

**US DEPARTMENT OF HEALTH AND HUMAN SERVICES**  
**CENTERS FOR DISEASE CONTROL AND PREVENTION**  
**National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention**  
**Division of Tuberculosis Elimination**

Amended 6/10/2021



**VIRTUAL MEETING OF THE**  
**ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS**  
**June 16, 2020**

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**RECORD OF THE PROCEEDINGS**

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# Table of Contents

<b>Minutes of the Virtual Meeting</b> .....	<b>2</b>
<b>Opening Session</b> .....	<b>3</b>
<b>NCHHSTP Director’s Update</b> .....	<b>4</b>
<b>DTBE Director’s Update</b> .....	<b>8</b>
<b>Updates from Global Tuberculosis Branch</b> .....	<b>11</b>
<b>Updates from NCHHSTP Epidemiologic and Economic Modeling Agreements (NEEMA) Consortium)</b> .....	<b>16</b>
<b>A Tool to Assist TB Programs with Integration of Whole Genome Sequencing Data</b> .....	<b>21</b>
<b>Ongoing Challenges with TB Drugs and Diagnostic Supplies: Results from National Survey</b> .....	<b>24</b>
<b>Update on ACET Workgroups</b> .....	<b>30</b>
<b>ACET Business Session</b> .....	<b>31</b>
Business Item 1: Approval of Previous ACET Meeting Minutes.....	32
Business Item 2: Advice Requested from ACET .....	32
Business Item 3: Report to HHS Secretary .....	33
Business Item 4: Status of Essential Component Document .....	33
Business Item 5: Impact of Public Charge Executive Order .....	33
Future Agenda Items.....	33
<b>Public Comment Session</b> .....	<b>34</b>
<b>Closing Session</b> .....	<b>34</b>
<b>Attachment 1: Day 1 Participants’ Directory</b> .....	<b>35</b>
<b>Attachment 2: Glossary of Acronyms</b> .....	<b>38</b>
<b>ADDENDUM 1: Roadmap for Advancing TB Elimination in the United States through Scale up of Testing and Treatment of Latent TB Infection</b> .....	<b>40</b>



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**ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS**

**June 16<sup>th</sup>, 2020**

**Minutes of the Virtual Meeting**

The United States (US) Department of Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC), National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention (NCHHSTP), Division of Tuberculosis Elimination (DTBE) convened a meeting of the Advisory Council for the Elimination of Tuberculosis (ACET). The proceedings were held on June 16, 2020 beginning at 10:00 AM EST.

ACET is formally chartered under the Federal Advisory Committee Act (FACA) to provide advice and recommendations to the HHS Secretary, HHS Assistant Secretary for Health, and CDC Director regarding the elimination of tuberculosis (TB). The charter authorizes ACET to make recommendations regarding policies, strategies, objectives and priorities; address the development and application of new technologies; provide guidance and review on CDC's TB Prevention Research portfolio and program priorities; and review extent to which progress has been made toward TB elimination.

Information for the public to attend the ACET meeting was published in the *Federal Register* in accordance with FACA regulations and rules. All sessions of the meeting were open to the public. See *Attachment 1: Participants' Directory*.

## Opening Session

**Carla Winston, PhD., M.A.**

Associate Director for Science, Division of Tuberculosis Elimination  
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCCHHSTP)  
Centers for Disease Control and Prevention (CDC)  
ACET Designated Federal Officer (DFO)

**Barbara Cole, R.N., M.S.N., P.H.N.**

TB Controller  
Riverside County Department of Public Health

Dr. Carla Winston opened the meeting by reminding everyone that the meeting is public, and all comments made during this meeting are a matter of public record. Members should be mindful of potential conflicts of interest (COI) identified by the CDC Committee Management Office and recuse themselves from voting and participating in these discussions. Members will state if there is a conflict of interest at the first roll call so that they may be noted for the record.

ACET Voting Member (Institution/Organization)	Potential Conflict of Interest
Ana Alvarez, MD University of Florida College of Medicine	No conflicts disclosed
Robert Belknap, MD Denver Metro Tuberculosis Control Program	No conflicts disclosed
Lisa Armitige, MD Heartland National Tuberculosis Center	No conflicts disclosed
Barbara Cole, RN, MSN, PHN Riverside County Department of Public Health	No conflicts disclosed
Jennifer Flood, MD, MPH California Department of Public Health	No conflicts disclosed
David Horne, MD, MPH University of Washington School of Medicine	No conflicts disclosed
Robert Horsburgh, Jr., MD, MUS Boston University School of Public Health	No conflicts disclosed

Lixia Liu, PhD, MP, (ASCP), D(ABMM) Indiana State Department of Health	No conflicts disclosed
Kristine Steward-East Advocate for Tuberculosis	No conflicts disclosed (no answer)
Zelalem Temesgen, MD Mayo Clinic Center for Tuberculosis	No conflicts disclosed (no answer)

The roll call confirmed that the 19 voting members and ex-officio members in attendance constituted a quorum for ACET to conduct its business on June 16, 2020.

Dr. Winston began her announcements by stating the ACET members that will be rotating off as of June 30, 2020. Firstly, Dr. Winston thanked Dr. Ana Alvarez and Dr. Jennifer Flood on behalf of CDC and DPDE for their contributions to ACET. They will be receiving certificates of appreciation via mail. She then welcomed to the committee Dr. Amina Ahmed, Pediatrics Infectious Diseases physician with Levine Children’s Hospital Atrium Health in Charlotte, North Carolina who is replacing Dr. Alvarez as of June 30, 2020. She welcomed Dr. Ann Loeffler, Pediatrics Infectious Diseases and Hospitalist Medical Director Outreach Education of Randall Children’s Hospital at Legacy Emmanuel in Portland Oregon, who will be replacing Dr. Flood. Dr. Winston welcomed Dr. Laura Cheever, Associate Administrator with the HIV AIDS Bureau who served as ex-officio member for the Health Resources and Services Administration. She has replaced Dr. Letha Healey. Dr. Winston then thanked Dr. Diana Elson, who is retiring mid-June 2020, for her committed participation and contributions to the success of the council as the Immigrations and Customs Enforcement Department of Homeland Security ex-officio to ACET. Letters have been sent to Substance Abuse and Mental Health Services Administration to identify a replacement in 2019, Office of Minority Health to identify a replacement in 2019, and the Agency for Healthcare Research and Quality to identify a replacement in 2018. This was the end of the announcements and Dr. Winston turned it over to Ms. Cole to proceed with the agenda.

Ms. Cole began by adding her thanks to the members who are rotating off the committee. She provided a quick overview by summarizing the forthcoming meeting agenda items. She then presented Dr. Jonathan Mermin, Director of NCHHSTP, for his presentation.

**NCHHSTP Director’s Update**

**Jonathan Mermin, MD, MPH (RADM, USPHS)**  
Director, CDC National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP)

Dr. Jonathan Mermin began his presentation by welcoming everyone and thanking them for being present. He acknowledged the difficulties of the time we are living in, not only because we are experiencing one of the worst epidemics of our lifetime, but also the continued racial inequity in our country. He reaffirmed that working for health equity and particularly the medically underserved is a core value of those working in TB, and expressed the discomfort felt by the killings of African American men, women, and transgender persons. Dr. Mermin stated that these deaths hurt our conscience and condemn our inability for change. He is reminded now, with Juneteenth in just a few days, that racism and discrimination are a stain in our country's history, but do not have to be a part of our future. He closed his introductory statement stating how most of us in public health can be tools of service to the world and he hopes we can continue to do this in our working life as well as within our communities.

### ***COVID-19 Response and Resources***

Dr. Mermin began with the center overview. Firstly, he recognized that CDC has likely not experienced such a long-term response that has involved so much of the agency. At the end of May, NCHHSTP had almost 200 people deployed, and almost 400 had been deployed previously. A lot of people who are working with communities and comfortable with infectious diseases are the ones serving in this response which, unfortunately, leaves gaps in the process of accomplishing their goals within the center. However, they adapted in the middle of a changing epidemic both for TB as well as other infections. He further stated that the centers tried to mitigate impacts of COVID-19 as well as the response on how they do their work.

