Written Testimony

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"The Threat of Drug-Resistant TB in Southern Africa"

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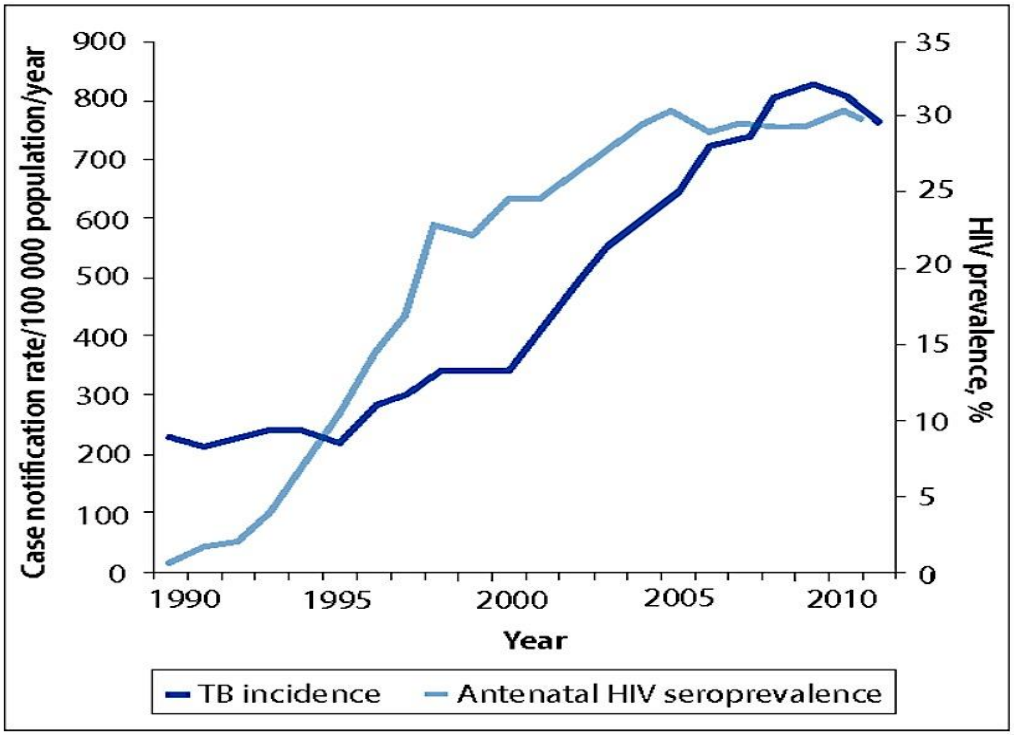
Thank you Chairman Smith, Ranking Member Bass, and other distinguished members of this Subcommittee. I am deeply honored to appear before the House Foreign Affairs Committee and your Subcommittee, which have provided such visionary leadership and remarkable support for the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) since its inception in 2003. Thank you very much for the opportunity to be here today to discuss global TB/HIV co-infection and PEPFAR's critical role in the fight against this deadly epidemic.

It has been estimated that a quarter of the world's population is infected with Mycobacterium tuberculosis, the organism that causes TB disease. Infection precedes the development of TB disease, sometimes by decades, and is clinically latent. Only about ten percent of infected people with functioning immune systems will develop active, symptomatic TB disease in their lifetimes. People whose immune systems are impaired from conditions like malnutrition and especially HIV infection are at particular risk of, and from, active TB disease. Persons living with HIV are 20-30 times more likely than people without HIV to develop TB disease, and when they do, they are much more likely to die. Your focus on this particular alignment of HIV and TB in Southern Africa is timely and critical for both diseases. In Africa, the prevalence of TB surged dramatically through the 1990s, driven by the HIV epidemic (see graphic).



Churchyard et al, "Tuberculosis control in South Africa: successes, challenges and recommendations." *South African Medical Journal*; 2014

In Southern Africa, the two diseases are so entwined that they are best considered as a syndemic – synergistically interacting epidemics, each worsening the other. In some communities in Africa with high burdens of HIV, rates of TB are literally hundreds of times higher than they are in the United States.

In 2016 alone, an estimated 2.5 million people in Africa developed TB disease, 30 percent of whom were HIV infected, resulting in an estimated 764,000 new cases of TB among persons living with HIV. TB is also a relentless killer of persons with HIV; it is the leading cause of hospitalization, and far and away the leading cause of death, responsible for approximately 40 percent of deaths in people with HIV. In Africa in 2016, there were almost 417,000 TB deaths, 320,000 of which were in persons with HIV. HIV patients are more likely to have extra-pulmonary TB, which is often harder to diagnose, and more likely to develop resistance to TB drugs, which makes TB extremely difficult to treat. The TB case fatality ratio is approximately 20 percent in most African countries – many times higher than in Europe and the United States. This is particularly concerning since we have the tools we need to cure and prevent TB – which means that those deaths arguably could have been avoided.

