TB Silent Killer: FRONTLINE Documentary and Panel Discussion
Kaiser Family Foundation
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PENNY DUCKHAM: Welcome to the Kaiser Family Foundation and today's event. Thank you for coming in the snow. I'm Penny Duckham and I run the Kaiser Foundation's Media Fellowships Program. Today's event is focused, as you know, on tuberculosis and the global challenge faced in diagnosing, preventing, and treating TB. We are looking in particular at the emergence of highly drug-resistant strains of TB and the particular challenge that they pose.

We're lucky today to have with us, the producer of a new FRONTLINE film, *TB Silent Killer,* which will air on most PBS stations this evening and you'll have the chance to see it in full then. Today we're going to watch short clips from the film and then we're being joined by a group of experts, so we will discuss some of the implications of the film.

I think, as many of you know, TB, and in particular, multidrug-resistant TB, has been described by the World Health Organization, USAID, and others as a public health crisis or emergency. I'm not sure that you would gain that from the attention that it gets in the media, except perhaps, on World TB Day which, of course, was yesterday and there was a flurry of coverage in some outlets at that point. With some 8.6 million people estimated to be contracting TB each year, this is an opportunity for us to focus on the issues. Again, we're

very glad to have that chance to do so in conjunction with our colleagues at FRONTLINE.

We are going to start today by watching a short clip, which is actually the trailer to the FRONTLINE film. If we could do so, we will start with that now.

[Video Starts]

MELUSI: When they told me that she has TB, I felt so miserable. TB is the disease that can kill my sister.

MALE SPEAKER: This March, in a special presentation from the stirring landscapes of Swaziland in Africa, FRONTLINE tells the story of a brave and struggling community that has let us into their lives.

GCEBILE: They take us away from our homes so that we cannot be dangerous to the people outside.

MALE SPEAKER: To shed light on a new epidemic of a very old disease.

FEMALE SPEAKER: The treatment has got severe side effects which makes it quite difficult for patients to adhere to their treatment.

MALE SPEAKER: A disease that is becoming resistant to treatment and is spreading.

FEMALE SPEAKER: In developed countries, they should be threatened with this worldwide spread of TB.

FEMALE SPEAKER: Anyone can get TB. Anyone can die from TB.

MALE SPEAKER: An intimate story of people fighting for their lives.

FEMALE SPEAKER: I am deaf because of TB. I lost my parents and my sister because of TB. I've been out of school now because of TB.

MALE SPEAKER: Isolated from those they love.

MELUSI: I miss my sister. I miss her a lot.

MALE SPEAKER: Stories of courage, loss, and hope that the world will hear.

FEMALE SPEAKER: In 21st century, we shouldn't have people dying from TB.

MALE SPEAKER: *TB Silent Killer*, a special presentation coming March 25th to FRONTLINE.

[Video Ends]

PENNY DUCKHAM: Welcome to you, Jezza Neumann who is joining us from London and is the producer of this new FRONTLINE film. Jezza, one thing that I think is rather striking is the focus on this film on patients who have actually already gone through the hurdles of being diagnosed. In many ways, the challenge of being diagnosed was indeed the theme of World TB Day yesterday, to reach the three million who were thought not to have been diagnosed. Even when that has happened and they are getting care, the options for treatment are so extraordinarily limited and grueling and that's certainly not just the case in Swaziland, but indeed globally.

Could you talk a little bit about your experience when you got to Swaziland dealing with this?

JEZZA NEUMANN: Absolutely, I knew very little about TB myself before I went there. It was a learning curve for myself and I think the thing that really struck me, the thing that I found most shocking was that it's not so much the disease that people are struggling with, it's the treatment. It's quite amazing that, actually, when somebody starts on their medication for TB, on multidrug-resistant TB, it is that they actually start to get better, and then after a little while, they start to get a lot worse. Worse means that we met people who were suffering from hearing loss which can often lead to permanent hearing loss. They were vomiting and unable to keep their medication down. They were getting this, kind of, rheumatism and arthritis in their bones and their joints, which rendered them unable to do the activities they might have been doing previously. Bheki, a builder we meet in the film, he can't do his job any longer. He's a great soccer fan and he can't play soccer any longer. Their lives are, basically, falling apart around them. They become very isolated because their friends and family don't want to be associated with someone with this airborne disease because it can spread through the air. You get to a point that not only are the doctors on the ground having to deal with treating these patients, but suddenly they've got this huge mental health

burden as well. The patients are becoming highly depressed, to the point that one doctor even told me that she had a patient who committed suicide.

PENNY DUCKHAM: You touched there on this issue of stigma and while appreciating that obviously TB is extremely contagious, the patients you profile and their families, how difficult was it for you to find people willing to be interviewed?

JEZZA NEUMANN: It was extremely difficult. The point of making a film like this is that the sadness is really in the realities. For a lot of the families who take part in the film, whatever change is film can invoke, it's unlikely to affect their outcomes. They're already struggling, they're already suffering, so there's a real altruistic level everybody's going to have in this. You hope that on one level that the filming process can be enjoyable, and that's about myself, Rebecca, who made the film with me and Zandile, a local fixer, is about us making sure that we engage with these families beyond just making a film. There are days that you would go there and not even film. There was one point that Bheki's mother was trying to get the harvest in and the rains were coming so, literally, we put the camera down and we were there chucking corn into a pile for two and a half hours so that it didn't get soaking wet. That's what you do, I think that that's why we can bring a different level of humanity into

these films is because myself and my team around me, we were just a team of three, because I self-shoot everything. We were there and we have this intimate relationship with them and, therefore, they can see an opportunity to do something good and be part of something that can invoke change. But it takes time to find those people, it's not easy. In the case of Bheki and Zandile, who I mentioned, their mother happened to be someone who worked in the community trying to educate people to use western medicine and to be open about these things. In that case, that family was like that, but it took awhile to find them.

