U.S. Global Health Policy: In Focus
"The U.S. Strategy for Combating the Global TB Epidemic"
Kaiser Family Foundation
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JEN KATES: Good afternoon and welcome to the Kaiser Family Foundation's webcast series, U.S. Global Health Policy In Focus. We are coming to you live from our broadcast studio here in Washington, D.C. I'm Jen Kates, Vice President at the Kaiser Family Foundation. In Focus brings you discussions and takes your questions about current issues and debates concerning the U.S. government's role in global health as a donor, partner, implementer, and often world agenda setter.

Each program features leaders in their fields who share their views and experiences with us. Today, we are very pleased to have an expert panel to discuss the U.S. strategy for combating the global TB epidemic. In addition to discussing the current U.S. response, including the status of the congressionally mandated five-year global TB strategy, we will also look more broadly at how this strategy fits into President Obama's new Global Health Initiative as well as the key

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challenges that remain in combating the disease around the world.

Today's conversation is live and interactive and we encourage you to submit questions now or as we go along. You can email your questions to infocus@kff.org. Please send them in. I'll be monitoring them during the show. I would now like to introduce our guests. First, we have Cheri Vincent from USAID's Bureau of Global Health. We also have Dr. Christine Sizemore from the National Institute of Allergy and Infectious Diseases at NIH. We have Christine Lubinski from the Center for Global Health Policy at IDSA, and Dr. Robin Wood from Desmond Tutu HIV Centre in South Africa. Thank you all very much for being here with us today.

PANELISTS: Thank you.

JEN KATES: So, to get us started and get us all on the same page, I'm going to start with you Christine to give us a sense of what is the global

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problem of TB today: What is TB? Why are we concerned about it? What's the status of the global epidemic?

CHRISTINE SIZEMORE: I wish actually we didn't have that conversation and TB would long be gone because it has been a disease that has been with humans for a very long time. Recently and also as part of the emergence of the HIV epidemic that I'm sure Robin can go into more, TB is on the rise again. We're not able to combat it effectively and it continues to kill over 1.7 million people each year. There are over nine million new cases each year and despite the availability of drugs, a vaccine that works well for children and also some diagnostics, we're not able to control the epidemic and it continues to be on the rise.

So while it doesn't seem to be a big deal and a big issue for the U.S. population, it is a serious and upcoming and severe problem for the globe as a whole. Also, since every economy becomes globalized and especially the United States is a very open

country, any TB cases in the world also affect the U.S., of course, and therefore it is a problem for the U.S. and a problem for international partners as well.

JEN KATES: Okay, so on that note thinking about the U.S., the U.S. has had a response to the global TB epidemic programmatically on the research side for many years. Can you give us a sense of that from the USAID perspective as the lead implementing agency Cheri?

CHERI VINCENT: Sure, thank you. The U.S. government is very committed to TB control. The support started in 1998. It was a minimal support. It was only $10 million but it was enough to get us started and to engage with the partners that had been working in TB control for over 100 years. Some of the partners like the KNCV Tuberculosis Foundation and the International Union.

So we started to work with those partners and WHO to start with care and treatment of TB. Eleven years later, we have a $177 million budget. So it's

gradually grown over the past 11 years and I think that the U.S. government seems committed to TB and we know that TB knows no borders like Christine was saying. So most of the foreign borne cases and most of the cases in the U.S. are foreign borne. So it's really, I think, in the U.S. government's interest, to be working in TB control as well as it's a humanitarian issue.

So our U.S.G. strategy is to diagnose and treat TB patients and to work within the Stop TB strategy that the World Health Organization has developed with other partners. So we're working in 20 focused countries where most of our funding goes but we have 40 total countries. The way we have chosen countries is based on the TB disease burden, multidrug resistance TB burden, and HIV prevalence as well as political commitment by the governments.

So we're working and we have a three-prong strategy. It's to develop an intervention of packages based on the Stop TB strategy. So, DOTS expansion and

enhancement - the DOTS stands for Directly Observed Treatment Short-course.

And then, also to expand MDR/TB diagnosis and treatment. In many countries we only have pilots. Only about eight-percent of the MDR/TB estimated cases in the world are actually on quality treatment right now. So we really need to scale up that.

Then the third prong is health system strengthening to make sure that we're developing cost effective, efficient programs within the health system. So we're working with the national TB programs in each of these countries to work within their strategic plans and to develop sustainable programs.

JEN KATES: So before we get to a little bit more about strategy and also here what NIH is doing, is it accurate to say that in 1998 when the agency first started really taking on TB as an issue, it was more on the TA partnering side? When you say you worked in 20 countries primarily and then 40 total, is that contracting with on the ground partners? Is it putting

staff in place? Can you give us a little sense of what that actually looks like?

CHERI VINCENT: Yes, for people who don't know USAID's makeup, we actually have offices in most of these countries that we're working in and these offices have health staff. So we're working in maternal and child health and HIV and malaria as well. So they do a range of different health technical assistance as well as program management. They engage with the government in terms of determining what they need to do looking at the other partners on the grounds - The Global Fund may be there or some of the other partners, The Gates Foundation.

So they work to see what are the gaps and determine where strategically can the U.S. government help to be the most cost effective to implement the national TB program. So they usually have a five-year plan. We look at the areas that are the gaps that we can help to assist and then we work with certain partners so we contract or give grants to different

partners to implement those projects. But, we develop the strategic vision with our other U.S. government partners. We work with CDC and whatever U.S. government partners are in the country at that time and to determine that and then work through U.S. contractors or grantees.