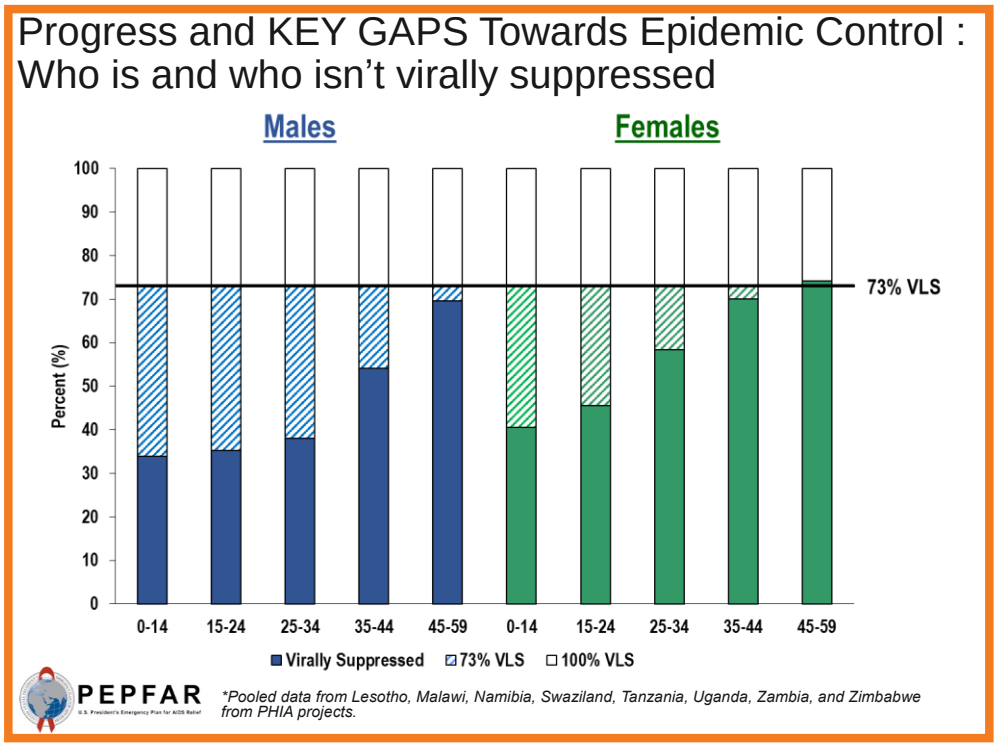
The persistent incidence and mortality of TB disease highlights two things: that TB remains an urgent public health concern in Africa and that we haven't yet done enough. Our goal is to provide the best care possible for our patients living with HIV and we are focused in three areas: (1) ensuring all TB cases are tested for HIV and treated for both infections, (2) preventing TB from developing in our HIV-infected clients by ensuring they are treated for HIV before their immune system deteriorates, and (3) screening our HIV infected clients for TB and

curing them when they are diagnosed or ensuring that they are given a course of TB preventive therapy. These efforts will interrupt transmission, lower TB prevalence, and help end this epidemic. In regions of the world where TB and HIV are tied together, HIV programs play a pivotal role in implementing the strategy to reduce TB through these focused interventions. As I will discuss, PEPFAR has committed to addressing TB in Africa by dramatically increasing HIV/TB investments and activities over the past decade and more recently by aggressively scaling up antiretroviral therapy for all persons living with HIV and accelerating the roll-out of TB preventive therapy.

Since 2005, PEPFAR has invested over 1.5 billion dollars on TB/HIV programming, and as a result, PEPFAR-supported countries around the world have made substantial gains in TB control. So let's review our progress. In focus area (1), testing all TB patients for HIV and ensuring rapid initiation of antiretroviral therapy for those that test positive, we are doing well. This intervention dramatically lowers the risk of death and has been a focus of PEPFAR for several years. In PEPFAR-supported countries in the second quarter of FY 2018, the proportion of TB patients with documented HIV status was approximately 95 percent, and the proportion of those with HIV infection who were started on ART exceeded 95 percent.