We had a young boy that we filmed with for nearly three weeks. After three weeks, his mother said, look, I'm really quite worried about some relatives we have in South Africa and can you guarantee to me that this film won't be seen in South Africa? I'm like, well, no, how can I? Even if I was to tell South African broadcasting they can't show it, there's still the internet, there's the web, there's all these mediums. We had to withdraw. There's no way I could openly film with this child any longer and with this family, knowing in the back of my mind that they would be false promises. That's hard, if you've invested that time and filming and you have to say, oh well, start again. But that's part and parcel of what we do and we understand that when we make these films. Ultimately if you take that time and then you meet the right people, like

Bheki and Zandile and then like Nokubheka and her brother, Melusi, then you start to create something much more powerful because everybody's in it together and the right reasons.

PENNY DUCKHAM: That's a great bridge for us to see a second clip which will just give a short piece of Bheki's story. If we would go to that now.

[Video Starts]

VIDEO PLAYING: [*subtitles*] Nokubheka's Story. Nokubheka is an orphan whose mother died of MDR-TB.

NOKUBHEKA: [*subtitles*] I think anybody can have TB, it's not choosy. I'm young—I don't know why it affects the young.

MELUSI: When they told me that she has TB, I felt so miserable, so dejected, so bad, because I know TB is a common disease which destroys people. If TB isn't treated, it can eventually kill the individual. TB is the disease that can kill my sister.

[Melusi reading to Nokubheka]

MALE SPEAKER: Their mother died from a multidrug-resistant mutation of tuberculosis known as MDR-TB. This form of the disease is far harder to treat. Melusi's greatest fear is that Nokubheka may also have the drug-resistant strain. She is already being treated for regular TB. Today, the nurse is bringing news about her latest test results.

NURSE: [*subtitles*] When Nokubheka came to the hospital we took her sputum and analyzed it to see what was causing the coughing. From that we found that she has TB. But we discovered that the TB is multidrug-resistant. There is normal TB, and then there is MDR. So Nokubheka's TB is MDR. MDR-TB is not as easy to treat as the normal TB. She'll have to have injections for a long time. For maybe four to six months.

MELUSI: [*subtitles*] I see.

MALE SPEAKER: The brother and sister share one room, so to protect Melusi from catching the potentially lethal infection, Nokubheka now has to go and live in an isolation hospital two hours away.

MELUSI: [*subtitles*] Being in the hospital for months, does that mean no school?

NURSE: [*subtitles*] Yes, that's a problem. How do you feel about going to the hospital? Hmm, Nokubheka? We want you to go to the hospital so they can take really good care of you. So you can have your injections and take all your pills properly. It's very important that you go to the hospital. Don't cry. You will get well. You will get well, my love.

MELUSI: [*subtitles*] I think the injections are frightening her.

[Video Ends]

PENNY DUCKHAM: We're being joined now by, to my right, Doctor Christine Sizemore, the chief of the TB, Leprosy, and Mycobacterial Diseases Section at the National Institute of Allergy and Infectious Diseases at NIH. Sitting next to her, Jonathon Gass who is currently a monitoring and evaluation specialist at Ariadne Labs in Boston and was prior to that, working for Doctors Without Borders, Médecins Sans Frontières, in Swaziland amongst other countries. And last but not least, my colleague, Josh Michaud, who is the associate director of the Kaiser Foundation's global health policy program.

Jonathon, I'm going to turn to you now. It's quite hard watching this film, partially because the patients are brave and, in this particular instance, a very young girl. It's also hard, the clips didn't cover it in much detail, but the film itself does, it's very hard for the doctors and the nurses and the providers in the field. Given your experience, specifically in Swaziland but in the field, can you talk a bit about the toll this very limited treatment set of options plays into the lives of the providers.

JONATHON GASS: Starting off, I think one of the biggest issues is the diagnostics for TB. Up until very recently, our very archaic methods for diagnosing the disease, as well as for detecting resistant strains of the disease, and so that lengthens the time from detection to actually getting a patient onto treatment. Secondly, the regimens that we use to

treat the disease were developed over 50 years ago. Again, they are quite outdated and very toxic as Jezza talked about, with multiple side effects which he went into which include psychosis, deafness, nausea, vomiting, et cetera. And then in addition to that, it just takes a very serious toll on the patients' lives because the treatment duration is so long. For drug-sensitive TB, which is your normal, quote, unquote, TB treatment, it's about six months or more, six to eight months of treatment. With multidrug-resistant TB, the treatment duration is anywhere between 18 and 24 months of treatment. Obviously, this takes an incredible toll on the patients' lives. They have to oftentimes stop working, et cetera.

Of course, witnessing it on the ground and seeing not only the toll that drug-resistant TB has had in Swaziland, but also the concomitant effects of HIV-TB co-infection, is quite a tragedy in Swaziland right now.

PENNY DUCKHAM: For both journalists and, indeed, providers in the field, the main protection is to wear a mask? But that means, of course, people can't really see you very clearly. Am I missing something, or is that really the main preventive step you both really take?

JONATHON GASS: Yes, you have to take, obviously, precautions by wearing a mask whenever you're in airspace with a patient. But I think Jezza, we were on a panel previously and he explained it quite well, that when you're interacting

with a patient or when you're a filmmaker and you're interacting with a subject, you look at people's mouths and it's one of the ways that humans sort of detect emotion and develop a sense of trust between the clinician and the patient, et cetera. When you're completely covered up with a mask and there's a small child, like Nokubheka you see in the film, of course she's going to be crying and a bit scared of the process. Of course, you have to take primary precautions for yourself.

JEZZA NEUMANN: But it is difficult because, as you can imagine, you are there to capture people's lives. Part of the process, too, not only do you wear a mask, but if you go into any of the Doctors Without Borders' clinics, they've got special vents in the ceilings so there's a through-flow of air, so you have at least three points of aeration in the clinic itself. In the National TB Hospital that I filmed in, you're supposed to limit your time on the wards. You should only really spend 15 to 20 minutes at a time, and then go spend 10 minutes out in fresh air.

