Decrease in TB Cases during 2020, United States

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

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Kathryn Winglee, a statistician at CDC in Atlanta. We'll be discussing a decrease in TB cases during the first year of the COVID-19 pandemic.

Welcome, Dr. Winglee.

[Kathryn Winglee] Hi, Sarah. Thanks for having me.

[Sarah Gregory] Your article is about looking into 2020 declines in TB cases during the first year of the COVID pandemic. You looked at something called IQVIA pharmacy data. First off, what's that?

[Kathryn Winglee] So IQVIA is a company that has several different databases containing de-identified outpatient prescriptions from across the United States. These data are provided either as number of prescriptions for a given medication or number of unique patients on each medication each month. And we can use the data to look at the medications used to treat people with TB disease.

[Sarah Gregory] How do you have access to it?

[Kathryn Winglee] So you do have to pay for access to IQVIA data. Once you have access, IQVIA has an interface that allows you to search each database and then download the results. So for example, I used the interface to identify all of the prescriptions that contained isoniazid, which is one of the medications used to treat people with TB disease—kind of analyzed those prescriptions by month.

[Sarah Gregory] You also looked at information in the National Tuberculosis Surveillance System. Who owns that and how is information tracked in it?

[Kathryn Winglee] So the National Tuberculosis Surveillance System, which is also known as NTSS, is a CDC data collection system. So all new cases of tuberculosis, which is also known as TB, that are identified in the 50 states, DC, Puerto Rico, the US Virgin Islands, and several US-affiliated Pacific Island areas must be reported to NTSS. These reports do generally include clinical and demographic information on each case, and then these data are used by CDC to track trends in the number and characteristics of cases. Preliminary numbers are reported each March in the Morbidity and Mortality Weekly Report, or MMWR, and the final numbers are reported each fall in the Division of Tuberculosis Elimination Annual Surveillance Report.

[Sarah Gregory] Okay. So you have access to that one because it's a CDC database, so there's no cost or request required for that, I guess, huh?

[Kathryn Winglee] Correct. There's no cost for access to these data. And in addition to these two reports, the aggregate data are also available through the Online TB Information System (also called OTIS) as well as CDC Atlas+. And requests for additional information can also be made through the Division of Tuberculosis Elimination if you email tbinfo@cdc.gov.

[Sarah Gregory] How did you become aware of the decline in TB in 2020?

[Kathryn Winglee] So CDC became aware of this decline when analyzing TB case data reported to NTSS in 2020. Because of the potential impact of the COVID-19 pandemic, we were really

focusing on comparing the 2020 numbers to previous years. And that 20% decline was reported in the March 2021 MMWR.

[Sarah Gregory] Why did you want to do an investigation into it in the first place?

[Kathryn Winglee] So the 20% drop was really unusual because TB has been slowly but steadily decreasing about 2-3% every year over the last 10 years. So this was a pretty large change, and it was so different that we decided it was important to try to investigate it. And this 20% decline likely represents both a true reduction in TB disease, as well as missed or delayed TB disease diagnoses.

So there's about four reasons that we could come up with to explain this decline. The first is widespread disruptions to healthcare during the COVID-19 pandemic. We know that the pandemic has strained a lot of public health services, including TB prevention and control services. A second reason is that there are a lot of similarities in symptoms between COVID-19 and the TB disease. There have already been some case reports that have revealed some people with TB disease were evaluated for COVID-19 but were not tested for TB, despite multiple encounters with healthcare systems. So these initial misassumptions might contribute to missed diagnoses, or delayed diagnoses.

The third reason is that efforts to prevent the spread of COVID-19, such as wearing masks and staying six feet away from others, can also reduce TB transmission as both COVID-19 and TB are both respiratory diseases. A fourth reason is the changes in the immigration and travel patterns. So global travel has greatly decreased during the pandemic, reducing the likelihood of TB diagnoses among people who are coming in from outside the United States. Understanding the underlying causes of this 20% decline will help the TB programs to better allocate resources and prepare for future cases.

[Sarah Gregory] What time period did you compare 2020 to, and why that one?

[Kathryn Winglee] We mainly compared 2020 data to 2019 data because the 2019 data is what's most recently available prior to the pandemic. We also used data from January 2006 to December 2019 to look at trends over time, and then I compared that with 2020. And this time period was chosen because IQVIA data aren't really available prior to 2006.

[Sarah Gregory] Okay. Going back to NTSS and IQVIA, how did you use the data together?

[Kathryn Winglee] So we first wanted to see whether the two datasets were correlated prior to 2020. So we don't expect the numbers in the two databases to match exactly because they're actually measuring different populations—for example, IQVIA doesn't capture the patients that are treated in the public health system. However, we still wanted to determine whether the trends match. And correlation between these databases suggests that the IQVIA prescription data can be used as a proxy for the trend in the number of TB cases reported. So if we can show that these databases were correlated prior to 2020, but not in 2020, then this would have been evidence that the decline in cases reported to NTSS in 2020 was caused by underreporting.