Dr. Mermin referenced Dr. LoBue's work as part of a sub-group of a working group that is responsible for how core clinical services are sustained during this response, but also on how to come out even stronger in the next few months. Dr. Mermin is also involved with the overarching working group as a Co-Lead and has responsibilities more so addressing the collateral damage that COVID-19 has caused on the economy, public health and directly on the availability of services and prevention. He reiterates how they have adapted in staffing by staggering/rotating deployment. They have streamlined hiring and onboarding in the agency as much as possible, however recognizing that most hiring and other core administrative services and operational activities are now focused on COVID-19, which leaves their ability to fill and do other activities even harder although there are some flexibilities. He mentioned some of the adjustments they have made such as postponing due dates for cooperative agreements and allowing data to be provided in different timeframes. He recognized the struggles of partners on the ground and how they surely feel these more strongly. Dr. Mermin also described some examples of mitigation efforts which include allowing flexible grants management/reporting, providing guidance and sharing lessons learned from the field, releasing guidance for syringe service programs (SSP) in this environment where face-to-face interactions are difficult, and supporting/expanding telehealth approaches like tele-PrEP for HIV, and working with local surveillance and program staff to think about what is essential. He emphasized the need to adapt their services in this environment in an effective way, which is hard.

Dr. Mermin then presented some resources for COVID-19, including guidance from DTBE for TB control programs on how to effectively adapt during this public health emergency,

the production of a liver disease in COVID-19 webpage to provide guidance around COVID-19 for people with HBV, HCV or at risk of Hepatitis A, provided information around what is needed to know about HIV during COVID-19, guidance for schools specifically about COVID-19, and issued “dear colleague” letters which, although an unusual way to provide guidance, are a way to provide useful information but through a less rigorous and time-consuming approach as is the case when developing formal guidelines. He also notified the group that, if people in the meeting think it would be helpful for CDC to present more useful information that has yet to be provided, they are certainly open to hearing them. Dr. Mermin stated they have had a major internal initiative to think about self-testing and exactly how they can respond to this environment by ensuring people have access to sample collection and, if possible, self-testing for their infections. Several factors to think about are whether the tests are available and, if they are, how they can get them to people. If not, how do they work on the research and the regulations through FDA to make them available and reimbursable in this environment. They have also been thinking creatively about what self-testing would mean for the TB arena, but it is quite hard because the test available for latent TB infection (LTBI), for which it would be most useful, are not amenable at the current time to either self-sample collection or self-testing.

### ***NCHHSTP Division Updates***

Dr. Mermin provided an update from provisional TB data from 2019 which showed a continued slight decrease in the absolute number of cases since 2018. He mentioned it would be prudent to have some discussion of what is happening to TB in the current environment and what it means for our programs. NCHHSTP was able to issue new HCV guidelines, which had focused initially on routine screening for baby boomers, as they were older and more likely to get ill and die without treatment, but they realized two things: (1) it is hard to screen in a routine way for a generation and (2) the opioid crisis meant an increase in HCV risk in younger people. Essentially, all ages are affected. The younger age group comprises the largest number and the middle ground also has very high rates. As such, they were able to modify and recommend universal screening for people of all ages at least once. Pregnant women are then recommended to be tested at least once during every pregnancy. He also mentioned they have a communication campaign that is trying to get this information out to providers and to the public.

Regarding HIV, Dr. Mermin stated that they issued the new data from 2018 and have sped up surveillance data provisions for HIV and thinks they will be doing so even faster over time. They are seeing a non-significant decline from 2014-2018 in HIV. With the onset of ending the HIV epidemic, he is hoping years 2019-2020 are seeing more decline. He recognizes that COVID-19 might have an effect but is hoping to respond effectively even though services are difficult to provide. He presented data on increased efforts to reduce disparities. NCHHSTP will be looking more carefully to understand how they can both accelerate the reductions they are seeing and respond to the ones that are going in the wrong direction. He also mentioned NCHHSTP issued a report on the risk of HIV infection among injection drug users, which shows that it is hard for many people to inject drugs without some risk of infectious diseases. It is harder for people to access syringes in some circumstances, especially if syringe service programs are farther away in distance than where people are living. There is data indicating that SSPs are struggling due to COVID-19 and there seems to be some indication of an increase in overdoses in the CDC



BioSense surveillance system, which he insinuated may be due to the fact that it has been harder to access naloxone as well as medically assisted therapy.

Dr. Mermin provided updates for the Division of Adolescent and School Health (DASH). The DASH strategic plan was released titled “The Path Forward”, focused on a collection of factors that impact not only how students live and their well-being while in school, but also how their behaviors and experiences in school influence the risks they will take as they get older. Increasingly we are seeing both positive effects of our programs in the schools and the limitations that only working in schools provides. A Healthy Youth board was launched on CDC’s Pinterest account which provides resources to educators promoting healthy behaviors and connecting youth to health services. From an STD standpoint, NCHHSTP provides continuing education credits for a variety of different activities. They have published new recommendations for providing quality STD clinical services focused on improving STD clinical services in primary care. Medscape is offering these CE credits for new recommendations. He added that NCHHSTP also issued some guidance on how to utilize telehealth and prescribing oral medication that could effectively treat STDs especially if these people have trouble accessing injectables. He ended his presentation by opening for questions.

#### ***ACET Discussion: NCHHSTP Director’s Update***

Dr. Randall Reves posed the first question in the chat which read as follows: “To what extent have the tools developed and in use by the Center and DTBE in particular, been useful as resources for the response to COVID 19 (tools in the broad sense, including databases, skills, training resources etc.)?” Dr. Mermin deferred the answer to Dr. LoBue, who responded that a lot of the materials, like contact tracing and STD materials, have been deployed to support contact tracing training and guidance. Things around isolation, personal protective equipment (PPE), and other many types of skills that have routinely been used for TB are being used in the COVID-19 response. He also mentioned the guidance that was provided in continuing clinical core services, which was general, but also had specific sections related to running TB and STD clinics.

Dr. Robert Benjamin commented in the chat that “offering of continuing education credits is an invaluable asset and inducement for education of healthcare providers,” which Dr. Mermin appreciated and acknowledged.

Dr. Julie Higashi added to Dr. Reves’ point that it is hard to tap into the idea that TB actually strengthens public health in general: it may be useful to know what ideas or what concepts in order to create the argument that by keeping TB infrastructure it actually strengthens the whole disease response. Is this an opportunity that we need to take advantage of in keeping our TB response strong? Dr. Mermin said there are three spaces in which they have responded to COVID-19:

1. Direct COVID-19 response, for which they have had staff and resources available
2. Linked engagement – how something that they strengthen for TB can also help the COVID-19 response. There is a way to use that for COVID-19 response.



3. Public health infrastructure, which Dr. Mermin sees as the biggest gap. He states that the public health infrastructure of the US has been decimated. It was never strong enough to respond effectively to COVID-19.

In an unapologetic way, he argued that if someone has a myocardial infarction and dies at home because they were afraid of going to the hospital, because of fear of Sars-Cov2 infection, they still die because of COVID-19. The same thing could be argued about not having a strong TB infrastructure. Monitoring of people who have active TB is reduced, people could use medications in ways they would not have previously, and collateral damage from COVID-19 rightfully should be improved. A lot of the people who do the core work of TB are ready and waiting to assist with others, and they do already. It is a cost-effective, not cost-saving, intervention to maintain public health interventions and infrastructure. Dr. LoBue added that “those who don’t know the past are condemned to repeat it.” He referenced previous outbreaks that we have faced, like anthrax and Ebola, where we see short term responses but not long-term infrastructure. He argued that if we had made longer term investments this would have improved.

As there were no further questions, Ms. Cole thanked Dr. Mermin for his presentation and transitioned to Dr. LoBue to present his update.

