

Tuberculosis Surveillance and Control in Puerto Rico

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hi, I'm Sarah Gregory, and today I'm talking with Dr. Emilio Dirlikov. Dr. Dirlikov is a CDC epidemiologist and we'll be discussing his historical review about the history of tuberculosis surveillance and control in Puerto Rico. Welcome, Dr. Dirlikov.

[Emilio Dirlikov] Buenas tardes. Thank you for having me.

[Sarah Gregory] Ok, let's start with the basics. What is tuberculosis?

[Emilio Dirlikov] Tuberculosis, or TB, is a disease caused by a bacterium that usually affects the lungs, and more infrequently, it also affects other parts of the body, such as the kidneys, spine, and brain. TB bacteria are spread through the air from person-to-person. For example, when a person who is infected coughs or speaks loudly or even sings, bacteria can be released into the air. People who are nearby may breathe in the bacteria and then become infected themselves.

There are two types of TB conditions: TB disease and latent TB infection. People with TB disease are sick from active TB bacteria. They usually have symptoms and may spread TB bacteria to others. On the other hand, people with latent TB infection do not feel sick, do not have symptoms, and cannot spread TB bacteria to others. If their TB bacteria becomes active, they can develop TB disease.

Symptoms of TB disease include a bad cough that lasts three or more weeks, pain in the chest, and coughing up blood or phlegm from deep inside the lungs. Additional symptoms are weakness or fatigue, weight loss or no appetite, chills, fever, and sweating at night. Both latent TB infection and TB disease *are* treatable. Most people with TB disease take a combination of drugs for six to nine months, and treatment for latent TB infection is often shorter.

While people may perceive that TB is a disease of the past, TB remains a major global health challenge. In 2017, the World Health Organization, or WHO, estimated that 10 million new cases of TB occurred worldwide—10 million new cases! Since 2015, TB has ranked above HIV as the leading cause of death from an infectious disease, and in 2017, approximately 1.6 million deaths were caused by TB, worldwide.

Beyond the sheer size of the global epidemic, there are two key reasons that challenge current control efforts: First, the emergence of drug-resistant forms of TB bacteria have made treatment more complicated. For example, with multidrug-resistant TB, or MDR-TB, the bacteria have developed resistance to two of the most important TB drugs, that is, rifampin and isoniazid. The second major challenge is TB among people living with HIV, as they're more likely than others to become sick with TB. Worldwide, TB is the leading cause of death among people living with HIV, and an estimated 300,000 deaths occurred in 2017.

Every year, the public health community observes World TB Day on March 24th to bring attention to the continued importance of TB. And just a little historic fun fact: This day commemorates Dr. Robert Koch's presentation of the isolation of TB mycobacterium on March 24, 1882.

[Sarah Gregory] World TB Day! Okay, so tell us about the situation with TB in Puerto Rico.

[Emilio Dirlikov] Well, similar to the rest of the U.S., surveillance data indicates that Puerto Rico is an area with low incidence of new infections. In 2015, the Puerto Rico Department of Health reported 52 cases of TB, and that's compared to 274 cases which were reported in 1994. So, between '94 and 2015, the incidence of reported TB cases per year decreased by five times, that is, from 7.5 to 1.5 reported TB cases per 100,000 population. For patients identified between 2011 and '15, the majority of patients were male, and most patients were over the age of 45. Six cases of multidrug resistant TB were identified, and among four...245 TB patients with known HIV status, 19 percent were HIV-positive.

Because of these promising reported data, the WHO has recognized Puerto Rico, along with 32 other contexts that have low incidence of TB, where they think that the goal of TB elimination, that is, having less than one case per one million population, could be possible by the year 2035.

[Sarah] Wow!

