TUBERCULOSIS CONTROL IN HIGH HIV PREVALENT AREAS

A STRATEGIC FRAMEWORK
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I. INTRODUCTION

Tuberculosis (TB) continues to be one of the most important global public health threats. The World Health Organization (WHO) estimates that the incidence of TB increased by 5 percent between 1997 and 1999, from 8 million to 8.4 million new cases. African countries severely affected by the HIV epidemic experienced a 20 percent increase in the incidence of TB; this rise is largely responsible for the TB increase globally.

TB was considered on the brink of elimination in the developed world until the late 1980s, when new HIV-related TB cases and multi-drug-resistant tuberculosis (MDR-TB) surfaced. In developing countries, however, TB has remained an important public health problem, exacerbated in the last decade by poverty, demographic changes and the rapid spread of HIV. Most TB patients in high HIV-prevalent countries are HIV-infected.

The relationship between TB and HIV has been recognized since the early days of the HIV epidemic. Today HIV is known to be an important risk factor, contributing to the development of active TB from latent TB infection. A person co-infected with TB (positive PPD skin test) and HIV faces a five percent to 16 percent annual risk of developing active TB disease. HIV also makes individuals with a recent TB infection more likely to progress rapidly to active TB disease. WHO estimates that more than 10 million people worldwide live co-infected with TB and HIV, more than two-thirds of whom are in sub-Saharan Africa (Tables 1 and 2).

HIV is not only fueling the TB epidemic but is also making TB control more challenging. The increase in new TB cases is likely to contribute to the overcrowding of health care facilities, draining human and financial resources from already under-funded health services. This overcrowding could prevent new infectious TB patients from seeking medical care, thereby contributing to lower case detection rates and risking further spread of TB into the community. Overcrowded health facilities will also increase the workload of health care workers, which may result in inferior case detection and treatment monitoring.

Some data suggest that HIV-related stigma may prevent TB patients from seeking medical care, resulting in delayed diagnoses and further TB transmission. Many TB patients have died during the course of treatment (Figure 1). Malawi, for instance, has reported more than 20 percent mortality rate among TB patients on treatment (Table 3). Finally, TB continues to be the leading cause of mortality among AIDS patients. Autopsy studies have shown that more than 30 percent of deaths in people with AIDS were due to TB.

The emergence of MDR-TB constitutes another challenge to TB control. MDR-TB is expensive to manage and generally associated with a high fatality rate. In the last decade, outbreaks of MDR-TB among HIV-infected patients were reported in the United States and Europe, and were associated with high-case fatality rates. Most of these outbreaks occurred in nosocomial settings such as prisons and hospitals. While the U.S. and Western Europe appear to have contained it, MDR-TB remains a major public health problem in Eastern Europe, especially in the republics of the former Soviet Union. In Africa, with the exception of Côte d'Ivoire and Mozambique, MDR-TB is not yet a public health problem. The situation in Asia is unclear but, given the burden of TB in the region, MDR-TB might become a more severe problem there.

TB is an important disease to target in areas with high HIV infection rates because it is one of the rare infectious diseases that is fueled by the HIV epidemic but does not remain confined to HIV-infected
individuals. Because TB is also one of the first opportunistic infections to appear in HIV-infected individuals — perhaps first suggesting the presence of HIV — addressing TB offers the opportunity for early HIV intervention. Controlling it in high HIV-prevalent countries will require that the Directly Observed Therapy, Short-course (DOTS) strategy be supplemented by other interventions, such as active TB case finding and treatment of latent TB infection among HIV-infected individuals.

II. STATE-OF-THE-ART: A COMPREHENSIVE APPROACH TO REDUCE TB AMONG PERSONS WITH HIV INFECTION

The introduction of streptomycin in the early 1940s and of multi-drug treatment in 1956 resulted in a tremendous decline in TB mortality. In the 1960s it was demonstrated that TB chemotherapy could cure a patient permanently.

WHO recommends a proven TB treatment regimen that is a combination of the following drugs: isoniazid (INH), rifampicin, streptomycin, pyrazinamide and ethambutol. Each regimen consists of two phases. The first is an intensive period of two to three months in which three to five drugs are given daily under direct observation. The second is a continuation phase of four to six months, in which either two or three drugs are given three times per week under direct observation, or two drugs are given daily for six months unsupervised. WHO recommends that all doses of rifampicin be given under direct observation.

