

# Tuberculosis Preventive Therapy among Persons Living with HIV, Uganda, 2016–2022

*[Announcer] This program is presented by the Centers for Disease Control and Prevention.*

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Deus Lukoye, an epidemiologist at CDC who is currently based in Uganda. We'll be discussing tuberculosis preventive therapy among people living with HIV in Uganda.

Welcome, Dr. Lukoye.

[Deus Lukoye] Thank you very much, Sarah.

[Sarah Gregory] Tuberculosis is still a deadly disease globally. How is it different though from pneumonia?

[Deus Lukoye] Yes, tuberculosis and pneumonia are both lung infections, but they are caused by different germs. Tuberculosis, which is commonly abbreviated as TB, is a chronic disease and is caused by a germ called *Mycobacterium tuberculosis*. It is ranked among one of the top infectious diseases in the world, and before COVID-19, tuberculosis was the topmost infectious killer in the world. And among the people living with HIV, tuberculosis is still ranked the worst killer in that population. In 2021 alone, about 1.6 million people around the world, including 187,000 people living with HIV, lost their lives due to TB. And when you translate that one on a daily loss, it's turned into 4,300 lives people lost on a daily basis. And actually around 10 million people across the world develop TB disease every year.

On the other hand, first we'll talk about pneumonia. Pneumonia is caused by a number of different types of germs, and this would include bacteria, viruses, and fungi, unlike TB which is caused by one germ. In terms of the presentation, pneumonia tends to differ a bit. Its presentation tends to be very dramatic. Symptoms seem to develop very fast, compared to the person with TB who may have symptoms over a long period of time, which has got public health implications.

[Sarah Gregory] It is very contagious. How is it spread to people?

[Deus Lukoye] Tuberculosis is actually a very contagious disease, and it is airborne, airborne meaning that any act that causes my breathing out (or someone's breathing out), as long as they do have tuberculosis, will cause TB infection to happen to another person. And even if one stayed or sat for a long time close to persons, and that person has TB, it is possible that one can transmit TB to the other person. And basically, TB doesn't know any borders. TB can be transmitted to any person, anywhere. And it is estimated that at least one in every three people in the world has got tuberculosis. That doesn't mean that they have got TB disease, but they have got the TB germ in their body, which at any time when the opportunity comes can become active and someone develops TB symptoms, putting close persons at risk of getting infected with TB, a person who you work, who you see maybe at the office, someone you are really close with most of the time. And at CDC, we know this very well and it has guided our control efforts of TB locally and globally.

[Sarah Gregory] When a person has active TB, how is it treated?

[Deus Lukoye] The good news is that TB is actually treatable and curable, unlike the closely associated disease that affects the same population as HIV. And there are medications which are standard or treatments which are standard that treat tuberculosis and some that completely cure

you of the disease. And usually, the person is treated with four to six antibiotics for a period of four to six months and will get completely cured of their disease. However, TB also has types. There is a type which is not sensitive to the commonest drugs that we know we use for the commonest TB that we have. That TB is called multidrug-resistant TB, sometimes abbreviated as MDR-TB.

Now, this TB is treated for a longer period of time, it is more difficult to cure, and it is treated with more drugs or more medicine than the drug sensitive TB. Just recently, it was treated for a period of two years, but of late, there are some new drug formulations that have come on the market that can be used to treat MDR-TB for a period of around nine months. But still, the cure rate remains low. You may find that for MDR-TB, out of the 10 people you treat, you might only cure one. And in Uganda here, about 500 patients of MDR-TB are diagnosed annually.

[Sarah Gregory] What happens if it isn't treated or an attempt at treatment?

[Deus Lukoye] That is a very good question, Sarah, and if someone is not treated, TB can become very severe and can lead to death. And because TB is airborne, the chances are many that if this person is not treated, they are going to keep transmitting. And due to the chronic nature of the illness (of the disease), this person could transmit the disease for a long time, among the people close by. Like I mentioned earlier, a person with TB can infect more than three people every year. And if we translate this one into the number of people who get...who have got TB at any one point in time in the world, the number of people who get TB from these people is really very big.

[Sarah Gregory] How many people each year are affected by a combination of TB and HIV in Uganda?

[Deus Lukoye] It is estimated that 30,000 people living with HIV (of the total people living with HIV) in Uganda gets TB every year. And just to take you slightly back into some statistics of HIV burden in this country, we have around 1.4 million people who are positive for HIV. And out of these, about 30,000 of them develop active TB every year.

[Sarah Gregory] And who is most at risk for contracting TB?

[Deus Lukoye] Yes, that's another good question. Everyone is actually at risk of contracting TB. However, the most vulnerable to get active disease or active TB when infected is anyone whose immunity has been compromised or has been reduced by one of the following conditions, that is commonly, now as we talk, which is HIV. But there are other immune-compromising conditions, for example, malnutrition. There are other debilitating conditions, for example, diabetes and cancer. They can also predispose someone to developing...to getting infected, but also when they get infected, to quickly become active with TB symptoms and TB disease.

