and 2 at local sites in South Africa. These geographically and programmatically distinct experiences in TB/HIV service integration are instructive, illustrate common themes, and show that the strategy can be successful, but they also show that programmatic, medical, staffing, resource, and scale-up challenges remain. In addition, they indicate that, although broad program principles of TB/HIV service integration are essential, program designs and components may vary by country and even within countries, as a result of differing TB and HIV disease prevalences, resources, levels of expertise, and differences in program settings (urban vs. rural and/or primary vs. district vs. specialty site). Large national programs can successfully provide rapid, uniform and widespread change and implementation but also must negotiate the subtleties of intricacies of TB/HIV interactions, which confound a uniform “one size fits all” public health approach. Conversely, smaller demonstration projects, even with successful outcomes, must grapple with issues related to generalization of findings, wider implementation, and scale up, to benefit larger populations of those in need.

Large and rapidly growing numbers of patients with TB and HIV coinfection require coordinated diagnosis, care, and treatment. In most settings, however, these services remain separate and often fragmented and are likely to lead to suboptimal outcomes. Collaboration between TB and HIV programs and integration of TB and HIV care and treatment is a proposed strategy to improve the diagnosis, treatment, and outcome for patients with both diseases [1, 2], but few studies have been performed to demonstrate its effectiveness. Most policy and practice recommendations for the management of TB and HIV coinfection are derived by consensus and are not fully evidence based [3–5]. Further, these have not yet been operationalized widely in the field. Challenges in implementing and defining the benefits of such a strategy are listed in Appendix A.

In this article, to illustrate both the successes and the challenges of the strategy of TB/HIV program collaboration and integration, 3 examples of model approaches to TB and HIV coinfection are described: 1 at a national level in Malawi and 2 at local urban and rural district levels in South Africa. In Malawi, recognition of the issue of coinfection has resulted in in-
increased communication and policy collaboration and rapid development and deployment of a national antiretroviral therapy (ART) program along the lines of existing TB programs but with the TB and HIV national and local programs remaining separate and distinct. In Khayelitsha, South Africa, at Ubuntu Clinic, a progressive process of integrating TB and HIV services has taken place. In Durban (eThekwini), in a large urban municipal TB clinic and in a district hospital in a remote rural area in KwaZulu Natal, partial integration of services was accomplished using the existing TB treatment infrastructure. In the South African programs, distinct from that in Malawi, scale up of these integrated models to provincial and national levels remains to be established. Although they are different in location and scope, each of these programs has grappled with similar sets of problems regarding the integration of services in areas of high TB and HIV infection prevalence, and each has developed instructive solutions.

These case studies also illustrate the need for operational research to address the challenges posed by the intersection of TB and HIV infection. Using observational and outcome studies, modeling, and cost-effectiveness methodologies, this research can help to make expeditious solutions to complex problems of program and policy implementation, often when complete information is not fully available, as is the case with TB and HIV coinfection.

MALAWI

Malawi is a small, impoverished country in southern Africa with a population of almost 12 million. It faces severe HIV/AIDS and TB epidemics. It is estimated that there are 900,000 adults and children living with HIV/AIDS, and as many as 170,000 people are in need of ART [6]. Between 1985 and 2000, TB case notifications, fuelled by HIV infection, increased by a factor of 500%, to ∼27,000 registered TB cases each year, with an HIV seroprevalence of 77% among patients with newly diagnosed TB [7].

Malawi has an established national TB control program (NTP) and, for 20 years, has been a model implementer of the directly observed treatment, short course (DOTS) strategy promoted by the World Health Organization (WHO) [8]. Despite this, case notifications and case-fatality rates have risen, prompting the Ministry of Health and the NTP to develop a 3-year (2003–2006) TB/HIV plan. Some of the key objectives of the plan are to (1) improve collaboration between HIV/AIDS and TB programs, (2) expand HIV voluntary counseling and testing (VCT) services for patients with TB and the general public, (3) provide cotrimoxazole preventive therapy to HIV-infected patients with TB, and (4) provide ART to patients with AIDS, including those with HIV-associated TB.