In most developing countries, TB chemotherapy is given at little or no cost for patients. WHO estimates the cost of TB chemotherapy at about US $11 per patient cured.

Studies have shown that, regardless of HIV status, individuals appear to have a similar clinical response to TB treatment. The TB treatment guidelines of the American Thoracic Society (ATS) recommend a six-month regimen of at least four drugs to treat drug-susceptible TB disease for patients co-infected with HIV. The guidelines suggest prolonged treatment for patients who present a delayed clinical and bacteriological response to TB therapy. Special care should be taken with HIV-infected patients receiving antiretroviral (ARV) drugs. Protease inhibitors and non-nucleoside reverse transcriptase inhibitors have substantive interactions with the rifamycins. Rifampicin should not be used to treat TB in patients taking either inhibitor.

While most western countries are progressing toward elimination of TB, the incidence of TB continues to grow in most developing countries. In 1993 WHO declared TB a global emergency and began promoting its remedial DOTS strategy, which aimed to detect 70 percent of active TB cases and to successfully treat 85 percent of them. The essential features of DOTS include:

- Government commitment to sustained TB control activities
- Case detection by sputum smear microscopy among symptomatic patients self-reporting to health services
- Directly observed, standardized treatment regimen of six to eight months
- Efficient information systems for monitoring and reporting treatment outcomes
- A regular, uninterrupted supply of all essential anti-TB drugs

DOTS, widely known to be cost-effective, has been a successful approach to TB control in China, Bangladesh, Vietnam, Peru, Tanzania and Kenya.
In light of the growing numbers of TB patients and their impact on health services, many countries are expanding TB control activities to involve community-based organizations. In Bangladesh, Haiti and Peru, community-based TB programs contribute to effective TB control. To address the HIV-fueled TB epidemic in sub-Saharan Africa, WHO has pilot-tested eight community-based TB treatment projects in six countries — Botswana, Kenya, Malawi, Uganda, South Africa and Zambia. Data from these pilot projects shows that community involvement in TB care is cost-effective. National TB control programs in Uganda, Kenya and Malawi are in the process of expanding their interventions.

Eight years after the DOTS strategy was introduced, 55 percent of the world’s population is still not covered by DOTS programs, more than half of the global estimated smear-positive TB cases are not detected, and an average of 70 percent of persons detected with smear-positive TB complete their treatment successfully. The DOTS strategy appears ineffective at containing TB in countries with high HIV prevalence; these countries have been reporting an increase in TB cases (Figure 2). For example, Tanzania, recognized for one of the best TB control programs in Africa, reported a 160 percent increase in TB cases (all forms) between 1984 and 1993. An estimated 24 percent of all new smear-positive TB cases during that period was attributable to HIV. Similar findings were reported in some sites in Southeast Asia. In Thailand’s Chiang Rai province, the incidence of TB began a long rise upward in 1991, following a decade of steady decline. The TB increase was closely correlated with an increase in HIV among TB patients.

Adding other interventions to the DOTS strategy — such as treatment of latent TB infection, active case finding and contact investigation — has helped control TB in the United States and Western Europe. Data from clinical trials have shown that anti-TB drugs can prevent latent TB infection from becoming active TB disease. Implementing treatment for latent TB infection, commonly known as TB preventive therapy (TB PT), may be an effective way to reduce the TB burden within that community. But when implementing TB PT, care must be taken not to drain limited resources from TB control activities, where diagnosis, treatment and cure of smear-positive cases must remain the priority.

The most common regimen for preventing TB and for treating latent TB infection is isoniazid for six to twelve months. Studies have shown that isoniazid preventive therapy is effective in reducing the incidence of TB in HIV-infected individuals. In these studies the protective effect of INH prophylaxis ranged from 30 percent to 83 percent, with significant benefit for HIV-infected individuals with a positive tuberculin skin test. A study in Uganda estimated the cost of a successful six-month preventive therapy regimen at US $18 per person. One cost study estimated that providing six months of isoniazid preventive therapy, compared with no therapy, saves between US $12 and $24 per person.

