

FINISHED FILE

SPH READS: EVERYTHING IS TUBERCULOSIS
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>> DEAN HYDER: Welcome. Welcome, everybody. I want to get this seminar started, so good afternoon. My name is Adnan Hyder. I have the privilege of serving as Dean of the Boston University School of Public Health. Welcome to this Public Health Conversation. This is under the theme of our 50th anniversary celebrations and also a theme on a special perspective on the future of public health. We are really delighted today to have this public health conversation on a topic that is of local, national, and global importance.

I'm delighted that today we are going to kick-start what we call SPH Reads. It's a book selected which all of the school faculty, staff, and students read, and today we are going to share this with our local, national, and global community. The book for this year is "Everything is Tuberculosis" by John Green, and I have my copy here, and I have read the book as well.

Tuberculosis is a centuries-old disease, and yet, despite all the advances of technology, medicine, prevention, public health, clinical work, we still, unfortunately, have not won the battle on this particular disease, and John Green highlights it incredibly well in this book. I look forward to this conversation with amazing panelists.

And, in order to introduce them and to begin that conversation, let me welcome Professor Yvette Cozier, our Associate Dean for Diversity, Equity, Inclusion, Justice, and Wellness. Yvette is an expert on epidemiology, looking at cohort studies. She's also spent a tremendous amount of time looking at social determinants of health, and I couldn't think of a better person to both select the book, but also moderate the conversation. So, Yvette, over to you. Thank you for moderating this seminar.

>> YVETTE COZIER: Thank you, Dean Hyder, for that great introduction. It's my pleasure to be moderating today's discussion.

So, before we get started, I'd like to just share a note on the program, how that will flow. I will start off by facilitating a group discussion with our panelists. Then, towards the end of the program, I'll turn to some questions from the audience. For audience members who would like to submit questions, please use the Zoom's Q&A tool that you'll find at the bottom of your screen.

Now I have the privilege of introducing today's speakers. Dr. Charles R. Horsburgh Jr. has over 30 years of experience in public health and medicine. He currently holds faculty positions in the Departments of Epidemiology, Biostatistics, Global Health, and Medicine at Boston University Schools of Public Health and Medicine. Dr. Horsburgh teaches courses in the Epidemiology of AIDS, the epidemiology of Tuberculosis, and Vaccine Epidemiology. His research focuses on Tuberculosis, non-Tuberculosis mycobacterial infections and opportunistic infections in AIDS.

Dr. Bruce Kirenga is the Principal at Makerere University College of Health Sciences. He is a pulmonologist, researcher, and founder of the Makerere University Lung Institute and an Associate Professor in the Department of Medicine at Makerere University. His work has contributed significantly to the understanding of airway diseases and TB control in Uganda and beyond.

And finally, Dr. Carole Diane Mitnick. She is a Professor of Global Health and Social Medicine at Harvard Medical School. Dr. Mitnick's research centers on the improvement of clinical management and programmatic policy for Tuberculosis and multi-drug-resistant Tuberculosis globally. Dr. Mitnick is a founding investigator of a movement to conduct randomized controlled clinical trials to improve drug treatment of drug-resistant TB. Now to our discussion. And I want to welcome all of you. Thank you so much for being here. Yes. Thank you. Thank you.

To start off, I'm going to jump in and focus specifically on the book, "Everything is Tuberculosis" by John Green. What is your favorite aspect of this book? And what would you say is the key takeaway, apart from the title of the book itself? And I'll start, as I see on the screen, I'll start with Dr. Mitnick.

>> CAROLE MITNICK: Thank you so much. So, I think that my favorite aspect of this book is its accessibility, and that I think that comes as a surprise to many people who are pressured by me or others to pick it up, that it is something that can reach a much broader audience than would normally read about TB, and I enjoy that and the humanity of it.

And I think that that relates to the takeaway in that John Green is very able to clearly articulate that the problem of TB in the 21st century is a human-made problem, and that it is a problem that if we chose to allocate resources to where the biggest burden lies, it's a problem that could be eliminated, and I think he makes that case so clearly in his story about Henry and also talking about many of the examples of innovations that are not reaching the people who need them on a population level.

>> YVETTE COZIER: Thank you. Dr. Kirenga.

>> BRUCE KIRENGA: Yes. I think what I found very interesting about this book is, as I was reading it, you start to think you are reading a medical book, but then you start to also see aspects of any other book that you can read that is talking about (?) and I think combining those two in one book is very special.

For the takeaway, I think it's not so different from what has been mentioned. I think pointing out in a clear way the broad drivers of TB is very important. The poverty and all these issues that usually do not receive the attention as TB modifiers. And I found that to be directly. Thank you.

>> YVETTE COZIER: Thank you. And Bob?