### DTBE Director’s Update

#### **Philip LoBue, MD, FACP, FCCP**

Director, Division of Tuberculosis Elimination (DTBE)  
CDC National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention

Dr. LoBue began his presentation with a summary outline and echoes Dr. Mermin’s introductory statements, adding that there is really no disease that better demonstrates disparities than TB and provided a few examples to substantiate this.

#### **2019 Preliminary TB Surveillance Data**

He presented case count and case rates per 100,000 persons for TB comparing years 2018-2019. There was ~100 case drop and the rate decreased slightly from 2.8 to 2.7. He then illustrated case counts from 2010, which showed slight decreases over the last 5 or 6 years. He also presented a US map to give some idea of the rate of TB comparatively across the states. Generally, more than half of the states have rates of less than 2 per 100,000 persons. Alaska, Hawaii, and California have the highest rates in the country (4 or greater per 100,000). Dr. LoBue showed TB rates per 100,000 over time, where the decrease has slowed down compared between 2007-2012 and 2012-2019. The rates for non-US born population is much higher than those born in the US at just under 71%. Next image shows decrease has slowed comparing 2006-2013 (8.5% decrease in rate) and 2013-2019 (4.8% decrease in rate). A similar graph for non-US born persons shows a similar trend of flattening over last 6 years. Regarding those who have HIV co-infection among people with TB, it has been decreasing over time and, for the first time, in 2019 we have fewer than 5% of people with TB also with HIV coinfection. Regarding multi-drug-

resistant (MDR) TB, data from 1993-2018 stratified by US-born and non-US-born shows that the percent has been between 1-2% over the last 10 years. In 2018 there was a total of 88 cases.

### **Impact of COVID-19**

Dr. LoBue noted that as of June 5, 42% of DTBE staff have been deployed for the COVID-19 response. Laboratory services have been limited to those with direct patient care or public health interventions only, so they have not been able to utilize these services for research purposes. All clinical trials and study enrollment have also been suspended but he is hoping to get things started again soon. Lastly, numerous conferences, site visits, and meetings have been either cancelled or postponed.

### **Impact of COVID-19 on Program Activities**

Dr. LoBue proceeded to congratulate Donna Wagner and Dr. Julie Higashi for their work with their monthly webinars and other information they have gathered. He mentioned that one of the things DTBE did was to have their project consultants contact grantees regarding impact of COVID-19 on TB program activities. They asked recipients (49 of 61) to assess the impact of COVID-19 on program activities, where responses were defined as no impact, partial, or high. Dr. LoBue stated that they found most programs were having at least a partial impact and a fair number of them were having a high impact, particularly for staff training and program evaluation. Looking at more clinical intervention activities, not surprisingly, he mentioned that targeted testing was more impacted compared to diagnosis and treatment. Case reporting surveillance had less impact than education and training which had a high impact. Finally, he mentioned a few studies that have been completed. First, he discussed the electronic directly observed therapy (EDOT) Study, a randomized controlled trial (RCT) which is a crossover study of in-person versus video directly observed therapy (DOT). He worked with NYC and they are currently in the analysis phase of the study. The second study is the Tuberculosis Trials Consortium (TBTC) Study 31, another RCT of two 4-month regimens versus standard therapy for drug-susceptible TB. They have completed enrollment and follow-up but have delayed genotyping of failure/relapse cases due to COVID-19. Preliminary results are expected by the Fall and should be available for the next ACET meeting in December 2020. He concluded his presentation and turned to Ms. Cole for questions.

### **ACET Discussion (Q&A)**

As Ms. Cole had been having issues accessing the chat room, she asked Dr. Winston to please read the questions.

Dr. Winston announced a comment brought up by Dr. Pete Dupree: *In my state, in efforts to address the huge state budget shortfall brought on by COVID-19, policy makers shortsightedly cut the TB budget. TB was the only infectious disease program to receive a budget cut in the upcoming fiscal year. That illustrates how much work we have to do at the local level to educate those who control budgets to protect our public health infrastructure specific to TB and the ancillary areas where TB could support responses.*

She also read Dr. Higashi's comment, which stated: *The issue at the local level is the understanding that TB amongst other priorities is important to include in allocation of funding. Our numbers appear small compared to other priorities"* She also thanked Dr.

LoBue for the earlier mention of her and Ms. Wegener's work.

She read a comment by Dr. David Bryden which stated: *Great points Jono, which really need to reach policy makers and funders. Now is the moment to make those arguments publicly in op-eds.* David Bryden: *I would suggest finding someone to submit a piece to the Denver Post about that.*

Dr. Shama Ahuja replied in the chat box saying: *I agree with David. We need to move beyond talking to each other and advocate better for public health broadly. We are taking a real hit in this crisis when it should have been our time to shine.*

Dr. Reves added: *I agree. We need to communicate that public health infrastructure is less about brick-and-mortar than the full spectrum of public health workers with actively performing patient-centered approaches to public health issues.*

Ms. Cole mentioned to the group that in her local jurisdiction they have received less evaluation of patients for TB and people with coughs, fevers and other symptoms are being evaluated for COVID-19 and not TB. She then asked if people seeing that TB is not of the first differentials in other areas as they are evaluating these patients. Dr. Higashi responded saying that they are currently 20 cases ahead compared to last year. She mentions she is seeing a mix of two things: (1) no consideration of TB as the initial diagnosis, so delayed TB diagnosis is occurring and (2) early diagnoses because people are more frequently seeking care due to COVID-19. As such, it does not seem that it is slowing down with COVID-19 from her perspective.

Ms. Cole asked if other people had questions, but there were no further questions. However, Dr. Winston proceeded to read further comments.

Dr. Andrew Vernon commented that *major contribution needed is in contact tracing, which is being impaired rather than strengthened in many locales. Once again TB has notable skillset in this regard that is much needed.*

Dr. Lawrence Kline added a question in the chat *given the strain on resources for Public Health and the current demands adding a major burden. Can you estimate the budget to CDC decline over past 5 years and if the recent legislation has added funding to Public Health that is material?* The budget is stable, but they are changing priorities. Before all of this, HIV was priority so there was additional funding there. Dr. Mermin weighed in on the expected budget decline over the next 5 years saying that it depends, and it also varies by administration. The nation itself is having a hard time economically but at the same time it needs public health. Some programs anticipate budget cuts and hiring freezes over time and we need to think about how to adapt to that. If we share the health and economic benefits of public health more widely and in the right places, perhaps it will not occur the same way and in all places. Ms. Cole thanked Dr. Mermin and asked for further comments.

Dr. Winston read a comment by Dr. Shama Ahuja, which read: *huge decrease in case counts in NYC, creeping up slowly as people start seeking care again.* Dr. Kathleen Ritger added to this statement in the chat, commenting *in Chicago we are running at about half*

of typical number of cases.

This concluded the discussion section. Ms. Cole then introduced Dr. Susan Maloney for the next presentation.

## Updates from Global Tuberculosis Branch

### **Susan Maloney, MD**

Chief, Global TB Branch, Division of Global HIV & TB  
CDC Center for Global Health

Dr. Susan Maloney introduced herself and stated her appreciation for the opportunity to present. She states that she did not update her slides for COVID-19 but will add information as she presents. Globally, TB is the top infectious disease killer in the world, which claims about 1.5 million lives a year; three people die every minute. One fourth of the world's population is infected with latent TB and 500,000 people have MDR TB. We have 10 million people who become ill with TB every year. TB is the leading cause of death for people with HIV. There are over 250,000 people with HIV who die of TB each year and there are 500,000 new cases a year. Drug-resistant TB is an epidemic as well as she had noted before. She mentioned some big challenges that are driving the spread of TB: more than 30% go undetected undiagnosed, only 56% of TB cases are treated successfully, and there are low adherence rates and poor oversight from the private sector as well.

Dr. Maloney proceeded saying that the WHO End TB strategy has set some bold goals. We should be hopeful to meet the goals by doing several things: optimizing current tools, pushing for universal health coverage, introducing new tools (vaccines, drugs, and treatment regimens) and through political will and supportive policies.