[Emilio Dirlikov] But, beyond these numbers, patient outcome data indicates that there is some challenges. As of June 2018, 70 percent of patients who started on treatment before 2015 had completed treatment, and that's compared to 73 percent of TB patients in the rest of the United States, that generally complete treatment within one year. Moreover, nearly one in five Puerto Rico TB patients died during treatment, and we don't have outcomes for 20 patients, which leaves a gap in our statistics.

[Sarah Gregory] Okay, so how does this TB epidemiology compare to the rest of the United States?

[Emilio Dirlikov] In general, sustained surveillance and control efforts have documented decreases in incidence of reported TB and mortality rates in Puerto Rico, as well as the United States. One indicator of progress is that there's been a significant increase in the age of TB patients over the last two decades. And this likely has resulted from both less transmission among younger age groups, as well as more activation of latent TB infections among the older age groups.

The largest drops in incidence of reported TB cases occurred during the late 1940s and early 1950s, and that's just at the same time that effective TB medications were discovered and introduced worldwide. For example, in 1953, the incidence of reported TB cases in Puerto Rico was 209 per 100,000 population. Just seven years later, in 1960, it had dropped to 82 reported TB cases per 100,000 population. So it dropped by more than half. Incidence then continued to decline, and in 2015, the incidence of reported TB cases in Puerto Rico was just 1.5 per 100,000, and now that's lower than three cases per 100,000 rate that is for the United States. And in fact, the incidence of reported cases of TB in Puerto Rico has been below that of the United States since the late 1980s. Along with these drops in incidence, mortality rates have also been declining. In 2015, the mortality rate due to TB in Puerto Rico was just 0.2 deaths per 100,000 population, compared to 0.1 deaths per 100,000 population in the United States.

[Sarah Gregory] So, what does "surveillance" mean in public health and what's its relationship to controlling TB?

[Emilio Dirlikov] The word *surveillance* is French in origin, and it dates back to the early and mid-1800s, just at the same time as public health was coming into being as its own domain. *Sur* means "above" or "over," and *veiller* means "to see" or "watch." So, for public health, in

combination “sur veiller” or “surveillance” refers to the important activities to “oversee” or “watch over” diseases that are affecting populations.

Today, surveillance is a term that describes a range of activities aimed at better understanding how diseases affect populations, including TB. As we collect more information, public health officials can analyze patterns of disease among different populations, over time and across geographies. Based on these patterns, when we see changes from what’s expected or what we expect to be normal, that’s when we want to investigate, figure out why people are becoming sick, and ultimately, try to prevent these diseases from occurring in the first place.

For tuberculosis, public health surveillance may also include clinical services. For example, during my time at the Puerto Rico Department of Health, I helped provide direct observation of treatment for several patients. This involved meeting patients in their communities to ensure that they were taking their medications and that we were documenting any side effects that were happening at the same time. And for me, as an anthropologist, spending time each day with these patients, I came to better understand their lives and their worries. And so, it was those types of stories that have really given me a look beyond the numbers, to something that I can take with me and drives my commitment for public health.

[Sarah Gregory] Why are you interested in the history of TB surveillance and control in Puerto Rico?

[Emilio Dirlikov] Well, to be honest, I’ve always been interested in history. But, in my role as a CDC epidemiologist, history provides an important, yet often overlooked, piece of evidence for understanding how diseases are affecting populations in the present. So, in other words, how can we use the past to improve our public health interventions in the present? In August 2015, I arrived to Puerto Rico to work at the Department of Health as part of a two-year field epidemiology fellowship, that is, CDC’s Epidemic Intelligence Service, or EIS. This program is referred to as CDC’s “Disease Detectives,” as our contribution to the agency is to look for “clues” and to better understand diseases affecting populations, especially in outbreak settings.