>> ROBERT HORSBURGH: Yeah, I found it quite interesting that John was able to portray Henry and his situation in the hospital in a way that was very generalizable. I have visited hospitals like that in South America, in Asia, in Africa, and the picture he painted was exactly the same that I've seen in all of those countries. It embodied both hopefulness and despair, because patients are fighting for their lives, and sometimes they make it and sometimes they don't, and it was a very accurate picture of what's really happening in many countries.

>> YVETTE COZIER: All right. Thank you. Thank you all for that. So, I'm going to just follow up and start talking about Henry -- really kind of one of the central figures of the book. For those who haven't read it, a brief introduction is that Henry Reader -- I think is the way his last name is pronounced -- is a young man in a hospital in Sierra Leone who, when first met, was mistaken for a young boy, but he really was, you know, a teenager, an adolescent, from the ravages of the disease.

So, just that being said, you know, and also that he suffered from multi-drug-resistant TB -- was his situation a worst-case scenario and representative of care in other regions? So, Bob, you said that that hospital seemed very similar. Was this what you see everywhere?

>> ROBERT HORSBURGH: It is definitely a scene that is played out over and over again. The good news is, in this situation, the ending was a happy one, but it often is not. And I think John Green portrayed it well in that you really didn't know what was going to happen. It sounded like it was going to be a tragedy, and then at the end, it turned out well, but that's not the case. In fact, that's not even usually the case.

>> YVETTE COZIER: So, following on that, here in the United States, we don't think about TB very often. This is to us an ancient disease. We hear about it usually in the context of other diseases. What really is the burden of TB in the U.S.? Dr. Mitnick?

>> CAROLE MITNICK: Yeah, it's true. Yvette, I can't tell you how many times, when people ask me what I do, the follow-up question is, is that still a problem? Or why? And it just happened on an airplane last week, back from Europe.

So, the burden in the U.S. There are about 10,000 cases of Tuberculosis each year in the U.S., and that number is growing. It continues to be a disease that disproportionately affects people who are disadvantaged in settings in the U.S., just like it does elsewhere in the world. And there are still people who die of TB in the U.S., again, a disease that has been preventable and curable for about 80 years, and we are still seeing deaths here and around the world on the order of 1.25 million people around the world each year.

>> YVETTE COZIER: And Dr. Kirenga, so as a pulmonologist in Uganda, one, how does Henry's experience relate to what you experience, you see, in your work? Let's start with that part. I have a second follow-up part, too, to that question.

>> BRUCE KIRENGA: Yeah. It is difficult, how the TB patient we've been seeing for over the years, although I can say in the last ten years there has been improvements in this situation. And this situation was typical when you talked about drug-resistant TB.

At the time when I was joining in my practice, we had no treatment for this and patients would go down as you see each

day and each day until they get weak and weak, until either they go from your care or you could see them depart. So, the situation is typical.

But the story described in the book -- although we now have less active TB patients who look like that, it is also a story that we are seeing from people who have recovered from TB, and they have remained with residual damage from their lungs and they live with this chronic lung disease, which actually also brings me to the question that, as I was reading the book, I wanted to see what actually happened two-three years for this patient, probably they may still have some residual problems.

>> YVETTE COZIER: Okay. So, curing, or clearing it, if successfully, there's still significant damage that can be done along the way, that individuals still have to live with for the rest of their lives, if I understand that. So --

>> CAROLE MITNICK: Yvette, if I may just add on that. I'm really glad Bruce brought it up, because it's not really something that's mentioned in the book, and I think it's something that those of us who have worked in TB have honestly been very slow to attend to. There is a groundswell, I would say, in action acknowledging this, that the current estimates are that about 60% of the estimated 100 million survivors of TB in 2020 had some kind of pulmonary compromise, some kind of long-term sequelae. So, there's the burden and then there's the lifelong burden that many, many people struggle with.

I can report, Bruce, that we actually got to meet Henry last year at the Union Conference in Copenhagen, and overall, he's doing well. He does still -- he has lots of health issues that arise, but overall, he's doing well and he's about to graduate from university in November.

>> YVETTE COZIER: Wow. That's a great follow-up. That's a great follow-up, because his story is so endearing and inspiring.

So, when we think about these things -- I'm just kind of putting on the hat of, you know, non-infectious disease, epidemiologist. So, first thing we think is, how do we prevent it? So, our most-recent experience with a large-scale respiratory disease was COVID. And masks became a big part of that, and isolation. Can any of you speak to what both the goals of isolating TB patients, as well as are masks effective, or is that part of preventive efforts?