[Sarah Gregory] I've heard that animals can get TB. Can they spread it to people? And can people give it to animals?

[Deus Lukoye] Yes. What we know so far is that animals can spread TB to people. And to be very specific, cows can spread TB to...these are cows which can spread TB to human beings through their products (especially dairy products). And this TB commonly affects the parts in the stomach from where it is transmitted to other parts of the body.

[Sarah Gregory] So tell us why people with HIV are more likely than others to get sick with TB. Explain to us how HIV works in the body.

[Deus Lukoye] So like I just briefly mentioned, due to their weakened immune response or immune system, people with HIV are more likely to become infected with TB and are more likely to develop TB disease when they get infected with a TB germ. Actually, research has showed that compared to the people who don't have HIV, a person with HIV is, over such time, more likely to become...to get TB disease when they get infected compared to someone who does not have HIV completely. So cognizant of this, with support from US President's Plan for AIDS Relief (which we call "PEPFAR"), CDC is tackling both HIV and TB epidemics in this country to sustain the impact. And we know if we make progress and get control of these conditions, we should be able to make progress against the others. For example, if we stop TB among people living with HIV, from a public health standpoint, it means that we should have less people transmitting TB in their community. And therefore, any person out there will be at less risk of coming in contact with a person who has got TB. And on the other hand, if we treat TB in the general population, we should have less HIV patients dying of TB because less HIV patients would be getting in contact with tuberculosis.

[Sarah Gregory] Your article is about TB preventive therapy among people living with HIV in Uganda. Let's start with what is the TB preventive therapy.

[Deus Lukoye] TB preventive therapy is a treatment that is given to individuals to reduce the risk of developing active TB disease if they are infected with TB. And WHO (which is the World Health Organization) recommends TB preventive therapy for all people living with HIV and household contacts at high risk and others with a weakened immune response, for example, we know children under the age of five years and people with other debilitating conditions. And for people living with HIV, research has shown that TB reduces the risk of...TPT reduces the risk of TB by about 60%. And if people do not develop active TB disease, it means they will not transmit TB to other people, and this makes TPT or TB preventive therapy a very key intervention for TB control.

And to compare TB treatment or treatment of active TB disease, which takes about four drugs, TB preventive therapy is simple. Sometimes there's only one drug that is taken for six months, and sometimes it's combination of only two drugs that one can take for a period of one or two months, depending...or three months, depending on the regimen someone has been prescribed. So at CDC, we at the forefront of efforts to accelerate the use of TPT and rapid provision of this life-saving preventive therapy for millions of people who are in need. And since 2018, CDC, as part of PEPFAR, has supported the initiation for over 11 million people living with HIV in PEPFAR-supported countries to access preventive therapy, including children.

[Sarah Gregory] And why did you focus on Uganda, specifically?

[Deus Lukoye] I focused on Uganda...first of all, Uganda is the country I come from, and Uganda is a low-income, high burden TB/HIV country, as I have described it. And Uganda has been very successful at providing TB preventive therapy in the last six years as recommended by the World Health Organization. By March 2022, over 95% of people living with HIV in care in Uganda were started on TB preventive therapy. And of these, about 89% of them had completed the six-month treatment. And I thought sharing this experience, including the lessons and the challenges we had in this process, was worth sharing with the world with, for example, countries who have not been successful in implementing this program could borrow lessons that Uganda can share with them.

[Sarah Gregory] Why don't you take a moment now to briefly tell us about your study—how you went about it and what you were looking for.

[Deus Lukoye] We know TB and HIV public health programs systematically collect data on their patients and the interventions and the services they receive, their outcome, and their impact. This programmatic data is what we analyze in our investigation to determine the impact or success of TB preventive therapy since 2016 to 2022. We identified people living with HIV who started and completed TPT (completed preventive therapy) from 2016 to 2022. And what we did next was to calculate the coverage which looked at how many eligible people or how many people living with HIV had started tuberculosis preventive therapy, and how many people had actually completed a course of TB preventive therapy.

We also looked at trends of TPT over time in terms of age, sex, and the region...in terms of coverage, we looked at age, sex, and the region where this intervention had been used. And finally, we looked at the TB disease itself. When you are giving an intervention like this one, you are very eager to know, is my intervention having an impact? And our impact in this intervention was to see whether we would find a decline of TB among people living with HIV in the period 2016 through 2022.

[Sarah Gregory] How did you scale up in Uganda to do the TPT coverage?

[Deus Lukoye] Yes. We were able to scale up TB prevention therapy in Uganda with...after receiving support from PEPFAR, CDC, and other partners. And from 2018 to 2022, this was part of PEPFAR supporting the initiation of TB preventive therapy across the world to about 11 million people, like I mentioned previously, including the children.

