THE CONSUMER OF HUMANS

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ABSTRACT

For decades, a dearth of scientific research, inadequate treatment and diagnostic tools have slowed progress in the fight to control tuberculosis globally. Scientists have developed important drugs, such as isoniazid, rifampin, and pyrazinamide, against the disease. But these drugs must be taken for several months, are sometimes ineffective, and can cause debilitating side effects. What's more, if people don't finish their treatments, it can lead to multidrug-resistant tuberculosis (MDR-TB), a form of the disease that is resistant to two of the four common drugs against TB, or, even more worryingly, extensively drug-resistant tuberculosis (XDR-TB), a form of the disease against which broader anti-TB drugs are powerless. Now, advances in immunology, chemistry, and biomolecular engineering are helping scientists to gain better insight into the complex cellular processes of *Mycobacterium tuberculosis* and the disease it causes. This could pave the way for the development of innovative diagnostics, vaccines, and new treatments for these tuberculosis superbugs. This thesis examines why tuberculosis kill millions of people till this day and scientists' best efforts alone can't win the war.

Thesis Advisor: Veronique Greenwood Title: Thesis Advisor

The Consumer of Humans

Los Angeles, California.

On a warm, sunny day in Los Angeles, the air is smogless, and clear. In Inglewood Park Cemetery, carpets of grass shimmer opulently along the smooth tarred roads of the cemetery. The footpaths are flanked by palm trees like rows of lamp posts.

As the afternoon breeze sighs, a mournful crowd gathers near a mausoleum in the cemetery. Since 1905, it's been the final resting place of thousands of Americans, including the singer-songwriter Ray Charles. But the vast, hauntingly beautiful cemetery – also called the Soul of the City of Angels – illuminates more than just the mortality of the great and the powerful. Because alongside the music stars there are graves that tell a sadder, grander story. On the 7th of May in 1914, a man who lived in Banning near Los Angeles died. He, too, was buried at the Inglewood Park Cemetery.

Don Clampitt had contracted a deadly disease around 1902. The culprit, according to his death records, was pulmonary tuberculosis (TB). As the disease tore through communities in America, it killed tens of thousands of people and left families devastated. Stories about "the cure" also spread across the nation. Railway companies extensively publicized favorable climates in western states, including Los Angeles, as "havens" that could cure the highly contagious infection.

In 1913, Clampitt made the journey to Banning with his family, hoping to improve his health. Along with other people infected with tuberculosis, he was admitted for treatment at the Southern Sierras Sanitoria – small houses built near the mountains with rooftops and big flaps in the sides to let in fresh air. Some patients at the sanitariums got better, but Clampitt wasn't one of them. The ferocious killer consumed him.

The disease known as tuberculosis is caused by *Mycobacterium tuberculosis*. When someone infected with active tuberculosis speaks, sneezes, or coughs, they release TB bacteria in thousands of tiny, moist droplets that hang in the air for several hours. Once a bystander breathes in these airborne bacteria, they can come down with TB.

Left with no treatment, TB advances. It attacks the lungs, causing severe damage that heralds weakness and other respiratory complications. Next is a hacking, wracking cough. If the infection spills into the bloodstream, it spreads to other vital organs of the body, including the brain, kidney, and spine. Amid the debilitating pain and coughs that bring up blood, the body begins to melt away. When the end comes, patients die in torment, unable to breathe.

Clampitt died more than 100 years ago. But tuberculosis still rages, killing one person roughly every 20 seconds – the global leading killer among infectious diseases today, despite the invention of antibiotics that can combat it.

Tuberculosis has a long history. It has been with humans for thousands of years. The ancient Greeks called it "consumption" and some people also called it the "White Plague." Others named it the

"Captain of Death," painting a picture of a fatal disease that has led millions of men and women – young, old, footballers, writers, musicians – to their graves. Today, it is estimated that tuberculosis deaths will cost the global economy nearly \$1 trillion in lost economic productivity by 2030. Seven years from now. This makes meeting the 2030 UN Sustainable Development Goals (SDGs) target to reduce TB infections by 90% highly unlikely.