[Sarah Gregory] You used modeling as part of your study. How does that work?

[Kathryn Winglee] So we used data from 2006-2019 to develop our models, and then we evaluated the 2020 data using those models to see whether 2020 kind of fits those trends from previous years. And we used two different types of models. The first is called a seasonal autoregressive moving average, or SARIMA, model. This model is a time-series model that uses

the prior measurements of the number of cases to predict future cases by using both the time of year and previous trends in the data. And with this model, what else can you see if the 2020 data are below the predictions from this model, in which case that supports our concerns that the declines seen are larger than expected based on the previous declining trend.

The second type of model we used is a linear model between NTSS and IQVIA data. This model basically draws a straight line between the two of them to look for a relationship between the variables. If the 2020 data did not align with the predictions from this model, then this would suggest there were differences in the decline between the two datasets.

[Sarah Gregory] How did you conduct this analysis?

[Kathryn Winglee] Data were pulled from IQVIA and NTSS as aggregate counts by month. And then all of the analyses were performed using the statistical programming language R, using some of the specialized R packages.

[Sarah Gregory] Briefly tell us about your study now.

[Kathryn Winglee] So after identifying that large decline in 2020 TB cases, we wanted to identify additional potential sources of data on trends in TB cases to help us better understand why there was this 20% decline. We specifically focused on the prescription data because the drug regimens used to treat people with TB disease are generally not used for other diseases or health conditions. In particular, two of the four drugs used to treat people with TB disease are isoniazid (also known as INH) and pyrazinamide (also known as PZA), and these two drugs are only used to treat people with TB disease, and so prescriptions of these medications generally indicate that the patient is being treated for TB disease. Of particular note, INH is used to treat both people with latent TB infection and people with TB disease, while PZA is only used to treat people with TB disease. IQVIA data also has the benefit of not being dependent on public health resources. And so, if it shows a different trend from the NTSS data, then it would have suggested that the decline we're seeing is due to underreporting to NTSS.

[Sarah Gregory] What did you find from your study?

[Kathryn Winglee] We first show that the number of patients identified from TB medications through IQVIA was strongly correlated with the number of cases reported in NTSS prior to 2020, and we showed that this relationship was specific to these TB medications. This supports our hypothesis that pharmacy data can be used as a proxy for the trends in TB cases. We next looked at the percent difference between 2019 and 2020 numbers and found that both databases had large declines in 2020 compared with 2019. There were particularly large drops in the number of patients in April and May.

We also saw similar decreases in April and May of 2020 when we looked at the total number of prescriptions in the IQVIA database. This suggests that the decreases we are seeing are not specific to people being treated for TB disease. Using our SARIMA time-series model, we showed that these large declines for both NTSS and IQVIA were lower than predicted. This provides support for the hypothesis this decline is much larger than would be expected, you know, from the previous declining trends that we've seen.

Finally, using our linear models, we found that PZA patient counts were close to the prediction, but INH patient counts were lower than the prediction, especially for June through December, suggesting that the declines in pyrazinamide prescriptions are in line with the declines in overall case counts, but the declines in INH prescriptions are even lower than expected. As a reminder,

INH is used to treat people with both TB disease and latent TB infection. So although NTSS only measures TB disease, these data hints that treatment for people with latent TB may also be declining.

[Sarah Gregory] Were there any surprises?

[Kathryn Winglee] The biggest surprise to me was the strength of the correlation between the datasets. While we did hypothesize that they were correlated, there were some major caveats. For example, many TB patients actually receive their treatment from the public health department, but IQVIA data doesn't include these prescriptions in its data. So there was no guarantee that there actually would be a correlation.

[Sarah Gregory] What were the challenges?

[Kathryn Winglee] The biggest challenge was trying to identify which metrics would be the best for comparing trends. For example, we didn't know whether or not we should exclude TB cases with resistance to common TB drugs from NTSS counts. In addition, IQVIA actually has a number of different metrics for measuring their prescriptions, so we had to identify which one best follows the NTSS trend. Thirdly, some prescriptions may occur in a different month from when the case is diagnosed, so we had to decide whether or not we wanted to aggregate by month or quarter. So these were all addressed by comparing the strength of the correlation between the two datasets for the different scenarios.

[Sarah Gregory] What factors contributed to this decline, do you think? I mean, I know you mentioned several things at the beginning of the podcast but let’s go back through those.

[Kathryn Winglee] Yeah. So the fact that the IQVIA data and NTSS data were correlated suggests that this is not a surveillance artifact caused by underreporting, which was one of our hypotheses. And that kind of leaves the options of true decline and underdiagnosis of TB as possible options. Underdiagnosis would result from patients avoiding medical care or being unable to access medical care, or from providers assuming that patients with respiratory symptoms had COVID-19 and therefore not even testing for TB. Both of these scenarios have actually been reported in the literature. And furthermore, in our analyses in the IQVIA data, the decrease was not specific to anti-TB medications, but also occurred when we were looking across all medications. This suggests that overall, there's going to be fewer prescriptions, and most likely coming from fewer diagnoses. This hypothesis, although not confirmed, is also supported by several other studies showing patients delayed or avoided medical care in 2020 due to COVID-19.