>> ROBERT HORSBURGH: I'll respond to that a bit. Masks are very useful in preventing the spread of infectious diseases that are respiratory, but in fact, in many communities where Tuberculosis is substantial, there are many people who don't realize that they are spreading TB because they're not that sick, they don't feel like they need to go to the doctor, and so the issue is that they don't see themselves as being sick, so they don't see themselves as wearing a mask, and that means that the disease is spread.

Obviously, just like with COVID, we'd like to have a vaccine, but we don't have a vaccine that will effectively stop the spread of TB, although we are hopeful that we may, in fact, have a vaccine in four to five years. There's a trial going on that the Gates Foundation and the Wellcome Trust have sponsored around the world, and so that might provide more hope.

But in reality, we now have better drugs, and we really just need to get out there and screen and find the people with TB and get them treated, and that's probably going to be more effective than either masks or a vaccine.

>> YVETTE COZIER: Okay. Either Dr. Kirenga or Dr. Mitnick, would you like to add anything to that?

>> BRUCE KIRENGA: I can add something. Sorry.

>> CAROLE MITNICK: No, no, go ahead, Bruce, please.

>> BRUCE KIRENGA: Okay. So, what I can add, like Robert has said, is at population level, TB is very uncommon, at least active TB, so masks would be very important to wear for together and know who has the disease and who does not have the disease. So, in the context of TB, masking is important, especially in treatment centers where people are caring for patients, but at population level, you don't know who you are going to give a mask and who will not have the mask and who has TB and who has no TB.

And this also is made worse by the new phenomenon of subclinical or asymptomatic TB. Now, data has shown these people have zero symptoms, but they can transmit the TB that is subclinical that they have. So, that was something that changed the way we think about masking, maybe in high-communication places.

>> YVETTE COZIER: Thank you. Dr. Mitnick.

>> CAROLE MITNICK: Yeah, I would just add one. We have one other kind of tool in our kit for prevention of TB, which is used more commonly in settings where there is a low incidence of TB, and that's preventive therapy. And so, people can receive a shorter course of fewer drugs -- the same drugs that we use to treat active TB, but a shorter course and fewer of them to treat infection. It's very, very effective, but generally speaking, healthy people don't like to take drugs if they don't have to, so it is hard for people to get through the regimen, even though it's shorter than that for active disease.

And I think part of the mentality around TB, which has really fallen short, has been a failure to recommend the use of preventive therapy in those settings, in addition to treating active disease, which I agree with Bob is extremely important for prevention of transmission and also for saving lives, but the use of preventive therapy around, say close contacts of people with active disease is a resource that we have not fully utilized.

>> YVETTE COZIER: Thank you. So, it is not activating or utilizing that resource. Does that have at all to do with cost? And what are the cost limitations of TB treatments?

>> CAROLE MITNICK: I think that the reluctance to use it has been in part what I have been accused of calling -- and I am not alone -- a paradigm of scarcity in Tuberculosis, where the idea is kind of, we can only do one thing at a time, and we have to live within the resource envelope that's available today, rather than saying that we're accepting the reality that we're actually not going to solve this problem if we don't go out and redirect resources from other places to apply all of the tools we need for the disease.

And so, while there is a price issue, there is a cost issue of doing it, consistently the data on Tuberculosis interventions show returns on investment of something on the order of between \$30 and \$50 return for every dollar spent.

And I guess I would just also add that it's not as if the resources don't exist in the world. They absolutely exist in the world, and they're concentrated in the hands of few, and were they redistributed, preventive therapy would be a totally viable option. There are also logistical issues about where that happens in the health system, how it gets managed in the health

system, that have not been adequately confronted.

>> YVETTE COZIER: Thank you for bringing that up, because that brings up a quote, one of the quotes from the book, around distribution of the drugs. And Dr. Peter Mugenyi from Uganda was quoted as saying, "Where are the drugs? The drugs is where the disease is not. And where is the disease? The disease is where the drugs are not." So, is this a matter of logistics? Choice? How do we solve that problem? Of distributing the drugs to where it's needed. What are the mechanisms that we have?

>> ROBERT HORSBURGH: I'll jump in here. It's a complicated process, and we're very fortunate in that in the last 20 years we've seen the development of some new TB drugs. In the 30 years prior to that, there were zero new TB drugs developed. And so, we're starting to see new drugs, but they go through a pipeline. They have to be developed and approved by regulatory agencies, and then they have to get to the WHO, who can distribute them to the countries, but they have a cost. And then, once they get to the countries -- if they get there -- you have to hire people to treat the patients and to diagnose the patients and to help them complete the treatment.

It's a complicated process. It's not just the drugs. The drugs are slower in getting out to the people that need them than they should be, and John Green points out in his book that it actually took a lawsuit to get some of these drugs approved by the government of India because they were expensive, and he doesn't mention that he, himself, has worked very hard to reduce those prices, in a very successful effort. So, it's a combination of cost and regulatory delays and the fact the systems that you have to go through to get drugs to the patients, who are by and large living in the poorest circumstances in the countries with the least resources.