Collaboration between TB and HIV Programs

The Ministry of Health is responsible for national policies, strategies, and implementation of TB and AIDS control. The NTP is a directorate of its own, with central and regional tiers of management and district or hospital TB officers being responsible for administering and implementing TB control at the peripheral level (usually health assistant grade, with 3 years of public health training and a 2-week TB orientation). Case finding, diagnosis, and follow-up of patients are performed within the general health services. The HIV Unit is under the directorate of the Department of Clinical Services and has responsibility for counseling, HIV testing, management of HIV-related disease, and ART. The NTP and the HIV Unit work closely on TB/HIV issues but remain separate. For example, both programs worked together to formulate national guidelines and national policy for cotrimoxazole preventive therapy, management and national scale up of ART, and coadministration of anti-TB drugs with first-line ART. For central and regional TB officers, the HIV Unit provided and paid for formal training in the administration of ART. Regional TB officers assisted in monitoring ART scale up in the early months of the program.

In this strategy, the newly developed HIV Program applied principles from TB control to HIV treatment and care (see Appendix B) and has not yet attempted integration of TB and HIV care. Integration at a national level was perceived to be a threat to the successful—although strained—NTP, because of health care worker shortages and the need to rapidly initiate ART in a significant number of patients.

Registration and Treatment of Patients with TB

Malawi has 44 hospitals that are TB registration and treatment centers employing standardized TB treatment in accordance with national guidelines (table 1) [9]. Patients remain in the hospital for the first 2 weeks of directly observed treatment (DOT) and are educated about the importance of good drug adherence, after which time they can go home to receive the remainder of initial-phase treatment from health center staff [10] or guardians at home. Continuation-phase treatment is with isoniazid and ethambutol and is collected every month from health centers or from the hospital. TB officers, medical assistants, or community nurses supervise the process of drug administration, recording, and monitoring.

HIV Testing and Cotrimoxazole Therapy for Patients with TB

Malawi performed operational research confirming the safety and effectiveness of HIV testing and cotrimoxazole therapy in reducing mortality among patients with TB [11–14]. The Ministry of Health then authorized phased countrywide implementation of HIV testing and cotrimoxazole therapy for all
Table 1. Comparison of 3 tuberculosis (TB)/HIV programs.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Malawi National Program</th>
<th>Durban (eThekwini) and Tugela Ferry, KwaZulu Natal Province</th>
<th>South Africa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Program scope</td>
<td>National</td>
<td>Municipal TB and rural district hospital clinics</td>
<td>Urban township TB and HIV clinic</td>
</tr>
<tr>
<td>Funding source</td>
<td>Ministry of Health; national TB and HIV programs</td>
<td>Municipal and provincial departments of health; foundation grants</td>
<td>Provinicial department of health; NGO (MSF)</td>
</tr>
<tr>
<td>Size of population with TB/HIV coinfection</td>
<td>Estimated to be 20,000</td>
<td>150 in demonstration project</td>
<td>2000–3000</td>
</tr>
<tr>
<td>TB and HIV care sites</td>
<td>Separate location for TB and newly established HIV clinics</td>
<td>Colocation in municipal TB clinic; partial colocation in rural district hospital</td>
<td>Colocation</td>
</tr>
<tr>
<td>HIV VCT</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>HIV care/treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>In TB program</td>
<td>On site</td>
<td>Integrated on site</td>
</tr>
<tr>
<td>ART</td>
<td>Refer to HIV program</td>
<td>On site</td>
<td>Integrated on site</td>
</tr>
<tr>
<td>ART regimen</td>
<td>d4T + 3TC + NVP twice daily</td>
<td>ddI + 3TC + EFV once daily</td>
<td>d4T + 3TC + NVP/EFV twice daily</td>
</tr>
<tr>
<td>TB treatment regimen</td>
<td>HRZE for 2 months; HE for 6 months (total, 8 months)</td>
<td>HRZE for 2 months; HR for 4 months (total, 6 months)</td>
<td>HRZE for 2 months; HR for 4 months (total, 6 months)</td>
</tr>
<tr>
<td>TB DOTS</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>HIV adherence support</td>
<td>Yes</td>
<td>ART DOT in municipal clinic; ART DOT plus adherence support (home-based family and community) at rural site</td>
<td>Adherence program</td>
</tr>
<tr>
<td>Outcome measures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB	extsuperscript{a}</td>
<td>Standard outcomes</td>
<td>Standard outcomes</td>
<td>Standard outcomes</td>
</tr>
<tr>
<td>HIV infection</td>
<td>Clinical outcomes	extsuperscript{b}</td>
<td>Clinical outcomes;	extsuperscript{b} CD4 cell count, VL (baseline and every 3 months)</td>
<td>Clinical outcomes;	extsuperscript{b} CD4 cell count, VL (baseline and at 1 year)</td>
</tr>
<tr>
<td>Integrated records</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Integrated staff</td>
<td>No</td>
<td>Partial</td>
<td>Yes</td>
</tr>
<tr>
<td>Operations evaluation and research</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**NOTE.** 3TC, lamivudine; ART, antiretroviral therapy; d4T, stavudine; DOT, directly observed therapy; DOTS, directly observed therapy, short course; EFV, efavirenz; HE, isoniazid + ethambutol; HR, isoniazid + rifampin; HRZE, isoniazid + rifampin + pyrazinamide + ethambutol; MSF, Médecins Sans Frontières; NGO, nongovernmental organization; NVP, nevirapine; VCT, voluntary counseling and testing; VL, viral load.