JEN KATES: Okay. I want to hear a little bit about the research effort because I assume that NIH has been doing research on TB for a lot longer than since 1998 but please—

CHRISTINE SIZEMORE: You would actually be surprised. In '85, I think the budget at NIAID for TB was somewhere around $60,000. It was really, really small. Through the re-emergence of tuberculosis in the U.S. in the early 1990s, it was in early 1990s around 1992 where also multidrug resistant TB cropped up in combination with the rising HIV/AIDS epidemic. That's when it was realized that we actually need significantly more effort and input into understanding the biomedical component of TB. That is that the

foundation of knowledge to understand what type of science is really needed to develop new health care interventions.

There was also the time when, of course, through multidrug resistant TB, it was recognized that our current interventions are failing. They no longer are doing the job that since the advent of antibiotic therapy for TB when it, for the first time in many, many years, it became curable, people had stopped working on those tools. They thought TB's an old disease. It's been taken care of. And then the health care systems in the U.S. and also globally, they basically started declining because it's sort of like you're a victim of your own success. Cases go down and it is perceived that no longer strong investment in research and especially new tools for development will come up.

So the NIH and especially NIAID the institute where I work at, we've started to put significant effort into tuberculosis research in about the mid-

1990s. They're now at a level of about $140 million per year and happen to be also the world's largest funder for R&D funding, not TB as a whole for research and development.

Our role is really to, almost like an architect of a building, we are one of those organizations that helps build the foundation upon which other programs can rise because without the knowledge about tuberculosis, how the pathogen interacts with the host and understanding detailed what is really necessary to intervene with a disease or prevent it. Without that knowledge, there's no way we can create new effective tools, diagnostics, just the health care interventions that then later gets translated to our partners in the U.S. government, the CDC, USAID, and of course also external ones and moved into the field.

So everything that covers support you might want to call research in tuberculosis is what is within our mission and what we're heavily engaged in.

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JEN KATES: Yes, please Robin?

ROBIN WOOD: I'd like to sort of back that to some degree. One is I'm not sure where the scales come out of this, the scale of the problem, I think, is as Christine was saying that funding in the U.S. probably dropped off because it wasn't a U.S. problem. But the country that I come from, we have 400,000 cases of TB each year. The city that I come from with three million people has twice as much TB as the whole of the United States of America. And, we have a lethal combination with about 73-percent of our TB being HIV-driven.

Whereas all the emphasis has been on effective case management and the DOTS program, it is actually failing in the southern tip of Africa, in the eight countries in the southern sub-region. Interestingly that shouldn't come as a surprise. Karel Styblo who discovered, and was the initiator of the DOTS strategy so that it would work in most settings but not where there was a generalized HIV epidemic and not in

settings where there was a high annual risk of infection of children. Both of those conditions are prevalent in southern Africa. It shouldn't come to a surprise to us that DOTS, whilst it's a fundamental building block on which to build is not sufficient to control this epidemic that we've got at the moment. The hampering is that we don't understand the drivers of the epidemic. We don't understand the upstream events. We don't understand the risk of exposure or infection. We don't understand the host-pathogen relationship and really, what Christine was saying is really welcome news.

I mean we need the U.S. to lead in the scientific approach, and it's really transforming the approach instead of just sticking with the programs that we've had, which have worked in many parts of the world but where they're failing we need to start thinking with an open mind and using appropriate scientific investigations.

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JEN KATES: Well actually this probably is a good segue to talk about the new strategy that the government is developing on TB. As I mentioned in the opening, there's a congressionally mandated five-year strategy I understand is due to Congress soon. At the same time, the administration is opening up the bigger question about a global health strategy. Can you give us a sense of where those pieces are? Then I think we want to hear from the other Christine a little bit about from where you're sitting, what you see as the biggest things that should happen.

CHERI VINCENT: Yes. The U.S. government strategy, we started the development process by bringing together the major—

JEN KATES: For TB?

CHERI VINCENT: For TB, together the major partners and agencies in the U.S. government. So USAID has been leading that process with a lot of input from the other agencies including NIH, CDC, PEPFAR, DOD. So we've had a series of meetings and discussions of where

we should go in terms of the next five years if we receive significant resources and a lot of it is under the Hyde-Lantos Authorization. Under that, the objectives of it are to also half prevalence by 2015 according to the 1990 levels but also in addition to that, we are to put 4.5 million smear-positive patients on treatment and 90,000 MDR/TB patients.

So they're very ambitious goals, which we would hope would be supported by the resources to do that. So the strategy supports that in terms of having what I had mentioned earlier of focusing on expanding the efforts that we have now but also making sure that we expand MDR/TB diagnosis and treatment. We only have nine-percent of the estimated MDR/TB patients on quality treatment right now, and we really need to expand that.

We also need to build on the health systems platform and to make sure we're doing it cost effective and efficiently. I think all of these are part of the Global Health Initiative. I mean some of the key areas

that Dr. Emmanuel talked about a couple weeks ago with you were to look at health system strengthening, make sure that they're cost effective and efficient so that we're integrating into the other U.S. government investments in health. So it's a kind of integrated approach.