>> YVETTE COZIER: So, another question, and I'm another sure. Maybe, Dr. Kirenga, you can begin with this. Recent cuts on the U.S. side, from agencies like USAID -- I'm not sure how many Americans are aware of what programs like that do here and abroad, but how do cuts in those programs impact exactly what Dr. Horsburgh is talking about, sort of both making the drugs available, delivery of the drugs? Is that something, an impact that you felt in Uganda? Oh, you're muted.

>> BRUCE KIRENGA: So, just before I talk about this, maybe I can talk about the issue of access to the drugs.

>> YVETTE COZIER: Yes.

>> BRUCE KIRENGA: Over the years -- and this is related to this question. Over the years, with the support from the USAID, from the Global Fund, the drugs really became available, especially for active TB patients, because the patients who would be sick, and they pull the drugs from the system.

Now, the challenge that remained that the people are not very sick, and as you know, they are end of the last -- up to about 50% of the active TB patients was estimated not have been diagnosed, so that was another challenge which needs to be solved.

Now, when it comes to the preventive drugs, the people are not sick -- they are not pulling the drugs. The health system has to get for people who are sick, people who have malaria, people who are suffering, people with other diseases. So, these people are not sick -- they are not pulling the drugs and making the drugs available is one of the many solutions. So, I thought I needed to add that.

But coming to the cut in the funding from the U.S. When

this happened at the beginning of last year, I want to really make it personal here, it was very devastating. I see one of the HIV treatment centers, went for a meeting and the Executive Director of this institution shed tears in the meeting. I have never known that how much impact this was having, because we are saying, now these guys when they come next month, what am I going to do? So, that is to put it in perspective. But actually, what happened in the beginning was a lot traumatizing.

Now, over the year, over the months -- not years, not years -- over the months, health systems have come up with resilience on how to push this back, but I know there are people who can speak better about this than I can do, especially in terms of HIV, the number of new infections which are not being diagnosed, the number of people who are not suppressed. But again, when it come as to TB -- I know that one I know for sure -- that we experience it deep in the gains that we have made. But like I said, over the months we have started now to see recovery going back to almost the normal.

Of course, I have to mention that over the months, some of the U.S. support has been reinstated through some other mechanisms, which is good, and we can see it coming back.

>> YVETTE COZIER: That's leaving us with some hope, but also devastating that we had such dips and setbacks in the progress. Dr. Mitnick?

>> CAROLE MITNICK: Yeah, I would love to just add something. Bruce, thank you for making it personal, because that's the thing is it was personal, and it was personal for literally -- or has been personal for literally millions of people who are affected by this, by the cruelty of these decisions.

And I guess in the spirit of some of the activism to which Bob referenced, on the part of John Green and his followers who call themselves TB fighters, there is something that Americans can do, and that is really calling our members of Congress and asking them to do their jobs and holding the executive branch of the government accountable to spend the money that Congress has appropriated.

So, the administration continues to withhold money that has been appropriated for global health funding, and that money -- little bits and pieces of it have been released to the Global Fund to fight AIDS, TB, and Malaria had been waiting for a lot of money from the U.S. Government, and about a third of what the U.S. Government owed was released recently and in part due to the pressure of American people on their members of Congress. Very few members of Congress are going public about these things, but they are privately putting pressure on the State Department. So, there are opportunities where we don't have to allow this process to continue.

>> ROBERT HORSBURGH: Just to put this in perspective. When USAID stopped its TB programs, over half of the support for international TB treatment from other countries disappeared. They were far and away the biggest supporter of TB treatment in the world and were supporting over half of the patients that were receiving that kind of support, so it was a huge thing.

>> YVETTE COZIER: Thank you. Thank you for helping to reinforce why this is so important, that funding be reinstated in full.

So, I'm going to pivot in a minute to audience questions, but there is one that has come up in the audience that's in line with what I'd like to ask. It's going back to the TB vaccine.

That's another thing that we think about. So, you know, we talked about masks and prevention, and then we also tend to think a lot about vaccines. You said that there's a vaccine that's under development. TB is a very old disease. Why have we not had a vaccine to date?

>> ROBERT HORSBURGH: Well, it's not easy when you have a disease that people can catch again. So, with measles, you can vaccinate people, and they won't catch it, and it's good for life, because people can only get measles once, but you can get TB again and again, which means that the natural resistant to TB is not so great, and therefore, it's difficult to mimic it with a vaccine. The same is true for HIV. We'd love to have an HIV vaccine, but we don't because there's no natural immunity, and so it's a much higher bar. There's hope for the new vaccine, but we'll see whether it actually does the job in a large trial that's now going on.