Imagine us filming with Nokubheka on the ward and at one point she was telling us her heartfelt memories of her mother. Her mother only passed away two weeks prior to us arriving there. She's telling us about her mother and the stories and what she remembered about her, and it gets to 19 minutes and 58 seconds, you can't go, oh, sorry Nokubheka, I've

got to leave now, get my fresh air, and can you just hold that thought? Yes, you have to follow certain protocols, but of course, you've got to know what risks you take and how you bend them. Ultimately, at the end of the day, we have a choice to be there, we have a choice to do what we do. Jonathon has a choice to work in the field he works and he could work in a different field. I have a choice to be there as a filmmaker, I could make a different film. Nokubheka, Melusi, Zandile, and all the others, they have no choice. They're there, come what may. They don't get on a plane and go back to their homes in nice comfortable western America or UK. I think that's the point. We're conscious of that, as people on the ground, and that's the amazing thing about people like Jonathon and the other doctors and nurses on the front. They are amazing people doing amazing work, working against these conditions day in, day out. It is a hard toss-up about what you do and patient care, just on a basic human level.

PENNY DUCKHAM: Did you feel, Jonathon, the sense of urgency that this is, indeed, recognized as a public health emergency, crisis, both within the country of Swaziland and by all of us in the rest of the world?

JONATHON GASS: In Swaziland, there is no doubt about it, that there's a definite sense of emergency. The Swazi government, several years back, invited MSF to come into the country to provide technical assistance with their provision of

treatment for drug-resistant TB because they didn't have the capacity to fund it, to staff it, et cetera. As I said before with the HIV problem in Swaziland, they're already pushing their funds towards that and it's quite limited in their resources. MSF's stance is basically, we want to get the word out about TB globally. This isn't just a problem in Swaziland, this is a problem in low- and middle-income countries and some high-income countries as well. Funding for treatment is completely prohibitive, especially in low- and middle-income countries right now. We want to give a call to action, that this is an issue that people suffer with and the biggest problem that I see is that many of the suffering around the world are amongst the poor, and the poor don't really have a voice. It's our role to give them that voice and put forth the TB manifesto that we're going to present at the World Health Assembly in May to call for increased research and development for new comprehensive TB regimens, which I think we'll get into later, talking about the drugs that we use to treat. And shorter duration treatments with less side effects, adherence is a huge, huge problem. And, of course, one that patients can afford because the poor shouldn't be shut out from receiving treatments.

PENNY DUCKHAM: That's a great segue to you, Christine. Christine is on the front lines of research and development in this field. Could you start by just briefly giving us a sense

of the challenge? Is the challenge a lack of funding or priority for research and development in this field, or is it the complexity, in fact, of this multidrug-resistant strain or strains of TB?

CHRISTINE SIZEMORE: I think it's probably a combination of all because TB, as you know or might not know, is actually a fairly complicated disease. It's not a matter of getting infected, you get disease, you get over it, you're done and you're protected for life, you can't catch it again. TB is almost like a dynamic process, you can carry the infection without being ill, you can never develop disease, or you could develop tuberculosis, and then you have to go on prolonged treatment. But that treatment, taking up to two years for drug-resistant TB or nine months for regular TB, we don't know why that really is. All we know is that the bacterium starts to respond, somehow, to therapy which requires those long therapeutics.

In order for us to develop new drugs and also vaccines and diagnostics, we need to understand a lot more about TB as the disease, and especially how the bacterium behaves. You can't target drugs effectively against the growth of the bug if you don't know what it does or where it is. Those are a lot of the areas that research is involved in and, unfortunately, it's a very complicated process.

Also, to learn more about human disease, you have to have a chance to have products that have made it far enough into the clinic. Only once you know what they do in humans, can you actually go back and look at the science and say, could I have predicted this? Did I predict the candidates properly? Or what is it that we have to improve to actually get better drugs out there? It's a very iterative process but the good thing is, we have gotten to the stage where actually products are now being evaluated in humans. It's a unique opportunity right now, to learn a lot from those.

PENNY DUCKHAM: Can you talk a bit more about that, because we've talked briefly before this event about diagnostics, treatment, prevention, and, indeed, vaccines. I'm asking you to cover rather a lot in a very short period of time about what might be in the pipeline and what we should be, hopefully, looking for. Where would you start, if we were going to—

CHRISTINE SIZEMORE: I think, of course with a positive note, because when you look at the realities of TB and how difficult disease is, and especially as was very powerfully shown in this film, how brutal the second-line therapy is on the patients and the fact that they'll get sicker from the drugs than they actually are from the disease. I think it's heartening to see that we have candidates in the pipeline right

now. Some of those have been approved for very special use for patients that have no other treatment options.

I think that one thing we have to realize that in order to really make a big difference in tuberculosis, only focusing on people with already disease and trying to get them better, is almost like putting band-aids on. To prevent the disease in the first place and to diagnose it early enough before the infections happen, especially in the households where the mom infects the children, they then go on to infect others potentially. To have a vaccine and to understand what it actually takes for the human immune system to fight the bacterium once there's an infection that is, of course, almost like the holy grail in biomedical research at the moment.

Again, it's very complicated because, as I said, you can get TB more than once, so you don't have a life-long protection. A lot of people never get disease, they keep the infection in their body without symptoms. You need to understand what's different between them, why is it that some people get TB and some don't. To tease that out again requires a lot of studies that involve human volunteers in communities. And then to figure out what is it scientifically that I can learn from these processes. It's where a lot of the efforts in science are actually going on, and it's often referred to as biomarker research. We may have heard that term. All it says is to try to characterize the various stages of tuberculosis

and say, what molecules could we tease out of the body that indicate, you're infected but you might not get disease. Or you're infected, but you can protect yourself. And then try to develop products, eventually we can say, can we mimic this? Or how do we address the bacterium, how can we kill the bug?

It's sort of this interplay between all those disciplines, that's really necessary to provide the underlying science that then helps us to create the products. We are working, at least the investigators that we are supporting at the National Institute of Allergy and Infectious Diseases, we support them in all aspects of science. It's very hard to say, prioritize. Where do you prioritize because you need all those disciplines? And they learn from each other and that is where, basically, we're trying to put our focus to do more for product development and fundamental science.

PENNY DUCKHAM: I'm going to draw you in here, Josh, because yesterday the *Financial Times* had a special section on TB and described TB as the poor relation of global diseases. I think that stems from a number of different factors, but clearly one issue is the adequacy of the funding and the role that the US plays in this as a very generous donor in global health, typically across the board. Could you talk more about the funding issues and where things stand, specifically in relation to TB?