	extsuperscript{a} Completion of therapy, cure, default, or death.

	extsuperscript{b} Completion of therapy or death.
patients with TB. National guidelines for this intervention were developed. An opt-out policy of HIV testing was adopted for patients with TB with referral to separate units for HIV counseling and testing. HIV-positive patients are provided with cotrimoxazole by the NTP employees who have been trained to deliver the intervention. A special register is kept by the district TB officer. The percentage of all registered patients with TB in Malawi who were tested for HIV infection increased from 8% in 2002 to 26% in 2004, with >95% of those testing positive having cotrimoxazole therapy initiated [15]. Recent national data for 2005 showed that 47% of 26,019 registered patients with TB were tested for HIV infection, 69% of those tested were HIV positive, and 92% of those patients received cotrimoxazole (Ministry of Health, Malawi, unpublished data). The use of cotrimoxazole for other HIV-infected patients received formal approval in early 2005 [16, 17]. The challenge now is to get the policy implemented, particularly because the TB and HIV programs have remained separate.

Implementing the National ART Scale-Up Plan

Preparatory work. After approval of the scale-up plan in February 2004, facilities were briefed, monitoring tools were finalized, and a national training module was developed. Training of personnel in the public and private sectors was conducted, including training of all central, regional, and district TB officers. The HIV unit performed assessments and accreditation of facilities for readiness to deliver ART and, by March 2005, all 60 sites were ready to deliver ART.

Drug procurement. As was learned from the TB program, an uninterrupted supply of drugs is crucial. Plans were developed to reduce the risk of stock-outs or drug expiration by a “push” system of drug procurement, by classifying facilities into low-, medium-, and high-burden units [23].

Initiating ART in new patients. Because clinical officers run >90% of the 60 ART clinics in the public health sector, a standardized approach, which works so well for the NTP, was adopted for ART. HIV-infected patients are assessed as eligible by ART clinic staff and participate in a group adherence counseling session, preferably with a family guardian [24], and all patients start treatment with Triomune.

Registering and monitoring case numbers and treatment outcome. Part of the success of NTPs is due to the excellent standardized systems of registration, recording, and reporting [25]. A similar system was developed for national ART scale up [20, 23]. Patient master cards, registers, standardized primary and secondary treatment outcomes, and quarterly cohort analyses are uniformly employed. The HIV Unit conducts quarterly supervisory visits to all ART sites, provides clinical support and performance feedback, and collates and reports all data.

Progress with the scaling up of ART. By July 2005, all 60 facilities in the public sector were delivering ART to their communities, and, by the end of September 2005, a total of 30,055 patients had ever had treatment started, only 5439 (18%) of whom had treatment started because of a diagnosis of active or past TB.