>> YVETTE COZIER: And where are the trials? Where is that trial taking place, do you know?

>> ROBERT HORSBURGH: It's in 30 different countries.

>> YVETTE COZIER: 30 different countries, okay. Okay. That's great.

>> CAROLE MITNICK: And Africa and Asia. And I guess I would add, to harken back Yvette, to your analogy with COVID. One of the realities of the situation is that as TB is disproportionately distributed among populations with little access to resources and little voice, and it is not affecting the large majority of Americans -- especially those with wealth and power -- there has not been a strong movement or incentive to improve upon the vaccine that's now more than 120 years old and that is used routinely pretty much everywhere in the world except in some countries in the Global North. It's used at birth. It doesn't require a cold chain. It's fairly easy to use, and it does seem to have some benefits in preventing serious disseminating TB in children, but as Bob said, it doesn't confer lifelong immunity, so it really does not do the job that's needed to be done, but there have not been adequate resources developed or allocated to kind of crack this nut in the same way that mRNA vaccines were developed for COVID in very short order.

>> ROBERT HORSBURGH: I will say, there are groups working on mRNA vaccines for TB, but they're a long way from being ready for use.

>> YVETTE COZIER: Okay. Okay.

>> BRUCE KIRENGA: Maybe I can talk a little bit about TB vaccines.

>> YVETTE COZIER: Yes, go ahead.

>> BRUCE KIRENGA: I belong to the WHO Group on TB and group on TB and vaccines, and we have reviewed quite a number of them. The last one was the one of India, where the results were not very promising, but it was published. And there is one that is now also completing phase 3 clinical trial, so there are efforts.

But to go back to the actual public issue of TB vaccines, things already mentioned. The investment has been very little to develop TB vaccines. I think chemotherapy took a lot of our energy, and when I started TB work, actually, we really believed that if you found 80% of TB cases and treated them, you will eventually, in ten years -- there are even models, actually -- eliminating TB. So, the attention to vaccines was little. That's one of the other issues.

One other issue with TB vaccines that I've learned in the last few years is there have been a couple, a few clinical trials of TB, one because of the end point that was being used of active TB. Like I said earlier, when you go to the population level, I don't want to say that has a problem -- I should be telling people this, a lot of TB, but the population level, the disease is rare.

Now, the new development that could be promising is coming, what if we included subclinical TB, if we had a definition for it, then the cases would increase and then effectively size would reduce the number of clinical trials of TB vaccines.

>> YVETTE COZIER: It's a very complex thing, for sure.

>> BRUCE KIRENGA: Yes.

>> YVETTE COZIER: Great. So, I just want to take a look at a couple of the questions that we have from the audience. I think this is a nice time to bring in a couple.

So, the first one: How can public health systems better address the social determinants of health, such as housing and nutrition, to reduce TB transmission in high-burdened communities? Start with you again, Dr. Kirenga, if you don't mind.

>> BRUCE KIRENGA: This is actually difficult for me as a clinician, but let me try.

>> YVETTE COZIER: Okay.

>> BRUCE KIRENGA: I think one key thing would be to improve the household living conditions, using resources available around the people, such that resources at household -- people have resources -- they can improve their housing, they can improve their nutrition, and they can look after their children better. I think I'll leave it at that. There could be better people who have a better answer for this.

>> YVETTE COZIER: Okay.

>> CAROLE MITNICK: I'm happy to --

>> ROBERT HORSBURGH: Go ahead, Carole.

>> CAROLE MITNICK: Sorry. I'm happy to add a little bit. I think, you know, there is, I guess a status quo informed by capitalist values that says that people should only have the resources that they've been able to earn on their own, right? That's kind of the dominant philosophy in much of the world, and that guarantees continued inequitable distribution of resources. That ensures that resources continue to be concentrated in the hands of very few who are able to actually even further concentrate their resources.

And I think there are examples, like in Brazil, where there were conditional cash transfers used, and the conditions were very, very minor, like kids having to go to school regularly, kids having to get vaccinated, where large groups of impoverished populations in Brazil got cash transfers and health benefits have been shown on multiple indicators, including Tuberculosis and reductions of TB. And so, it's actually not that complicated.

It's more of a will kind of issue, that by redistributing resources and allowing people -- as Bruce said -- to live in better conditions and to have more sustained access to food and employment and health care, that you would see it. That's what you saw in the middle -- or in the early and mid-20th century in the U.S. and in Europe. You saw very, very steep declines in Tuberculosis as living conditions improved, even before there were any TB antibiotics.

>> ROBERT HORSBURGH: I was just going to say, as living

conditions improve, as the economic status of people improves, TB goes away, but that's obviously a very difficult thing to make happen. Some countries do a better job at providing good health care and good transportation than other countries. In the countries where the rich people at the top are keeping all the money to themselves have a lot of TB.