Now, before getting to the island, I had been working on TB as part of my dissertation on TB control in China. So I was familiar with the WHO’s End TB Strategy, which had been released earlier that year, and, moreover, how Puerto Rico had been highlighted as an area for TB elimination. In getting to the island, I began working with the Puerto Rico Department of Health, TB Control Program, as well as experts at CDC’s Division for TB Elimination. My supervisor at the time and co-lead author for this article, Doctora Dana Thomas, was the TB Control Program’s Chief Medical Officer. And she really encouraged me to think critically when interpreting surveillance data on reported TB cases, especially as my first project, in getting to the island, was to evaluate TB surveillance. So, as part of this evaluation, I started reading about the history of TB and the more I read, the more I became fascinated, and, moreover, the more I came to think of TB history as a crucial part of how we needed to properly evaluate the system and interpret these numbers moving forward.

[Sarah Gregory] Okay, so on that note, tell us about your study.

[Emilio Dirlikov] Our study drew on both qualitative and quantitative information. We began with a systematic search of literature that was published in English or Spanish on TB, going back

to 1898, and that's when Spain ceded Puerto Rico to the United States through the Treaty of Paris.

[Sarah Gregory] Surveillance.

[Emilio Dirlikov] Indeed. We read extensively, beginning with archival reports describing TB control in the 1910s and '20s. So, in addition to these review of policies and descriptive reports, we also wanted to analyze available surveillance data to better understand how TB epidemiology was changing over this time. So, with some archival digging, we were able to analyze data on TB deaths starting in 1932, when Puerto Rico was included in the U.S. annual mortality statistics, and we also analyzed data on the number of reported TB cases since 1953; that is when CDC's National TB Surveillance System was established. And finally, we compared data from Puerto Rico to data from the United States. And by doing this, this allowed us to have a comparison group, something that we could contrast and really understand how well Puerto Rico was progressing against the United States.

[Sarah Gregory] And what was the goal of your study?

[Emilio Dirlikov] We had several goals for our study, focused on bringing attention to better understanding current TB epidemiology and progress to TB elimination on the island moving forward. The first goal was to provide a comprehensive documentation of the history of TB surveillance and control, using both qualitative and quantitative data sources. This could be helpful for the Department of Health and other local stakeholders, such as academia and medical associations, as they try to think critically about how indicated historic challenges could continue to impact TB epidemiology in the present.

The second goal was to highlight the extraordinary progress in controlling TB on the island, while indicating these potential challenges that could require some further support, or even additional investigation. Finally, we wanted to position this article to join a larger global discussion on TB control and TB elimination. So, in low-incidence settings, like the Puerto Rico or the United States, it's important to understand how TB surveillance and control strategies have developed over time, and how we can use that understanding of history to better interpret current epidemiologic data and share those lessons with other contexts.

[Sarah Gregory] Are there reasons that TB may be underreported in Puerto Rico?

[Emilio Dirlikov] In speaking with TB patients during their clinical visits or while providing direct observation of treatment, my coauthors and I realized that many of these patients had had symptoms for quite some time before they were diagnosed, meaning that they were undetected and not reported in official figures, despite having TB disease. Through our historical review, we found that delayed diagnosis and underreporting had been a longstanding problem on the island. So we turned to current epidemiologic indicators. In particular, we focused on indicators that might help us understand delayed diagnosis.

And just for a bit of background: TB bacteria can be detected through a staining technique or grown in the laboratory using cultures. And this is how we confirm diagnosis. Patients with more advanced disease are more likely to have positive results to either one of these techniques. TB can also be diagnosed clinically using symptoms alone, which is especially important early on in the course of the disease, when it's difficult to isolate the TB bacteria.

Back to Puerto Rico... On the island, a smaller proportion of cases are identified clinically, which may denote insufficient clinical awareness of TB symptoms. In Puerto Rico, that's five percent of cases are clinical cases, compared to 16 percent in the United States. Puerto Rico has a higher proportion of culture-positive cases, 85 percent versus 77 percent in United States. And this might indicate delayed diagnosis, as the likelihood of detecting TB through culture increases as disease advances over time.