Integrating ART and TB Treatment Services

The initial registration and treatment of patients with TB is performed in TB offices, and HIV testing is performed at the separate HIV VCT units based in the hospital. HIV-infected patients with TB are then sent to the ART clinic for staging and will be assessed in either WHO clinical stage 3 or stage 4. As a result of concerns about drug-drug interactions between rifampicin and nevirapine and the possible development of the immune reconstitution syndrome, ART is deferred for 2 months, until the continuation phase of TB treatment. At this point, the patient starts receiving isoniazid and ethambutol, which avoids the drug interaction issue but prolongs TB treat-
ment. This creates an immediate problem, because many patients with TB are back in the community, feeling better and receiving anti-TB drugs from the nearest health center. The need to come to the hospital ART clinic for treatment initiation and monthly ART is a barrier to access [12]. This may explain the fact, as noted above, that only 18% of those who ever have ART initiated are patients with active or previous TB.

Because TB and HIV care are presently organized as separate systems, HIV-infected patients with TB who attend the hospital for TB treatment and ART currently have to attend the TB office to receive their anti-TB drugs and the ART clinic to receive ART. These visits are synchronized to occur on the same day, but the patient has to join 2 queues, which prolongs the hospital visit. Discussions are going on about whether anti-TB drugs and ART can be administered from the same clinic. However, TB officers are health assistants, with no or little clinical training, and the management of adverse effects will require the presence of a clinician. Moreover, a separate ART recording and monitoring system will have to be placed in the TB clinic, and mechanisms will be required for referral to the ART clinic once TB treatment is completed. If TB treatment is to be administered from the ART clinic, ART clinicians and nurses may be too busy to be able to take on the extra burden.

It is currently felt that the only way to improve access to ART for HIV-infected patients with TB in the community is to devolve initiation and follow-up of ART to health centers. This is part of Malawi’s 5-year ART scale-up plan (2006–2010), but it will not be easy to implement. Decentralization on a national level will require working out operational issues such as training and supervision of medical assistants who staff the health centers, ART drug procurement and security, and clinical supervision.

The 5-Year Plan: 2006–2010

The Ministry of Health 5-year plan aims to initiate ART in 45,000 new patients every year and, by 2010, to reach a target of 245,000 patients with ART ever initiated. The lack of human resources, poor infrastructure of many facilities, and provision of regular supervision and effectiveness of the first-line regimen (particularly with reference to TB drug interactions) make this a formidable task. The NTP has plans to use rifampicin and isoniazid in the continuation phase of TB treatment. The issues of whether to use rifampicin and nevirapine together (or to introduce efavirenz), to integrate treatment delivery from a single office instead of 2 offices, and reaching rural poor populations will be challenging to TB/HIV service integration and will require well-planned and -executed operational research, as well as attention to the practical details of integration if solutions and progress are to be made.

SOUTH AFRICA

South Africa has the highest burden of both HIV disease and TB in the world. It is estimated that >5 million persons are living with HIV disease, of a total population of ~43 million [26]. South Africa is ranked ninth among the 22 countries with the highest TB burden, accounting for 80% of all cases worldwide [27]. TB has been endemic for many decades, and transmission has been enhanced by poverty, overcrowding, poor living conditions, migration, and, more recently, HIV infection [28]. In 2004, the TB notification rate in South Africa was 551/100,000 population. Within South Africa, the Western Cape Province has the highest TB notification rate (988/100,000 population), and the province of KwaZulu Natal, with a notification rate of 723/100,000 population, has the largest number of newly diagnosed cases. HIV seroprevalence among patients with newly diagnosed TB varies from 60% to >80%.

Since 1994, there has been a strong vertical NTP in South Africa at the national and provincial levels. In most cities and urban areas, there are vertical TB services, whereas in rural areas they are integrated with other primary health care services. In 2001, a comprehensive strategic TB plan was drawn up. Despite strong investment, including support and training, and the implementation of DOT, by 2003 the cure rate for smear-positive cases had not exceeded 65% in most parts of South Africa [26].

In November 2003, the National Department of Health released the Operation Plan for Comprehensive HIV and AIDS Care, Management and Treatment [29], which explicitly includes the use of ART. By March 2006, public sector health services had initiated ART in ~140,000 patients, 20% of the estimated >800,000 in need of ART [30]. Of these, at least 20% also have TB infection.