JOSH MICHAUD: I think there's a paradox when it comes to TB and the support that it receives. If you look at the overall global trends on the epidemiology of TB, they're positive. The millennium development goals, for example, called for a reduction in TB deaths, the rate of TB death from 1990 until 2015, of reducing it by 50-percent. At a global level, we're over 40-percent reduction from the 1990 baseline, which indicates that there's been some significant progress. Certainly some countries, where there's a large TB burden, have made significant progress, China being a shining example of that.

There's been this great progress, yet there's still this massive unmet need. The World Health Organization estimates that annually, about $8 billion is needed to fully fund TB programs in low- and middle-income countries, yet we're very far from that figure. If you add everything together at the global level, again we're talking about maybe $4 to $5 billion, so there's a big resource gap. That's always been present in TB, and it looks difficult to fill in the years to come.

As far as the US government goes, it's a very important funder of TB programs and I'll separate out the support for programs in countries from the research and development portfolio that Christine's been talking about. On the support to program side, the US government has identified and is

working with about 26, 27 countries, and supporting them through funding that's provided, and oversight by USAID mostly. That supports the prevention, the diagnostic, and the treatment programs in these countries. They're really focusing on the high-burden countries.

In the last few years, it's really been ramped up since about 2000, but it reached a peak funding level for the USAID global health funding of about $250 million in 2012. Since then, it's been stable at that level and gone down a little bit. The President released a budget request for fiscal year 2015, which is the first step in the budget process for determining the actual funding level which will come after Congress appropriates that money. Of course, there's a lot of time between now and then. In that presidential funding request for TB programs, it was set at a level of $191 million, which represents a significant cut. Of course, that's not the final figure, but there is concern about the fact that there is a cut in global TB programs just when there is a recognition of, we may be at a turning point in terms of diagnostics, in terms of different approaches in TB, and whether that's going to be enough to really fill the resource gap that's out there.

PENNY DUCKHAM: I don't know whether you would also touch, Josh, on while the film is focused on Swaziland, clearly this is by no means confined to southern Africa as a problem. Perhaps you could just briefly give us a sense of how this

plays out across the world and, indeed, the implications for the US.

JOSH MICHAUD: The first part of that, yes, Swaziland has recorded the highest rate of TB among countries, according to the World Health Organization which is really the source of information about TB. This idea of the 3 million missed is interesting. If 8.6 million people are thought to have developed TB disease, yet we're missing 3 million of those, that 8.6 million estimate is based upon an extrapolation or modeling and is based on the foundation of incomplete information. It's very difficult to know exactly what the burden is, and the more you look for it, meaning TB and MDR-TB in particular, the more you tend to find, so many people aren't counted in those estimates. Any estimates that you do see out there are best guesses and they're based on the best information that's available, but are often revised or should be revised and with more complete information, we'd have a better idea.

The global TB problem, the highest rates are in many of the countries in southern Africa and also Asia, if you're looking at TB, both drug-sensitive and drug-resistant TB. If you're talking about drug-resistant TB, MDR-TB in particular, the highest rates are actually found in eastern and central Europe. In fact, in countries like Moldova, there are estimates of one-third of the newly diagnosed TB cases in those

countries being multidrug-resistant which presents a very significant public health challenge.

PENNY DUCKHAM: Christine, can you speak a little bit about the challenge of diagnosing, and particularly the efforts to find quicker diagnostic tools?

CHRISTINE SIZEMORE: Yes, it's a very important issue. Right now, the best way, or the most frequently used way of diagnosing TB is really focused on detecting the bacterium in the sputum of patients. But what that, of course, means is that if you don't have pulmonary TB, and I can't isolate the bacterium, or I have very low levels of the bacterium in sputum, I won't find TB either. What's necessary is almost to go away from the necessity of looking at a very specific sample that the patient has to provide, that has a lot of bacteria in it. The research that's ongoing and that will be required to really improve diagnosis is to say, how else can I identify whether someone either carries the infection and is not yet ill, or has TB that may not necessarily by pulmonary TB, because once you have pulmonary TB, of course, you excrete the bacteria and you can infect others. How can I catch patients earlier?

But beyond the tools that are necessary is really, again, the science, like what molecules do I really, or can I find in the body that indicate the various stages of disease? Because in diagnostics, the difficulty is if you have to merge

technologies, which is basically the platforms, like is it a little strip that you can put a drop of blood on or any other sample. So you have the technology but you have to know what to look for. And what do you put in that diagnostic? How do you actually populate, almost like the technology with the biological molecules, so it identifies TB. And that requires a different type of marriage in science, almost, that you need in drug development and vaccines, because you need technologists and you need scientists, and they have to be able to talk to each other.

It's a lot of effort that is going on in that area of science to really assure that we're not dependent on just bacteria coming out of lung infections. But also to take the bug when it's in the body and it's not otherwise visible. And can take blood or urine or something that's very easy for the patient to produce to help with the early and faster diagnosis.

PENNY DUCKHAM: I'm going to open this up in a minute to questions and we will have two roving mics going around. While we wrap up this first part of the panel discussion, I guess my question to you, Jezza, is why did you go to Swaziland, beyond the fact that this is obviously a big challenge in Swaziland?

JEZZA NEUMANN: I have a tradition of making films to make a difference. The ethos of the company True Vision that I work with and films I made in the past is, basically, to give

the voice to the voiceless. Or find something that's happening in a society that really can benefit from a voice and can evoke change. I've worked in Zimbabwe, China, Tibet, Gaza, I made a film here in the US on poverty and it was told through the eyes of children and that was very much about their future, education, et cetera.

When Doctors Without Borders mentioned about TB and brought it to our attention and I looked into it, I could see this really was something that was neglected, that wasn't at the forefront of people's agendas. And there's a very human and real story there, there's a real human cost to what's going on. At that point, I feel that that's where I can do something, where you have an issue that people have been bringing reports about, there's facts and figures and they're landing on desks and becoming coffee cup holders. That's when I can make a difference because I can bring the human face of the issue and combine that with the reports and get the reports, the stats, the facts, let the guys who are good at that do that. I'll bring the human cost of what we're talking about, put them together, and surely people have to sit up and listen.

