Role of the US President’s Emergency Plan for AIDS Relief in Responding to Tuberculosis and HIV Coinfection

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The intersection of tuberculosis (TB) and human immunodeficiency virus (HIV) infection has eroded gains made in TB control, because previously well-functioning national TB programs have been overwhelmed by the dual challenges posed by TB and HIV coinfection. The US President’s Emergency Plan for AIDS Relief (PEPFAR), through its direct support of >2.4 million persons receiving HIV treatment and, in 2009, support of >308,000 HIV-infected persons receiving TB treatment, works closely with national governments and other partners to strengthen the response to TB and HIV coinfection. PEPFAR-supported activities fall within the World Health Organization’s 2004 framework for collaborative TB and HIV activities, including critical interventions to (1) develop organizational methods of collaboration across the 2 programs, (2) reduce the burden of HIV infection among patients with TB, and (3) reduce the burden of TB among persons with HIV infection or AIDS. To date, PEPFAR and partners have made important gains in coverage and scope of HIV testing, referral, and antiretroviral therapy for patients with TB. TB screening of HIV-infected patients is also beginning to increase, although greater progress needs to be made in increasing access to isoniazid preventive therapy and strengthening TB infection control. Continued strategic integration of TB and HIV interventions into PEPFAR-supported programs is essential to easing the patient burden of dual infection, improving patient outcomes, and, ultimately, decreasing rates of TB in areas with a high prevalence of TB.

Human immunodeficiency virus (HIV) infection and tuberculosis (TB) have each contributed to the suffering and premature deaths of millions of individuals and have shaken the foundations of the hardest hit societies [1]. Each disease presents formidable challenges alone, and together, the 2 diseases have strained already fragile health care systems in resource-limited settings and made efforts to accelerate prevention and control activities even more challenging.

The US President’s Emergency Plan for AIDS Relief (PEPFAR) is best known for implementing a robust US government response to the global HIV epidemic. As of September 2009, PEPFAR directly supported antiretroviral treatment (ART) for >2.4 million persons in the countries with the greatest burden of HIV infection [2]. It is less well known that, from 2005 through 2009, PEPFAR increased bilateral funding for TB and HIV programs from $26 million to $150 million per year. In 2009, PEPFAR supported TB treatment for >308,000 HIV-infected patients. When combined with the beneficial effects of ART on reducing TB incidence and expansion of laboratory, information systems, and supply chain management capacity by PEPFAR, this TB and HIV-specific funding and program support demonstrates an increasing and substantial US government investment in combating the combined threats of both TB and HIV infection. Our objectives are to put PEPFAR’s response in the context of the World Health Organization’s (WHO) Interim Policy on Collaborative TB/HIV Activities and to outline major areas of emphasis in future programming.
INTERSECTION OF TB AND HIV INFECTION

PEPFAR provides support and has an in-country presence in >87 countries in Africa, Asia, Central and South America, and Eastern Europe. During fiscal years 2004–2008, approximately two-thirds of PEPFAR funding was directed toward sub-Saharan Africa, which is the heart of the generalized HIV and TB coepidemics. In addition, substantial funding is used to combat TB and HIV infection in countries with concentrated HIV epidemics, such as Vietnam and Ukraine.

TB is the most common opportunistic infection and the leading cause of death among HIV-infected persons in sub-Saharan Africa [3]. Estimates of the number of HIV infection–related TB cases and deaths have recently been revised upward, in part because of large increases in HIV testing. The WHO reported that, among the 9.27 million incident TB cases registered in 2007, an estimated 1.37 million occurred in persons with HIV infection—almost double the number previously estimated. It is estimated that the African region accounts for 79% of this global burden of coinfection [1].

In sub-Saharan Africa, PEPFAR supports >13,500 HIV care and treatment sites (including 5200 sites that provide ART), many of which provide an ideal platform for further community or institution-based TB prevention, diagnosis, and treatment. Because TB incidence increases with decreasing CD4 cell count, both patients in care over time and those starting ART, often with CD4 cell counts <100 cells/μL, are at high risk of incident TB [4, 5]. Similarly, TB clinical settings provide an opportunity to identify a large number of HIV-infected persons who need HIV care and treatment and who may be eligible for ART on the basis of low CD4 cell count and clinical stage [6–8].

PEPFAR’S TB AND HIV ACTIVITIES IN THE CONTEXT OF THE WHO INTERIM POLICY ON COLLABORATIVE TB/HIV ACTIVITIES

PEPFAR’s current and planned support for TB and HIV activities involve the 2 basic tenets of the WHO Interim Policy on Collaborative TB/HIV Activities, which outlines essential interventions to optimize collaborative TB and HIV programming: (1) establishing mechanisms for collaboration, (2) decreasing the burden of TB among persons with HIV infection or AIDS, and (3) decreasing the burden of HIV infection among patients with TB [9].