Despite these data, application of INH prophylaxis has been limited in most developing countries because of poor adherence, concerns about toxicity, and unresolved questions about cost and benefit. Short-course regimens using two or three anti-TB drugs have been used and studied. A treatment regimen using rifampicin and pyrazinamid for two months has been shown to be as effective as nine months of isoniazid. The ATS, the Centers for Disease Control and Prevention (CDC) and the Infectious Disease Society of America now recommend four regimens for treating latent TB infection (Table 4). In 1998 WHO and UNAIDS made the following recommendations, which WHO is piloting through its TB/HIV initiative known as ProTest:

- Preventive therapy should be part of a package of care for people living with HIV/AIDS.
- Preventive therapy should be used only where it is possible to ensure appropriate monitoring and follow-up and to exclude active TB cases.
Information about TB and preventive therapy should be available to people with HIV.

Settings with HIV voluntary counseling and testing (VCT) services should provide preventive therapy.

Detection and cure of infectious TB cases should remain the priority for TB control programs.

National authorities must regulate the procurement and supply of TB drugs to prevent the development of drug resistance.

Given the common challenges presented by TB and HIV, one might expect that the majority of TB patients in areas where both TB and HIV are prevalent would have access to HIV services such as VCT. But a review of TB services conducted by UNAIDS in parts of Southern Africa found that HIV education and VCT were not offered to TB patients. In Côte d'Ivoire, Malawi and Thailand it has been shown that offering HIV counseling and testing to TB patients could be successful; more than 80 percent of TB patients there consented to HIV testing.

III. FHI GOALS AND OBJECTIVES

FHI’s goal for targeting TB is to reduce the burden of TB in HIV-infected individuals and affected communities. Its strategy has three main objectives: to strengthen the capacity of TB programs, to expand TB services to HIV-infected populations, and to integrate HIV prevention and care interventions into TB control activities.

IV. FHI’s TECHNICAL AND PROGRAMMATIC APPROACHES

Guiding principles

The guiding principles of FHI’s TB control strategy are to reduce transmission of mycobacterium tuberculosis by detecting and effectively treating all infectious cases and to avert new cases by providing TB preventive therapy to treat latent TB infection. In high HIV-prevalent areas, this strategy must be accompanied by interventions that address the impact of HIV on the natural history of TB and the needs of TB patients living with HIV. Such interventions will involve:

- Working at the individual level to assess and address individual health-seeking behaviors, perceptions of TB, and interaction between TB and HIV
- Working at the community level with a behavior change communication strategy to change perception of TB and of the link between TB and HIV, encouraging greater community involvement in the care of TB patients with and without HIV
- Placing significant emphasis on building local capacity to design, implement and evaluate effective interventions linking TB and HIV control
- Collaborating with ministries of health (national TB and AIDS control programs), other government agencies, NGOs, donors and the private sector to design strategies that strengthen TB control activities and integrate TB and HIV control interventions
- Improving the policy environment to secure adequate resources for TB control
• Reducing stigma and discrimination associated with TB and HIV
• Improving the institutional capacity of developing countries to design, implement and evaluate TB/HIV programs

FHI approaches

FHI recognizes the value of a coordinated approach to HIV and TB and appreciates that TB services must be provided in conjunction with the country’s national TB program. This strategy will build upon the country’s existing TB control programs, HIV prevention and care programs and community efforts. Collaborating institutions will devise specific activities with input from national TB and HIV/AIDS programs and district health authorities to ensure that interventions address national and local program needs and strengthen existing TB and HIV programs.

FHI will use its long experience implementing activities and working with communities to provide interventions that successfully integrate TB and HIV activities. As part of a comprehensive care and support strategy, the TB effort must be linked to prevention activities. In some areas, TB/HIV interventions could be the first care intervention of the comprehensive care and support program.

FHI’s TB strategy will address the following four program areas:

• Strengthening TB case detection and case-holding capability of national TB programs
• Establishing HIV services at TB service points
• Introducing TB control activities at HIV service delivery points
• Managing HIV-related TB through training and capacity building

To ensure successful implementation of the first three program areas, FHI will:

• Conduct an assessment to identify opportunities and barriers to effective implementation
• In partnership with local stakeholders, determine which interventions are feasible
• Develop and implement a program action plan with a monitoring and evaluation component
• Build the capacity of local organizations or government to ensure sustainability of the interventions

The four program areas are explained in detail in the sections that follow.

Strengthening TB case detection and case-holding capability of national TB programs

An effective TB program is essential for controlling TB, especially in high HIV-prevalent areas. To be effective, it must achieve higher cure and detection rates, since both decrease the probability of TB transmission. In addition, higher cure rates prevent the development and transmission of multi-drug-resistant strains.