That's what I saw here in Swaziland, there was a place to do it and there was a place to get understanding, and try and get this on a level. These are the things that we try to do and looking at the characters that we have in the film and

the people that we followed. If you look at the idea that Bheki loves soccer and soccer's his church, for me, that would bring that home a bit because I get it. I get that Americans have busy, crazy lives and they're going to come home from work and it's 10 o'clock at night, this is going to go on television, and I'm asking you to watch something that's quite a hard watch that you've got to invest in. How can I make that something that you can get something from, not just learn about this strange place? How can I bring Swaziland into your living room?

And that's about the people that are in the film. If you see Bheki, you'll identify with him. How many people have Monday night football and get what he's talking about, his church? If you look at little Nokubheka who loves flowers, loves the color pink, plays with dolls and dances, she can be any little girl next door. I think if we can get that right and follow those kids and give justice to their stories, then hopefully, people will be captured into this and the adage is, if I can capture the heart, your heads will follow. So that's the premise of what we're trying to do. Ultimately, I saw that Swaziland TB was something where I felt that I could make a difference and my team could make a difference for Bheki and Zandile, that we could do something that could hope to evoke change.

You've got to remember, when we talk about these regimes, this treatment, I think it's really important to bear in mind that by the time Nokubheka, when you see her in the film, would have finished her treatment, she will have had up to 240 injections and consumed 14,600 pills. How many people out there struggle to take their multivitamin? And that's not a lifesaver, you know?

You can really see what we're talking about is really real issues, really real problems, and it always seems that with TB, from what I've learned on the ground, is we seem to be one step behind all the time. We talk about diagnostics, it touched on here. They brought out a machine called the GeneXpert. It was supposed to be the holy messiah of diagnostics that now they don't need to grow culture for six weeks, they can find it out in three days. It's too late in Swaziland. There are already strains of MDR that are not picked up on GeneXpert.

That's just another case of, yes, great stuff is being done, and let's not diminish the work that's being done. But the fact is, it's too little, too late at the moment. We need to start being proactive. I think that's the issue in the West, I've seen it time and time again, and I'm guilty of it. We're reactive, we wait for the flood to happen and the houses are washed away and the peoples' lives are destroyed before we do anything. With TB, I think that everyone would agree, that

really we can't wait until it's a problem here in America. If you do, it's a serious problem, because these guys aren't going to be able to give you a new drug in a day. It's something that needs to be invested in now, to stop it. It really needs to be one of those issues that we're preemptive about, we're not reactive.

PENNY DUCKHAM: But Jonathon, as new drugs and new diagnostics do come down the pipeline, there are obviously the challenge for the people in the field to incorporate that into the treatment regimen and not allow new resistance to emerge. Could you just address that?

JONATHON GASS: Yes, like I said before these, sort of, old TB drugs or this category of old drugs that we use to treat drug-sensitive and drug-resistant TB and, sort of different combinations, have obviously produced some level of resistance in multiple strains that are out there. The worry is that there are two specific new drugs, new, new drugs that have been developed by pharmaceutical companies, that will be incorporated into current regimens with old drugs that have a resistance profile to them already. The idea being that one drug, mixed with these old drugs that are, all we have right now but not good enough, is simply not a very comprehensive improvement for the regimen as a whole. And also, these two new drugs that have come out have quite low barriers for

resistance themselves. I don't know if that gets to exactly what you were asking?

PENNY DUCKHAM: Well, it raises issues, and Josh, maybe you have—

JOSH MICHAUD: I wanted to add, thinking on what Jezza and what you had said, it's amazing to me that in the film it's depicted that the health system is working fairly well, in that it can diagnose, or at least work with patients such as they're shown in the film and have the drugs available to treat those patients in the TB hospital that has a fairly high level of functioning. Beds are made, et cetera, it's clean, it's got windows and that's not necessarily the case in TB programs. A reflection of the funding gap that's out there, I think in many places you don't even see that level. Maybe it's a testament to MSF working with the Swazi government on this, that it's working so well.

There are global funders out there, the World Health Organization is working on this, the Global Fund support is the largest donor in support of TB programs out there, they provide 60-percent of the donor support for TB programs. Even that, it's not enough. It's almost an anomaly in a way, right?

JEZZA NEUMANN: Yes, but it was a lesson that the Swazi government had learnt from other countries. In fact, when you speak to Tamber who runs the TB program there, he's very proud of the fact that they have not had a stoppage in drug supply.

Drug supply, he saw how that had caused serious problems in other countries, so that was something that they were quite keen on was the drug supply. Obviously MSF has supported that in a big way, but the big other element is that what they really want to do, and what they've learned through Doctors Without Borders is that decentralized care is really the way to go.

You don't want people traveling on multiple buses like little Nokubheka does in the film to get to the hospital because then she could be infecting people all the way there. They want to have this decentralized care program, so for them, that's the issue, MSF completely propped that up in Swaziland. They have the four by fours that go out to the villages with the MSF/Doctors Without Borders personnel on board and injecting families outside in the rural areas, and that's the thing that Swaziland is finding really hard to deal with.

They've maintained a good drug supply, but if Doctors Without Borders left tomorrow, they'd have no way of getting those drugs to the patients. That's their issue. Their issue is they need funding for that. So each country, and like you say, yes on the face of it, it looks like it's working, but it's not working completely. I think anyone in the country would also argue that because it went on for so long, there are so many patients out there in Swaziland who are yet to be diagnosed.

PENNY DUCKHAM: Do you want to comment on that, Jonathon?

JONATHON GASS: Yes, I'll just say that the National TB Hospital, as you saw in that clip, looks all built up and it's there as a resource and there are drugs, as you say. But when I was there, for example, there was a three or four month period where every single nurse in that entire hospital went on strike and the patients were just lying in their beds. That's the reality of the situation because the nurses didn't have personal protective equipment for themselves to buy. So maybe there were drugs and through the drug pipeline came down, but a nurse doesn't wear a mask is going to be a nurse who is ultimately infected with TB or drug-resistant TB.