Khayelitsha

The Khayelitsha subdistrict of the Western Cape Province is representative of many poor urban areas in South Africa, with a large proportion of the population having migrated from rural areas in the past 20 years. The population is estimated to be 450,000–500,000, with the majority living in “informal” dwellings. In 2005, Khayelitsha had a rate of newly reported TB cases of 1283/100,000 population, and 76% of patients with TB are coinfected with HIV.

Health services. As with many health services in urban areas in South Africa, there is no comprehensive primary health care service. TB, sexually transmitted infection, family planning, VCT, and pediatric services are provided by the local authority, whereas all other services are provided by the Provincial Department of Health. Discussions have been ongoing for a number of years, regarding the integration of services under one
management structure, but this has not occurred. There are 8 TB services and 3 separate HIV services providing ART in Khayelitsha.

In February 2000, Doctors Without Borders and the Provincial Government of the Western Cape initiated a comprehensive service for persons infected with HIV within the 3 primary health care centers in Khayelitsha. In May 2001, these sites became the first public sector services to provide ART in South Africa. By July 2006, ~3800 persons had had ART initiated. TB and HIV services functioned independently, apart from some less-than-optimal referral of patients between services. At both the TB and the HIV services, the patient load was high. Because of the large number of coinfected patients, it was soon learned that a comprehensive TB/HIV service was required. There were many reasons underlying the implementation of greater collaboration between and/or integration of TB and HIV services (see Appendix C).

In 2002, consultations were held with the staff at the TB and HIV services to explore whether it was feasible to integrate the 2 services, and the scope, process, and performance of the TB and HIV services were assessed and the benefits and hindrances of integration evaluated [31]. The stepwise integration of TB/HIV services commenced in 2003 as a pilot project, at Ubuntu Clinic, one of the 3 primary health care centers [32].

The following steps were taken to integrate services:
- Consultations were held with the staff at both services to explain the benefits of integration. Initially, the staffs were very reluctant to integrate, because they felt it would lead to greater workloads in services that were already overloaded.
- VCT was reinforced in the TB service.
- All patients with TB and HIV coinfected were provided with cotrimoxazole prophylaxis.
- CD4 cell counts in coinfected patients were determined.
- Access to ART was increased for patients with CD4 cell counts <200 cells/mm³, via improved referral mechanisms.
- Standardized guidelines were developed, and staff training was provided.
- The contiguous TB and HIV clinic buildings were merged, and integration of TB/HIV services was accelerated. Coinfected patients continued to attend both services, but the records from both services were drawn when a patient attended a consultation at either of the services.
- The TB and HIV records were integrated.
- All patients were seen at the same service by the same clinicians.
- Adherence procedures for patients receiving ART were adapted and introduced for patients receiving TB treatment.
- Monitoring systems were coordinated.

**Results of integration strategy.** Lessons have been learned from both TB and HIV services that have enhanced management of coinfected patients in an integrated strategy. The majority of patients accessing HIV care are now tested for HIV at TB services. In Khayelitsha, initially, <30% of patients with TB were tested for HIV infection, but this has increased to 56% of patients at the Ubuntu Clinic, with 87% of those offered accepting testing, in contrast to 8% and 40%, respectively, in Gugulethu, a similar township without integration. Integrated services have provided easier and quicker access to HIV care and easier access to ART, with a substantial increase in enrollment [32]. Referral delays and loss to follow-up of coinfected patients have been reduced, and earlier treatment initiation has become more common. In addition, patients who begin receiving TB treatment can be more easily prepared for ART and subsequently have ART initiated. The standardized regimen offered to coinfected patients at the integrated clinic is stavudine, lamivudine, and efavirenz. The institution of cotrimoxazole therapy in coinfected patients has been increased; however, isoniazid prophylactic therapy, although shown to be effective in decreasing active TB disease among HIV-infected persons, has not been successfully utilized. To improve TB diagnosis in the context of HIV disease [33], diagnostic algorithms have been established that broaden the diagnostic armamentarium beyond the positive results of sputum smear examination, and staff members in the TB program feel more confident about diagnosing extrapulmonary TB. In addition, sputum culture has been made available for the diagnosis of TB, and a smear-negative algorithm has been put into place to allow for the early initiation of empirical TB treatment in HIV-infected patients while waiting for the culture result. With integration, monitoring while receiving treatment for both diseases is enhanced, with better clinician awareness of treatment interactions, adverse effects, and immune reconstitution inflammatory syndrome.