Despite this, she assured that there is a lot of reason to hope. Since 2000, over 60 million lives have been saved through TB and TB/HIV treatment. As of September 2018, CDC alone has screened for 6.5 million people living with HIV (PLHIV) for TB. The global TB response has been bolstered by new diagnostics like Xpert MTB/RIF. They have new anti-TB drugs and regimens that can improve adherence to treatments. Also, diagnosis and reporting of MDR TB has doubled since 2010. There are promising new TB vaccines under development in collaboration with the private sector, and there is also increased political interest and commitment to ending the TB epidemic. PEPFAR is working very hard to push TB preventive treatment (TPT) and LTBI treatment and reach 5 million PLHIV by 2020. This has really been spearheaded by their group at CDC.

She presented a summary of the United Nations General Assembly TB United Nations High Level Meeting, which was a big success. They are looking now to see if they are on track to meet the goals that were set. The meeting produced a declaration with UN Member States unanimously committing to diagnose and successfully treat 40 million people, including 3.5 million children with TB by the end of 2022 and to provide TPT to 30 million people by 2022. That includes 6 million PLHIV, 4 million children under 5yrs, and 20 million household contacts. It is the first time they have tangible targets for TPT. The political

declaration produced from this meeting called for mobilization of 13 million dollars per year to finance universal access to TB prevention, diagnosis, treatment, and care and an additional 2 billion per year for research into new tools.

Dr. Maloney then presented the branch's mission to provide scientific leadership and expertise for developing, evaluating, and implementing evidence-based and innovative approaches to find, cure and prevent TB and also to build and sustain surveillance and laboratory systems and workforce and research capacity. They are aligned with WHO strategy, PEPFAR strategy, US government TB strategy and the US National Action Plan (NAP) for MDR TB. She mentioned they do not have a large envelope of funding, a big part of their funding goes to supporting their experts, and so she presented a map demonstrating their geographic priorities. These priorities are in place to focus their resources and maximize their impact. Priority countries are those that have a high burden of HIV associated TB where they can focus and build on their PEPFAR platform. They also have a few focus countries which may or may not have overlapping HIV and TB epidemics, but they do have a high burden of TB and MDR TB, in-country CDC staff, political will to collaborate, and existing and ongoing investments. The three focus countries are India, Vietnam, and China.

Dr. Maloney then proceeded to discuss the mission and how they are approaching things. They want to change the trajectory of TB epidemic. They want to implement a comprehensive epidemic response and find that they can really bend the curve not just on finding and treating active TB cases, but also preventing disease and controlling infections.

Dr. Maloney stated that the first area they have put as strategic priority is TB in children to improve screening, testing, diagnostic tools, and contact tracing to help find missing cases. Children are of the most vulnerable groups to TB. As part of the Gates-funded PERCH study, she described that they have demonstrated TB is one of top 10 causes of pneumonia in children under 5. She saw this as an important finding and something that should be pushed a lot more. In Kenya, they are identifying the fastest and most effective way to diagnose TB in children, collaborating with multiple partners assessing innovative specimens and tests. She also presented their work in South Africa which has also led to WHO guideline changes for treatment of drug-resistant TB among children. In Mozambique and Uganda, they are implementing and evaluating approaches to TB diagnostics and household-based contact investigations to identify children at risk for TB. They are partnering with The International Union against TB and Lung Disease and have now developed a Child and Adolescent TB Centre of Excellence and have already hosted several webinars around HIV and TB. They are working with WHO and international organizations to put together this roadmap for childhood TB to address the gaps in childhood diagnostics and includes revised childhood TB treatment guidelines for partner agencies.

Dr. Maloney proceeded with the second strategic pillar: optimizing treatment for TB. She reiterated that TB is the leading cause of death of PLHIV. People with HIV are 20 to 30 times more likely to develop TB than those without HIV. They are showing increased screening and treatment for people with HIV as a routine part of care. They have noticed TB notifications increase and deaths decrease between 2015 and 2017 through the



PEPFAR strategy of “the right thing at the right place at the right time”. She noted that the number of notified HIV positive TB cases on ART has grown in recent years. These are among the 30 TB HIV hybrid countries where, overall, they have 85% of TB patients known to be HIV positive on ART.

Proceeding with the third pillar, Dr. Maloney stated that since the UNHLM and the commitments made, PEPFAR has committed to putting every person who has HIV on TPT by 2022. PEPFAR is aggressively scaling up TPT. They have addressed 2.5-3 million PLHIV and will likely help reach UNHLM targets. A 6-point strategy was presented:

1. Helping countries establish their baseline country assessment
2. TPT implementation toolkit and operational guide
3. Raising awareness
4. Working to provide technical assistance (Dr. Maloney displayed a graph looking at the aggressive increase in Kenya putting all PLHIV on TPT)
5. Working on partnerships
6. Planned scale up and achievements saying they will hopefully reach the target of putting 60 million PLHIV on TPT despite COVID-19 by 2022.

Dr. Maloney then introduced a big thing the group has been working on the building and strengthening infection control strategies (TB BASICS) group. She stressed that, especially now with COVID-19, no healthcare worker should become infected with TB or any other disease by simply going to work. There has not been the attention we need on infection control and we do not have enough for public health when we have these outbreaks, as Dr. LoBue commented earlier. Whether it is Ebola or COVID-19, we continue to face the same problems around infection control. TB BASICS launched in 2013 and was cross-divisional between DTBE and DGHT. TB BASICS is using innovative tools and a mentoring model to assist countries with high HIV, TB, and MDR TB burden and to assess and improve their TB infection control practices in healthcare facilities using a continuous quality improvement approach. She then presented a few tools and dashboards that they are utilizing for TB BASICS. She stated that the important part of TB BASICS is that it emphasizes sustainable local capacity development and is now being scaled-up in more than 15 countries in Asia and Africa. This platform has been used very successfully to pivot for COVID-19 response, especially in India and Vietnam.

Dr. Maloney added that an important part of what the group does is strengthening laboratory and surveillance system capacity. She mentioned that one of the things they have been doing is looking at how Xpert MTB and RIF are being rolled out. They have been working with other USG agencies and the Global Fund to map out where the machines are and look at the prevalence of disease for HIV and TB as well. This has become very useful due to the Xpert cartridges that are also being rolled out for COVID-19. They also have a very robust laboratory quality improvement and accreditation mentoring program in their division, developed by their international lab branch called Strengthening Laboratory Management Toward Accreditation (SLMTA) and Stepwise Laboratory Improvement Process Towards Accreditation (SLIPTA), which are not only building very strong laboratory networks across Asia and Africa for HIV and TB, but also building infrastructure for all types of diseases. They have taken a great focus on data collection and utilization of data to drive their programs. This type of data can be used for

decision making, finding hotspots, targeting interventions, and increasing impact and cost-effectiveness. Dr. Maloney presented one of the recent activities they have put together, Engaging Local Experts to Validate and Analyze TB data to End TB (ELEVATE), and the dashboards that can be put together using this local data to inform program modifications or improvements.

Dr. Maloney then proceeded to discuss what they are doing in each of their priority countries. Regarding CDC's India Portfolio, she divided their activities by Find, Cure, Prevent, and Build/Sustain areas. In the Find area, some of the activities she discussed were their work with household contact tracing to manage active and latent TB, engaging the private sector in diagnosis, treatment and monitoring of MDR TB, and testing the feasibility of advanced molecular tools to improve case finding. In the Cure area, she discussed their work with the ECHO group to establish a functional ECHO model for MDR TB and TB/HIV and are working to improve quality of care for MDR TB clients. In the Prevent area, she mentioned that they are very active in implementing interventions to prevent TB transmission in healthcare facilities, reiterating how this was also pivoted to support COVID-19. Lastly, in the Build/Sustain area, they are also working to support India in a number of areas, including collaboration and establishing some capacity for whole genome sequencing in India.

Regarding CDC's China Portfolio, she mentioned some of the work they are doing in China. She highlighted that they have a lot of nice collaborations around optimizing Xpert diagnostic algorithms which have not really taken off. They are also getting technical assistance for MDR TB guideline updates. Lastly, they are working closely across nation on TB infection control interventions to prevent transmission and are building TB surveillance systems and lab quality and capacity through the CDC Field Epidemiology Training Program (FETP). They have now launched the first FETP cohort specifically focused on TB.