So they banded together and they decided to go on strike, which is obviously a huge issue because they're already underpaid as it is. So then they're going without payment for awhile and MSF stood in and continued the operation in the hospital for some time. But there's obviously stigma attached to it, nurses feel that they want to be paid more because they're at higher risk treating patients with drug-resistant TB, et cetera. I means, it's a very complex issue, yes.

JEZZA NEUMANN: In the context of the film, so you understand, of course there are lots of issues. In Swaziland it's HIV that causes the reduced immune system to give you the full blown disease, but that's not the case, necessarily, in

Eastern Bloc countries where it could be living conditions. Or it's not necessarily the case in China or India, but I'm looking at a micro story, so I have to tell this, in the back of my mind the whole time I'm putting the film together is, I don't want to let you off the hook, I don't want you to go, oh, well, it's only HIV, we don't have HIV, we don't need to worry about that. I don't want you to go into it and go, oh well, the hospital waste, the government they're not paying their nurses correctly, that's why there's TB, it's their fault, it's Swaziland's fault, we don't need to worry about that. You have to be really, really conscious the whole way through. I don't want you to be heading off on a path in one direction or the other, which is why, you know, and it comes up. I've had people, even Keyes who runs the TB for MSF in Swaziland, he said to me, well you don't really cover decentralized care properly, do you? Well, no, Keyes, the point is that neither of my characters got treated in that way, they actually went to the hospital.

You can't cover everything, but you have to be really conscious the viewer isn't taken off on a different path. Obviously, in these discussions, these things come out. But when you're watching it in the context of the film, I want you to be engaged, primarily, with Nokubheka, with Melusi, with Zandile, with Bheki, with all these people with real names and real lives who have real hopes and real desires for the future.

So that what you take away from it is, my goodness, really? Because that's what's going on, and how you can engage in that in a way that will make you want to look at this further and maybe read into it more and then learn the things that the Josh's of the world can tell you. So that's the point within the context of the film, you're trying to, in a way, make this incredibly complicated story as simple as possible.

PENNY DUCKHAM: And on that, I'm going to open this up to questions from the floor. If you would, there are roving mics, if you could speak into the microphone and if you would introduce yourself before you ask your question. I appreciate that we've all seen the film and you haven't, more and more reason to watch this evening.

SHARON LADIN: Hi, my name is Sharon Ladin, I'm with Summit Strategies. I was wondering if you could talk a little bit more about the pipeline and what needs to be done in terms of encouraging private pharmaceutical companies to get involved with this, what the balance is between public and private investment, and how you address the fact that you're hitting a moving target. Somebody may be developing a drug to target what is a current strain, and by the time that drug is through the pipeline and gets approved, you now have a new MDR strain that you're fighting against and you're still behind the curve.

CHRISTINE SIZEMORE: Very good questions, and I'll try to keep the answer manageable. When you look at the current

pipeline, it is focused, of course, on individual drugs. But what is often not reflected in the pipeline is that there is also a variety of organizations that are trying to develop new regimens from the beginning. So not one drug at a time that you then combine or add to existing drugs but say, if we shuffled the deck completely differently, can we come up with new regimens that are able to treat the disease either faster or with fewer side effects. That is the big effort that is going on in the field as well.

The balance between public and private investment and especially the issue of pharmaceutical companies involved in tuberculosis drug development is, unfortunately, a difficult one and not just limited to tuberculosis, but infectious diseases in general. There's a perception, and it's probably from a pharmaceutical perspective, a true statement that the market may be too limited. It takes a lot of money to make a drug, and while I could argue that if I can't recover my costs, it's not worth for me to be in the game. That said, though, the drugs that were just recently approved provisionally to help people without other treatment options who have MDR-TB, came from large pharmaceutical companies. But there are also smaller biotech companies in public/private partnerships that are working in that space.

The balance, and especially our contributions at National Institute of Allergy and Infectious Diseases, since we

are one of the largest funders of biomedical research in that space, is we try to help people, what we call, de-risk their products. And that's basically, if you have an interesting candidate but you're lacking the resources to get either medical evidence or information so you can take it into the clinic, we try to help them to get to that stage. With the expectation, then, that there are other funders and other partners who take on those molecules or those regimens to develop them further.

In the TB product development area, luckily there is a consortium or a good collaboration among the largest funders or the major funders, pharmaceutical industries, biotechs, public/private partnerships, and then also, some of the more patient communities, to say, how can we really populate every step along the way to drive new products to patients as fast as we can. Is it easy? Absolutely not. Very challenging, takes a lot of time and a lot of products fail. That's, I think, where one of the issues that you've pointed out earlier is, it's going to take some time to get new drugs. It's not a matter of, if you throw a lot of money at an issue you can force innovation. It's almost like steady support, steady effort and emphasis on new product development and recognizing that things would have failed, but the community has been able to learn from failed clinical trials, from lessons learned in vaccines and diagnostics and drugs to say, okay, how are we

going to do better? The need is there, the emphasis is there, are all the players at the table? Not always, but so far we've been able to at least do what we can with the resources available.

PENNY DUCKHAM: Other questions?

RALPH PAEZ: Hi, my name's Ralph Paez. It would seem important to identify the carriers who show no symptoms. Is there any work being done in that area or how do you test an entire population to determine the carriers?

CHRISTINE SIZEMORE: Yes, that's actually another very good question and one that's, again, a combination of science, technologies, and then also the realities of tuberculosis in the field. Even if you had a tool to say, I can identify all the carriers, you need someone who produces it, someone who can sell it, and then programs that can actually apply it to people. So how do you say, who do I test? The emphasis on trying to find out who carries the bacterium without having disease is actually, by the research community, taken up very seriously. It is one of the priority areas of multiple funders.

It's basically, if we can detect individuals with the highest chance of progressing to tuberculosis, we can give them even the existing prophylactic treatments. There are drugs that you can take for several months and it should at least prevent the initial episodes of the disease. Again, since you

can get TB more than once, this is not a one-time process. You're infected once, you may be able to deal with it, you can get it again. In the end, focusing on those individuals, I think, is a good goal but having a vaccine that prevents disease from occurring in the first place in all types of individuals, infected or not infected, would probably be the most effective tool that we can get our hands on, and they're working on developing. All the other aspects, again, are important, but maybe harder to implement, again, than having an effective vaccine.