And, women's issues. So making sure that women who, in some countries, don't have access to health care and are able to have access to health care, finding ways, new approaches to making sure that women and children have access to TB care. So that's the foundation, the areas that we're working on.

Some of the other pieces to it is that PEPFAR is developing their HIV strategy and so they are the lead organization for TB/HIV. So we're working with them in terms of making sure that there's synergy between those strategies and how to address the TB/HIV co-infection issue from both sides of the strategy.

In addition, we're looking at, we really need to enhance TB infection control, making sure that the

settings where people are, that we're reducing infections, looking at pediatric TB and, as I mentioned, all within the health systems realm. So trying to be efficient and effective. So I think they go hand in hand these two, the global health initiative and the TB strategy.

JEN KATES: Let me ask this because I think that, in theory, they do. On the time front, are they actually happening that way? So our viewers know the background and the detail here, the TB strategy and the HIV strategy were part of PEPFAR reauthorization. So Congress required those. Do those have a specific time that they need to be delivered to Congress? Do you know?

CHERI VINCENT: Well I think we're hoping to finalize in the next month or so. We have a draft and we're circulating it again among the U.S.G. partners and so I think we're lining up the timelines and the global health initiative is moving quickly. So I think they are lining up, yes.

JEN KATES: Okay. Is that what you're hearing Christine?

CHRISTINE LUBINSKI: At least theoretically I think the TB and the HIV strategies are actually due this week, October 1. Although, we have certainly heard, and I'm not sure Congress is going to come screaming to USAID or to OGAC, "Where's my strategy?" They're a little preoccupied. We have certainly heard that there's being an effort made to, I think, release ultimately a more integrated package that addresses all the components of the global health initiative, perhaps, by the end of the year.

JEN KATES: Have you been sharing the strategy of TB with the community?

CHRISTINE LUBINSKI: They have and I did have an opportunity to participate in a listening session with a PowerPoint presentation on the TB strategy. And, I guess what I would say is that while it's heartening to hear that you're working with your colleagues at NIH and OGAC, I mean one of the nature of the way global TB

or tuberculosis in general is dealt with by the federal government, it's a little bit fragmented. I understand there are very strong interagency discussions and agreements but if you look at the USAID strategy, it is a USAID strategy. So it's about global TB control. It reflects only in small part the critical issue of HIV/TB co-infection, which is going to be more prominent in the OGAC strategy and reflects virtually not at all the kind of urgent need to ramp up both basic science research as well as research and development in TB drugs, vaccines, and diagnostics. So in order to get the whole, so it's good as far as it goes, but in order to get the whole picture, you have to go to a variety of sources to do that.

I think the unanswered question is, "Where are the resources to implement that strategy?" I think it's important for the audience to know that the bill that really called for a significantly ramped up U.S. government effort on global tuberculosis authorized $4 billion.

JEN KATES: PEPFAR reauthorization?

CHRISTINE LUBINSKI: Right, for that activity over a five-year period. And, certainly in the last budget, we did not see in the administration's request even remotely a down payment on that. We saw a request for a mere $10 million. And again, this would be on global TB programming. We also know that NIH research has kind of languished in terms of funding too.

So, I think we're worried. Many people fought really hard especially in the face of the HIV/TB co-epidemic for TB to be a prominent part of the reauthorization. I think it's an open question about whether the goals of that authorization are going to be realized because it's unclear whether these folks and others, who are not in the room, from CDC are, in fact, going to have the resources necessary to really make for what Tony Fauci has called a transformative response to tuberculosis.

CHERI VINCENT: I just wanted to say one thing on the research. That is something that I overlooked

when I talked the last time. I mean, if we had the resources, we would really like to increase our operational research for programmatic relevant activities. I mean we have had discussions of where NIH and CDC and USAID's roles are in research, and we see that definitely we would like to see more rapid diagnostics and shorter regiments and vaccines to reduce mortality, of course. So we would definitely support them where NIH or other U.S.G. partners leave off, we would pick up to make sure that they're relevant for the field. But, that's definitely important and it's a missing link in TB.

CHRISTINE SIZEMORE: If I may add to that as well. It made the field of TB research or just TB, what the U.S. government is involved in tuberculosis, the U.S. may appear fragmented but since the resurgence of TB in the U.S. in the 1990s, there has been established a U.S. government TB taskforce. As part of the TB taskforce, all agencies that are involved in TB care in the U.S. and also internationally, and that

includes the agencies that Cheri already mentioned, USAID, CDC, NIH, the big funders and the big implementers, but there's also Indian Health Services, Immigration Services, Department of Defense, anybody who might ever interact with tuberculosis patients. We have at least annual meetings as the TB taskforce that have been going on since the 1990s where we regularly discuss each agency's and organization's mission, how we fit in amongst each other and especially how we can facilitate the translation of knowledge, that we're in charge of basically creating, into either implementation or changes in policy or then also into field implementation. So that is an ongoing process.

And also the various research agendas that have informed the U.S. government strategies are basically a compilation of the research agendas of each individual agency. They're all mapped towards a common goal. So yes, you will always see different content in each of the agencies' research agendas but that is of course permission. But then as a whole, we talk on a

regular basis and make sure that our individual contribution really maximizes output and really leverages the resources, the expertise that we have to the maximum extent.