The proportion of cases identified among TB patients following death was also higher in Puerto Rico. That is five percent on the island versus two percent in the United States. And finally, TB among people born outside of Puerto Rico or the rest of the United States is not very well understood. Most foreign-born TB patients in Puerto Rico were from the Dominican Republic, where the incidence of TB is much higher than in the United States or Puerto Rico. It was estimated at 45 cases per 100,000 population in 2017.

[Sarah Gregory] And what was the number in Puerto Rico?

[Emilio Dirlikov] Yeah, and that's compared to 1.5 cases per 100,000 population in Puerto Rico.

[Sarah Gregory] Yeah, that's what I wanted to know. Okay.

[Emilio Dirlikov] So, we might anticipate that unidentified cases of TB exist among documented and undocumented migrants from Dominican Republic to Puerto Rico.

[Sarah Gregory] Beyond their epidemiologic indicators, what are the broader socioeconomic factors impacting TB?

[Emilio Dirlikov] Well, I'm glad that you asked that question, Sarah. As we know from histories of tuberculosis the world over, stemming from the late 19th century, TB thrives in contexts marked by poverty. And just to give you some facts about poverty currently in Puerto Rico. In 2017, 43.5 percent of the population was living under the poverty line, and that's compared to 12.7 percent in the United States—43.5 versus 12.7. Puerto Rico's government debt, which was announced at \$72 billion in June 2015, further limits the local government's ability to service...provide services to its population, including for public health. So, although we would need further investigations to better determine any association between TB and poverty currently on the island, these starkly higher poverty rates could further impact TB epidemiology, including promoting delayed diagnosis and underreporting.

[Sarah Gregory] If you were going to do a future study, would that be something you would look into?

[Emilio Dirlikov] Certainly! And I hope that other people on the island and with CDC support, will continue this...to learn more about what's going on.

[Sarah Gregory] And Dr. Dirlikov, what were the main findings of your study?

[Emilio Dirlikov] The main finding is that underreporting and delayed diagnosis should be considered when interpreting reported numbers. We should further investigate to learn more about these areas, especially as they might affect progress towards TB elimination.

Now, additionally, our paper documents the rich history of TB control on the island. And, Sarah, I'd like to share two of my favorite anecdotes that have relevance to today's control efforts. The first is the impact of hurricanes to public health, including on TB. Historic reports emphasized

the devastation caused by hurricanes during the 1920s and 30s. For example, Hurricane San Ciprian crossed the island as a Category 4 storm on...in September 1932, and the following year, the Department of Health reported the highest recorded mortality rate due to TB, that is, 333 deaths per 100,000 population. And, as you remember, right now it's at 0.1 death per 100,000 population. And also, by comparison, during that year, in the United States, TB mortality was estimated at 57 per 100,000 population. Public health officials at the time linked this peak in mortality rates to the destruction caused by Hurricane San Ciprian.

[Sarah Gregory] Okay, so flash forward for us now.

[Emilio Dirlikov] On September 20, 2017, Hurricane Maria made landfall, also as a Category 4 hurricane, devastating infrastructure across the island, including public health. Recently, CDC's *Morbidity and Mortality Weekly Review*, the *MMWR*, published a report on the innovative efforts undertaken by the Department of Health to ensure patients received treatment in the aftermath of the hurricane. Continued surveillance and patient monitoring will be needed to better understand the potential effects Hurricane Maria had on the island.

The second anecdote I'd like to share highlights the importance of Puerto Rico as a site for advancing the science of TB. From 1957 to 1960, the U.S. Public Health Service conducted a controlled trial of treatment for latent TB infection using isoniazid prophylaxis. And through this study, they recruited known TB patient contacts in the United States, here in Georgia, as well as in Mexico and Puerto Rico. Contacts who received isoniazid had 60 percent lower incidence of active TB disease over the course of trial. The study's Puerto Rico principal investigators wrote the following prophetic words in one of their reports, and I quote: "A large reservoir of tuberculosis cases for the next generation is already seeded in Puerto Rico... The infant with a positive tuberculin in 1962 may be the grandfather who will develop cavitary disease and infect his grandchildren in the year 2012."