For decades, a dearth of scientific research, inadequate treatment and diagnostic tools have slowed progress in the fight to control tuberculosis globally. Scientists have developed important drugs, such as isoniazid, rifampin, and pyrazinamide, against the disease. But these drugs must be taken for several months, are sometimes ineffective, and can cause debilitating side effects. What's more, if people don't finish their treatments, it can lead to multidrug-resistant tuberculosis (MDR-TB), a form of the disease that is resistant to two of the four common drugs against TB, or, even more worryingly, extensively drug-resistant tuberculosis (XDR-TB), a form of the disease against which broader anti-TB drugs are powerless.

Now, advances in immunology, chemistry, and biomolecular engineering are helping scientists to gain better insight into the complex cellular processes of *Mycobacterium tuberculosis* and the disease it causes. This could pave the way for the development of innovative diagnostics, vaccines, and new treatments for these tuberculosis superbugs.

However, researchers face stubborn hurdles such as lack of funding, slow clinical trials for vaccines, and regulatory bottlenecks. Contributing to that is the fact that people in rich countries don't think much about tuberculosis – for decades, thanks to antibiotics, the disease has been under control where they live. There is a disconnect between the burden of the disease and the perceived importance of addressing it globally.

Another major barrier blocking the global eradication of tuberculosis is that even in countries where it runs rampant, the disease is often seen as a cause for shame. The bacterial infection has always been a signature disease of the poor, easily passed in cramped households where people do not have adequate nutrition, sanitation, and access to healthcare. Women, children, and people with underlying health problems or compromised immune systems such as HIV/AIDS, diabetes, and other conditions are most at risk, and asymptomatic carriers can spread the disease for years without realizing it. When the disadvantaged have a stigmatized disease, it rages on despite scientists' best efforts.

Rapid tests for TB and better vaccines could be a game changer. But as scientists race to develop these tools, the numbers continue to rise. In 2020, when the coronavirus pandemic swept across the world, it prevented people infected with TB from getting treatment and upended the progress made in fighting the disease. Over the intervening years, tuberculosis has taken over again from COVID-19 as the deadliest illness on the planet.

On the fifth floor of a tall red brick and glass building – just 15 minutes north of the Inglewood Park Cemetery – Mireille Kamariza is setting up a new infectious disease lab. A chemical biologist, she has just started a new position in the Department of Bioengineering at the University of California, Los Angeles (UCLA). "I grew up knowing this disease called TB," says Kamariza, as she leads me along a corridor into her new lab. "TB is not a disease of the past, it's just ignored," she says.

Kamariza wants to tackle this tough problem. In the United States, some years after Don Clampitt succumbed to the disease, massive public health campaigns and new drugs helped bring the tide of infections under control, and though there have been outbreaks of multi-drug resistant TB, cases numbers today are relatively low, about 7,000 a year. But the disease remains difficult to eradicate in other countries around the world – the infection can be tricky to detect, it's complicated to treat, and it simply hasn't been a top priority, even among governments and healthcare providers. In the poor, urban settings that often have the highest burdens of the disease, few can afford to even be tested.

In her research, Kamariza seeks to design new tools to detect the disease and prevent its spread. Over the past few years, using molecular bioengineering, she has developed rapid, diagnostic tests that could be used for quick detection of tuberculosis.

Kamariza has an unmistakable demeanor of someone who's lived an unusual life and isn't afraid to face difficult challenges. Over the past years, she has had an impressive start to her career and by many standards is at the top of a handful of leading tuberculosis researchers in the world. In 2019, she was named a Junior Fellow at Harvard University, where she conducted independent research at the Broad Institute of MIT and Harvard, a top biomedical and genomics research center, and received mentorship from leading researchers Pardis Sabeti and Ben Neale.

Now, at UCLA, her big picture vision is to bring these tests to the people who need them in poor, developing countries. But developing the diagnostics and getting them to the hospitals is a huge undertaking and it's still early to tell whether she will succeed.

"TB is still killing people today, millions of people in globally," Kamariza says. "It's baffling to me." She feels dismayed that COVID-19 grabbed the research world's attention so swiftly and completely, but tuberculosis has been overlooked, with little attention given to the search for new tools and interventions for years. Tuberculosis research funding trends, between 2005 to 2021, showed that funding for TB research has reached \$1 billion, but it is far short of what's needed to worldwide.