For the patient there is less traveling and waiting time. TB and HIV consultations are now scheduled to occur at the same time. TB registers, appointment systems, and patient-held cards have been adapted to meet the needs of HIV care and ART delivery. This coscheduling of visits is beneficial to staff and patients alike but has been very hard to monitor in a very busy clinic and remains to be demonstrated to improve outcomes. TB registers and quarterly reports have been adapted for the ART program. The experience from the successful promotion of adherence to ART is being adapted for TB adherence and support. TB support groups are being made mandatory at treatment initiation, and educational materials are being provided to patients starting TB treatment. The importance of a good patient-provider relationship emphasizing understanding and responsibility, which has characterized HIV therapy, should not
be underestimated and is incorporated into TB care in the integrated model.

There have been benefits for staff and clinicians as well. Cross-training of TB and HIV staff has been accomplished, and both are now able to rotate between services. The increased diversity of roles, pooling of staff, and broadening of training have also increased competence in the management of coinfected patients, led to an increase in staff morale and retention, renewed doctors’ interest in TB, and provided a structure for those who wish to pursue a career in TB/HIV medicine. This expanded role of staff training to enable the management of both diseases is one way of decreasing the drain on TB program staff resources.

KwaZulu Natal

The province of KwaZulu Natal is the most populous of the 9 provinces in South Africa and is also most severely affected by the HIV infection pandemic. More than 2.5 million people are believed to be living with HIV disease, and the HIV seroprevalence among patients with newly diagnosed TB ranges from 65% to 85%. To address the issue of integration of TB and HIV services, a series of demonstration projects have been designed, implemented, and completed or are in progress in both urban and rural areas [24, 34, 35]. In these demonstration and operational research projects, the already existing TB infrastructure is used as the site of introduction and monitoring of HIV care and treatment.

Prince Cyril Zulu Communicable Diseases Clinic. The Prince Cyril Zulu Communicable Diseases Clinic is a public municipal TB clinic in Durban (eThekwini). The clinic manages >11,000 new cases of TB annually. DOT is provided on site or through referral to community care settings once the diagnosis of TB is established. Although HIV VCT is available, uptake has been slow and inconsistent, and HIV care and treatment have not been available. In a pilot project of TB/HIV service integration, HIV VCT was offered to sequential patients with newly diagnosed smear-positive pulmonary TB [34]. Standard procedures and definitions used by the clinic and recommended by the South Africa NTP [36] were employed. With the collaboration of the TB program and staff, the components included the following:

- strengthening the TB program with additional staff training
- training TB clinic staff in HIV care and ART
- standard TB treatment as per the clinic protocol, consisting of an intensive phase of 4 drugs in single combination tablets administered under direct observation from Monday to Friday for 2 months, followed by rifampin and isoniazid in single combination tablets for the remaining treatment period (usually 4 months)
- an ART regimen consisting of once-daily didanosine, lamivudine, and efavirenz (600 mg)
- ingestion of both TB and HIV medications at the same time in the morning, under direct observation by the clinic staff nurses
- clinical and laboratory assessments of both HIV infection and TB outcomes and drug toxicity
- provision of social support by ongoing counseling, informal patient support groups, and payment, as needed, of transportation costs
- transfer to the Infectious Disease Clinic at the Nelson R. Mandela School of Medicine, Durban, for continued ART after completion of TB treatment

At the end of concomitant TB and HIV therapy, 80% of patients had nondetectable viral loads and a mean CD4 cell count increase of 148 cells/mm³, and 19 (95%) of 20 patients had been cured of TB. Follow-up of the pilot project beyond the 6 months of the project has demonstrated the durability of the TB and HIV benefits for close to 2 years [37]. The most common medication adverse effects reported were dizziness and poor concentration, attributed to efavirenz, but they did not require drug discontinuation. High levels of self-reported medication adherence were documented, and 237 (88%) of 269 patients’ scheduled clinic visits were kept. A more definitive National Institutes of Health study has now commenced as a large randomized trial of immediate integrated TB and HIV treatment versus sequential TB and HIV treatment performed at separate TB and HIV treatment sites [2].