Now, more than 50 years on, the use of prophylaxis to treat latent TB infection is being prioritized as...both domestically and globally as a key strategy for TB elimination.

[Sarah Gregory] Okay, so how about a "lessons learned" generally here?

[Emilio Dirlikov] We have three major lessons learned. The first is that data from TB surveillance has directed control efforts. In the 1930s, that was mortality data that showed the extent of the problem of TB. Starting in the 1950s, more systematic reporting of cases documented the dramatic decreases following the use of effective TB medications. And more recently, public health officials have used TB genotyping to better understand TB transmission, including across jurisdictions and over time.

The second lesson learned was the use of newly developed strategies and techniques has produced evidence-based practices to improve surveillance, control, and patient care. For example, TB treatment using...for latent TB infection...was adopted following studies conducted in the late 1950s, especially for persons identified at risk during public health investigations looking at the contacts for known or newly identified TB cases.

The third lesson learned is that public health commitment has been crucial for TB control and surveillance efforts. It's often said that progress towards TB elimination is a marathon, with many committed public health officials contributing to this long history.

[Sarah Gregory] And the overall public health implications of your study are what?

[Emilio Dirlikov] Although there are fewer and fewer cases reported of TB on the island, there's still a lot of opportunities to improve TB surveillance and control. Reaching TB elimination will require sustained public health surveillance and control efforts, including case detection, case management, and treatment. Novel tools are being used to further improve public health interventions, including genotyping and molecular surveillance, electronically-facilitated case consultation, and the use of smartphone technology for direct observation of treatment. In crafting effective interventions, public health officials, clinicians, and other stakeholders on the island and beyond should continue to consider underreporting and delayed diagnosis and how that might be used for interpreting current epidemiologic data. Like we mentioned, further investigation will be needed to clarify the extent of potential underreporting and how that might affect progress towards TB elimination.

[Sarah Gregory] Okay, Dr. Dirlikov, you mentioned being an anthropologist, early on. So, tell us a little bit about that. Tell us about your history—why you do what you do, how you came to be at CDC, and what your interests are.

[Emilio Dirlikov] Yeah, so I actually went into anthropology after starting my career as an undergraduate at the University of Michigan, dual majoring in Chinese studies and biology. And I didn't really know exactly what I wanted to do just yet—I was only 18, 19 at the time. But I found myself in Beijing in spring of 2003. As you might recall, this was when a new disease was starting to spread across China and beyond. And this disease eventually was termed “severe acute respiratory infection...syndrome” or “SARS.” So, it was that experience of being in Beijing in 2003 that led me to think about the different ways that we interpret numbers, that we collect numbers, and people ultimately experience disease. So, my bent from biology was being applied to Chinese studies in order to think about how people throughout the world think about disease, and how we, in public health, can use those understandings to better improve upon our public health interventions.

So, I joined CDC, as I mentioned, in 2015, through the EIS program. And since then, I've been very, very fortunate to work on a variety of different priority areas, including TB, rabies, and imported malaria in Puerto Rico. I got to go to Guinea for Ebola response in 2015 and '16; I've been to Mozambique and Liberia for measles; dengue in Burkina Faso; and I had the great honor to lead efforts to better understand neurologic complications of Zika among adults throughout the 2016 epidemic in Puerto Rico. So, currently, I work as an epidemiologist on global HIV control, which also brings me into contact with tuberculosis control globally, again.

[Sarah Gregory] Thank you so much for taking the time to talk with me today, Dr. Dirlikov. Listeners can read the March 2019 article, Tuberculosis Surveillance and Control, Puerto Rico, 1898–2015, online at cdc.gov/eid.

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

[Announcer] For the most accurate health information, visit cdc.gov or call 1-800-CDC-INFO.