Regarding CDC's Vietnam Portfolio, Dr. Maloney mentioned they are mostly active in Hanoi. They are focusing on piloting some novel TB and active and latent TB case finding and treatment. She also said that they are working on TPT for PLHIV and have a collaboration with DTBE and DGMQ to provide TPT for US-bound immigrants from Vietnam.

What is next? Dr. Maloney believes there are several things we need moving forward. First, we really need innovation on a scale that we have not seen in TB but may have seen in other diseases. We need rapid mobile point of care diagnostics and a way to use less invasive specimens. We need new treatments, drugs, and less toxic treatments, which are all things that they look to the domestic group for their research capacity. Lastly, we need an effective vaccine to prevent TB disease and infection.

Dr. Maloney finished her presentation acknowledging the progress we have seen on the global TB front, but there is a lot more progress to get done. The group is focusing their resources on areas where they can bring core capacities and expertise to bear. She was optimistic and hopeful that they can meet the UNHLM targets and goals. She concluded her presentation and Ms. Cole proceeded to the discussion.



### **ACET Discussion (Q&A)**

Dr. Winston began reading the comments and questions posed in the chat box.

Dr. David Bryden asked: *can you tell us about the impact of COVID-19 in Haiti and how CDC is working to maintain TB and HIV services there?* Dr. Maloney responded that, broadly, they have been working very hard to support countries like Haiti. She said they have at least monthly check-ins and have developed webinars. She acknowledged that there has been an impact and that TB case detection has gone down by almost 15%. They have been putting together considerations documents to talk about how to advocate for TB services to be considered essential and how to move towards technology. They have also done month by month scripting, which they have been doing for HIV but are now doing so for the TB population. She offered to put Dr. Bryden in contact with their POC who is stationed in Haiti for further information. She says that they have submitted some funding proposals to CDC to look at what innovations other countries have taken to keep TB and HIV services accessible moving forward, and she is hopeful that this will go through and they will have more information soon.

Dr. Robert Belknap asked in the chat: *“Do the efforts to scale up TPT include an assessment of the real and perceived barriers for patients and providers that need to be addressed. This remains a challenge for US TB Programs and I wonder if there are opportunities to learn and to share.”* Dr. Maloney agreed with this statement. She sees that there are a lot of opportunities to work and share. There is funding to look and assess the scale of TPT and hopes they will be able to see, over the next 3-4 years, the impact of TPT in TB incidence, prevalence, morbidity, and mortality as well as to look at perceived barriers and the reluctance for healthcare workers to start people on TPT.

Dr. David Horne asked in chat: *“I believe that Kenya is gearing up for 3HP roll-out. How are CDC supporting introductions of regimens other than 6H/9H globally? DOPT or SAT? RFP costs?”* Dr. Maloney replied that yes, Kenya, before COVID-19, and other countries were planning and still are planning to move this 3HP rollout forward and CDC and PEPFAR are supporting this rollout. She mentioned they have a workstream that is focused on how to support introductions and other regimens. They are promoting SATs right now and, although there was some confusion as to what RFP was, it was clarified as rifapentine. Dr. Maloney said she also addressed that earlier and PEPFAR is using its muscle to bring those costs even further down.

Dr. Reves asked in chat: *“On a conference call a few weeks back, the TB program director in a South African program mentioned how they were contributing to COVID-19 activities, and were learning about contact tracing, something not previously done. This suggests a potential future benefit of this interaction. Are there any indications of positive as well as the negative impacts?”* Dr. Maloney replied that yes, if there is good to come out of COVID-19, it is the importance of contact tracing. She is hoping that the training and capacity being built around this for COVID-19 will spill over and be sustained for TB moving forward. She reiterated that they are working on operational research projects for contact tracing and they will continue to do that.

Dr. Ana Alvarez commented that she was excited about Dr. Maloney's work to find TB in children, and Dr. Maloney said it is also a nice area where she would like to build on collaborations from the domestic side in order to bring some of those insights into the global community.

Ms. Suzanne Marks asked: *"is telemedicine being used for TB services overseas?"* Dr. Maloney responded that she believes it is used in a scattered way. From what she knows, a lot of it being used is through SMS but she is really pushing and promotion for telemedicine to be used more, especially the ECHO platform.

Ms. Cole thanked Dr. Maloney for the presentation. Before the lunch break, she recapped some key points from the presentations. From Dr. Mermin's presentation, she highlighted that we are in the middle of an area of opportunity and must think of what things we can build on. She stated we must think about how we can advocate for TB while also helping the public health infrastructure. She also brought up the summary about the clinical impacts from COVID-19 and how we are linking care, telehealth, and contact tracing, as TB program staff do a lot of these things already. She summarized Dr. LoBue's presentation around the latest statistics for TB and highlights that we have been monitoring the decline which has been slowing down over time. She stated that their work and activities has been strongly impacted by COVID-19. Lastly, she restates that Dr. LoBue provided updates on some studies and shared some take-home messages from global TB. Ms. Cole also wanted to highlight the gamechangers presented – new treatments, new drugs and how to utilize them, shorter less toxic treatments for adults and children, and the potential vaccine, which is still missing from our arsenal to fight TB. She finished the summary by encouraging everyone to think about how to prioritize all this moving forward in 2021. Ms. Cole concluded this first part of the meeting and proceeded to break for lunch. She reminded everyone to join on time for 12:30pm roll call. There were no further comments.

### **LUNCH BREAK**

Following the break, Dr. Winston proceeded with roll call and confirmed quorum. Ms. Cole introduced Ms. Michelle van Handel and Ms. Suzanne Marks for the next presentation.

## **Updates from NCHHSTP Epidemiologic and Economic Modeling Agreements (NEEMA) Consortium)**

### **Michelle Van Handel, MPH**

Associate Director

Program Performance and Improvement Office

CDC National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP)

### **Suzanne Marks, MPH, MA**

Epidemiologist/Health Economist

Division of TB Elimination

Ms. Van Handel, Associate Director of the Program Performance Improvement Office of NCCHSTP, thanked everyone for allowing them to present updates from the NCHHSTP Epidemiologic Modeling Agreements (NEEMA). She introduced Ms. Marks who will be presenting with her.

She began by providing an overview of their presentation, where she will update on achievements of NEEMA 1.0, TB-specific achievements, provide updates on NEEMA 2.0, and specific TB projects that are under way for NEEMA 2.0.

Ms. Van Handel stated that in 2014 they started the first cooperative agreement to find the most cost effective approaches to reducing HIV, viral hepatitis, STDs and TB in all settings by supporting a wide range of modeling activities, including those that assess costs and burden of disease, costs and cost-effectiveness of interventions, population-level program impact, and optimal resource allocation across various interventions and populations.

NEEMA is a collaborative between the five divisions, the Office of the Director in the Center, external stakeholders including state and local departments of public health, and the recipients. She introduced NEEMA 1.0 recipients, who also worked collaboratively with academic institutions. These recipients were

1. Coalition for Applied Modeling for Prevention (CAMP) led by Patrick Sullivan from Emory University and in collaboration with Johns Hopkins University, University of Washington, and the Georgia Department of Public Health.
2. The Prevention Policy Modeling Lab (PPML) led by Joshua Salomon from Harvard University and in collaboration with the Boston Medical Center, Brown University, Yale, and the Massachusetts Department of Public Health.
3. The Consortium to Accept Prevention Economics (CAPE) led by James Kahn from the University of California at San Francisco and in collaboration with UC Berkeley, Stanford University, the California Department of Public Health, and the San Francisco Department of Public Health.

Ms. Van Handel hailed NEEMA 1.0 as extremely productive, with more than 60 manuscripts (20 related to TB projects) being completed or in progress, 73 abstracts and presentations, of which 12 presentations and 20 abstracts/posters at conferences were specific to TB. This has also resulted in 500 tweets, coverage by over 60 news outlets, over 870 citations and more than 16,000 downloads.