Inside her new lab - a large, spacious room with big windows at the far end – the effervescent 33year-old Kamariza speaks gently. Bespectacled, and dressed in a black puffer vest and blue jeans, Kamariza is explaining how she plans to attract funding and recruit students to carry out research. As she walks around the lab space, her eyes brighten as a surprisingly laugh burbles out of her. She believes in the promise of what might happen in these four walls.

Before we head out of the building, Kamariza wants to show me her workspace, where she has been writing grant applications and meeting her new students. Inside the small office, a long

whiteboard hangs on the wall and a table sits right at the middle with chairs. The room is small, but her dreams are big. It's the kind of place where she could sketch the molecules of the bacterium's membrane on the whiteboard, teach, and brainstorm with her future students about their research work and how it can contribute to the fight against tuberculosis. "If the US has managed to eliminate TB, it is something we can do globally," says Kamariza.

At the hallway on the fifth-floor, a few people are gathered around tables, enjoying light lunch and drinks. The gathering, Kamariza tells me, is being hosted by her department for students and faculty interaction. It's Kamariza's first since she arrived at UCLA. As we approached the small crowd, some colleagues wave at her as if to tell Kamariza to come join them for coffee. She waves back, with a broad smile. The task she has set herself is a big one, but she has a lifetime of seeing the price of inaction.

It is past 3pm by the time we sit at a blue plastic table on a paved area outside the UCLA Henry Samueli School of Engineering building, where Kamariza is setting up her lab. The chattering of students and their droning footsteps walking to classes and dorms dims slightly behind us.

Kamariza was born in Burundi, a small landlocked country in East Africa. While growing up, many people around her community, including some close relatives, contracted tuberculosis and died. Worldwide, tuberculosis is one of the top causes of death and the leading infectious disease killer, followed by COVID-19 and HIV/AIDS. In 2021, TB killed nearly 2 million people and more than 10 million had the disease. The burden is highest in low-and-middle-income countries. Africa, including Burundi, accounts for 25% of global TB cases.

In developing countries, doctors depend on cumbersome, time-consuming tests to diagnose tuberculosis infection. One of such methods is the Ziehl-Neelsen (ZN) test, developed more than 100 years ago. The ZN test is laborious, it requires extensive processing and it gives false results – tells people they have TB when they don't – more than is optimal. While other tests like TB cultures (which involves growing the bacteria in the lab) are more reliable than ZN tests, they can take six weeks to produce a result. Kamariza says in some communities, samples have to be sent to far away laboratories for testing, and it takes several weeks or months to get results back. And while people wait, the disease spreads in their households and communities.

There is also a massive shadow population of people around the world who have TB but don't know it. Globally, 1 in 3 people living with tuberculosis and every 2 in 3 people with drug-resistant TB are not being detected. According to the World Health Organization (WHO), there's an urgent need for fast tests that use saliva instead of blood for rapid detection and diagnosis of tuberculosis. The lack of fast tests for the diagnosis of TB and drug resistant TB remains a major challenge.

As well, the ability of diagnostics to distinguish living TB bacteria cells from dead ones rapidly has implications for tuberculosis diagnosis, says Bavesh Kana, a professor of immunology at the University of Witwatersrand in Johannesburg, South Africa. "It allows doctors to see whether the anti-TB medications they administer to patients are working," he says, which would hasten a

diagnosis of drug-resistant TB. Standard TB cultures, which use drugs to test for drug-resistant TB, can take up to six weeks, says Kamariza. "Somebody could have passed away already," she says, and an especially dangerous form of the disease could have spread to even more people.

Just after a bloody civil war in Burundi that killed nearly 300,000 civilians, Kamariza immigrated to the US at age 17. In the fall of 2006, she arrived in San Diego, California, and moved into a small studio apartment with her three brothers. There, she graduated high school, and started pursuing higher degrees in science. At the University of California, San Diego (UC San Diego), she earned a bachelor's of science in biochemistry and chemistry. She also spent her summers doing biology research, through a diversity scholarship awarded by the US National Institute of Health (NIH).