JOSH MICHAUD: I'd add that, yes, there's the tool aspect and then there's the public health practice which you mentioned. But there are certain public health practices which are practiced in this country, for example, with contact tracing where if you have a TB diagnosis you go out and find who that person has maybe contacted. That may not necessarily be the practice in countries, mainly due to resource constraints. That is where you would find a whole lot of additional cases.

I don't know if you saw that there has been an announcement made about children and TB and on the estimates that are out there previously. Yesterday a study was published saying that there's an estimate now of a million children with TB, which was double the previous estimate out there. It was really a matter of building a better evidence base. One of the

aspects of contact tracing is often, if you have an adult with TB then a child with it in the household who may also have TB, but that's not necessarily followed up on in every case. In this country, yes, but other countries, not necessarily.

PENNY DUCKHAM: Do you have anything to add to that, Jonathon? I wondered what's the practice and—

JONATHON GASS: In Swaziland, in particular, we do contact tracing, especially with children. One of the biggest issues is that pediatric patients don't necessarily produce mycobacterium in their sputum, so we have to go to an extra level of investigation and do a gastric lavage or what have you, in order to diagnose them with the disease. And so there's an added with issue with the pediatric patients area.

PENNY DUCKHAM: Could you talk a little bit, Christine, about TB treatment in this country and the degree to which it is totally comparable or different from what we've been talking about in the context of Swaziland or other countries?

CHRISTINE SIZEMORE: I can touch on it, it's not our area, at my institute we don't provide treatment, but we work, of course, with our colleagues at the Centers for Disease Control and Prevention. The few instances that I'm aware of where patients, especially with very complicated tuberculosis or multidrug-resistant tuberculosis were treated, is that we have the advantage of providing what you might want to call individualized therapy. That is, patients are really watched

very closely for how much drug they have to take, how high the drug levels in the blood are, are they most effective against the bacterium? So I think patients in the US, actually have great advantages because they don't get a standardized cocktail of drugs until they respond.

But if they're not responding properly, we can switch things, we can dose higher, we can manage the side effects, because that's one thing that's often not addressed in TB treatment. It's not just having the drugs available to treat the disease, but how do you manage the side effects? Can you give a patient something so they don't vomit and they can keep their drugs down? In the US, I think we're actually in a very fortunate place. Globally, TB cures are often highly standardized and before someone is identified with drug-resistant TB, it's not just a matter of getting a diagnostic test that says your bug is resistant, but they failed therapy for drug-sensitive TB multiple times. They keep getting drugs for nine months, they're not going to get better. They get it again, they still don't get better. And then they become suspect. And at that point they have drug-resistant TB, if this developed during therapy, or if they came with it, they've already infected a lot of other individuals. There isn't this individualization of being able to really cater to individual patient's needs as we do in the US, I think, is not available elsewhere.

PENNY DUCKHAM: Question in the back group.

BEN BROWN: Hi, my name is Ben Brown from Results for Development Institute here in DC. I was hoping any of the panelists could share a success story or two from a low- or middle-income country at a district level or a country level, where you've seen programs have achieved a high degree of success.

JOSH MICHAUD: One example I've referenced already, which is China, since 2000 has made a lot of investments in its public health infrastructure and about TB in particular. They've exceeded the millennium development goal of reduction, they've achieved a greater than 50-percent reduction in their TB death rate, which is quite remarkable. They still have a very large number of TB cases and a lot of work to do, but the progress made in China has been somewhat of a success story. At least it's an example of, if you invest in public health infrastructure, and TB is often an indicator of lack of investment in public health infrastructure and an indicator of poverty, where health systems aren't that strong. Another example might be Brazil at the country level.

JONATHON GASS: And I'll just talk on that for a second. I actually think the question is very good because it's important that we also focus on the success stories. And there are successes, of course, patients can get cured. We have a campaign at MSF called, TB and ME, which is an online

resource for both laypeople and patients themselves, and clinicians to go on and write about their experiences, either with TB, treating TB, having a family member with TB, multidrug-resistant TB, et cetera. There are plenty of patients on there that have successfully achieved a cure at the end of their very laborsome treatment. But I do think it is good to also focus on those that did make it through that battle.

JEZZA NEUMANN: Yes, and I actually in the context of the film, once you get to see the film, there is a point in the film where there's a group session in the clinic. There are a lot of MDR sufferers and their care and their group session. In fact, the person running the group session is an MDR survivor, she was someone that was treated successfully in Swaziland and then what she does, is she's used by Doctors Without Borders to do this mental health therapy with the patients. They are constantly getting feedback and saying, hey, look, this is tough, this is hard, we know it, and I know it because I've been through it, but I'm here today to talk about it. Of course, there are those and then that is used to try and help people get through it.

PENNY DUCKHAM: Any more questions?

DAN COLLINS: I'm Dan Collins, I'm with the Lilly Foundation, thank you. Thanks for the presentation, it's been great. Knowing that the US government's gone down in its

funding and probably won't go up too much, I'd be interested in all the panelists' perspective on this, if you were in control of that budget, what would be the one or two things that you would focus on, where the real solution opportunities are? Knowing some of these things may not be budget-dependent, what would be the greatest bang for the buck do you think in resolving, or at least making the most progress towards resolving issues primarily around MDR-TB?

JOSH MICHAUD: Well, I'm going to avoid your question completely and answer a different question. That is, I mentioned the client and the quest for the bilateral budget, but the US, of course, supports the multilateral Global Fund, for significant funding levels. There has been an increasing emphasis on using a multilateral instrument like the Global Fund for HIV, but also TB. Within that portfolio of the Global Fund, TB is around 16-, now bumped up to 18-percent of the funding for the Global Fund. So compared to HIV and malaria, it's the smallest proportion, but that becomes a very critical part of the Global Funding level and of the US contribution to TB control.

There are, within that Global Fund portfolio, efforts to both address MDR-TB and also this relationship between HIV and TB. In fact, countries with high burdens of TB and HIV are now required to submit joint proposals on those two for

funding. I'm sorry I didn't answer your question, but, I don't know if anybody else has anything?