The objective of this program area is to improve access to quality TB services and facilitate adherence to TB therapy. Working with national TB programs, FHI will achieve this by:

• Developing specific communication approaches to sensitize communities and individuals to the importance of adhering to TB therapy
• Promoting community support for TB treatment based on the WHO’s model of community-based TB care
• Engaging in targeted efforts to find active cases, aided by communication programs that address treatment-seeking behavior and community understanding of TB
• Forging links between national programs and hard-to-reach groups, such as prisoners and migrant workers
• Strengthening existing TB services in the private sector by nurturing public-private sector partnerships

Establishing HIV services at TB service points

Most TB patients in high HIV-prevalent countries are HIV-infected and do not have easy access to HIV education, VCT and services to help them manage HIV-related illnesses. Establishing HIV services within TB service points will address the needs of most TB patients. HIV VCT will help alleviate the anxiety of most TB patients (many are aware of the link between TB and HIV) and motivate HIV-negative patients to adopt life-saving skills. Knowing their status makes it possible for HIV-positive persons to plan for the future and alter behavior to protect others. It also makes HIV more visible in communities, reducing its stigma. HIV education, by filling gaps in knowledge and dispelling misunderstandings, also can reduce stigma and discrimination. Providing appropriate HIV care will boost the credibility of health workers in TB programs.

The objective of this program area is to improve TB patients’ access to quality HIV services that provide and promote appropriate information, diagnosis and treatment of HIV-related illnesses. FHI will achieve this objective by:

• Providing HIV education at TB service points
• Promoting and providing HIV VCT to TB patients at TB service points
• Improving management of simple HIV-related illnesses at TB service points and/or establishing an effective referral mechanism for managing HIV-related illnesses

Introducing TB control activities at HIV service points

The majority of HIV-infected people living in areas where TB is prevalent are likely to develop TB during their lifetime. Introducing TB control activities at HIV service points will help strengthen TB programs by increasing TB case detection and cure rates and by reducing the number of people who develop TB from reactivation of latent infection.

The objective of this program area is to improve HIV-infected persons’ access to quality TB services that provide and promote appropriate information, diagnosis, prevention and treatment of TB. FHI will achieve this by:

• Promoting the provision of TB education wherever HIV services are offered
• Providing training in TB control activities (case detection, TB treatment supervision, monitoring and evaluation) to HIV/AIDS support groups and NGOs in conjunction with national TB programs
• Strengthening TB care delivery (treatment and monitoring) in HIV home-based care or community-based care
• Providing TB preventive therapy to people living with HIV/AIDS

**Managing HIV-related TB through training and capacity-building**

The objective of this program area is to establish capacity for implementing effective and sustainable services for managing HIV-related TB by increasing the understanding of interaction between TB and HIV interaction. FHI will achieve this objective by:

• Developing a training plan for TB/HIV interaction that establishes priorities for each level of services
• Conducting and/or facilitating workshops for trainers in skills necessary to implement activities related the TB/HIV program

**V. ILLUSTRATIVE ACTIVITIES**

**Cambodia.** In collaboration with the Gorgas Memorial Institute at the University of Alabama, FHI is developing a TB pilot project to address hard-to-reach populations (squatters, prisoners and PLHA and their families) in Phnom Penh. The goal is to improve TB treatment-seeking behavior and treatment compliance among these vulnerable groups. Planned activities include: a sputum survey to determine TB prevalence; behavioral research to assess treatment-seeking behavior and perceptions of TB; development of behavior change communication; community mobilization and education; improvement of referral, case finding and case holding; and expansion of the DOTS home delivery program. Local partners in this project include the National TB Program, the JICA support project to the NTP, the National Center for HIV/AIDS, Dermatology and STD, and local NGOs and CBOs.

**Kenya.** The FHI project in Kenya is expanding to address the growing HIV-related TB epidemic. FHI is helping to rehabilitate the National TB Reference Laboratory and to expand TB diagnostic services in the Coast and Western Provinces. FHI is also incorporating TB services and co-trimoxazole preventive therapy services into HIV VCT centers at two primary health care facilities in Mombassa.