Kamariza joined the lab of Carolyn Bertozzi as a graduate student. Because of her experiences of the real-world impact of tuberculosis and a knack for finding solutions to complex problems, Kamariza was drawn to the development of technologies that can be used to diagnose tuberculosis quickly and deployed in resource-poor environments. "I was really interested in studying TB and understanding why it's still a major problem," she says. "I was really lucky that I found a chemist who was interested in exploring tuberculosis."

Bertozzi, now at Stanford University, shared the 2022 Nobel Prize in chemistry. She uses chemical biology techniques to study sugars that coat the outside of cells and understand complex molecular processes in living cells. One of the applications of this approach is investigating how different organisms, including pathogenic bacteria, can be identified by sugars on their cell membranes. In one of their studies, her group found that *Mycobacterium tuberculosis* uses a unique type of sugar, called trehalose, on its surface.

When Kamariza joined the Bertozzi group at Stanford University, she started reading papers and brainstorming with Bertozzi and other graduate students about ways that they could use trehalose to detect mycobacterium cells. "We understood the molecules, how they worked and how to manipulate them," she says.

Kamariza and her research group designed a range of trehalose sugars. They tagged each of them with a fluorescent dye known as DMN, for short. When the dye enters a cell membrane, it lights up, glowing bright green. "It becomes quite happy and fluoresces – you can see it," says Kamariza.

Kamariza and her team fed their DMN-labeled sugar, which she calls "probes," to mycobacterium tuberculosis cells in the lab. If the cells take up the special substance, something only living cells can do, they turn green within one hour, making it possible to visualize and spot live tuberculosis infection. Non-TB cells, or TB cells that have already died, don't light up, Kamariza says, because the sugar never makes it into their membranes. "It was really exciting," she recalls. "You could see the whole cell and that's what tells you if the TB bacteria cells are alive or not."

But Kamariza knew that she had to see if the tests would work in real world. In 2015, she packed her probes and bags and was on a plane to South Africa, which has one of the world's highest rates of tuberculosis. There, she met Kana at the Center of Excellence for Biomedical TB Research in the University of Witwatersrand. They collected samples of sputum – a gummy mixture of saliva

and mucus – from a small group of people suspected of having tuberculosis to test the probes. Her tests detected live tuberculosis within 30 minutes.

In 2018, the research team lead by Kamariza published their <u>study</u> in the prestigious journal Science. Further <u>studies</u> in 2021, using two new types of dye probe that they designed, showed a 10-fold increase in fluorescence, compared to DMN, making the tests easier to interpret, and they were able to spot TB cells within 10 minutes. This means that the person who gave the sample could still be in the room when they get their result, instead of hundreds of miles away, having spread the disease for weeks or months.

In these trials, the probes have proved successful in detecting tuberculosis and provide a simple and fast alternative to existing tests. Now, she wants to go a step further and deploy the rapid diagnostic tests in clinical settings in low-and -middle income countries.

"I'm imagining a community health worker somewhere in rural Kenya or South Africa, carrying a backpack with these diagnostics. And then they walk around in communities testing people and get the results within one hour," says Kamariza. "My work here at UCLA and this lab that I'm starting up right now is actually to build the kit."

She knows it will be an uphill battle: Kamariza has strong opinions on the lack of investment in tuberculosis research and the chronic underinvestment in science in Africa. The continent spends a meager 1.3 percent of its over \$3 trillion GDP in research; it contributes <u>only 2 percent</u> of the world's research output and, in turn, produces just 0.1 percent of all patents. Over the past few years, African countries have struggled to scale up basic testing capacity for COVID-19, and TB hasn't been a high priority for governments.

"Resources directly affect the outcomes of a disease," she says. "I mean, on one hand, I understand the argument that we're so poor...governments have limited resources. On the other hand, poor or not, people will get sick and die. So, there has to be local support in research and infrastructure for our own people," she continues.

She left Burundi to pursue a career in science and understands the power of investment in research and education to develop human talents. "How does a girl from Burundi become a professor at UCLA," she laughs. "It's education – that's what empowers people."

Asked when the diagnostic kits would be commercially available, Kamariza says: "The short answer is, I don't know – it's a long road and there's a lot we have to go through." The diagnostic tests have to face tougher trials, including regulatory approvals and endorsement from the World Health Organization.