CHRISTINE LUBINSKI: I mean I don't think it's any doubt that we have fantastic people really committed to addressing this disease in government and that they talk together a lot. In fact we could paper this town with reports that have been released even recently about combating tuberculosis. A wonderful report from the federal TB taskforce on combating drug-resistant TB, a very important Institute of Medicine report on the same subject all demonstrating the kind of collaboration. What we don't have is the leadership and resources to really implement that plan either for research or for program and make it a reality.

JEN KATES: Let me ask a question. This is maybe a devil's advocate question but one, if you look at the structure of the U.S.G. response to global health issues to date, where we've seen big pushes,

whether programmatic pushes and resource pushes, it's been, in part, it seems because a disease-specific initiative has been created: PEPFAR with a coordinator. Malaria with a coordinator. And, at the same time, I think there's a growing recognition and it was said very clearly in the Global Health Initiative that we need to be integrated and not always disease-specific. There's a tension there.

So how does one then, everyone wants their issue and their area to get more attention, to get a high priority, how does that fit in? We actually have a question from someone that I think gets at this a little bit. Someone emailed this question, Louise Baker at the WHO, "Given the administration's priorities and current discussions around the global health initiative, what should the advocacy community do differently to ensure that TB gets the attention it is due?" So I don't know, if . . .

CHRISTINE LUBINSKI: Well I'll certainly jump in here.

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JEN KATES: And, Robin, feel free.

CHRISTINE LUBINSKI: I think we could use a coordinator or a sort of visible high-profile leader on this. I think TB suffers from its' absence and one could argue about whether or not we should have gone down this road with AIDS and malaria but we did. So we have one of the three major infectious disease killers in the world that doesn't have that visibility.

What does that translate into? Well it translates into spokespeople from the White House talking about HIV and malaria and not even saying the word tuberculosis. It translates into there being an assumption somehow that TB has been addressed by the U.S. government in a big way globally and we're moving on to new issues like neglected tropical diseases or maternal and child health when, in fact, there has been nowhere near a commensurate response in TB compared to HIV, for example, either in research or programming.

So I think tuberculosis attention, leadership suffers as a result of not having that visible, more

centrally located person, whether it's in the White House or somewhere else. Although, I appreciate that each of the agencies probably cringe about the thought of a sort of a super leader that is beyond their agency.

JEN KATES: I don't know if you have anything you want to say. I think that it really comes up against this tension of do you have lots of different coordinators and meanwhile there's a GHI broader vision that's going on. I don't know if anyone else wants to comment or you, Robin, want to mention how South Africa deals with some of these challenges or if it's just a totally differently organized response.

ROBIN WOOD: I think that the discussion of TB control is sort of not appropriate for South Africa. TB incidence has gone up six-fold in the last 20 years. We're galloping away from Millennium Development Goals. The situation is an emergency and under emergency situations like that - it's been declared a national emergency, it's been declared a regional emergency - I

think focused approach is really necessary to try and take this on.

We are using tools, which are not working, and we're trying to do more efficient use of those tools as opposed to looking and trying to understand the epidemic, which is the key to controlling any epidemic. This is what I think Christine was pointing to. There's a great need for us to understand the things that are driving this. I think focus is really needed.

JEN KATES; Actually, two other questions that just came in that have to do with on the research side because I think we're all leading a little bit towards the need for new diagnostics and new tools. Jamie Rosen from Aeras Global TB Vaccine Foundation asks, "Although new tools to prevent, diagnose, and treat TB are urgently needed, U.S. government funding for R&D of new drugs, et cetera, diagnostics and vaccines have been fairly limited. What are the prospects for increased U.S. investment in this area?" And, a similar question from Dr. Randall Reves from the Denver

Metro TB Control Program of the Denver Public Health Department, "What can be done to rapidly accelerate the development and implementation of new tools?" So again, coming back to this question, it's a little bit about resources, a little bit about priorities, where are we kind of on the cusp of getting to where we need to be?

CHRISTINE LUBINSKI: Well let me just offer an example because I was really surprised by this. So the Bill and Melinda Gates Foundation has gotten very involved in tuberculosis and has certainly made a major contribution to the field. And, you mentioned the writer from Aeras and Aeras is about TB vaccine development. You have the TB Alliance for Drug Development. And, you have FIND [Foundation for Innovative New Diagnostics] working on diagnostics. There's very exciting activity in the pipeline in all three cases. Well in all three cases, the Gates Foundation has told these entities that they will support Phase I and II trials to look at safety and

efficacy, but that these entities are responsible for identifying the resources, which for this disease, just have to come from the public sector, to actually do phase III trials. Right now, there is no way that USAID or CDC or even NIH have the additional resources to support. I mean a Phase III trial for TB vaccine would take more money than the entire R&D budget of USAID right now.

So we could find ourselves in a position where we get down the pipeline and actually have some potential new regimens, which we need, not just drugs, we need brand new combination regimens and to think about that like we do in HIV. Or, a rapid point of care diagnostic. And, in fact, there are not resources in the public sector to actually definitively test those in Phase III trials or bring them to the poorest countries and the poorest people in the world. So that's the sort of deficit we face on the research and clinical trial capacity side.

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The U.S., by the way, has the biggest budget for tuberculosis research in the world. So I'm not suggesting we ought to do it all, but I think it just demonstrates how much the current resources doesn't meet the need.

JEN KATES: Christine, can you tell us a little bit about the clinical trial capacity situation right now with TB research?