And the scale-up of TPT coverage among people living with HIV in Uganda presented many challenges which we had to overcome in order to make progress. So when TPT medicine was made available in Uganda, we noticed that the demand was not there for this medicine. Both healthcare workers and the patients were not interested to have this program implemented. Patients were not asking for it (for TB preventive therapy), much as the healthcare workers, who were not also prescribing these medications.

So we decided to do something about this to ensure that people living with HIV benefit from this very important intervention. So our priority was to identify and address challenges at the different levels of the health system, and this is what we did. We, first of all, created awareness and rapidly scaled up TB preventive therapy in a campaign, which we called the 100-day TPT campaign we implemented in 2019. We did this from July to October 2019. And during this period, the country took ownership of TB preventive therapy and implemented the following: one, there was full integration of TB preventive therapy into HIV and TB programs. Previously, these were programs we were working with separately in prevention of TB among people with HIV. In addition, the country mobilized resources through partners to ensure availability of medicines. And because we knew there were knowledge gaps out there where the beneficiaries were, there was a need for disseminating information, so there was dissemination of materials that educated and informed both patients and healthcare workers in provision of TB preventive therapy, eligibility, as well as the possible adverse events.

In addition, in order to create demand for TB preventive therapy, we also leveraged the civil society (these are people who speak the same language with the patients) so that they could easily understand each other to create the demand among people living with HIV who sought

these services in the facilities. But to monitor the program and to monitor whether we are meeting our target, we developed a nationwide TPT data capture dashboard, where we monitored weekly performance in terms of TPT enrollment at the health facility level, and it provided timely feedback where we saw suboptimal performance. During the campaign, we prioritized...we didn't go everywhere, but we made priorities over the high-volume facilities that contributed 80% of all the people living with HIV in the country. That's how we did it.

[Sarah Gregory] Let's back up a little bit. Who, living with HIV, is most likely to get TB? Men, women, young, old?

[Deus Lukoye] Regardless of...as long as someone has HIV, regardless of sex, age, all have equal risk of developing active disease when they get exposed. Therefore, it is important to ensure that all people living with HIV have access to TB preventive therapy, and we also need to ensure that when they initiate this treatment, they go ahead and they complete it to prevent them from developing active TB disease.

[Sarah Gregory] So along those same lines, was there a certain age or gender that was more likely to seek the TPT?

[Deus Lukoye] Yes, Sarah, this is a very good question which recognizes the inequalities which often exist in HIV and TB epidemics, where we sometimes find women and children have less ability to access services, and yet they bear the greatest burden of disease. So in the case of TB preventive therapy, however, our data showed that demand for these services was even across all age groups. It is important to note, however that we have... at CDC, we have the authority to address the gaps in terms of providing services, addressing the inequities or the inequalities in patient access or service access by patients, including TB preventive therapy in this context.

[Sarah Gregory] Ultimately, were Uganda's TPT scale-up efforts successful? And if so, what factors contributed to this success?

[Deus Lukoye] Yes, I'm happy to mention or to say that Uganda's TPT scale-up was tremendously successful, and this was made possible with support from partners, including PEPFAR and CDC. The majority of persons with HIV receiving antiretroviral therapy—those are patients within the program—and over 90% of those who started had completed TB preventive therapy by March 2022. And through CDC's partnership with the Ministry of Health, we had a...CDC's partnership with the Ministry of Health and other partners was a very big, driving force towards this achievement. And what I'm saying is that without a partnership or without people or without partners coming together, it was not possible to mobilize resources for us to be able to realize that kind of tremendous and fast progress of the TPT program that had failed to take off for the long period since PEPFAR began supporting the country in 2003.

[Sarah Gregory] Did you find anything else you want to tell us about and was there anything surprising?

[Deus Lukoye] Yes, there were some reports of adverse drug reactions, which I can say is not very surprising because in any public health intervention, you would expect some of these adverse events to come through. We have seen this in immunization programs in the country, and in other programs which are widely scaled up, especially in a rapid mode. However, we also attribute it to having sensitized the messages that there could be a possibility of some of these adverse events, and also having built the capacity for the country to be able (or for the facilities

to be able) to report whenever these adverse events happened. However, there was capacity to manage them, and we did not realize any severe damage to the program.

[Sarah Gregory] Did the COVID pandemic impact the TPT coverage?

[Deus Lukoye] Yeah, this is actually very relevant, because a part of our implementation period that we are reporting was covered by COVID. But we are proud to report that the impact of COVID-19 on TPT coverage was not significant. First, by the time COVID-19 had reached Uganda, most people living with HIV had already received a course of TB preventive therapy. But most importantly, the country quickly developed interim guidance to ensure that TB and HIV activities would continue, even during the COVID-19 pandemic. For example, patients were able to receive their TPT medication at the same time as their HIV medicine (and we called this one alignment of TPT and ART treatment) to avoid any unnecessary trips to the clinic.