Kamariza founded the biotech startup OliLux Biosciences in 2019 to translate her work to public use and develop other rapid, low-cost, reliable tools for detection of infectious diseases that are tailored for the complex needs of developing countries, including these new probes.

Still, she notes that her team at the company currently recruiting patients to launch a large clinical trial of the test in Vietnam and Uganda – both countries with endemic cases of tuberculosis. "And

as soon as we get a good number of patients, that's when we start analyzing the results," says Kamariza. "So, I imagine one to two years would be when we start getting results from clinical trials," she continues.

Kamariza believes that Africa could eradicate tuberculosis. But lots of work remains. She ticked off the conditions: investment in scientific research and development, strong political commitment, and infrastructure, she says. Might things change soon? "I don't know if it's going to be in my lifetime," she says. "I think there has to be some sort of local mindset that changes how we view science and so we can put money into it."

While scientists like Kamariza are developing promising tools for testing tuberculosis, others are investigating what to do after a diagnosis, and how to protect the families and communities of TB patients. For them, the question is how vaccines – technologies that can shield the vulnerable from a disease, and even, in some cases, keep the infected from getting worse – can help turn the tide against tuberculosis.

As a child growing up in rural South Africa, Thomas Scriba witnessed people die from tuberculosis, when the disease was surging and tearing families apart. "I was at risk of contracting the disease as a kid," says Scriba. It was hard for him to fully understand what was happening.

Now a clinical immunologist at the South African TB Vaccine Initiative (SATVI) in the University of Cape Town, in Cape Town, South Africa, Scriba has been working to develop potential vaccines to control the disease. In the past two decades, he has co-led thirty trials that aim to find new tuberculosis vaccine candidates. But his work has been bedeviled by the disease's complexity.

There is already a vaccine against TB, called Bacille Calmette-Guerin (BCG), which was developed more than a hundred years ago. Although BCG is safe and used in immunization campaigns across many countries, it has many limitations. BCG is only administered to children below age 16, and its efficacy remains controversial. The vaccine comes in a freeze-dried powered form and must be mixed with sterile water to be administered, meaning it's temperature-sensitive; it can even be readily destroyed by sunlight. These factors create significant barriers to distribution of BCG vaccines, particularly in poor communities most affected by tuberculosis. "It's not good enough," says Scriba. "That's why developing new vaccines that are more effective is critical to ending the tuberculosis epidemic around the world," he says.

Part of the problem lies in TB's own biology. *Mycobacterium tuberculosis*, after it manages to establish itself in the lungs, grows slowly. Many people who get infected never develop obvious disease. Only about 5 to 15% of infected persons develop active tuberculosis in their lifetime, and even for them, it takes two to three years. This later phase of TB is known as pulmonary tuberculosis.

That quirk of biology—that the pathogen can lie dormant for an entire human lifetime—has helped it survive over the long term. "The bacteria's inherent metabolic complexity has enabled it to survive and live successfully in the human population for centuries now," says Sarah Fortune, a professor of immunology at Harvard University and director of TB research program at the Ragon Institute of MGH, Harvard, and MIT. According to national tuberculosis prevalence surveys in many countries in Africa and Asia – both regions carrying the highest incidences of the disease – about 50% of clinically confirmed cases of people infected with the disease do not show any symptoms, and can spread the TB bacteria without knowing. This makes it all the more difficult to find people infected with the disease and recruit them for vaccine trials.

Conducting the clinical trials for potential experimental tuberculosis vaccines has not been an easy task. They take a very long time to complete, lasting between five to seven years in most cases. And recruiting people for the vaccine trials is slow and difficult, says Scriba. "Doing the trials is like the disease – it is slow and chronic," he says.

Scriba co-leds a trial group known as Immune Correlates Consortium, a programme coordinated by the Bill & Melinda Gates Medical Research Institute, which aims to identify the immune responses needed to trigger protection against tuberculosis. It has conducted second-stage clinical trials across African countries including Kenya, South Africa, and Zambia to test a subunit candidate vaccine, called M72/AS01E. The <u>study</u> published in 2019, showed that administering two doses of the experimental vaccine elicited immune responses and offered 50% protection against pulmonary tuberculosis in adults with prior TB infection, over three years period. "It's the most promising one we've had," says Scriba, who is the principal co-investigator of the Immune Correlate Consortium studies. "But there are many people who haven't had any prior TB infection. We don't know if it would work in those people or not," he says.