>> YVETTE COZIER: Yeah, so, poverty is kind of a, you know, that's a big driver, and I'm not sure, does that give companies and governments an excuse to look away, because where property is so much, it's like, just throw their hands up around the condition.

>> ROBERT HORSBURGH: I would say that the government of India has been making noises about providing food supplements, at least to TB patients, which would help them get cured, but it would be even more helpful if they would provide food supplements to everybody that doesn't have enough food, because then there would be many fewer TB cases.

>> CAROLE MITNICK: Yeah, yeah. Absolutely. And a recent clinical trial demonstrated exactly what Bob is saying.

>> YVETTE COZIER: So, that kind of goes back to what you were saying before. For every, like, dollar spent on TB care, it generates like an order of magnitude bigger/greater in terms of benefits, but those benefits specifically are in diseases that does not happen, right, and people who get better, so.

>> ROBERT HORSBURGH: Yep. The World Bank showed 30 years ago that treatment of Tuberculosis is the most cost-effective medical intervention that exists.

>> YVETTE COZIER: Wow. Wow. And here we are.

>> CAROLE MITNICK: Here we are.

>> YVETTE COZIER: Yeah. Another question from our audience -- there are lots of questions coming up in the chat asking about policy innovations, that we need to make a difference. And we were talking about some things, food and others. But in the book, John Green talks about failures of imagination and how moral blindness contribute to the ongoing epidemic. This particular person would be interested in hearing what you think about what we need to do to address these failures of imagination.

>> CAROLE MITNICK: That's a big question, and I love it. I think there are multiple angles, but I do think it comes back to kind of what I said earlier about as long as the dominant philosophy is, is a capitalist one that results in people only believed to merit the resources that they kind of earn on their own, we're going to be a little stuck. And so, I think some of that really does need to shift to make substantial changes.

Tweaking around the margins of things like the models for development of innovation, where that innovation -- so, there are two examples in the book -- one is one of the newer anti-TB drugs, and the other is one of the newer TB diagnostics called Gene Expert. Both of those new tools were developed with substantial public and philanthropic investment, and yet, Johnson & Johnson, the manufacturer, was still allowed to have exclusivity on the drug Bedaquiline for the full 20 years of the patent and then tried to extend that process through patent evergreening, where it really basically just tried to exercise and enforce secondary patents that prevented generic manufacturers from beginning to make the drug more cheaply.

And so, as long as those models are allowed to exist -- even though so much of the funding came from your pocket and my pocket, as well as those of philanthropic

organizations -- it's going to continue to take a really long time for innovation to reach people who can't pay for it out of pocket and whose governments are not allocating enough resources to help to be able to purchase these, so those are other areas where I think we're sort of ripe for improvement.

>> YVETTE COZIER: Dr. Kirenga?

>> BRUCE KIRENGA: Yes, I could add on one point is, we really need to see how to emphasize community resilience. Looking at the communities that we have grown in here in Africa, most of the distortions in these family structures are quite recent, and communities here could not only use local materials to build safe houses, they could use their land to grow nutritious foods and animals. And the despair that we see in households now I think is being brought by the distortion of what, I think Carole is talking about, of people who are holding too much to the people who don't have, and the people who don't have now lose even the little that they had, that was trying to have resilience in them.

And I think if we go back and train communities to be resilient, to look around their communities, what structural adjustments can they make to improve the health determinants around them, it could be a good addition. I thought I would add that because if you look at where we live, it would take a bit of some time to get all of the resources that you need to improve the situation of the people, but what resources do we have around where we live that we can use and teach people? For example, if you have a modern house, could we teach you to ventilation? Because now we know ventilation is very important. Over.

>> YVETTE COZIER: Thank you. Thank you. Bob, do you want --

>> CAROLE MITNICK: If --

>> YVETTE COZIER: Go ahead, Carole.

>> CAROLE MITNICK: Sorry. I did want to add one other thing that's very peculiar to TB -- because a lot of the things that we're talking about -- the other things are relevant to other diseases.

The peculiar thing, again, comes up quite a bit in the book, and this is the tendency in the Tuberculosis community to require directly observed treatment for people with TB. That means that every single dose of treatment -- and we haven't talked about this explicitly, but that treatment has historically been six months for drug-susceptible TB; it was 18 to 24 months for drug-resistant TB; we now see regimens of four months tomorrow drug-susceptible TB and for drug-resistant TB.