[Sarah Gregory] What about the future? Will numbers stay lower or bounce back as some kind of normalcy resumes?

[Kathryn Winglee] While we have ruled out one possible reason for the decline, we have not identified the true reason, and it is also entirely possible that this decline had more than one cause, which makes it difficult for us to predict what's going to happen in the future. However, if there is a lot of underdiagnosis happening, then TB cases may increase in the future, at least temporarily, as patients will be sicker longer, resulting in increased chances of them infecting other people. CDC will be monitoring this closely and will be working with partners in state and local public health departments to adapt TB priorities and prevention measures as needs change.

[Sarah Gregory] This decline is in US only, correct? That's what you looked at. Do you think it's applicable globally?

[Kathryn Winglee] So at the time this paper was written, numbers had not been released globally, but the World Health Organization has now reported an 18% decrease globally in the number of people newly diagnosed with TB between 2019 and 2020. And this is despite the fact that they have reported large increases between 2017 and 2019. Multiple other countries have now also published scientific papers reporting on their investigations into declines in reported TB in their areas. However, a concern for the first time in a decade, global TB deaths increased in 2020. Here in the US, we don't yet know the number of 2020 TB deaths, as we typically allow a two-year reporting lag for programs to report deaths during treatment for TB disease.

[Sarah Gregory] So we don't exactly know apparently what the decline is caused by, but are there measures public health can adopt to help continue a decline if there actually was one and create a trend?

[Kathryn Winglee] So ending TB in the United States requires a dual approach, both of diagnosing and treating every case of TB disease and also preventing future cases through expanded testing and treatment for people with latent TB infection. We also need to engage communities disproportionately affected by TB. As part of that, CDC recently launched a new communications campaign called Think. Test. Treat TB. This is aimed at raising awareness of TB prevention and promoting testing and treatment of latent TB infection. CDC, state and local TB control programs, and the TB Centers of Excellence for Training, Education, and Medical Consultation can provide guidance, educational resources, and training for healthcare providers.

[Sarah Gregory] What are the best ways for TB to be treated and monitored?

[Kathryn Winglee] The timely diagnoses of TB disease helps to save lives and prevents spread in the communities. It's important for healthcare providers to include TB in their list of differentials and maintain an index of suspicion, especially for patients who may be at a higher risk.
And CDC is continuing to work to improve diagnostics and treatment for TB disease. In February, CDC provided guidance for a new treatment regimen specifically for extensively drug-resistant TB. In February, we also released a new four-month regimen to treat drug-susceptible TB disease. You can find more information on both of these at cdc.gov/tb.

[Sarah Gregory] March 24th is World TB Day. Does CDC do anything to recognize this day?

[Kathryn Winglee] We consider World TB Day an opportunity to educate people about the impact of TB both in the United States and around the world. CDC is featuring stories from our 2022 US TB Elimination Champions, who are being recognized for their work and commitment to eliminate TB in their communities. And for more information, digital resources, and a list of events, you can visit cdc.gov/tb.

[Sarah Gregory] Tell us about your work, Dr. Winglee. What do you do, what your background is, and what you like most about it?

[Kathryn Winglee] So for my background, I have a Bachelor of Science in Microbiology and a Bachelor of Science in Computer Science from the University of Washington, and a PhD in Cellular and Molecular Medicine from Johns Hopkins School of Medicine. This means my background is a mix of biology and analytics. I am currently a statistician (data scientist) at CDC, which means that I get to help analyze data for projects related to TB, such as this one.

And my favorite thing about this is being able to work with a lot of talented people on a range of projects that can have a real-world impact.

[Sarah Gregory] As we cautiously aim toward being out and about again, are you doing anything recently for fun that you haven't done for a long time?

[Kathryn Winglee] That's a good question. For me, I recently saw a movie in a movie theater for the first time in a while. It was really great to actually be able to have an audience to share that experience with.

[Sarah Gregory] Was it an Oscar nominated movie? I have to ask.

[Kathryn Winglee] No. It was the most recent Spider-Man movie.

[Sarah Gregory] Ah. Yeah, I haven't done that yet. I haven't braved a movie theater. I'm kind of cautious of them at the best of times.

[Kathryn Winglee] I will admit I saw it much later than everybody else, so it was still relatively empty.

[Sarah Gregory] Okay. Well, thank you so much for taking the time to talk with me today, Dr. Winglee.

[Kathryn Winglee] Thank you for having me on. It was a pleasure to talk with you.

[Sarah Gregory] And thanks for joining me out there. You can read the April 2022 article, Decrease in Tuberculosis Cases during COVID-19 Pandemic as Reflected by Outpatient Pharmacy Data, United States, 2020, 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.