

PEPFAR-Supported HIV and TB Laboratory Networks Significantly Contributed to COVID-19 Testing Preparedness in 16 Low- and Middle-Income Countries

[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. Erin Rottinghaus Romano, a microbiologist at CDC in Atlanta. We'll be discussing the contribution of PEPFAR-Supported HIV and TB molecular diagnostic networks to COVID-19 testing preparedness in 16 countries.

Welcome, Dr. Rottinghaus Romano.

[Erin Rottinghaus Romano] Thank you, Sarah. It's great to be here.

[Sarah Gregory] For those who aren't familiar with PEPFAR, what is PEPFAR and how does CDC implement it?

[Erin Rottinghaus Romano] PEPFAR is the United States President's Emergency Plan for AIDS Relief. It's quite a mouthful, that's why we abbreviate it and call it PEPFAR. It was established in 2003 by the White House with bipartisan support. So PEPFAR has invested over 100 billion dollars and supported over 50 countries since 2003 in their ongoing battle with the HIV/AIDS epidemic. This includes 22 countries with ongoing HIV and TB epidemics. So while it is focused primarily on HIV, there is a TB component for PEPFAR. And it's important to connect these two diseases, as TB is one of the leading causes of death in those living with HIV across the world. So I feel like this is a general description. Maybe if I were to describe PEPFAR in a nutshell, I would say that PEPFAR provides support for the prevention, diagnosis, treatment, and care of people living with or at risk for acquiring HIV, as well as the health systems that are necessary to support those components of the HIV program.

One unique feature of PEPFAR is that it leverages a whole government approach. So it's managed by the US Department of State's Office of the Global AIDS Coordinator and implemented by seven other US government departments and agencies. So CDC is one of these implementing agencies in PEPFAR, and this is how it's implemented in CDC. So at CDC, it's primarily implemented through the Division of Global HIV and TB. And this division has experts working on the frontlines in more than 45 countries and regions around the globe as well as at headquarters, which has a goal of bringing an end to the dual epidemics of HIV and TB worldwide. Maybe a little bit more specific to this paper, DGHT through PEPFAR has routinely and continues to routinely support laboratory networks in PEPFAR-supported countries. So we do this to promote patient access to quality clinical testing services and associated care.

[Sarah Gregory] Your EID study looked at the role that PEPFAR laboratory networks played during the COVID-19 pandemic. What did you find?

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[Erin Rottinghaus Romano] I think one clarification I want to make for all of the listeners is with the term 'PEPFAR network' and 'PEPFAR-supported network'. The way PEPFAR works is we work as a partner to support host countries' HIV and TB responses. And so, throughout the manuscript, we use the term 'PEPFAR-supported laboratory network' or 'PEPFAR-supported laboratories' instead of PEPFAR laboratories, and I'm hoping that this helps to communicate that PEPFAR doesn't have its own separate laboratory system or laboratory setup in these countries that we support, and instead we're supporting the National Laboratory Network or labs within the host government country. I do just want to make that clarification to make sure that the listeners understand how PEPFAR provides support for the countries in terms of labs.

So to get back to your question, what did we find out? Briefly, we found out that country programs in many countries used PEPFAR-supported laboratory resources for SARS-CoV-2 testing during the COVID-19 pandemic. So I feel like that's my one-sentence answer. I'd like to provide a little bit more detail, though. I do want to provide some context, which I think is important to truly understand the results of this study. First, I want to acknowledge that 16 countries participated in this study. So all of the results that I'm speaking about today from the study are representative of these 16 countries—15 of them were from sub-Saharan Africa plus the Dominican Republic. And then, we also looked at different PEPFAR resources and how they were utilized. And we looked at, I would say, three broad categories of PEPFAR resources. We looked at the use of centralized HIV molecular laboratory and associated resources, and how they were used for SARS-CoV-2 testing. We looked at the use of decentralized HIV and TB molecular laboratories and resources and how they were used, as well as the use of HIV laboratory information systems.