Ms. Van Handel then proceeded to highlight some of the accomplishments outside of TB. NEEMA has estimated population sizes for men who have sex with men (MSM) by state and county with additional stratification by race and ethnicity to inform HIV and STD public health intervention needs. They have also modeled the possible impact of interventions ranging from the potential effective preexposure prophylaxis (PrEP) for preventing HIV to the const effectiveness of chlamydia screening for women who have sex with women, men who have sex with women, and MSM. A number of their projects have also informed guidelines. She presented an example where a cost-analysis found that a single dose revaccination strategy for HBV costs \$28-\$156 less per individual than the previously recommended three-dose dose

strategy while being equally effective. After the publication of this analysis, the Advisory Committee on Immunization Practices now recommends the single-dose strategy.

### ***TB Specific Achievements During NEEMA 1.0***

Ms. Van Handel then handed it over to Ms. Marks for the next section. However, due to audio connectivity issues, Ms. Marks asked Ms. Van Handel via the chat to present her slides. All references to presented data and graphs are cited on each slide and are either published or being evaluated for publishing.

During NEEMA 1.0, all 3 recipient groups worked on different types of models with different assumptions to look at different geographic areas. One looked at national level, one looked at four different states, and one looked at California. Ultimately models projected TB would not be eliminated from US before 2100. All 3 recipients found greatest TB reductions through acceleration of targeted testing and treatment (TTT), particularly of persons who are non-US-born from high TB incidence countries.

PPML found that intensified TB control activities could reduce US TB incidence by 77% (66%-85%) from current levels by 2050. Looking at the possible impact of the US Preventive Services Task Force guidelines for TTT on California, UCSF modeled that a 23% increase in TTT in high-risk CA residents could prevent around 40% of new cases in 10 years. TB pre-elimination in California, which they defined as less than one case per 100,000, might be achieved by 2065 with a 10-fold TTT increase of non-USB and persons with medical risks or a 4 or 10-fold TTT increase in all Californians. These models are useful for looking at various scenarios and results that might be possible in different populations.

All 3 recipient groups, each using their own models with the same data on California, found that accelerated TTT for LTBI among non-US-born residents was projected to produce sustained reduction in TB incidence. A graph was presented comparing TB projections from the three models using California data after one-time TTT of 25% of non-US-born persons that showed consistent findings despite different assumptions from the models. It also showed that LTBI and migration were more significant drivers of TB incidence than transmission and that existing policies for immigrant pre-arrival testing and TB treatment are justified and that pre-arrival LTBI testing and treatment might have a large impact. Differences in model results reflect a gap in data or uncertainty in key parameters, such as LTBI incidence and prevalence and reactivation rates.

Findings from Johns Hopkins models of accelerating TTT in CA, FL, NY, TX through TTT to half of non-US-born adults could lower TB incidence by 20% to 27% over a 10-year period in these four states. Also, replacing current LTBI treatment regimens with 6 weeks of daily rifapentine dose, which is currently in clinical trials, reduced 2020-2035 TB cases by 27% in the model if it enabled TB programs to achieve 3.5 times greater population coverage, higher (92.5%) treatment initiation, and better (95%) completion. The number needed to screen to prevent one TB case in CA, FL, NY, and TX was also presented. Persons diagnosed with HIV were found to be the most cost-effective for TTT, and represented the smallest number needed to screen in order to prevent one TB case. Among the populations examined, persons with diabetes had the largest number needed to screen.

The TB modelers also estimated the impact of a six-week regimen of rifapentine to treat LTBI in the US. Modeling with higher completion rates, low adverse event rates, and high initiation along with greatly increased coverage of populations at highest risk, incident TB cases could be greatly reduced in the future.

Also discussed were cost effectiveness analyses conducted. One such study by PPML found that for all non-US-born persons, Interferon Gamma Release Assay (IGRA) testing and 3HP/SAT treatment was cost effective compared with no TTT. In non-US-born persons with HIV, dual testing with IGRA and TST, with positivity defined as TST+ or IGRA+ was most cost-effective. UCSFs modeling found the most cost-effective strategy was a one-time 2-fold increase in TTT of non-US-born persons. In modeling by Johns Hopkins that looked at CA, FL, NY, and TX, TTT cost-effectiveness was highest among people living with HIV, moderate among non-US-born, incarcerated, or homeless, and lowest among diabetics. Finally, a paper by PPML estimated that effective global TB control can avert thousands of US TB cases and reduce the US economic burden of treating those cases.

Modeling the impact of a more predictive test for TB progression was then presented. This is one of the papers that is under publishing consideration, but the initial results noted that a test with 10% positive predictive value for TB progression might reduce the number of individuals treated to prevent TB by 82% to 94%. If combined with greater (90%) treatment acceptance and completion, we could save hundreds of thousands of dollars in averted LTBI treatments in the hypothetical cohort of 10,000 people.

To summarize the consensus of the various TTT modeling results, there was greatest effectiveness among non-US-born people, and the greatest efficiency and cost-effectiveness was found testing by TTT for PLHIV. Regarding testing, IGRA appears to be more cost effective than tuberculin skin testing. Regarding treatment regimen, treatment with 3HP, either self-administered or by direct observation, is more cost effective than treatment with isoniazid alone. These results were used to support current guidelines, like whom to screen by USPSTF, how to test by ATS/IDSA/CDC, testing and treatment by ATS/CDC, and treatment by NTCA/CDC.

Some takeaway lessons were that NEEMA modeling benefited greatly from collaboration with state and local TB controllers such as the CA Department of Public Health (DPH), MA DPH, as well as NY, TX, and FL DPHs. While models relied greatly on surveillance data to which they were calibrated, additional data to reduce uncertainties are needed on the size of and LTBI prevalence of risk populations (some of which has been published or is in progress), sensitivity and specificity of diagnostic tests, risk of TB progression, and costs of interventions and disease. Another major challenge is how best to implement the modeled scenarios.

Websites for the tools are available on the NEEMA website and other locations.

### **NEEMA 2.0**

Ms. Van Handel presented on NEEMA 2.0. In October of last year, they started second 5-year cooperative agreement to build on the work from NEEMA 1.0. She stated the objectives of NEEMA 2.0, which are to increase the availability of scientifically valid mathematical models, increase access to web tools that are 508 compliant, and increase dissemination of manuscripts documenting models and tools applicable to NCHHSTP. She also noted there was a shift in



recipients from NEEMA 1.0 to NEEMA 2.0. CAMP, now led by Eli Rosenberg, and PPML were both funded for NEEMA 2.0 and the primary TB modeling group has remained consistent for Johns Hopkins University and the Harvard School of Public Health. Ms. Van Handel provided information on TB NEEMA 2.0 projects. One is with CAMP/JHU to estimate the impact of preventing TB transmission by modeling averted TB cases and costs by alert system, such as whole-genome sequencing, for large outbreaks. A second project is to further develop PPML Tabby2 models for each US state and D.C., projecting TB/LTBI cases and costs and impact/cost of TTT interventions. Lastly, she described a third project of the PPML group working on estimating reactivation rates by population.

### **Opportunities**

To close, Ms. Van Handel stated that the projects supported by NEEMA have contributed knowledge on the extent of LTBI burden, impact of targeting TB prevention efforts, and potential for new tests and treatment regimes. They have also increased tools for state TB programs to better understand the potential impact of TB prevention interventions. She concluded by stating that NEEMA plans to build on this work to help achieve TB elimination. On behalf of Ms. Marks, Ms. Van Handel quotes “a journey of a thousand miles begins with a single step” and thanked the group for listening.

### **ACET DISCUSSION (Q&A)**

Ms. Cole thanked Ms. Van Handel for her presentation and announced five minutes for questions starting with those shared via the phone. The first question was posed by Dr. Andrew Vernon. He inquired about the assumptions underlying the models, specifically around a presumption of 93% efficacy. He asked if the models consider re-exposure and the possibility that therapy is not completely sterilizing? Ms. Van Handel responded that she believes they did sensitivity analyses to assess a range of values and that treatment efficacy is not 100%. She noted she would have to revisit the manuscripts and follow-up on the assumption related to re-exposure. She also recognized that these are the discussions that the group has when developing assumptions for each of the models. Ms. Marks also added to the response in the chat saying that 93% efficacy means that 7% are not cured.