CHRISTINE SIZEMORE: That is actually, and you may have heard it articulated by Dr. Fauci as well especially during the Pacific Health Summit that was held not too long ago, the NIAID has a fairly significant investment in clinical research and trials for a multitude of diseases. Discussions that are currently going on within our institute is really how to leverage the existing infrastructure - a lot of it is invested very heavily in HIV/AIDS - how we can create more pluripotent, what we call pluripotent, research sites because tuberculosis doesn't conveniently come as just the only infectious disease

that a patient has. In endemic countries, it's often basically appears in combination with HIV/AIDS, diarrheal diseases, hepatic diseases.

So, in order to address TB of the real world and really make a transformational step upward, we need to start looking at the disease in a larger context again and making, and trying to leverage our existing investment in clinical trials and really facilitating that and providing extra resources to researchers is something that we're currently dealing with and discussing very heavily.

JEN KATES: Actually you mentioned real world, so I want to turn to Robin and get that perspective from one of the countries that is really facing one of the most serious problems related to TB and TB/HIV. So can you tell us sort of what that looks like and how, so it gives us some sense of what all of the research and the programmatic tools are going toward or needed for?

ROBIN WOOD: So we have generalized epidemics of both diseases. So we have generalized HIV disease and we have generalized TB. The intersection between those is particularly in the newly urbanized populations, poor people who've moved into substandard housing. I think that part of the knowledge that we're just getting some insights into is that it's glibly said a third of the world's population are infected with TB. Well when I look at our communities that are living like that, it's almost 100-percent of them are infected with TB. So by the age of five going to school, 20-percent of them are infected or one-percent's had TB. By the age of 15, before they've become sexually active, 55-perccent of them have either had TB or are currently infected. And, by the age of 25, the time of sort of peak risk of HIV infection, over 80-percent of them have either had TB or currently have TB.

So I mean this is dreadful. I don't think a new drug or a new diagnostic is going to make a

difference to that dramatically. We have to understand how did that infection take place. Focus has been taken off. We've taken our eye off the ball. We're looking at the treatment of the end stage of the disease and making sure we do that efficiently, which is great, but we've sort of ignored this. It hasn't been looked at since the 1950s.

So these rates of TB infection are pretty much like you had at the turn of the last century in New York and large cities of Europe. Perhaps in the 1950s before national TB control programs. This really is an emergency that needs focus. The first thing we need to do is to use the tools we've got. We've got molecular epidemiological tools, which we're not using in a systematic way.

I think leadership, and the role of the NIH to take this leadership, is to identify those components of the equation that we don't know and get a rational strategy to find out about those. We're going to need to do that and perhaps we need to even look at the

tools that we used in the past that did control TB before we had TB treatment. TB has been decreasing since 1790 in industrialized world. Many factors have been successful.

So I'm a little bit concerned that expecting the silver bullet to come that's going to make everything get better, and the new diagnostic's going to make it all go away, strikes me as, I'd love to have those, but surely we can use our existing technology in a rational way to look at the scope of the drivers of the epidemic at the moment.

JEN KATES: Can you talk more about that? So, you're saying that there are new diagnostics, new vaccines, but at the same time we need to address what we can with what we have. So what are the biggest barriers that you face in doing so?

ROBIN WOOD: Well I think it's a sort of human perseveration - that we are failing and losing and we just try and do exactly the same thing a little bit more efficiently. It strikes me as though that's

doomed to failure, that we need a new sort, we need a transformational research agenda. And, whereas these strategies have worked very effectively and worked in many parts of the world, but where they're failing, we need to rethink, step back, understand our epidemic and then have a focused, strategic control program, which is not just rehashing the stuff that's not actually managing to control at the moment. And, sure enough, there's no doubt that effective and efficient treatment of infected cases is quite important, but, I mean, to get these rates of infection means that something's going on, and we're not doing any epidemiological systematic approaches to that to try and understand that. I think that needs to be a major component.

JEN KATES: Christine, if you want to add anything in on that? One of the questions that we got in is from Karen Goraleski from Research!America and I think this gets at it a little bit from the more global perspective. This is looking at successes of PEPFAR and I would add maybe the challenges, "What lessons

learned are there for ensuring a comprehensive TB strategy?"

I'll just put out that one of the big challenges I think that people are, the last few years, grappling with is that we haven't achieved a sufficient level of coverage in scope and scale and intensity on the prevention side with the existing tools that we have, at the same time needing new ones. Maybe that's one to really think about for designing a global strategy here but I don't know if you want to speak to that?

CHRISTINE LUBINSKI: Well I mean, I think the first thing I would say is what we learned from PEPFAR is that when we put our minds to it and we invest in resources and leadership, we're able to do what many people said was impossible to do, which is to save millions of lives in developing countries. I mean you remember very well, Jen, that there was a time when the notion of implementing any kind of antiretroviral rollout was considered impossible.

I guess I would suggest that similarly, to kind of support Dr. Wood's point, I mean we need, one of the things that's shocking to me as a nonscientist, but somebody who's been doing advocacy in AIDS for 20 years, is how much more we know about a virus that we've only been studying in earnest for a quarter of a century compared to a bacteria that's been around for thousands of years.