Secondly, they were also able to receive their medications at home, delivered by a community resource person that we had during that period, to make sure that there was matching with the standards during that period, which required less visits to the facilities, in the spirit of social distancing and other prevention measures against COVID-19.

[Sarah Gregory] You mentioned some challenges. Were there any other challenges to the success of the program?

[Deus Lukoye] Yes. Our data indicates that much as we have implemented the TB preventive therapy widely, we have yet to see...I don't know whether it's a challenge, but we have yet to see a significant decline of our TB burden among people living with HIV. But this is not surprising, because during the course of implementing TB preventive therapy, there is dedicated screening of everyone who is living with HIV for TB all the time, because as one of the requirements before you start TB preventive therapy, you must confirm that they do not have TB. So in the process, you will be able to find those who have got TB, and those contribute to the other category that will develop TB among people with HIV to add on the number that maybe could have been previously been missed. But still, during the course of that period, there has been a coincidental improvement in TB diagnostic capacity in the country, and this one might also have contributed to finding more TB patients than previously (especially among this population), but we are still hopeful that in the near future we will be seeing a decline of TB among the HIV patients in this country.

[Sarah Gregory] What can other countries that are looking to reduce this burden of TB among people living with HIV learn from all of this?

[Deus Lukoye] Yes, we can share so many things which other countries could actually learn from us. But I can just share these things. One, if we are going to stop TB among people living with HIV in the world, we need to find all the people living with HIV and enroll them on HIV treatment early. Why? Because this will improve their health overall and ensure their ability to fight TB disease. When people take antiretroviral therapy or HIV treatment, their immunity does not decline or does not substantially reduce to a level that can result into people developing active TB disease.

Secondly, all the patients who have been confirmed with HIV should be enrolled in TB preventive therapy as long as they are eligible. And we should not only stop initiating them, but we need to ensure that they go ahead and complete this treatment to ensure effectiveness. And lastly, we need to find and treat all TB patients in their communities because these are the

sources of the infection. If we are able to treat all of them, it means that even if you have got HIV patients out there in the community whose immunity is compromised, they will not come across the source of the infection, and that is the patient with active TB disease. So if you do these three things, we should be able to see a significant decline in TB among HIV patients.

[Sarah Gregory] So again, along those same lines, how would you like other programs to implement what worked in Uganda? What do you think is a good starting point?

[Deus Lukoye] Yes, that is another good question and very practical. Each country is different, we have different contexts. But there are some lessons we can share that other countries can borrow from. It is important that programs work with the communities to develop effective plans for addressing these epidemics in their communities. These plans can include, first of all, a very strong collaboration between TB and HIV programs at the national level because these are two related conditions, and if these programs don't work closely, some of these interventions get compromised. So a very good collaboration between the HIV and TB programs will ensure that there is no gap in regards to implementation of TB preventive therapy.

However, it is also important to create demand among the beneficiaries. As long as you have not convinced the people who would benefit from this treatment, it will be difficult for your program to succeed because you can still have your medications, but as long as they do not take it up, it may not be helpful to them. But lastly, we also need to have the capacity to monitor programs, and this can be done through a very good data capture system, because you need to know how many patients you are initiating, how many patients are completing, what's the impact of your program in general of TPT provision among people living with HIV. So if you do not have the data capture system (the data capture platform) to help you monitor, you are not able to identify where the gaps are, and you cannot have this done in a timely manner. So I think if countries picked these, probably there could be some progress in their implementation of TB preventive therapy among people living with HIV.

[Sarah Gregory] Tell us about your job and what you do and how you became involved in this study.

[Deus Lukoye] I am a medical doctor and a public health specialist. I hold a PhD in epidemiology, and I work with the Centers for Disease Control and Prevention in Uganda as a public health specialist. My primary focus is TB elimination, specifically in this country, because this is where I have some level of control. And my job is to provide technical support to the Uganda Ministry of Health and implementing partners towards delivery of high-quality patient centered TB/HIV services. So by virtue of my position, I was part of the team that led the TPT scale-up in this country, and I was therefore interested in monitoring the progress that we were making and evaluating whether our progress is making an impact. And perhaps most importantly, using the data to improve our efforts to accelerate the progress of TPT implementation among the HIV patients.

[Sarah Gregory] Thank you so much for taking the time to talk with me today, Dr. Lukoye.

[Deus Lukoye] Thank you, Sarah. Thank you for hosting me.

[Sarah Gregory] And thanks for joining me out there. You can read the March 2023 article, Tuberculosis Preventive Therapy among Persons Living with HIV, Uganda, 2016–2022, online at [cdc.gov/eid](https://www.cdc.gov/eid).

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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