The World Health Organization, praised the results saying that they are an important "scientific breakthrough" and pave way for further development of the new TB vaccines and the potential use of the M72/AS01E vaccine candidate in countries with high cases of tuberculosis. However, further trials are required and adequate financing is needed to bring the vaccine into use in the global fight against tuberculosis.

In 2020 the World Health Organization, who was not involved in the trial, licensed the vaccine to the Bill & Melinda Gates Medical Research Institute. But it recommended that it's important to determine whether the M72/AS01E vaccine protects people who have not been infected with tuberculosis across different ethnic and geographical regions.

A previous <u>study in 2018</u>, showed that another candidate subunit vaccine, called H4:IC31, could protect against tuberculosis in pre-clinical models, and observational studies suggested that primary BCG vaccination may also offer partial protection against tuberculosis infection. Researchers say that the findings provide a basis upon which to re-evaluate the use of the current BCG vaccine for populations. And further studies are required to fully understand the immune system and host interactions in both vaccine candidates in order to guide the development of future trials and new tuberculosis vaccines. Studies are now being followed up for larger trials, says Scriba.

Recently, a breakthrough vaccine showed promising results in first-stage clinical trials, raising the hopes that it could be an effective tool in the fight against the vexing and dangerous disease. The new TB vaccine was tested in 45 healthy adults, who were monitored over a six-months period. According to the <u>findings published</u> in the journal *Nature Communications*, the new TB vaccine showed that the freeze-dried formula was stable at room temperatures (37C) for three months, well-tolerated, safe, and it stimulated antibody responses. Some researchers are also aiming to build on the success of mRNA technology against COVID-19 to develop an mRNA <u>vaccine</u> that could protect people against TB.

Still, there is a lot of work to be done to have a new vaccine for tuberculosis. But Scriba is hopeful. "I feel very confident that at the end of the decade, we would have a new TB vaccine on the shelf that can be deployed to save lives and protect people," he says. "If we can turn off the transmission tap, if we stop people from transmitting the TB bacteria, we could make a real impact on eradicating the disease," Scriba says.

Although scientists like Scriba and Kamariza – and many others elsewhere – are developing innovative tools for testing and vaccines against tuberculosis, the disease is a systemic challenge as much as a scientific one. Poverty increases the risk of contracting the disease. For the vulnerable people infected with tuberculosis, getting access to testing and treatments that prevent the disease from advancing is a race against death – yet the disease also puts the patients in a difficult social position.

For example, in areas with high rates of HIV and TB in South Africa, such as Khayelitsha – a large township in Western Cape – and the suburb of Masiphumelele in Cape Town, people infected with TB are often neglected by family members and stigmatized in the community. People are afraid of catching the disease, and because tuberculosis and HIV travel together in these communities all of the fear that people have for HIV gets transferred to TB.

In 2014, Anastasia (Tasha) Koch was a PhD candidate studying tuberculosis at the University of Cape Town (UCT) in Cape Town, South Africa. But soon, Koch came to feel that she could make more impact with her work by leaving the lab to work directly with local communities affected by tuberculosis. She and her colleagues created Eh!woza, a non-profit organization centered on science communication, youth advocacy, and community engagement to tackle local problems. Eh!woza holds events in local communities in South Africa to engage the public and policymakers about their scientific research, and discuss the social impacts of infectious diseases such HIV and TB on people affected.

Koch strongly believes that socio-economic problems such as lack of healthy living environments, poor nutrition, and lack of access to healthcare are major barriers to eradicating tuberculosis in poor communities and in developing countries. She argues that in rich countries, improved socio-

economic conditions – not just medical tools – helped fast-track the fight to control TB. "People think that it's just antibiotics and testing, but people infected with the disease need more than that – they need good living conditions, nutrition, and access to sanitation," says Koch a molecular biologist and managing director of Eh!woza.

One reason for the stigma against people infected with TB is the lack of education about the disease. Eh!woza recruits teenagers from areas with high TB burden in South Africa and train them to produce films and documentaries to raise awareness about tuberculosis and decrease stigma. "The training workshops blend experiments, talks, and storytelling to educate and engender conversations about tuberculosis," says Koch.