Establishing mechanisms for collaboration. PEPFAR supports efforts to build TB and HIV programs by working in partnership with Ministries of Health, national AIDS control programs, national TB programs, and other key local and international partners. This approach has enabled PEPFAR to fund and provide technical assistance to comprehensive national efforts to integrate TB and HIV activities, including the development of national policies, guidelines, and operational tools, to improve the standardization of approaches across countries. For example, to support efforts by the government of South Africa to improve TB and HIV control, PEPFAR TB and HIV experts recently participated in a WHO-sponsored review of the National TB Program in South Africa [10, 11]. PEPFAR also supports expansion of national and international TB and HIV surveillance activities to determine rates of HIV infection among patients with TB and uptake of related interventions (eg, systems of referral and back-referral).

In many countries, the key to scaling up TB and HIV activities has been the establishment of coordinators responsible for facilitating, monitoring, and supervising staff at health care facilities. Many PEPFAR-supported programs have also instituted regular monitoring visits. These visits have focused on the review of routine reports to verify implementation of interventions (eg, HIV testing in TB clinical settings), verification of drug supply and infrastructure and/or equipment, and dissemination of new technical guidance and/or updates. This process strengthens the programmatic connection between TB and HIV responses and can serve to motivate and provide an incentive to collaborate. Similar monitoring and supervision procedures will be important for other interventions as they are expanded.

PEPFAR collaborates closely with the Global Fund to Fight AIDS, TB and Malaria (GFATM), both at headquarters and in the field. The US government is the first and largest contributor to the GFATM, providing ~$3.5 billion since 2001. Through 2007, the GFATM had committed $1.4 billion to TB grants, with the intent of strengthening national capacity to control TB. In addition, a proportion of US government funding is used to support provision of technical assistance to GFATM TB grants through the Stop TB Partnership. In a number of countries, PEPFAR also contributes to TB and HIV coordination efforts through in-country leadership in GFATM Country Coordinating Mechanisms. These efforts help to better leverage PEPFAR funding and programming by reducing overlap and improving GFATM grant performance.

The US government also provides funding and technical support for the WHO Stop TB and HIV Departments and the Green Light Committee for multidrug-resistant TB (MDR-TB), which supports a variety of interventions aimed at strengthening TB and HIV coordination and policy development. PEPFAR funding for technical assistance supports countries’ capacity to develop applications to the Green Light Committee and provide surveillance and treatment for MDR-TB. PEPFAR also works with the World Bank, the United Nations Joint Programme on HIV/AIDS, the International Union Against TB and Lung Disease, and the private sector.

Lastly, at the headquarters level, PEPFAR has created a steering committee of leaders from its TB and HIV, HIV Care and
Support, and HIV Treatment Technical Working Groups to spearhead joint planning for HIV and TB and to serve as a resource for headquarters and field staff. Planned activities for 2010 include joint technical assistance visits to countries and joint strategic planning to improve communications and synergies among technical areas.

**Decreasing the burden of TB in persons with HIV infection or AIDS.** PEPFAR-supported institutional platforms that have expanded access to HIV care and treatment also provide important infrastructure to address the second tenet of the WHO collaborative activities framework: decreasing the burden of TB in persons with HIV infection or AIDS. First, support of the scale-up of ART and decreasing the reservoir of severely immunosuppressed individuals has undoubtedly had a major impact on reducing TB among these individuals in regions with a high prevalence of TB [12–14]. PEPFAR’s TB- and HIV-specific activities have built on WHO’s “3 I’s,” including intensified case finding, isoniazid preventive therapy (IPT), and TB infection control. The 3 I’s are central to PEPFAR’s Technical Considerations document, which PEPFAR Country Teams use to build their programs and on which yearly PEPFAR Country Operational Plans are evaluated for funding.

PEPFAR’s Technical Considerations state that Country Operational Plans should integrate intensified TB case finding among HIV-infected persons and scale-up of IPT and TB infection control as critical components of quality HIV care and treatment. Related elements of these interventions include strengthening of laboratory services to support TB diagnosis and treatment, including stronger integrated laboratory referral networks; development of standardized clinical algorithms and supportive paper or computer-based forms; and offering of provider training in the appropriate care and treatment of coinfected individuals. There are many examples of PEPFAR implementing partners that integrate TB and HIV services. In Mozambique, a pilot program is under way to improve adherence to IPT in an ART facility and to develop screening tools that increase case detection and pathways into treatment and preventive services. In South Africa, a program was developed to bring TB and HIV services to a remote Kgalagadi desert community. As a result, there has been a large increase in the number of HIV-infected residents screened for TB, and of those tested, one-third have received a diagnosis of active TB. The program has also led to a substantial increase in the number of patients with TB who receive HIV counseling and testing.