Dr. Robert Belknap thanked Ms. Van Handel for a great presentation and asked in the chat: *“Have the modelling activities identified places where we need to be collecting data differently to better inform and adapt? This has happened quickly with COVID-19 but obviously much slower with TB.”* Ms. Van Handel replied and asked him to clarify if by place he meant geographic location or something else? Dr. Belknap replied that he was thinking of both and was wondering if there was usefulness in bringing data from lower-burden states and use kind of a feedback cycle to improve the models. Ms. Van Handel replied that with regards to the places, NEEMA wants to expand the modeling in the Tabby2 tool to all 50 states and D.C. and as he had noted, modeling for high-burden states is easier because of more data and results in a more stable model, so they have been working down the morbidities list to add in states and address those gaps in data as they go to lower-burden states. With regards to the different types of data, Ms. Marks added in the chat that all 50 states and D.C. are currently being modeled in the Tabby2 tool. Ms. Van Handel chimed in to say they are exploring the different types of data to guide new models as well. Ms. Marks added that the lower burden states pose difficulties because

modeling requires calibration to historical cases and low numbers is a problem (for modeling, but not for TB elimination).

Ms. Cole asked for any other comments or questions, but there were no further questions. She apologized for technical difficulties and transitioned to next presentation by Dr. Kathryn Winglee.

## **A Tool to Assist TB Programs with Integration of Whole Genome Sequencing Data**

### **Kathryn Winglee, PhD**

Statistician

Centers for Disease Control and Prevention

Dr. Winglee began her presentation stating that despite decreasing incidence in the US, TB outbreaks continue to challenge public health. For example, 24 confirmed large outbreaks were counted by surveillance between 2014-2016. The response to these large outbreaks can quickly deplete resources and last for many years so there is a need for better tools to help investigators understand their data and investigate ways to reduce transmission.

She stated that, when conducting investigations of TB clusters, our two most basic public health objectives are to find and treat existing cases and prevent additional cases by interrupting transmission. She provided one approach to achieving these objectives: characterizing transmission networks and determining how TB is spreading within a cluster. It allows us to focus on using resources to more quickly and efficiently identify new cases and interrupt transmission to prevent additional cases.

Dr. Winglee stated that characterizing transmission networks is a complex problem that involves looking at a lot of different data, including surveillance data, the relationships among cases from contact investigations, timing of symptoms, and whole genome sequencing (WGS) data, which shows the genetic relationship between TB isolates and can be used to rule out recent transmission but does not facilitate inferences related to directionality. All this data must be combined in order to answer the question of where and when transmission occurred and generate transmission networks. Currently, she finds many investigators try to do this by hand, but this is very time-consuming and challenging. As such, she introduced the Logically Inferred Tuberculosis Transmission (LITT) algorithm to help investigators easily and systematically analyze each of these pieces of data. LITT is based on the thinking and logic an investigator would use when investigating a cluster or outbreak. She stated LITT uses the same data as the investigators. They have data from CDC databases for surveillance and WGS, and from user databases they have data on epi links and timing of symptoms. These data can be used by LITT to identify and rank potential source cases which can then be used to generate a transmission network. Before moving on, Dr. Winglee clarified definitions for a given case and a potential source. A



given case is a case for which we are trying to identify a source, and a potential source was defined as case that LITT considers as a possible source for the case.

Dr. Winglee provided an overview of LITT process of identifying a likely source case in a stepwise fashion. For step 1, they identify the most likely sources case for each given case by filtering out cases that are pediatric, exclusively extrapulmonary, distantly related by WGS, and infectious period after given case. This helps narrow down potential sources. The second step is to rank potential sources on genetic distance by WGS, timing of infectious period, infectiousness, and epi link strength and risk factors. The result is a filtered, ranked list of potential sources. It also provides likelihood and score in addition to ranking. The algorithm then repeats steps 1 and 2 for the next case in the cluster.

Dr. Winglee described 3 main tables as sources of input needed to utilize LITT. First is a case data table which contains all the case-specific information like infectious period, if it is pediatric, whether it is extrapulmonary only, sputum smear results, and presence of cavity on chest radiograph. The second table is epidemiological links which contain the relationships between cases and are characterize as definite, probable, or possible. The third table is a single nucleotide polymorphism (SNP) distance matrix. It represents the genetic distance (measured in SNPs) between each pair of sequenced isolates. She noted that LITT can run on clusters that do not have WGS data available as well.

Dr. Winglee provided a snapshot of the LITT interface, which is designed to be point and click and not require any programming skills. She also provided descriptions of output tables, but only described in depth the heat map in the interest of time. She provided a snapshot of a heatmap from a made-up cluster of 10 cases and described how the heatmap displays the data and how to read and interpret it.

To validate LITT, Dr. Winglee mentions they collected information from 56 clusters ranging in size from 2-69 cases for a total of 534 cases. At least one case in each cluster had at least one presumed source case identified from investigation for a total of 181 cases with an investigation presumed source. This was the gold standard. Of those 181, LITT ranked 145 (80%) as a presumed source. Of those not ranked first in the list of potential sources, 12 ranked second, and 2 ranked third. The remaining 22 presumed sources were ruled out by LITT. Thus, the LITT network produces similar output to what is done by field workers.

However, she mentioned they were interested in learning more about the situations where LITT and investigators identified different most likely source cases. There were 32 discrepancies, which was enough data to allow them to conduct a discrepancy review. Of the 32, 13 refuted LITT's most likely source, but these discrepancies were attributed to the availability of TST results for investigators (which is not incorporated into LITT) or, errors in data and/or missing epi links that led to incorrect conclusions. Two given cases had 2 most likely sources from LITT, one of which was refuted and the other corroborated due to TST conversions. The review corroborated 17 (53%) of the discrepancies of LITT's most likely source, meaning that the review agreed with LITT. She clarified that these were often situations where data has changed and, consequently, highlights that LITT is only as good

as its input data. As a result, she recommended that LITT results be reviewed. She also noted that LITT can help with quality assurance and more when data is constantly changing, which can often be tough to do by hand.

She presented where the tool is available (OAMD Portal) and stated that the code is publicly available in a GitHub repository in case users want to run the code themselves. Training materials and other help documents are also available. The user manual provides extensive documentation on how to perform the data and is designed to answer user questions and get them started. They also have blank input files to help users get started, which she displayed to serve as an example.

In addition, she presented the cluster investigation tool (CLINT) to help users manage their investigation data. It is an Excel workbook designed to keep cluster investigation data organized in a real-time way while getting visual summaries of data. She walked the group through a display of this tool. To further help users become comfortable with LITT, DTBE has two training datasets that demonstrate key features and provide examples for users to understand the tool in depth.

Although LITT is performing well, she acknowledges that it has a few limitations:

1. Investigation presumed source determination has some uncertainty
2. LITT is only as good as the input data
3. It takes advantage of commonly available data but may be refuted with additional data
4. It will not detect missing cases
5. It cannot replace local investigation.

She used these limitations to reiterate that LITT results should always be reviewed.

Dr. Winglee also summarized the benefits of using LITT. First, she highlighted that it provides a systematic method for integration and analysis of surveillance, WGS, and investigation data, generating a ranked list of potential sources for every case in the cluster. These results, as she had demonstrated earlier, are highly concordant with investigation presumed source determinations. It can help investigators save time on data analysis as it removes the need to write or run code, its runtime is quick, and the results can be quickly updated as new data becomes available.

She noted that LITT is only part of a larger workflow that they have developed. Data visualization is an important component of this workflow, which they achieve using MicrobeTrace. MicrobeTrace was developed by Division of HIV/AIDS Prevention and is an easy and flexible way to visualize data. She displayed an example that illustrated how MicrobeTrace uses color coding and other features to visualize data produced by LITT and how it helps to better understand transmission.