In focus area (2), ensuring everyone is begun on antiretroviral treatment immediately upon diagnosis to prevent the destruction of their immune system and prevent opportunistic infections including TB, we have not done as well – and this has been a core focus of the program over the past 2 years. While finding and curing TB in our patients is a critical strategy, preventing TB from developing in the first place is the ultimate goal. Providing antiretroviral therapy to all HIV-infected patients before impairment of their immune systems is the single most impactful intervention possible: antiretroviral therapy for those that are HIV infected bolsters the immune system and reduces the risk of developing TB disease by about 65 percent, and it reduces mortality in those who already have the disease. We have seen that Option B+ – antiretroviral therapy for expectant mothers – when offered to all pregnant women, regardless of CD4 cell count, dramatically reduced the risk of TB reactivation and death in women. Clinical trial and modeled data strongly suggest that wide-scale implementation of antiretroviral therapy will sharply reduce TB incidence and transmission in communities with high burdens of both diseases. Early antiretroviral therapy also protects communities by decreasing both HIV and TB transmission within those communities. By lowering the number of hospitalizations and preventing deaths, we are preserving the integrity and economic capacity of families and communities.

We constantly seek more accurate data, at national and sub-national levels, to better track our progress and more precisely identify and address the key gaps and obstacles. We have conducted comprehensive community-level impact surveys (PHIAS) to better understand the gaps in achieving our goals, as demonstrated in this graphic below:



We are missing HIV-positive individuals among males 0-34 years old and females 0-24 – these are mostly "healthy" individuals infected with HIV, but the virus is quietly destroying their immune system and if we don't find and treat them now, early in their disease, they will present later, sick with opportunistic infections, including TB. This is a core focus of the PEPFAR program; if we meet this challenge, stable health systems in Africa and health-seeking behaviors of communities will follow. Such systems and behaviors are needed to combat all the non-communicable diseases and ensure early identification of new infectious diseases and zoonotic events (critical for the global health security agenda) will be there.

Scaling up antiretroviral therapy is the cornerstone of PEPFAR's TB/HIV efforts, and for the past two years, we have been insisting that programs start antiretroviral therapy in all people living with HIV (PLHIV) as soon as possible after confirmation of HIV status, regardless of CD4 cell count. This Test and Start policy is now the standard of care, and we are aggressively pursuing implementation of this policy and practice in all countries where we work.

We are seeing the effects of the scale-up. Rates of TB increased starkly across Africa after HIV exploded in the 1990s; we are now seeing the reverse of this trend: the World Health Organization has reported falling TB incidence as antiretroviral therapy is expanded where there is a high dual burden, and published data from Eswatini, Kenya, and Malawi clearly show decreases in new TB cases in the areas where HIV scale-up has been most effective. The effect of antiretroviral therapy on mortality is equally evident: UNAIDS has reported that AIDS-related deaths have fallen by 48 percent since the peak in 2005, and deaths specifically attributed to TB among people living with HIV fell by 33 percent. These effects will be amplified as we further scale up antiretroviral therapy to all PLHIV. And this success actually comes with a cost-saving: modeling data from Botswana show that in addition to preventing

tens of thousands of TB cases, antiretroviral therapy given to all PLHIV will save tens of millions of dollars in TB treatment costs over the next 15 years.

In order to accommodate the increase in the number of patients who are being treated with antiretroviral therapy as a result of Test and Start, we are decongesting the healthcare facilities by spacing out follow-up appointments for the vast majority of PLHIV who are doing well and shifting monitoring of adherence and symptoms to community health workers. This will not only free up clinic appointments for those that are newly registering, it will also develop healthcare infrastructure in the communities where TB and HIV patients live, facilitating treatment adherence and diagnostic evaluation of those with symptoms and those who were exposed to either disease.

The third area of focus is the early diagnosis of TB in persons with HIV and increasing access of TB preventive therapy. By emphasizing routine screening for the symptoms of TB disease in all PLHIV at every visit to a PEPFAR-supported facility, we are able to find TB disease early and refer directly for diagnostic workup and treatment, key to preventing drug resistance. Our recent data show that 76 percent of our patients were screened for TB at their last visit. We remain focused on improving the frequency and quality of TB screening and are collecting site-level data to focus our interventions.

We are using sensitive diagnostic technology followed by effective treatment to save more lives and lower TB transmission. The GeneXpert platform is a cartridge-based diagnostic tool that uses molecular technology to diagnose TB disease. It doesn't require a laboratory setting, and can be placed at or near the point of care. It is much more sensitive than traditional diagnostic methods, and the newest cartridge is as sensitive as the best laboratory-based tests. In 2012, PEPFAR partnered with USAID and the Bill and Melinda Gates Foundation to reduce the cost of each test from 17 to 10 dollars, and has directly funded the purchase of more than 500 GeneXpert machines in over 20 countries and well over 100,000 cartridges. The GeneXpert platform can now be leveraged to document and monitor HIV viral load, which is especially important and lifesaving for early infant diagnosis, amplifying the effect of this considerable investment. PEPFAR continues to play a critical role in providing technical assistance to ensure that this platform is efficiently scaled up in a coordinated manner.