**Rwanda.** FHI is addressing the interaction between TB and HIV through two pilot projects in Rwamagana and Kabgayi. The goal is to incorporate TB services and prevention of opportunistic infections into HIV VCT services in district hospitals. Activities include: increasing TB patients' access to HIV VCT services; active screening for TB among partners of HIV-infected TB patients; providing TB preventive therapy to HIV-infected individuals identified at VCT centers; and increasing TB and TB/HIV awareness in the community.
VI. INTERVENTION-LINKED RESEARCH

Intervention-linked research activities will be specific to each program area and will seek to improve the design, implementation and evaluation of these programs. Intervention-linked research might include:

**Strengthening TB case detection and case-holding capacity of TB programs**

- Investigating health-seeking behaviors related to TB, including symptom recognition
- Developing and testing community-level approaches, such as media and interpersonal communication, to promote TB symptom recognition, treatment-seeking behavior and treatment compliance
- Describing the roles played by various health care delivery systems (TB clinics, pharmacies, primary medical providers, private practitioners, traditional healers) and other sectors in providing TB services

**Establishing HIV services at TB service points**

- Investigating ways to motivate health care workers at TB service points to provide HIV education, promote HIV VCT and provide quality care for TB patients
- Developing appropriate training materials for health care workers and for patient education related to TB

**Introducing TB control activities at HIV service points**

- Determining the appropriate screening strategy to exclude active TB in HIV-infected persons
- Studying the acceptance and compliance/adherence of HIV-infected individuals to the full-course TB preventive therapy
- Determining how VCT services and HIV and TB incidence rates are affected when TB preventive therapy interventions are introduced
- Determining the rate of secondary TB in partners of TB/HIV co-infected individuals

VII. MONITORING AND EVALUATION

Indicators for monitoring and evaluation (input and/or output) will be defined and collected for each program area. Some examples of monitoring and evaluation indicators for each program are:

**Strengthening TB case detection and case-holding capability of TB programs**

- Proportion of TB cases detected through new TB case detection strategy
- Proportion of TB patients who complete TB therapy
- Proportion of smear-positive TB patients who are cured
• Proportion of TB cases lost to follow-up
• Proportion of TB patients who die during TB treatment

Establishing HIV services at TB service points

• Proportion of TB patients who received HIV education and HIV VCT
• Number of TB health care workers trained to provide HIV education and HIV VCT

Introducing TB control activities at HIV service points

• Number of HIV-infected TB cases referring their partners for TB and HIV screening
• Proportion of secondary TB cases among partners of HIV-infected TB patients
• Proportion of clients who start TB PT and comply with the treatment
• Number of health care workers trained in TB PT
• Number of incident cases of TB among clients receiving TB PT
• Number of incident TB cases with MDR TB
• Proportion of people presenting with toxicity to TB drugs

VIII. LINKAGES AND PARTNERSHIPS

Because TB prevention and control is an important part of an overall HIV care and support strategy, links will be established during the design and implementation phases with:

• **VCT services.** These may be an entry point both for TB patients to HIV services and for HIV-infected individuals to TB services.
• **Behavioral change communication program.** This might increase TB/HIV awareness, TB case finding and adherence to TB treatment.
• **Sexually Transmitted Infection (STI) programs.** Working with STI programs can enhance STI service providers’ understanding of TB and improve referral for STI clients with TB symptoms.
• **Programs for orphans and other vulnerable children (OCV).** Collaborating with these programs can improve detection and management of OVC exposed to TB.
• **Other community-based services.** Working with CBOs can improve case-finding, increase adherence to TB treatment and reduce stigma by increasing the community’s understanding of the relationship between TB and HIV.

FHI will work with projects supporting national TB programs to ensure that proposed activities strengthen existing efforts. It also will work with international organizations involved in TB control, including WHO in Geneva (whose STOP TB department is implementing the ProTest initiative), WHO regional TB advisors, UNAIDS/HQ and regional advisors, the International Union Against Tuberculosis and Lung Diseases, and the CDC.
IX. FURTHER READING


### Table 1.
**Estimates of TB and TB/HIV burden by WHO region**

<table>
<thead>
<tr>
<th>WHO Regions</th>
<th># HIV(+) in new TB cases</th>
<th># TB/HIV co-infection</th>
<th>TB/HIV rates (per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>515,000</td>
<td>7,300,000</td>
<td>1,194</td>
</tr>
<tr>
<td>Americas</td>
<td>25,000</td>
<td>510,000</td>
<td>64</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>16,000</td>
<td>107,000</td>
<td>23</td>
</tr>
<tr>
<td>Europe</td>
<td>10,000</td>
<td>84,000</td>
<td>10</td>
</tr>
<tr>
<td>Southeast Asia</td>
<td>64,000</td>
<td>2,400,000</td>
<td>162</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>9,000</td>
<td>307,000</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>640,000</td>
<td>10,700,000</td>
<td>183</td>
</tr>
</tbody>
</table>