There is no doubt that the robust effort in HIV research delivered, delivered life saving treatment, delivered an amazing level of understanding of the pathogenesis of the virus, and all kinds of things I as a nonscientist could not enumerate. But, nonetheless, and it's kind of shocking to me, as I talk to Dr. Wood and other experts, you mean we don't know that? We don't know even the issue between latent and active disease.

I think we know, both from AIDS research and from PEPFAR, that if there is leadership and resources, the brightest minds around the world will embrace these

challenges and look at learning more about this scourge. So that, to me, is the lesson.

JEN KATES: Unless anyone else wants to add into that? I actually want to get to another key player in this that, obviously the U.S. is involved with, is the Global Fund. The Global Fund began operations in 2002 and had TB as part of its mandate. And, what have from your different perspectives, I know the U.S. has said that the Global Fund is a key multilateral arm, in a sense, of the U.S. response.

I'd also like to hear from Robin about how in the South African context, the Global Fund has shifted the response to TB or has it really been seen more in HIV? Anything anyone wants to add. And, what the status or thinking forward about the role of Global Fund in all of this?

CHRISTINE LUBINSKI: Well I guess just as a baseline piece of information, I think it's important for the audience to know that the Global Fund finances more TB treatment than anybody else on earth. So

they've made a huge contribution to expanding TB screening and treatment across the world. So they're actually a much bigger player in tuberculosis than they are in, relative to other funders, than HIV and malaria. So they're very, very important.

I think people outside the field somehow assume that all the Global Fund money goes to HIV and that's not true. I mean in the last round, actually the majority, more grants went to malaria than TB or HIV. But, it's a very important player in TB. I think the shortfall in the Global Fund is going to have repercussions for TB control programs all over the world especially in the highest affected area. I mean I'll let Robin speak to South Africa. I think that in general, South Africa is not a huge beneficiary of Global Fund resources. I know they're not on the HIV side. I'm not sure on the TB side.

ROBIN WOOD: Well there are some large funded programs from the Global Fund. My clinic of 5,000 patients is largely funded by Global Fund. So they are

putting some funds in there. Obviously, there's been a big emphasis on testing for HIV in TB cases. That's been interesting that it's the impact of that is that my antiretroviral program, the majority of individuals who come into there to benefit from antiretrovirals have already had TB. So the impact there of what we do in the clinic is obviously going to be very limited as far as population control. So, again just as you're focusing in HIV to upstream and prevention, we have to do exactly the same thing with TB. We have to go upstream and find out what's happening with infection. Treating end stage, testing lots of patients in TB clinics is great, it does a lot of good for them and their survival, but it's not attacking the control of the program at a population level. That, I think, is quite important.

We have to go upstream. That's difficult to do. That means moving out of the comfort of the clinics and getting into the community. But, I think that's probably something that we need to do in a big

way. That was what was done in control programs in the industrialized world a century ago.

CHERI VINCENT: Could I talk about the Global Fund?

JEN KATES: Yes.

CHERI VINCENT: So many people may not know that the U.S. government is the largest supporter of the Global Fund. We have, I think it's $3.5 billion have been put towards grants to countries and of all of the grants, I think that Christine was mentioning the TB grants are about 15-percent of the total. So we're the smaller sliver, still the orphan.

CHRISTINE LUBINSKI: As always.

CHERI VINCENT: Still the orphan, but have benefited significantly from the Global Fund.

I think what we encourage is, at the global level, as well as the country level, is maximize the coordination because our little bit of resources can go a long way if we can help to remove bottlenecks to Global Fund implementation and to help to pick up where

the Global Fund isn't supporting and being able to work and fill those gaps of the national TB program.

For example, in Indonesia, our support is, we have like a matrix of "alright here's the things that need to be done in the next five years to meet certain objectives, and here's the pieces that the Global Fund is going to take on, and here are the pieces that the U.S. government is supporting." So the problem with that is if one part kind of doesn't meet its' objectives then the other part has to pick up. But, coordination is really key with these resources to make sure that we're leveraging them. Obviously, for making sure that quality first line drugs are available, the Global Fund has been critical in getting drugs through the global drug facility as well. So that's been a major success of TB control.

JEN KATES: We actually just had a question come in from somebody at Stanford from Eran Bendavid. I think it might be a repetition of some of the things you said but it's important to underscore. It said,

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"It seems like there are many strategies being promoted but we don't know that these strategies work and historically, their effectiveness is moderate at best. I am interested in the opinion of Dr. Wood and others on the panel on what are the most important pieces of information we need to know in order to understand TB control."

I think we've been saying some of these things, but I think restating them and getting them out clearly is what this person is wanting to hear.

ROBIN WOOD: Yes. Well I think TB control has to be focused differently in different settings. So there's no doubt that efficient case management has worked in many parts of the world, but where there is the jewel problem of a generalized HIV epidemic and these high risks of infection, what can we do?

Well the two factors that are driving it are the immune suppression of these patients with HIV. We have a tool to deal with that and that's antiretrovirals. In communities I've looked at with

widespread initiation of antiretrovirals, we've actually turned around the increase in TB rates that have been going on for the last 10 years and we've managed to turn them around and get them down by about 20-percent, but that's with very high coverage. That's coverage which would require South Africa to be treating two-and-a-half times as many people as it is at the moment.

So what it unfortunately means is if we're going to deal with that immune compromised individual, we either have to stop the infection of HIV or we have to have much wider access to antiretrovirals. If we let off on that and don't recruit at a fast enough rate then the number of people that move into that suppression increases and TB will take off again. So it's a way of dumbing things back.