So, shortened, but imagine building that into your daily life of having to go to a health center that might only be open from 8:00 a.m. to 2:00 p.m. every day for four or six or nine months, regardless of how you feel, regardless of what your other responsibilities are. Because there has been this notion that that's the only way to ensure that people with TB finish their treatment. It's not a very trusting framework. It's an artifact of moving care out of the hospital, which did do a lot to increase access to care for TB, by moving it into communities. But as Bruce was saying, there are many other mechanisms that could be used that would help people with TB complete treatment without having such a draconian approach to making people go to health facilities every single day for the duration of a treatment.

>> YVETTE COZIER: Wow. And what was the consequence if they

did not make it? I mean, during those observed times?

>> CAROLE MITNICK: So, we had -- so, in Peru, which is where I first started working on Tuberculosis and drug-resistant Tuberculosis, if people either couldn't make it or people actually knew the treatment wasn't working -- they knew they were getting the wrong treatment because they had resistant TB and maybe everybody around them had resistant TB and they knew they weren't getting better on treatment -- they were forced to sign a document that basically said, "I will fully acknowledge that I'm abandoning treatment," like against the recommendation of my medical providers.

So, the consequences -- that's an extreme version, but it's often just a lack -- it's a lack of trust, that health care workers don't trust patients to complete their treatment, and they, therefore, treat them poorly, without dignity, without respect, rather than saying, let's work together, let's find a solution. You know, whatever your job is, you have to be at your job from 9:00 a.m. to 3:00 p.m., let's try to find somebody in the community, or why don't you check in if you're having trouble? But it really is quite exceptional in TB to require this direct observation on a daily basis, as the norm.

>> ROBERT HORSEBURGH: And the reason it came up is that the treatment is so long. And after two months of receiving treatment, most patients feel a lot better, and they think, I'm done. I mean, all the other antibiotics that we give, we give them for three weeks and that's it. And so, the patients need support to understand and enable them to continue to complete the treatment, because with TB, if you feel better after two months and you stop, you have a pretty substantial risk of having the TB come back. But you know, patients don't see this, and therefore, we need support -- not directly observed therapy, but support to the patients to help them get through it, and the drugs aren't always easy to take, either. It's not the easiest regimen in the world, not only because it's so long, but because it makes people sick. And once they start feeling better, they think, "Well, I'm done!" I can't blame them.

>> YVETTE COZIER: Good points. And there's another question, and this is moving a little bit further, you know, into the book, and it has to do with Henry's father. So, this person says, I was fascinated with Henry's father. Part of me was disappointed he wanted to resort to non-evidence-based therapies, but I also understood where he was coming from due to past injustices shown from medical institutions towards people of Sierra Leone in the past.

This, of course, harkens back to our continual comparison in this time we've been together between TB and COVID. So, how do you rebuild trust in health care systems like this? How do you -- you know, the story talks about Henry's father eventually coming around, but for those who are working directly with patients, how do you build that trust in the first place? In the clinical setting. I'll pass it to you, Dr. Kirenga, first.

>> BRUCE KIRENGA: Okay. So, in the clinical setting, to build the trust with patients, one, we have to have empathy; we need to understand what they are going through. That is in the first days. And we need to make sure the care is organized around the experience that they go through.

But down the road, patients, if they are illiterate, if they do not go to school, they would detect where -- there are so many dimensions -- where the issue of people with drug-resistant TB say I will not take the medicine because I

know it doesn't work. So, people detect a system that is looking after them and treatment that is beneficial to them. But outside the issues of building trust, are stakeholder engagement, involving the communities -- especially in Africa. The communities are organized in a way you may not see when you first go to the community, but then something there (?) a traditional leader, that we need all of those people to understand their experience.

In Kampala here, there is a community where, when I started working there for TB, I went telling them about TB, how I should screen them and how I should cure them. And in that community, for Uganda (?) almost 60% of the people there had had TB before, so they were saying, what is this man talking about? Actually, this is a quote, "This is our disease." So, so-and-so got our disease. Then at that time, we used to admit them. They took him to hospital for two months and he came back. So, what are we talking about? I will get a disease, I will go to hospital for two months and then I will come back and continue with my work. So, trying to understand what communities understand about the disease is very important. And of course, other social things around the disease it how people interpret it, what are the implications.

If you go back to -- I'm going to go away from infectious disease to noncommunicable diseases, especially ones related to (?). In some parts of the world and here, until a few hours ago, people who had a little bit of mass were being viewed as being healthy. So, the new concept of saying you need to do this and be healthy, you need to understand the implication of someone who is 90 kilos looking 70. It might be a disaster to him. So, I think systems, health systems, should be set up around the people they are trying to serve, not transplanted from one to another.

>> YVETTE COZIER: Very good point. Would anyone like to add to that?