Tugela Ferry, Church of Scotland Hospital, and Philanjalo.

Sixty percent of South Africa’s population lives in rural areas, where high levels of both TB and HIV infection are present and resources and health care are quite limited. The Church of Scotland Hospital is a 300-bed government district hospital serving ~300,000 traditional Zulu people in a remote, resource-limited setting. The HIV infection rate is 83% among patients with newly diagnosed TB. TB care is supported by the province and follows South African TB/DOTS program guidelines [36]. The treatment completion rate was 59% in 2002.

In 2001, an HIV clinic was established, providing infection prophylaxis and clinic- and home-based palliative care with the participation of Philanjalo, a local nongovernmental organization. Within this context, an operational study to evaluate TB and HIV treatment integration was established. On the basis of a strategy similar to that of the Durban TB clinic, the TB program was strengthened, and training of physicians, nurses, and community health workers was accomplished. A secure supply of ART and laboratory backup was put in place. To facilitate integration, patients receive a once-daily ART regimen...
of didanosine, lamivudine, and efavirenz, along with standard TB treatment. Additional special features include family and community home-based TB and ART support and care. Patients disclose their HIV infection diagnosis to at least 1 person in the household, who serves as a treatment supporter and who undergoes treatment literacy training with the patient before institution of ART. Under supervision, patients construct and package a month’s supply of their own regimens in individual daily packets, together with others in supportive groups, in a communal setting typical of Zulu culture. Patients ingest both TB and HIV medications concomitantly once daily at home with family support and are visited by community treatment supporters and seen monthly at the hospital. On completion of TB treatment, patients are transitioned to continue their ART regimen by self-administration with continued family adherence support.

Successful treatment outcomes for both TB and HIV infection have been documented in this project. At 12 months after treatment initiation, 89% of patients had undetectable viral loads, and 83% successfully completed TB treatment. There were few grade 3 or 4 adverse events, and adherence to study visits and medication were both >90% [38]. However, unexpectedly and ominously, the majority of deaths in the program have been the result of suspected or confirmed multidrug-resistant TB, and subsequent prevalence surveys have confirmed the high prevalence of TB caused by an extensively drug-resistant strain of Mycobacterium tuberculosis among HIV-co-infected patients, associated with recent nosocomial and community transmission and high fatality [39]. Rather than nullifying the value of further collaboration and integration between TB and HIV programs, this finding emphasizes the need to address long-neglected issues of infection control and the urgency in implementing strategies aimed at reducing the risk of TB transmission to patients with HIV infection [40, 41].

The Future

The effectiveness of integration in improving outcomes is strongly suggested by these small-scale demonstration and operational projects but remains to be fully defined and confirmed. If scaled up, the rational and successful TB/HIV integrated systems of care developed at Khayelitsha and in KwaZulu Natal could assist the overall large-scale rollout of ART and the improvement of TB services in South Africa and could result in improved TB and HIV infection outcomes. However, there may be understandable resistance from policy makers in embracing these models on a provincial or national scale without further evidence of their effectiveness and in light of increased concern regarding potential nosocomial transmission of TB in integrated programs. Operational research demonstrating improved cost-effective patient and population outcomes in comparison with conventional parallel systems of care and treatment is required.