So I do want to go through and provide a few definitions here that, again, I think will hopefully clarify any acronyms I may use later or any language I use later. So when we're talking about centralized HIV molecular laboratories, these are generally a higher-throughput laboratory—so they can test a lot of specimens because they have big instruments, and this is usually housed in a fairly big laboratory space. So that's what we mean by centralized laboratories. When we're talking about decentralized, we're talking about (in this particular paper) laboratories that utilized a specific instrument, which was the Cepheid GeneXpert instrument. So this instrument can have different capacities as of the modular instruments, but in general, it has lower capacity to test specimens. So they can test fewer specimens compared to the centralized instrumentation. Both centralized and decentralized laboratories and instruments played important roles in the COVID-19 pandemic, and this is why we looked at them both together and separately in the paper.

A few clarifications, again, that I also want to make around what we're calling an 'HIV molecular laboratory'. There are two laboratories that fit into this category, and are laboratories that perform HIV viral load testing, as well as HIV early infant diagnosis testing. So an HIV viral load test is a test that we do to see the amount of HIV virus in the blood of an HIV-infected patient. So this is used to monitor patients who are on treatment, with the goal of if you're on HIV treatment, ideally you will have undetectable levels of the virus in your blood, and that would be a good sign, right? It means the treatment is working. For HIV early infant diagnosis, this is also a molecular test, and it is used to diagnose infants who were born to HIV-infected mothers. I may refer to that as EID, so when I say 'EID', it's not referring to *Emerging Infectious Diseases*, it's referring to early infant diagnosis.

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I think one final clarification I'll make before going into and truly answering your question is about the associated resources. We looked at both the use of the actual physical laboratory space and instrumentation, but we also looked at the use of additional resources that were already in place because of PEPFAR. So this includes maybe staff (so, the people performing the test); it can include standard operating procedures that were already developed and in place because of the HIV work; and it can include training materials and sample transport pathways and mechanisms of moving samples from a clinic to a lab. So when I talk about associated resources, that's what I'm referring to.

So to go back to answer your question, we found that countries used PEPFAR-supported resources for SARS-CoV-2 testing. All 16 countries reported using PEPFAR-supported centralized and decentralized laboratories or resources for SARS-CoV-2 testing. 11 reported using PEPFAR-supported laboratory information systems for SARS-CoV-2 testing—so, laboratory information systems are an electronic system that help laboratories manage specimens, and they also manage workflows in the laboratories. So these are important components to have, especially in laboratories that are running or testing a lot of specimens. We actually had a total of 109 PEPFAR-supported centralized molecular HIV laboratories reported as performing SARS-CoV-2 testing from the 16 countries; 138 decentralized PEPFAR-supported labs that reported performing SARS-CoV-2 testing in the labs in the 16 countries; and together these contributed to over 3.4 million SARS-CoV-2 tests performed during the one-year period that we looked at, and that period was from March of 2020 to April of 2021.

So with all of this, I do want to end just by saying the purpose of the paper was just to quantify which resources were used. There's really no good or bad use of PEPFAR resources. Country governments and ministries of health determined which resources were used for SARS-CoV-2 testing in their respected countries. They did this by assessing and balancing the testing needs for SARS-CoV-2 and additional tests...and additional existing diagnostic testing, such as HIV and TB. But obviously, there are a lot of other tests that also need to be performed, and they balanced this with the availability of reagents, the capacity of the labs to perform the necessary testing within an appropriate timeframe. Again, there's no good or bad use. We're simply just quantifying which of these laboratory resources chosen by the Ministry of Health to support SARS-CoV-2 testing were supported by PEPFAR.

[Sarah Gregory] Why is all of this important?

[Erin Rottinghaus Romano] I think it's important for many reasons. First, it's important for the PEPFAR program to review how our laboratory program was utilized during a non-HIV or TB emergency response. We think that these data demonstrate that PEPFAR-supported laboratory strengthening efforts in low- and middle-income countries (which are primarily what PEPFAR supports) are not only beneficial for HIV and TB-related programs and services but can also have a broader health benefit.