On World Tuberculosis (TB) Day in March, Eh!woza held an event in Khayelitsha. It was a dry and sunny Friday, but the community ground was full of young, adult men and women. Koch's Eh!woza team put on loud Amapiano music, and the audience got up and danced. A female health worker took the microphone, she encouraged people to take their treatments and explained some basics about TB and how it spreads. Koch distributed posters in local South African languages. A few researchers spoke about their work and ongoing vaccine clinical trials. Then people started asking questions. "One person asked, 'it's fine that you come here to tell us to take our medicines and to finish it, but how do we do that if we don't have the money for transportation and to buy the food we need'," Koch recalls.

I know what she means. I've seen it myself. In 2018, I joined the National Youth Service Corps (NYSC) as a volunteer to serve my home country, Nigeria, for one year. I was posted to a hospital inside a large military base on the outskirts of Jos, north-central Nigeria. I arrived at the hospital to find it occupied by a platoon of soldiers. Some of them looked to be about in their early 20s, their bony fingers tucked on sophisticated FN rifles, with no trigger guards. Turns out they live on the hospital compound. The town has endured many years of brutal religious conflicts. And the people of Jos have been largely left poor, since British colonialists began mining tin in the region in 1905.

The next morning after I arrived, a young military officer was showing me around the square of buildings within the hospital's perimeter wall whitewashed in blue paint. As we walked inside one of the building's dimly lit corridors, we passed children and women; some in faded dresses sitting in rows on long blue metal chairs waiting to see doctors. "TB DOT," one sign read in all capital letters, at the far corner of the corridor, on the top of the door of a small, dusty ill-kept office.

DOT, also known as directly observed therapy, is the World Health Organization's recommended strategy for the treatment of active tuberculosis and management of cases of people infected with the disease. The approach allows health workers to prescribe TB drugs and ensure that patients complete their TB therapy, without any unnecessary gaps, and thereby decrease the chances of treatment failure. This is especially crucial for patients with drug-resistant TB, underlying health problems such as HIV/AIDS, and persons on intermittent TB treatment regimens.

I requested to be assigned to the TB DOT in the hospital for my service year. During my stay at the TB DOT, I was tasked with keeping the records and medical appointments of people infected with the disease and admitted to the hospital. I also documented prescribed TB drugs for the

patients. I watched many people swallow dozens of pills every day. I remember one wet and cool morning. An old man inside the DOT, was swallowing, swallowing again, his throat moving with the force of getting the pills down one by one.

Taking the tuberculosis drugs was never an easy task. The drugs' side effects can include, but not limited to, nausea, headaches, and depression. And many people infected with the disease lack adequate motivation to swallow the daily drug cocktail meal. To make sure the patients didn't miss their daily doses and treatment regimens, I called them up on the phone to show support and encouraged them to come to the clinic.

Although the drugs were provided free of charge through a national TB programme to stop the spread of tuberculosis in the country, some patients told me they couldn't afford to walk or pay for transport to the hospital every day. I tried to help, when I could, but on my own I couldn't transport everyone to and from the office. Consequently, some patients missed their treatment regimens and some people infected with the disease did not finish their treatment and sadly passed away. It was heartbreaking. I felt helpless and I wondered about how complicated tuberculosis treatment is. People infected with the disease are among the most disadvantaged in our society. So, the drugs alone aren't enough; they need social and economic support.

In the years since the death of Don Clampitt, the social conditions of millions of Americans – and people living in rich countries – have improved significantly, even though people don't realize it. And, in turn, TB rates have also dropped. However, this is not true for the millions of people infected by TB in poor countries. Today in the US, people don't think about TB. This is possible in Africa, and the developing world, too. Tuberculosis is preventable and treatable, but efforts must be coordinated, fast-tracked, and multifaceted in approach toward eliminating the disease globally.

Science is crucial towards eradicating tuberculosis globally. But innovation alone can't win the war. It's not just about having medical interventions – diagnostics, drugs, and vaccines – the social conditions of people living with TB need to change. Socioeconomic barriers must be shattered for the poor and disadvantaged. Poor countries must put TB at the top of their agenda while galvanizing for financial and political support from rich countries. If the disease continues to persist in poor countries, it's only a matter of when a more deadly form of TB will emerge. And then, in little or no time, it'll find itself in Los Angeles.