JONATHON GASS: I just want all of the money. [Laughter] A good answer would be that this GeneXpert diagnostic machine that Jezza spoke of, also tests for resistance to two of the first-line medications that we use. It's able to diagnose someone within, I believe, two hours. So you have the patient who won't leave your clinical environment, that you can then start on treatment either right away or start them counseling and developing a treatment plan, et cetera. They've done these studies saying that if you're diagnosed using GeneXpert, you're three times more likely to get treatment on time then if you're diagnosed with these, sort of, more archaic methods. The problem is, the GeneXpert machine has gone down in price significantly but it's still very, very, very expensive.

PENNY DUCKHAM: Are you going to take a stab?

CHRISTINE SIZEMORE: Oh yes, absolutely. We get that question a lot, believe it or not, what is the highest priority and where should you focus and where should you put all your money for the biggest bang? The way we try to manage this question in our minds is often, start with two categories, public health and patients.

If you look at the public health impact that you can make in TB, which is basically prevent new cases from

occurring, it's the multitude of approaches you can take, diagnose faster, treat faster, have a vaccine. But then you look at the patients and the reality of the patients is, we tend to focus on, you are a patient when you have advanced pulmonary disease or multidrug-resistant TB. But you also have family members that need to be protected, you have communities that need to be protected, you have people that want to be diagnosed faster.

Once you start prioritizing and saying, I should put all my money into drugs, you are focusing on individuals with disease. It doesn't work. Only focusing on diagnostics means I'm still only focusing on people with disease, but you're not working on the patient level of, I don't want to get disease in the first place. So to prioritize and say, if we have better drugs, problem solved, not the case. With better diagnostics, again, it's not going to help you, either. I think if you follow the global strategies for tuberculosis control and especially the modeling, in those documents it is very clear that one individual intervention or one type of intervention is not going to be sufficient.

You have to almost focus in multiple dimensions. You need the new drugs, the new regimens, the vaccines, the diagnostics, and the underlying science that actually gets you to that place. The post-2015 global strategy for tuberculosis got simplified quite a bit. It's going to rest on three

pillars, a third of which is supposed to be improved research to help facilitate product development. To focus on one area or the other, saying we need to invest more here, will take away from the other areas. When you look at it from a higher level perspective, it's not something that is probably going to get us the results that we want.

PENNY DUCKHAM: Jezza, want to take a stab from your perspective?

JEZZA NEUMANN: Yes, as a filmmaker, I'm such an expert in these things. At the end of the day, you can put logic to it. Ultimately, there are a lot of people doing a lot of important things and they all need money. This is a global threat and it's happening across the globe. I think the reality is the only way it's ever going to get to the point that everybody wants it to be, is there needs to be a forum of all the experts.

The R&Ds need to get together with those implementing it in country, and we need to map out the world and go right, Swaziland, what do we need there? A serious issue there is decentralized care. So we know we need a budget for that there. What do we need in Eastern Bloc? What do we need in India? And they need to sit down together and go, right, we've got this amount of money and we need to do this amount of on-the-ground stuff, right. How much can we then put into developing the next bit, the new drugs, the vaccinations?

It needs to be done properly, though, where you actually know the money you're being told is real money, it's not money that's going to suddenly disappear a bit. Sorry, man, I thought I had 50 quid in my pocket, I've only got 20 now. And that's the problem with all these issues, that the money that's there is suddenly not quite the money you thought it was when you came to pay for the new drug supplier, pay for the new four by four. It seems to me that what everybody wants is one cohesive platform to work together, but knowing what have we got, what is the cash there that we can use, and how are we going to make sure that that cash is best used?

For example, there are plenty of countries, and I know Swaziland is one of them, they've applied for funds but they're up against the fact that maybe at different times in their governments the funds haven't quite ended up where they should have done. So now they're being hit by that. They might have a really good TB program, but they can't get their hands on the money. How do we then police the funds that are there? How do you police that within the countries? Rather than going, well, we're not going to give you the money because it might not end up where it's supposed to. The whole time you're doing that, these TB programs are getting hit and patients are infecting other patients. It seems to me, we kind of almost need to draw a line in the sand and say, okay, that government was crap, that one was, that one's not, that one is. Let's draw a line

in the sand and let's now work out how do we do this, how do we fix this, how do we get the money to where it needs to be?

PENNY DUCKHAM: I think I would just add that the problem is, perhaps, exacerbated by the lack of media coverage. Yesterday was World TB Day, so you know there's suddenly a spate of coverage by some news organizations, but on the whole there's very little coverage, I think, of TB. Perhaps, linked to that, Josh could correct me on the figures here or Jen Kates, my colleague here. Kaiser polls show that the American public thinks that an extraordinarily high percentage of the federal budget goes for foreign aid and global health, in particular when in fact less, as I think you all probably know, less than 1-percent of the budget—

JOSH MICHAUD: On average, 28-percent.

PENNY DUCKHAM: And 28-percent think, I mean, that is really a mismatch in reality and it definitely plays into this debate about where the US budget should go. Do we have other questions, or is everyone waiting with a great anticipation to see the film this evening? And then you could, of course, follow up, I'm sure there will be other opportunities to address many of these questions.

JEZZA NEUMANN: We'll have live Tweeting during the film, and then the day after, on Wednesday, there is a webinar where there'll be myself and a couple of proper experts, rather than me, to answer any questions. If you do watch the film,

which I hope you all will, it's only 80 minutes, it's not a lot of time, it's a small part of your life. If you watch it and then you have other questions and thoughts, you think, oh, I wish I'd known this yesterday, you can come online at 3 o'clock tomorrow and, equally, there is an opportunity to Tweet Out during the film while it's going out. Although I get really angry about that because I think you should be watching the film. [Laughter] But I know we need it, so. Honestly, so Tweet Out or there's the web at 3 o'clock the next day.

PENNY DUCKHAM: I'm going to thank our panelists for joining us today. And thank you for coming out in the snow to join us and hope that you will, indeed, have the chance to watch this very powerful film. Thank you again.

[END RECORDING]

[1] The Kaiser Family Foundation makes every effort to ensure the accuracy of written transcripts, but due to the nature of transcribing recorded material and the deadlines involved, they may contain errors or incomplete content. We apologize for any inaccuracies.