Additionally, this topic of multi-disease testing—which is what was happening, right? So the labs and the instruments were testing for SARS-CoV-2 as well as HIV, and additionally as well as TB in some cases—is becoming increasingly important, as a lot of these molecular platforms that are used for HIV and TB laboratory tests can perform many other tests (so, well beyond SARS-CoV-2 and HIV and TB testing). And this concept is called 'multiplexing' or 'multi-

disease testing'. And so, for us, we think that this study provides evidence that multi-disease testing on existing instrumentation can happen, and it can happen quickly when necessary.

And beyond just the instrumentation, this study showed that countries were using existing diagnostic networks. So a diagnostic network includes more than just instrumentation, it includes the laboratories; it includes the sample transport networks that are involved in transporting specimens to and from the lab. So the countries use these diagnostic networks in the PEPFAR-supported countries for SARS-CoV-2 testing, and it demonstrates the feasibility of what we call 'diagnostic network integration', which is the concept of integrating multiple diseases and specimen types into the diagnostic network to support countries' public health needs. And then lastly, we think this study helps to illustrate that many low- and middle-income countries have diagnostic laboratory networks in place that can adapt and respond to emerging threats. So COVID-19 is just a good example of this, and it was a good illustrative example of this. So those of us that work in these countries or with these countries (such as I do) know this well, that these laboratory networks are there and exist and are excellent examples of lab networks. But we think it's still important to study and share how systems, including lab networks, were used and adapted in the face of a pandemic with the scientific and public health communities.

[Sarah Gregory] So let's talk about the pandemic for a second, here. It seems that the time and resources invested to build PEPFAR laboratory networks was vitally important for countries during the pandemic. But did health officials have to pause the work for PEPFAR (helping to treat HIV patients), given the focus on COVID-19?

[Erin Rottinghaus Romano] This is a really great question. It's probably a little different for each country, and it's probably a little different for the timeframe that you would want to look at. So at this point, the pandemic has been going on for years. So it's probably different now from what it looks like when COVID-19 first hit.

So because of these, I'll speak more to the program as a whole, and we encourage countries to investigate exactly what their response looked like and also encourage countries to publish their unique experiences. But as far as the PEPFAR program, in March of 2020, PEPFAR released guidance and then updated this guidance weekly thereafter to guide our country teams on how to continue the life-saving services for the clients that we serve. And the importance of doing so while balancing the need for COVID-19 testing and support. So right from the very beginning, PEPFAR was coming out with guidance, telling countries (or guiding countries) on how to continue the services, how to adapt the services to the changing times and to lockdown measures to ensure that our clients were still being served, right, as it is critical that TB and HIV patients are still being diagnosed and treated. This manuscript focused on diagnostic testing and laboratory networks, so I'll focus my answer on this aspect of the PEPFAR program. I will say other manuscripts have and will touch on the impact of COVID-19 on HIV and TB treatment, so I encourage listeners to go and read through the details of this manuscript. I can say that just our programmatic data shows that the number of patients supported on HIV treatment increased during the COVID-19 pandemic. So we do know that that happened as a program.

As far as what we saw in the paper, we could not directly measure the impact of SARS-CoV-2 testing on established HIV and TB testing numbers in this study because our data only included testing numbers during the one-year period from March of 2020 until 2021. And it didn't include testing trends from before the pandemic. With that said, we did show that over 9.3 million HIV

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viral load EID and TB tests were performed in PEPFAR-supported labs during this period compared to a little over 3.4 million SARS-CoV-2 tests. So there certainly wasn't like a complete pause in testing during this one-year period. Our programmatic data also tells us that the number of patients with a documented HIV viral load test increased annually during the pandemic. With all of that said, we do acknowledge that there are reports in the literature citing decreased TB and HIV viral load testing coverage. A lot of this was attributed to national lockdowns and isolation practices which prevented patients from accessing services during the height of the pandemic. So if the patient can't access services or doesn't access services, the tests won't be ordered, blood won't be collected, and therefore won't be performed. And there also are reports of instruments and human resources being prioritized for COVID-19 testing in some countries in the literature.

Going back to what I was saying earlier, individual countries have different answers and it's critical for countries to assess how COVID-19 impacted the current testing and treatment services for all areas of health, and take the lessons learned from the experience to improve their systems and practices for the next pandemic.