For now, tuberculosis rages on. The long war is far from over.

References

Inglewood Park Cemetery. Website, (2023). https://www.inglewoodparkcemetery.com/

Ray Charles Home. Website (2023). https://raycharles.com

People Legacy. Where is Don L. Clampitt Buried? https://peoplelegacy.com/don_1_clampitt-4O3p4N

Elsemerecanyon.com. Website. *Clampitt Family History*. https://www.elsmerecanyon.com/oil/clampitt/clampitt.htm

Patch.com. 'Southern Sierras Sanatorium' Ad Evokes Early Banning Promoters' Vision (2011). https://patch.com/california/banning-beaumont/old-banning-southern-sierras-sanatorium-photo-evokes-8d713ead07

ScienceDirect. Tuberculosis An Overview, (2023). <u>Tuberculosis - an</u> overviewScienceDirecthttps://www.sciencedirect.com > topics > tuberculosis

TB Alliance. New TB Pandemic. https://www.tballiance.org/why-new-tb-drugs/global-pandemic

Centers for Disease Control and Prevention. *History of World TB Day*. <u>https://www.cdc.gov/tb/worldtbday/history.htm</u>

The Lancet. Economic impact of tuberculosis mortality in 120 countries and the cost of not achieving the Sustainable Development Goals tuberculosis targets: a full-income analysis, (2021). https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00299-0/fulltext

Centers for Disease Control and Prevention. *Drug-Resistant TB*. <u>https://www.cdc.gov/tb/topic/drtb/default.htm</u>

Kana, B (2019). *Major battles have been won against TB. But the war isn't over.* <u>https://theconversation.com/major-battles-have-been-won-against-tb-but-the-war-isnt-over-113765</u>

Neti, J. David, E. *A qualitative review: The stigma of tuberculosis* (2011). <u>https://pubmed.ncbi.nlm.nih.gov/21040040/</u>

Pai, M. Kasaeve, T. Swaminathan, S. *Covid-19's Devastating Effect on Tuberculosis Care - A Path to Recovery* (2022). <u>https://www.nejm.org/doi/full/10.1056/NEJMp2118145</u>

Centers for Disease Control and Prevention. *About the Think. Test. Treat TB Campaign.* <u>https://www.cdc.gov/thinktesttreattb/aboutCampaign.html</u>

Treatment Action Group. 2021 Report on TB Research Funding Trends (2021). https://www.treatmentactiongroup.org/resources/tbrd-report/tbrd-report-2021/

World Health Organization. Tuberculosis. https://www.who.int/news-room/fact-sheets/detail/tuberculosis

Advances in Parasitology. *ScienceDirect Ziehl-Neelsen Stain*, (2023). <u>https://www.sciencedirect.com/topics/immunology-and-microbiology/ziehl-neelsen-stain</u> Centers for Disease Control and Prevention. *BCG Vaccine Fact-Sheet*. <u>https://www.cdc.gov/tb/publications/factsheets/prevention/bcg.htm</u>

Roman, F. Tait, D. *The New England Journal of Medicine. Final Analysis of a Trial of M72/AS01E Vaccine to Prevent Tuberculosis (2019)*. <u>https://www.nejm.org/doi/full/10.1056/NEJMoa1909953</u>

Hatherill, M. Nemes, E. *The New England Journal of Medicine. Prevention of M. tuberculosis Infection with H4:IC31 Vaccine or BCG Revaccination* (2023). https://www.nejm.org/doi/full/10.1056/NEJMoa1714021#:~:text=H4%3AIC31%2C%20a%20candidate% 20subunit,offer%20partial%20protection%20against%20infection.

Fox, C. Sagawa, Z. *Nature Communications. Safety and immunogenicity of a thermostable ID93* + *GLA-SE tuberculosis vaccine candidate in healthy adults* (2023). <u>https://www.nature.com/articles/s41467-023-36789-2</u>

Bagcchi, S. SciDev.net. *Can mRNA vaccine tech take on tuberculosis?* (2022). https://www.scidev.net/global/features/can-mrna-vaccine-tech-take-on-tuberculosis/