Table 2. Estimated TB cases, TB-related deaths and HIV-related TB in selected countries

<table>
<thead>
<tr>
<th>Countries</th>
<th>TB cases (thousands per year)</th>
<th>TB-related deaths (thousands per year)</th>
<th>% new TB case attributable to HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>124</td>
<td>19</td>
<td>4.8</td>
</tr>
<tr>
<td>Cambodia</td>
<td>58</td>
<td>9</td>
<td>3.4</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>160</td>
<td>49</td>
<td>29.3</td>
</tr>
<tr>
<td>India</td>
<td>1,828</td>
<td>437</td>
<td>2.4</td>
</tr>
<tr>
<td>Kenya</td>
<td>86</td>
<td>28</td>
<td>39.5</td>
</tr>
<tr>
<td>Nigeria</td>
<td>259</td>
<td>69</td>
<td>13.5</td>
</tr>
<tr>
<td>South Africa</td>
<td>172</td>
<td>72</td>
<td>44.2</td>
</tr>
<tr>
<td>Tanzania</td>
<td>99</td>
<td>31</td>
<td>36.4</td>
</tr>
</tbody>
</table>

Source: Stop TB 1999
Table 3.
Case fatality rates (CFRs) in new smear-positive pulmonary tuberculosis (PTB) Patients registered nationally in Malawi: Relationship to HIV sero-prevalence rates in TB patients (all forms) measured in different sites

<table>
<thead>
<tr>
<th>Year</th>
<th>National notification and CFRs in new smear-positive PTB patients</th>
<th>HIV sero-positive rates in TB patients (all forms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of patients</td>
<td>CFR (% died)</td>
</tr>
<tr>
<td>1986</td>
<td>1788</td>
<td>6</td>
</tr>
<tr>
<td>1987</td>
<td>1959</td>
<td>6</td>
</tr>
<tr>
<td>1988</td>
<td>2720</td>
<td>8</td>
</tr>
<tr>
<td>1989</td>
<td>3312</td>
<td>10</td>
</tr>
<tr>
<td>1990</td>
<td>4355</td>
<td>10</td>
</tr>
<tr>
<td>1991</td>
<td>4071</td>
<td>11</td>
</tr>
<tr>
<td>1992</td>
<td>5366</td>
<td>12</td>
</tr>
<tr>
<td>1993</td>
<td>5462</td>
<td>16</td>
</tr>
<tr>
<td>1994</td>
<td>6285</td>
<td>16</td>
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<tr>
<td>1995</td>
<td>6278</td>
<td>19</td>
</tr>
<tr>
<td>1996</td>
<td>6702</td>
<td>21</td>
</tr>
</tbody>
</table>

Table 4.
Recommended drug regimens for treating latent TB infection in adults

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Duration (month)</th>
<th>Interval</th>
<th>HIV-negative</th>
<th>HIV-positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>9</td>
<td>Daily</td>
<td>A (II)</td>
<td>A (II)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Twice weekly</td>
<td>B (II)</td>
<td>B (II)</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>6</td>
<td>Daily</td>
<td>B (I)</td>
<td>C (I)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Twice weekly</td>
<td>B (II)</td>
<td>C (I)</td>
</tr>
<tr>
<td>Rifampin-pyrazinamide</td>
<td>2</td>
<td>Daily</td>
<td>B (II)</td>
<td>A (I)</td>
</tr>
<tr>
<td></td>
<td>2-3</td>
<td>Twice weekly</td>
<td>C (II)</td>
<td>C (I)</td>
</tr>
<tr>
<td>Rifampin</td>
<td>4</td>
<td>Daily</td>
<td>B (II)</td>
<td>B (III)</td>
</tr>
</tbody>
</table>


A = preferred;
B = acceptable alternative;
C = offer when A and B cannot be given
† I = randomized clinical trial data;
II = data from clinical trials that are not randomized or were conducted in other population;
III = expert opinion
Figure 1. Probability of survival of HIV positive and HIV negative TB patient during TB treatment
Figure 2. TB case notification in selected sub-Saharan African countries (per 100,000)