[Sarah Gregory] How do you hope this information from your study will be used?

[Erin Rottinghaus Romano] So we hope that presenting these data collectively and on behalf of the country teams and ministries of health will help to highlight the strengths of public health laboratory systems in many low- and middle-income countries, and how a disease-specific program like PEPFAR can contribute to these important systems in the face of a pandemic. And we talked about before, our study showed that testing for multiple diseases on the same instruments and integrated diagnostic networks were feasible. And so, we hope that countries and disease programs not involved in this manuscript can see this as a proof of concept for an integrated diagnostic approach is feasible and recommended in that country. Furthermore, we hope that countries and disease programs involved in the study can take the lessons that they learned from implementing an integrated approach to diagnostic testing and apply this to further enhance and improve their laboratory network and their laboratory testing. And of course, we want them to share lessons learned with themselves, but as well as for other countries to use.

[Sarah Gregory] What do you think are the lessons learned for leveraging longstanding platforms such as PEPFAR for other emerging threats or pandemics?

[Erin Rottinghaus Romano] So as you mentioned or as you alluded to, PEPFAR has worked with ministries of health to strengthen laboratory systems in low- and middle-income countries for 20 years now. So we do this by supporting and providing technical assistance for laboratory quality and accreditation, specimen transport, human resources, supply chain, instrumentation, reagents that are necessary to perform the lab test, information systems, waste management and biosafety. So we're really covering the entire spectrum of a laboratory program and strengthening it. As mentioned before, historically this work has been focused on HIV and HIV-related laboratory testing and networks. As I also mentioned, these laboratories and systems are a part of the National Laboratory Network.

So one of the ways to leverage (or lessons learned from leveraging) a program such as PEPFAR, is that just as ministries of health did in response to COVID-19, they need to continue to monitor and understand their National Laboratory Network in terms of the infrastructure that's in place, the instrumentation that's in place, the testing capacity that they have, and where the capacity exists and where the additional capacity exists, as well as the testing demand. So the demand is

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the number of patients that need to receive a test and where that demand exists in the country and does it line up with your existing capacity and aiming to understand all of this in order to respond to...to be honest with you, their current threat as well as emerging threats or pandemics.

And this is actually not a new concept for PEPFAR. So we've been doing this actually for years, and even before the pandemic started, we've established and promoted a practice of assessing and optimizing diagnostic networks—so, optimizing meaning trying to make them more efficient so we can serve the patients that need them—and it has been a minimum program requirement for our country teams for several years, like I said, even before the COVID-19 pandemic. So what this means is that our teams are strongly encouraged to support ministries of health and understanding their network and monitoring it and improving efficiency and efficacy of the diagnostic network. It includes practices like disease integration that we saw happening during COVID-19 for both emerging and existing threats. So it's something we have been doing for a long time. It's something we encourage countries to continue to do in and outside of PEPFAR.

And then, one other important component—and it is sort of related to this diagnostic network optimization work and practice—is a process that we call 'stakeholder engagement', which really just means that all of the entities that play a role in the laboratory network. That means the clinics that collect the specimens, the people who transport the specimens and the entity that manages that, the laboratorians that perform the tests, and then how you get the results back to the patient—all of this is part of a laboratory network. And even the entities or stakeholders that are involved in ensuring that the reagents are in the laboratory and that they have the appropriate plasticware and others to actually run the assay. So all of these are what we would call 'stakeholders' for the diagnostic network.

And one thing that I think wasn't explicitly talked about in the paper but definitely happened was that all of these entities need to be involved in decisions about the diagnostic network. And the more that we can work together and make informed decisions with each individual entity's knowledge, it will better serve the patients who need these tests in a timely manner. So...and I think some countries probably did this well. I think some countries did what they could do in the face of a pandemic. So one lesson that I think we've learned is that we encourage countries to go back, go look at the communication plans that happened, see if there are ways to improve that, and moving forward, right? Encourage all countries to have a technical working group of these individuals who meet routinely to bring together all of the people involved in your laboratory network to review the network and to make decisions, both during routine operations and in the face of global pandemics.