PEPFAR is also making treatment more accessible by pushing to integrate clinical care for TB and HIV. In the countries where we work, TB and HIV are often separate programs with separate clinic systems that are frequently not co-located. This means that historically, patients with HIV and TB disease needed to engage two different and often uncoordinated care and treatment systems. As recommended by the World Health Organization, PEPFAR is integrating TB/HIV care by providing care for both diseases in one clinic. We are building capacity in partner governments through effective policy change and focused training, which will allow treatment of HIV in TB clinics, greatly diminishing the burden put on patients and promoting adherence and retention in care.

The risk of TB disease and its attendant mortality can be further reduced by adding TB preventive therapy to antiretroviral therapy. This is a key intervention. The combination of TB

preventative therapty and antiretroviral therapy has been shown to reduce the risk of TB disease by almost 95 percent, and TB preventative therapy has been shown to reduce mortality in PLHIV by 37 percent, independent of antiretroviral therapy and CD4 cell count.

If immediate antiretroviral therapy is the cornerstone of PEPFAR's TB/HIV efforts, then TB infection control and TB preventive therapy are the capstones. We are actively monitoring all PEPFAR-supported facilities to ensure that they each have and are compliant with policies for preventive therapy and infection control. TB preventive therapy for people living with HIV has been a World Health Organization recommendation for years, but with the newer global targets and the ambition to end the TB epidemic, it has become a more prominent component of TB control efforts. PEPFAR has always recommended TB preventive therapy for our patients, but in the past, most countries did not have a specific policy, and we did not closely follow how well preventive therapy programs were implemented. That has changed. Almost all of the countries in which we work now have national guidelines recommending preventive therapy for PLHIV.

In 2016, PEPFAR revised the suite of TB indicators and now mandates reporting on initiation and completion of TB preventive therapy as well as TB screening and initiation of TB therapy in those diagnosed with the disease. These additions were part of a deliberate attempt to drive programming and encourage fully integrated TB/HIV care in PEPFAR countries. In the past year, we have seen a remarkable increase in PEPFAR targets for TB preventive therapy: despite limited advanced planning and no requirements for targets for FY 2018, 21 countries have initiated or expanded TB preventive therapy programming, and the targets for FY 2019 are substantially higher in almost every country.

A number of markedly successful programs have been introduced: the Democratic Republic of Congo, Malawi, Mozambique, and South Africa have all had steady progress incorporating TB preventive therapy into routine care with approaches that are well documented and replicable. More notably, Kenya had tremendous rapid success rolling out TB preventive therapy through a well-designed, carefully crafted collaboration between the country's national TB and HIV programs. Their approach resulted in an increase in the number of PLHIV who initiated TB preventive therapy from a total of 10,000 PLHIV in 2014 to more than 880,000 by this year, with treatment completion rates approximating 90 percent for most implementing partners. We are promoting TB preventive therapy in all of the countries where PEPFAR is implementing programs and will continue to monitor and expand to ensure that all of our patients have been treated.

With correct application of sufficient resources, the fight against TB/HIV is a battle we can win. We must make a commitment to finding and treating all persons with HIV before they have immune impairment and get clinically sick, and we must find and effectively treat all persons with TB disease – we simply cannot afford not to. We need to facilitate effective treatment to unburden our patients. Care should be integrated and mainstreamed, and adherence should be promoted in ways that do not require patients to report for observation. Inadequate or

erratic treatment has led to the development of drug-resistant disease, which now threatens to undermine the progress that is being achieved.

Once it develops, drug-resistant TB spreads exactly the same way as drug-susceptible TB: to anyone who shares air with a sick patient. It is expensive and extremely difficult to treat patients with drug-resistant TB on a large scale – but the financial and public health consequences of our failure to do so will be devastating. It is an imminent and growing threat to public health. Recent reports suggest that by 2050, the consequences of drug-resistant microbes, most importantly multi-drug-resistant TB, could have a more catastrophic impact on global financial mechanisms than the 2008 housing crisis.

But such a crisis can be avoided. All the interventions I've mentioned are proven concepts – none are controversial or questionable, they simply need to be fully scaled. Effective scale-up of these interventions will allow us to gain control of the TB epidemic in high HIV settings. The goal of PEPFAR is to save lives and, by doing so, revive communities afflicted with a high burden of HIV. By greatly expanding antiretroviral and TB preventive therapy, while diminishing the burdens placed on patients, we are cutting transmission of both diseases and getting ever closer to realizing a world free of HIV and TB. The continued focus on effective and innovative TB/HIV programming will help consolidate those achievements and further global efforts to end the TB pandemic.

Chairman Smith, Ranking Member Bass, and other distinguished members of this Subcommittee, thank you for the opportunity to appear before you today. We are profoundly grateful for the ongoing support and engagement of the House Foreign Affairs Committee and this Subcommittee for PEPFAR's work.

Thank you. I look forward to your questions.