Then we've got the second component of what can we do to decrease the risk of infection, the early upstage effects. Really, I think that those are things

that have been dealt with elsewhere and we need to put those into the mix of efficient case management.

So, I think those were two components that I would focus on. On the one we've got a tool, which works, and the other one, we have to relook at perhaps some of the tools we had previously that controlled, meanwhile hoping that we will get better drugs and better testing. But, we can fight the battle, to some degree, with the tools that we've got.

JEN KATES: Cheri, I want to hear also how the strategy that you're developing now is looking at that approach in the priority countries.

CHERI VINCENT: Well, I wanted to talk about some of the successes of TB because I think that it's important for the audience to know that 55-percent of the TB burden is in Asia, which has a very different dynamic than Africa, which is about 31-percent of the cases. So in Asia, I mean you're dealing with, you don't have the co-infection issue. You do, in some

countries, have multidrug resistance TB that needs to be dealt with.

So I mean overall, we are seeing that more cases are being detected and treated successfully. So that is important to know. We are noting that globally, incidence has been declining slightly. So different regions obviously have been doing, I mean Europe and Eurasia have not done as well as, for example, Asia.

So I think that's important to note that we do have tools. And also, what Robin was talking about that recently released by the World Health Organization, the TB Infection Control policy, that hopefully we'll be able to scale up and put into the mainstream of case management that you were talking about to.

JEN KATES: Can you talk more about that?

CHERI VINCENT: About the TB Infection Control Policy?

JEN KATES: Yes.

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CHERI VINCENT: So basically, the TB Infection Control Policy that WHO and partners have recently released is to make sure that we are preventing infections in congregate settings. There is a household component. It's limited, but looking at administrative, environmental, and other interventions so that we have safe settings for health care workers and people that come there to seek care or if it's another type of setting. So, preventing infections. Also, in laboratories it's very important to make sure that we're meeting biosafety standards; that we're not putting lab workers at risk for being infected while working.

So tools are being developed. They're being recreated, many of them, and we do need to scale up. We have a lot of pilot projects. We have a lot of pilot MDR/TB projects. We have some pilot TB infection control activities but we really don't have the resources to be able to scale these interventions up

and to learn new information that will create better tools.

JEN KATES: Yes?

CHRISTINE SIZEMORE: I'm sorry. If I may add very briefly just from the research perspective. I mean the perfect scenario will be if we put ourselves out of business, which would really be prevention of infection in the first place because, if you consider that the current TB control strategies are very much reactive, you are dealing with a patient who has managed to infect countless others. So, a strong focus and understanding how to prevent infection from a programmatic perspective.

And then, of course, also understanding the majority of individuals with a normal healthy immune system who are exposed to the tuberculosis bacteria, but will not get disease. We don't understand what it is that they do well and what those who actually develop active disease don't do well. And that, of course, is the foundation for figuring out how to make

vaccines. It has not been possible yet because even infection with mycobacterium tuberculosis, won't protect you lifelong. So there is no natural immunity.

But, just really a continued focus and a continued appropriate balance to prevention strategies in addition to curative. Basically, dealing with the existing case loads in patients is what makes research allocation and the whole work in R&D for TB very difficult because there's no one aspect that sort of deserves or needs more emphasis than another. They're all equally important because we're dealing with the existing problem of TB right now and also forward thinking how to basically turn the tide and, especially in settings with large numbers of immune suppressed individuals, prevent infection in the first place.

ROBIN WOOD: Many of our targets are treatment targets. But, in fact, what we're trying to do for long-term control of TB is to produce the next generation of children who have less infections than

their previous generations. That's not part of the target but it's actually what we should be doing.

JEN KATES: Actually here's a question that came in sort of the flipside of your question about targeting antiretroviral clinics where it's getting at one end of the problem. It's from David Bryden at the Center for Global Health Policy and he asks, "I've heard," and I've heard this from several reports too, "I've heard that people coming in to HIV treatment sites may be getting infected with TB as they sit in the waiting room. Is there anything being done about this and what do we need to do for better infection control and better community awareness of to prevent the spread of TB?"

So it's sort of the other side of that coin where people are coming for their treatment and getting it. Co-location we all think would be a good plan and then there's this other element.

ROBIN WOOD: Well that's quite an interesting question because the problem we had before is that we

wouldn't have known. It was only in exceptional circumstances where everybody dropped down dead to get a ferry that we realized it was a problem. There is no systematic monitoring of the transmission and I think transmission is really the key of everything, as Christine was saying.

So, Tugela Ferry was picked up, this dreadful mortality rate, but that was why it was picked up. There the biggest risk factor appeared to be previous hospitalization and interface with the hospital system. So we need to have good science, good monitoring, and we've got the tools to look at that and certainly if it's a problem then we have to put in the appropriate infection control modalities, which is what happened at the Church of Scotland in Tugela Ferry. So they have reacted to that, which could have gone on for another few years if those patients hadn't have dropped dead.

So again, it's a little bit like the MDR story. If you don't look for it, you're not aware of

it. When you start looking for it, you get very scared and you start having lots of problems.

CHRISTINE LUBINSKI: I mean, I do know that - I mean the office of the Global AIDS Coordinator isn't kind of represented on this panel and they're a big player in this - that certainly there has been an effort, maybe a little late in the game, to start looking though much more carefully at infection control and any clinics that are being rehabbed with PEPFAR money are now meeting standards.