[Sarah Gregory] On a personal note, tell us about your job and some of your favorite projects.

[Erin Rottinghaus Romano] So I work in the International Laboratory Branch within the Division of Global HIV and TB at the CDC. So as the name implies, we focus on laboratories. And our goal is to strengthen laboratory systems and ensure quality of testing in PEPFAR-supported countries. So one way that we do this—and one thing that we're quite proud of—is that we maintain accreditation at our laboratories in Atlanta. So laboratory accreditation is a similar process to other accreditations for hospitals or schools or manufacturing sites—you work towards a set of standards, and then you get assessed from an outside entity. And so, our labs in Atlanta have been accredited for over 10 years. And in doing this and in making sure that our labs are accredited, we can better support our country teams to get their labs accredited.

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So I can read about it and maybe provide guidance, but one of the things I really like about my job is that we're in the labs doing the practices and it helps us to provide practical support to our country team. So we can provide practical solutions for how to monitor laboratories' temperatures for every refrigerator and freezer that you have in an efficient way or in a way that ensures it gets done on a daily basis. So that's one of the things that I really like about our branch that we do and that I've enjoyed doing in the past. I will admit, I'm no longer in the lab anymore.

So my particular role now within the branch is on the Data and Monitoring Team. And so, part of what we do is we assist our PEPFAR-supported countries in implementing laboratory information systems—so, these are the electronic systems that help to manage specimens and workflows within the laboratory. So we work with the country teams and the ministries of health to choose a system that works for them and that they can support within the country and that works for the laboratorians that are using it as well.

We also provide a lot of technical assistance on reporting an analysis of PEPFAR-specific programmatic data. So one of the unique things about PEPFAR I think is that we're very data driven, and we have a lot of indicators and programmatic data that are collected. And so, my team provides a lot of the assistance to country teams and at headquarters on how to interpret the laboratory data and how to use the laboratory data. We also support diagnostic network optimization (that's what I was discussing previously). We provide a lot of support for the countries on how to begin the process, how to go through the process, how to ensure that you're communicating with all of the necessary stakeholders and entities. But we also liaise with other donors that support diagnostic network optimization. So we've learned that it's much better when we work together instead of working in parallel in countries. So that's one of the parts of my job that I actually enjoy as well.

A favorite project that I think I could talk about is that I like to develop or be involved in practical approaches. Sometimes you get...I don't want to say orders, but there's a programmatic initiative that sounds very vague, and so I really, really like to turn that into practical solutions that people can use. And so, one of these was my team and I developed and implemented just this simple approach to assessing a diagnostic network. So I've been talking about diagnostic network optimization; this process actually uses specialized software with specialized algorithms to truly optimize your network and tell you where to best place instruments based off of the testing demand. But not every country has access to the software...I mean, not every country has the ability yet to use the software, as it requires specialized expertise. And until that happens, we've developed a really simple approach for countries just to look at their diagnostic network using Excel. We just look at what capacity do you have in place; does that capacity...is that sufficient to test the patients that need a test (yes or no)? If not, are there ways we can improve that by extending laboratory working hours or by bringing in new equipment? We look at testing coverage—so, how many of the patients that needed a test got a test in the last year. And we also look at efficiency—so, even if you have capacity and all of the patients that need a test got a test, we need to make sure that the test is being done in an appropriate timeframe so the clinicians can act on it for the patient care. So we set up a really basic and simple tool for countries just to be able to do this and get a basic understanding of their network without using complicated software. So I feel like that's probably one of my favorite projects.

[Sarah Gregory] Well, thank you so much for taking the time to talk with me today, Dr. Rottinghaus Romano.

[Erin Rottinghaus Romano] Thank you. It was my pleasure.

[Sarah Gregory] And thanks for joining me out there. You can read the December 2022 supplement article, Contribution of PEPFAR-Supported HIV and TB Molecular Diagnostic Networks to COVID-19 Testing Preparedness in 16 Countries, online at cdc.gov/eid.

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

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