The lack of standard HIV monitoring and evaluation systems for collection of data on TB has also been a major challenge, and PEPFAR programs have worked closely with the WHO to advocate for inclusion of TB data in national monitoring systems for patients with HIV infection. Rwanda is one of the few countries with a strong monitoring and evaluation platform and has reported that 85% of HIV-infected patients are screened for TB at their initial visit and 59% are screened at follow-up visits. PEPFAR views TB screening of HIV-infected patients as critical to quality delivery of HIV service. PEPFAR is working with implementing partners and others to ensure that programs collectively reach high levels of TB screening and that these data on service are fully integrated into national HIV and TB monitoring systems.

Expansion of TB screening activities is also a prerequisite to wider implementation of IPT among HIV-infected persons. Evidence exists for the benefit of expanded use of IPT as part of HIV care and treatment [15]. To date, uptake of IPT has been hampered by programs’ concerns about their ability to rule out active TB before initiation of therapy, in part because of insufficient laboratory or clinical and/or radiological capacity, and by lack of national guidelines, training, or prioritization of the intervention. PEPFAR supports global efforts to overcome these concerns through improvements in laboratory infrastructure and capacity to rule out active TB.

TB infection control is another high-priority intervention aimed at decreasing the impact of TB on HIV-infected and uninfected patients and health care providers. PEPFAR is currently funding and providing technical support for global efforts to develop guidelines and operational tools that will assist countries in establishing TB infection-control programs. PEPFAR is supporting the training and development of cadres of engineers in methods of improving TB infection control in renovated and new structures. PEPFAR is also asking its HIV care and treatment partners to conduct site-level TB infection-control assessments and to implement the package of infection-control interventions recently described in the revised WHO Policy on TB Infection Control [16].

**Programs aimed at decreasing the burden of HIV infection among patients with TB.** Critical to PEPFAR’s success in scaling up prevention, care, and treatment of HIV infection has been the identification of HIV-infected persons in the general population and among persons at high risk, such as those with TB. Through a WHO and PEPFAR partnership, 3 countries successfully accelerated the implementation of collaborative TB and HIV activities during 2005–2007. In Kenya, HIV testing of patients with TB increased from 41% to 84% during the period. Similarly, in Rwanda, 88% of patients with TB were tested in 2007 (increased from 45% in 2005), and in Ethiopia, testing rates increased from 3% to 16%.

A key component of successful scale-up of HIV testing of patients with TB was the development of a standard implementation package. This implementation package guided countries through the critical steps necessary to scale-up HIV testing of patients with TB (eg, establishment of national policies and guidelines, establishment of collaborative in-country TB and HIV working groups, development of a training-of-trainers...
plan, ensuring supply chains for HIV test kits and reagents, implementation of rapid point-of-care testing, and development of infrastructure and patient flow). In addition, guidelines for provider-initiated counseling and testing and monitoring and evaluation further enhanced countries’ ability to implement important components of the program. Because of the high rates of HIV infection among persons suspected of having TB who attend TB clinics, PEPFAR is currently supporting Kenya’s efforts to pilot HIV testing of all persons suspected of having TB (in addition to testing of persons with TB). If this pilot is successful, Kenya, among other countries, may broaden national guidelines to include HIV testing of persons suspected of having TB.

Linking patients with TB who are identified as having HIV infection to care and treatment is another essential component promoted by PEPFAR programs. In Kenya, 42% of HIV-infected patients with TB who are identified as HIV infected through the PEPFAR and WHO collaboration initiated ART by the end of 2007. In Ethiopia, 28% of HIV-infected patients with TB received ART (increased from a baseline of 19% in 2005). In Rwanda, 36% of HIV-infected patients with TB received ART by the end of 2007 (increased from 13% in 2005). With the rapid expansion of ART availability in these countries, it is likely that the proportion of HIV-infected persons with TB who are receiving ART will be substantially higher in 2009. Using lessons learned from these 3 countries, PEPFAR is prioritizing expansion of these linkages and their measurement to all PEPFAR-supported countries in the future.