And a lot of activity has gone on to do very simple things like establish, separate people who are obviously coughing from others, have people wait outdoors if weather permits, things to increase ventilation. Simple things that aren't extraordinarily expensive. But, I think the infection control is an absolutely huge priority.

And of course, then if you look in communities and see how the individuals most at risk in the townships where Dr. Wood works, it's not surprising

that there's an urgent need for strategies to deal with infection control in the community as well as in the health care setting. But, there's something really horrible about the notion of going to get your HIV antivirals and picking up TB while you're there.

CHRISTINE SIZEMORE: Even to take that even one step further, again in those countries where you have a still more limited HIV burden - for instance, in prisons in Eastern Europe - what is the immune suppressed risk factor in your country for instance, and increases mortality is really drug resistance; the high occurrence and the high transmission rates of already drug resistant mycobacterium tuberculosis in those settings. And that is, when you're immune suppressed, I think you have a higher chance of dying, of course, because you get more severe disease. But, in Eastern Europe, then it's the lack of drugs to do anything for those patients if they have serious forms of disease and drug resistance and there are not enough drugs available. So it really, you're absolutely right

Robin, it depends on the setting. And, each setting will require its' own attention, its' own focus, and it also has its' own research questions.

JEN KATES: Know your epidemic, which is the mantra in HIV.

CHERI VINCENT: Yes, I think it's important to note that in some Eurasian countries, the multidrug resistance rates are higher than 30-percent, up to 36-percent we're seeing in Azerbaijan and Kazakhstan. So this is a crisis as well and it's something that we really need to focus on because many of those people, if they are on treatment, they're not on quality treatment. And it's, I think, one of the main focuses of our U.S. government strategy.

JEN KATES: Here's a question that someone sent in that gets at how we engage the public in some of this. This person asked about engaging a mom in Detroit, Michigan, I'd like to say that that mom in Detroit is going to watch this webcast but maybe she won't.

So Karen Gorlesky, again from Research!America, asked, "How do you engage that mom in Detroit who, to support a local TB strategy when her family's facing their own significant health and economic challenges," and goes on to ask, "In other words, how do you engage that mom or their member of Congress or Congress in general on this key issue."

CHRISTINE LUBINSKI: Well I think the first thing to do is always to put a human face on it. I think if that mom in Detroit heard Robin Wood talk about how many of those five-year olds are already infected, and if she also knew that TB was the leading infectious cause of maternal mortality in many places, that that somehow brings it home. I mean in the same way that the Global Health Initiative is focused in part on women and children, I think there's a very compelling case can be made about women and children. And then, of course, the other thing you need to do as an advocate is to educate moms in Detroit and others that the money that the U.S. spends on global health is

really a very, very small fraction of its' overall budget.

So it's not necessary or appropriate to think about choosing health care for a mom and her child in Detroit versus saving the lives of the children who live in Robin Wood's community. We don't really have to make that choice. And, that a fairly modest investment, and I think if you look at what USAID's accomplished, actually produces good cure rates, saved lives, children who grow up healthy with mothers and fathers who are there to raise them. So I think that's certainly an important way to approach it.

JEN KATES: Actually from research we did looking at the entire U.S. global health budget, it's something, like less than a percent of the entire federal budget.

We only have time for maybe one other question. We're wrapping up and we're getting a lot of email questions about specific things around prevention, what are the best techniques. So there'll

be resources on our website and all of you have it. I actually want to end with what would be success in the next three to five years if we could come back say we really made a difference in combating the global epidemic. I want to start with Robin because you're probably closest to the on the ground. What would you see as success in South Africa?

ROBIN WOOD: Well I think the foundation on which we have to build things is the ability to diagnose clinical cases and the effective case management of those. I wouldn't want to take away from that, but I think that we need U.S. leadership in international health care and we need that leadership, I think, to show particularly in the research agenda. I think that, as you put out when you started, this disease being around for a long time and really we've been treading water for quite a long time. I think of what Tony Fauci's talks were about.

So I would look for a research-led approach to this. And, looking at all the things that we know

work, implement them, and obviously look for new things and look at things that we've previously used.

JEN KATES: Last word from anybody else because we're really at the end now.

CHERI VINCENT: Yes. I would just say that we need to make sure that we turn off the tap. We make sure that we turn off the tap in terms of diagnosing early and treating the patients and also getting people on MDR/TB treatment as well.

CHRISTINE LUBINSKI: And the research agenda needs to be coupled with a rapid way to get the findings of that research to the places in the world that need it the most. I think that's the other important point with TB for success.

JEN KATES: Well we'll certainly, through our In Focus series, come back to some of these questions and particularly as the Global Health Initiative is rolled out too, the larger initiative and your strategy, because then it'll be how those all fit

together to get at these very real challenges will be something we'll want to continue to explore.

So I'm going to thank you all for being here today and sharing your perspectives. Thanks for coming from South Africa to join us. And, I want to thank everybody else for all your questions. On our website, globalhealth.kff.org, you'll find additional resources on today's In Focus. We encourage you to share the video and transcript with your own audiences. We also hope that you will join us for future webcasts of U.S. Global Health Policy In Focus.

I'm Jen Kates of the Kaiser Family Foundation. Thank you.

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