>> CAROLE MITNICK: Well, just some of it to me seems like -- and I'm not a clinician, so forgive me. I feel like I'm stepping out, stepping out of line here. Some of it is really about empathy, and it's, you know, giving these examples of people who are struggling to complete a treatment according to the schedule of that treatment and having health care workers being willing to engage with them to try to troubleshoot together, or if nothing else, just to listen is really huge, and I think that's one of the things that comes across in the book, in the relationship developed between one of Henry's doctors, Dr. Jerome, and the father, and just how angry the father was and how much of that was directed at Dr. Jerome, but Jerome continued to try to engage with the father and to try to find a place where the father could meet him, father to father, for example.

>> YVETTE COZIER: Yeah, good point. Very good point.

>> ROBERT HORSBURGH: The other thing I think to realize is that people's perceptions of TB are accurate. When you talk to people in communities that have a lot of TB, they say, "Oh, if you get TB, you're going to die," because people don't get diagnosed until very late, and sometimes, even with treatment, they die. And so, it not unrealistic for them to believe this, and yet, we as doctors say, "oh, 95% of the people can be cured!" But that isn't the way people see it in the community, and that's why TB has a terrible stigma, because people say, oh, it's an infectious disease and you're going to die and I hope I

don't get it.

>> YVETTE COZIER: Yeah. So, Bob, there is a question here that someone wanted -- you cited the report. I don't know if it was the World Health Organization that showed TB treatment is the most cost effective? Is that the --

>> ROBERT HORSBURGH: Yeah, the answer was posted in the chat. It is the 1993 World Bank report. And it summarized nicely in a figure that shows up every couple of years in the Global TB Report about how, what are the most cost-effective drugs, showing that TB is the most cost effective. So, that, it's actually -- because the World Bank report is heavy reading, but it's a very nice graphic in the Global TB Report.

>> YVETTE COZIER: Great. So, my last question for each of you. At the top, at the opening of this session, Dean Hyder mentioned that we're celebrating here at Boston University School of Public Health, our 50th anniversary. And we're asking leaders from across public health to look towards the future. How do you think TB will continue to evolve and change over the next several decades? I know, in as a big question.

>> ROBERT HORSBURGH: Who goes first?

>> YVETTE COZIER: You can.

>> CAROLE MITNICK: I think you should. I was going to give Bob the last word as the BU representative. I'm going to surprise myself and say I'm hopeful. I do think there -- despite all of the disincentives to develop innovation and all the gaps that I have highlighted on structural levels, there's a lot of exciting stuff going on in TB. There are long-acting agents under development. There is the possibility of a vaccine. There are models that are making care more accessible and that are bringing to bear all of the tools we have against TB, bringing these to bear in the individual communities, so I think we'll see a more -- I predict a more precipitous decline in TB over the coming 50 years, and congratulations to BU on the first 50 years.

>> YVETTE COZIER: Thank you. Dr. Kirenga?

>> BRUCE KIRENGA: I can also say I'm very hopeful, for the same reasons -- new treatments, better diagnostics that are near point of care, and of course, the possibility of a vaccine and improved living. However, there will still be pockets of places where TB could continue to be a problem, especially in Africa, places where there is war, places where they have disasters.

So, as the global decline happens, those pockets will start to become visible, and probably people will have to be within.

>> YVETTE COZIER: Thank you. So, Bob, you've got the last word.

>> ROBERT HORSBURGH: So, I started working in TB 35 years ago, and it was a pretty hopeless situation, and the patients were hopeless, and there weren't good drugs, so we've come a long way, but I don't think we're going to make good progress until the communities that are affected by TB stand up and demand as communities that they get the resources they need to get TB out of their communities. And we're starting to see it happen, but it's going to be a struggle. They're going to have to fight to get the attention that they deserve, and I hope they will.

>> YVETTE COZIER: The call for advocacy. And with that, I thank you all for your expertise. Dr. Kirenga, being later in the evening than we are here, but it's a pleasure speaking with all of you, so thank you so much. Dean Hyder?

>> DEAN HYDER: Thank you so much. My role is, first of all,

to thank Carole, Bob, and Bruce for an amazing conversation. Thank you for your expertise, for the work that you do in TB and many, many other conditions all around the world. Thank you Yvette, for leading us, both at the school, but also at this Public Health Conversation.

And I do think that it's important to remember the words in the book, that the cure is where the disease is not and the disease is where the cure is not. And this fundamental dissonance is true for TB, but it's also true for many other conditions, and that's why public health at this time is so important.

Thank you all for participating. What an incredible audience. I saw about 150 people join and engage with amazing comments, discussions, and it looks like we had a global audience today. Thank you for joining. It's a pleasure, on behalf of Boston University's School of Public Health, to host these conversations. Join us next month. On October 21st, we will have another conversation on maternal and child health. Until then, thank you and all the best. Bye-bye.

(Session concluded at 2:01 p.m. ET)

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