CONCLUSION

These geographically and programmatically distinct experiences in TB/HIV program collaboration and integration indicate that the strategy can be successful, but programmatic, medical, staffing, resource, and scale-up challenges remain. Large national programs must address the subtleties of TB/HIV interactions and the programmatic complexities that confound a uniform, “one size fits all” public health approach, and small demonstration projects with successful outcomes must face the challenge of wider implementation and scale up. To accomplish these in a sufficiently timely manner in the face of the rising tide of morbidity and mortality due to TB and HIV infection requires careful attention and operational study. It should be apparent, as well, that a basic array of issues must be addressed. Increased collaboration between national TB and HIV programs is necessary. Colocation of services simplifies integration, as do standardized regimens that are sufficiently flexible to take into account the special issues of TB/HIV service integration and utilization of existing human resources in families and communities to support treatment success. Training of staff to a needed degree of familiarity and expertise with both TB and HIV infection diagnosis and treatment is essential, as are effective monitoring systems and standardized and measurable outcomes for HIV infection as well as TB. The varied experience described illustrates that a single program design is not likely to fit all countries or settings. Broad program principles of TB/HIV service integration are essential, but program designs and components may vary by country and even within countries, as a result of differing TB and HIV disease prevalences, resources, levels of expertise, and differences in program settings (urban vs. rural and/or primary vs. district vs. specialty site).

To be fully successful, these programs must be designed within the constraints of available resources with comprehensiveness, continuity, competence, compassion, and cost-effectiveness.

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APPENDIX A
OPERATIONAL BARRIERS TO TUBERCULOSIS (TB)/HIV CARE AND TREATMENT INTEGRATION

- Separate national TB and HIV programs with corresponding separate personnel, funding streams, facilities, and responsibilities
- Concern about disruption and overburdening of already strained TB and public health care services
- Unfamiliarity of TB-trained providers with HIV infection diagnosis and treatment strategies
- Limitations and difficulties in diagnosing both diseases, particularly around issues of HIV counseling and testing, stigma, and limited strategies for the accurate diagnosis of smear-negative TB
- Limitations and difficulties in treating both diseases concomitantly, including overlapping and additive drug interactions and toxicities, high pill burdens, and immune reconstitution inflammatory syndromes
- Separate TB and HIV cultures and traditions

APPENDIX B
TUBERCULOSIS (TB) CONTROL STRUCTURE COMPONENTS TRANSFERRED TO THE NEW NATIONAL HIV PROGRAM, MALAWI

- Standardized diagnosis and case finding (smear microscopy and well-defined types of TB)
- Standardized treatment (3 treatment categories to cover all types of TB): first-line ART regimen only for World Health Organization stage 3 and 4 disease (fixed-dose combination of stavudine, lamivudine, and nevirapine) and ART using the first-line regimen delayed to the continuation phase of TB treatment, when the HIV-positive patient with TB begins receiving isoniazid and ethambutol
- Standardized recording and reporting system (treatment cards, registers, cohort analysis, and monitoring using standardized treatment outcomes)
- Standardized system of drug procurement
- Management by paramedical officers
- Free drugs for patients

APPENDIX C
RATIONALE FOR INTEGRATING TUBERCULOSIS (TB) AND HIV SERVICES IN KHAYELITSHA

- Increase voluntary counseling and testing among persons with TB so that they can access HIV care
- The high rate of HIV infection among patients with newly diagnosed TB makes TB programs an important entry point to HIV care for adults.
- Accelerate access to antiretroviral therapy (ART) in coinfected patients
  - Integrated services provide easier and quicker access to HIV care and ART.
- Reduce TB incidence and opportunistic infections among coinfected persons
  - Institution of cotrimoxazole, isoniazid preventive therapy, and other opportunistic infection prophylaxis enhanced.
- Diagnose and treat TB earlier in coinfected persons
  - TB is more difficult to diagnose in coinfected persons.
  - The emphasis of the TB program on sputum smear-positive pulmonary TB results in missed or delayed TB diagnoses.
  - Integration of TB and HIV services may provide more flexible and comprehensive diagnostic strategies for coinfected patients.
- Facilitate an integrated approach to the management of coinfected persons
  - Vertical services for HIV infection and TB result in patients being seen by different services and clinicians.
  - With integration, coinfected patients can be treated for the 2 conditions simultaneously.
  - The TB services tradition of caring for large numbers of patients and experience with standardized monitoring/tracking systems can be used for coinfected patients.
- Improve cure rates for patients with TB
  - TB completion rates are poor and can be improved if patient-centered ART adherence approaches (treatment literacy, support groups, and adherence aids) are employed for patients with TB.
- Provide benefit of integration strategy to staff
  - Staff and clinicians may benefit from cross-training and increasing skill sets.

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