To further increase the timely uptake of HIV care and treatment services for HIV-infected patients with TB, several countries, including Tanzania, Zambia, and Kenya, are piloting the provision of HIV care and treatment services in TB clinics. In these models, some or all of the components of HIV care and treatment (eg, provision of trimethoprim-sulfamethoxazole preventive therapy, CD4 cell count testing, and ART) are available at TB clinics for HIV-infected patients with TB. TB providers are trained to provide HIV care and treatment and may receive supervisory support from national AIDS program staff. Referral and follow-up are strengthened to ensure that patients who initiate HIV care and treatment at a TB clinic are transferred to the most convenient HIV clinic to continue their HIV-related care after TB treatment is completed.

Lastly, TB clinical settings also provide an important opportunity to explore ways in which messaging of prevention of HIV infection can be integrated into TB care and treatment. In Kenya, where such a project is being pilot ed, the results will likely inform the development of operational tools that could be used to expand the project nationally and to other countries for integration of prevention of HIV infection into TB clinical settings.

CROSS-CUTTING ISSUES

Development and innovative use of human resources. Many countries have severe health care worker shortages that hinder the delivery of health care. In response, PEPFAR supports the strategic shifting of tasks to lower-level cadres of health care workers [17]. Task-shifting has been widely implemented at community and institutional care delivery sites. For instance, several countries have developed cadres of community health workers (eg, TB treatment supporters and home-based AIDS care workers) to implement key interventions, including health education about the link between TB and HIV infection, HIV counseling and testing, support of patient adherence to therapy and monitoring of adverse effects of therapy, and TB screening of HIV-infected persons. This model for community health workers will be more widely promoted in the next phase of PEPFAR.

A number of countries have innovatively task shifted basic laboratory services, such as smear microscopy and HIV counseling and testing, to lower-level staff. In Zambia, for example, nonlaboratory personnel (eg, environmental health staff) are trained to conduct sputum smear microscopy. In Namibia, lay counselors are being trained to provide individual or group HIV counseling in TB clinics to reduce the burden on TB providers.

Strengthening laboratory services. Lack of diagnostic capacity is a significant barrier to the response to the challenges of HIV infection, TB, and drug-resistant TB. A massive scale-up of quality-assured, integrated HIV and TB laboratory services is an essential step in effectively addressing the diagnostic challenges of TB, HIV infection, and MDR-TB. PEPFAR supports efforts to improve TB diagnosis among HIV-infected persons through introduction of methods, such as liquid culture, fluorescent microscopy, and polymerase chain reaction methods (line probe assay), that have been shown to have increased sensitivity and to rapidly detect TB and MDR-TB. PEPFAR continues to work with international partners to identify opportunities to introduce new laboratory methods adaptable to low-resource settings. Through the provision of substantial and continued funding for products that improve the diagnosis and treatment of TB, PEPFAR is able to increase the long-term attractiveness of the markets for new diagnostics and therapeutics and to encourage technological innovations.

Meeting nutritional needs. In PEPFAR-supported programs, food and nutrition activities are increasingly an integrated aspect of clinical services for adult and pediatric patients before and during ART. Food by Prescription programs, initially developed in Kenya, are now being adopted and adapted by many PEPFAR programs. Additional opportunities to expand these programs to coinfected clients need to be intensified as integrated approaches are built on PEPFAR’s platforms.
CONCLUSIONS AND EMERGING ISSUES

Over the past few years, there have been substantial investments in international health programs through the US government and other multilateral efforts. These investments have supported care and treatment for millions of individuals through development of infrastructure and human resources to care for persons with TB and HIV infection and other related illnesses. Over the past several years, the scale-up of TB and HIV collaborative activities has accelerated because of input by national governments and international partners, such as PEPFAR.

National and international partners will need to accelerate efforts to increase capacity to prevent, diagnose, and treat HIV infection-related TB, including drug-resistant TB. For its part, PEPFAR has identified TB and HIV coinfection as a priority for scale-up of ART in its new Five Year Strategy [18]. Therefore, PEPFAR will continue to support efforts to decrease the distance between HIV treatment services and TB treatment networks, through the support of integrated national systems and service delivery platforms. Efforts must focus on implementing the appropriate intensified case finding and infection control measures in facilities providing HIV care and treatment, which are hosts to concentrations of highly vulnerable persons.

TB remains the most significant cause of morbidity and mortality among HIV-infected persons living in sub-Saharan countries with a high prevalence of both diseases. HIV care and treatment programs must continue to view TB prevention, screening, diagnosis, and treatment as standard-of-care. As PEPFAR moves into a new phase, emphasizing sustainability and greater country ownership, the US government looks forward to working closely with host countries and other partners to determine mutual responsibilities and priorities, especially those that will accelerate key TB and HIV collaborative activities.

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