The final part of the workflow is Location and Time to Epi (LATTE), which she stated is another tool they developed to help identify epi links from location data which can then be set into LITT's epi link table. LATTE identifies all overlaps in space and time from a list of

dates cases were in a particular location. It is designed for any setting and can handle multiple different locations. It can also convert lists without dates to epi links. Its design is similar to LITT and can be found in the same location.

Dr. Winglee concluded by summarizing their workflow. They developed LITT to integrate different types of data and rank potential sources for each case, MicrobeTrace to visualize the data, and LATTE to help identify epi links. She noted that these tools are used as supplement and are only as good as input data and do not replace local knowledge. Moving forward, they are working to complete the documentation, explore ways to integrate LITT with other tools and systems to reduce data entry burden, and identify and train partners interested in using any part of this workflow. They are also interested in applying LITT prospectively. She finished her presentation by thanking their partners for their contributions.

Ms. Cole thanked Dr. Winglee for her presentation and brought up the advice requested from ACET prior to answering questions, listed below:

#### **ADVICE REQUESTED FROM ACET**

1. General comments on use of the tool
  - a. Dr. Lisa Armitage was very excited about these tools and commended them for their tool.
2. Suggestions for promoting use of the tool
  - a. Donna Hope Wegener commented: *“as another mechanism for distributing this work, the NTCA's epidemiology section, SETC, is interested in a presentation on data visualization. this might be a great presentation for you to share on a webinar with the SETC members.”*
  - b. Julie Higashi commented in the chat: *“education and training might be supported by NTCA conference, CTCA conferences for LITT, LATTE, and microbe tracing.”* Dr. Winglee responded that they have done a few but are open to broadening the audience.

Ms. Cole asked if this type of tool would assist with contact tracing and other activities done during COVID-19? Dr. Winglee replied that it is very designed towards TB, but it could be customized, although it would take a lot of work. However, she notes that LATTE and MicrobeTrace could help with data visualization needs with less customization.

Ms. Cole restated the usefulness of these tools and thanked Dr. Winglee for her presentation. She sent the group for the break and reminded everyone to be back at 1:55pm for roll call.

#### **BREAK**

Following roll call, Dr. Winston confirmed that quorum was reached. Ms. Cole then introduced Ms. Donna Wegener who is the next presenter.

### **Ongoing Challenges with TB Drugs and Diagnostic Supplies: Results from National Survey**

**Donna Wegener**

Executive Director

National Tuberculosis Controllers Association (NTCA)

Ms. Wegener, Executive Director of NTCA, began her presentation by thanking the committee for including this report. She noted it is a timely presentation as their challenge continues and hopes they will all appreciate the presentation. She stated they have taken some liberties with the last of the content. As the TB drug supply challenges have continued, they felt it more prudent to present more recent data. To this end, they have included multiple different data sources which, woven together, paint a full picture of the complexity and universal nature of drug access challenges and the consequences for programs and those individuals they are treating. Despite this, she stated they know there are diverse ways to report challenges which, unfortunately, makes for a patched report of challenges.

***NATIONAL SURVEY ON TB DRUG AND DIAGNOSTIC SUPPLY CHALLENGES***

Ms. Wegener presented the results of the national survey from January to December of 2019. Data were collected throughout December of 2019 and the end of January 2020 as they sought to increase the response rate of their programs. In the end, there were a total of 110 responses reflecting geographic diversity and program-level diversity with respondents representing state, county, big city, and territorial TB programs. She displayed a graph that demonstrated program-level responses for the questions about challenges accessing TB drugs and purified protein derivative (PPD) solutions. Although these data indicate that many programs have been impacted by the TB drug and diagnostic challenges, there are jurisdictions for which no challenges were reported. They are interested in what protective factors contributed to their ability to access TB drugs and diagnostics.

Ms. Wegener then presented the next graph, which underscored the vulnerable nature of current TB drug supply. During 2019, challenges were reported for first- and second-line medication as well as those for LTBI. This was happening at the time where the new LTBI guidelines were released and 3HP was a recommended treatment. Programs had more challenges accessing and affording rifapentine, 39% reported challenges accessing rifampin, about 31% of the programs reported challenges accessing bedaquiline, and 29% reported challenges accessing isoniazid (INH). She noted that, although the top issues for accessing drugs vary, 76% of respondents indicated that the cost of the drug to the patient was one of the top 3 issues to report.

Following, Ms. Wegener presented a graph that showed that the number one-way programs and patients were affected by drug access/affordability issues was the large amount of staff/program time spent in accessing drug. However, over half of respondents reported there were delays in the start of treatment due to these access challenges, and 35% avoided prescribing the drug in treatment regimen because of barriers. She finds that implications of this

may be important for patient care as lesser regimens might be recommended due to the challenges of the preferred regimen.

Ms. Wegener stated that the two most frequently picked solutions might be a heavier lift for all of us, which were a centralized national supply stream and additional patient assistance programs. Two potential solutions, however, that had approximately 50% of the respondents supporting them were a national TB drug website and further guidance on how to procure drugs. She recognized that there still seems to be a lot of uncertainty about the most appropriate way to procure medications but finds that these are both achievable in a relatively short amount of time. NTCA's survey committee, under the direction of Katelynne Gardner-Toren with the Seattle TB Program, are preparing these and other results from the survey for publication.

A second reporting mechanism is the TB Drug and Diagnostic Shortage Report Form from NTCA's website. It was established in 2014 but has had intermittent use over the years. She mentioned it is accessible on NTCA's homepage and because they were starting to hear of so many more reports in the first part of 2020, they have encouraged as many people to fill out a report so they can systematically start to track these reports. Since 2020, there have been 35 reports that came from 16 different states. While the majority were from their state, city, or county TB programs, Ms. Wegener added they also received reports from external partners and 93% were reports of shortages. She presented a chart that showed rifapentine consisted of 52% of the reports of drugs in shortage, but ethambutol accounted for a quarter of those reports.

#### **TB NURSES COMMUNICATION PLATFORM**

Ms. Wegener described that another mechanism they have to learn about drug shortages is through Nurses Communication Platform. During a 1-year period from May 2019 to the end of April 2020 there were 47 email exchanges on this TB nurse listserv all of which were focused on drug shortage. She stated they found these reports were from a variety of states and programs, reflecting geographic diversity, and found very similar drugs were reported in shortage. Despite the diversity of data sources, they are starting to achieve some consistency in reporting and are starting to see uniform challenges across the US.

#### **SNAPSHOT: COMMUNITY OF PRACTICE DATA ON TB DRUG SHORTAGES**

A final data source she shared was the information obtained through their community of practice calls, which were previously mentioned by Dr. LoBue and Dr. Higashi. She mentioned that NTCA started using this forum for their TB controllers and program managers. It is facilitated by Diana Fortune, their nurse consultant, and she mentions it uses the project ECHO model. Ms. Wegener stated that during two of the calls in March and April they asked: since January 1, has your program experienced challenges accessing TB medications, which 69% indicated they did have challenges. In April, they asked the same question but just looking at the period of time since April 1 and 83% indicated they had challenges. Again, similar drugs were reported to be in shortage.

Ms. Wegener also presented a case study with information obtained from one TB program which has its own pharmacy and buys in bulk for the whole state. She says they started reporting rifabutin access challenges in April and contacted NTCA to see if other states were

facing similar challenges. Afterwards, they learned this state was not unique in its experience, although the size of their state and the nature of the case mix being treated in that program certainly did seem to be more significantly impacted. Rifabutin is a critical drug for some patients, so transitioning away from this drug was unlikely, although the program did what they could during the spring knowing that this drug was in shortage, so they tried to transition patients off of the drug as much as possible. She stated the program reported that on any given month 3,000 to 5,000 capsules of this drug could be distributed but in May, due to shortage, this number dropped to 1,275. They did not anticipate that they would be able to supply all the drugs that were needed, so NTCA also put out a request to their programs for any programs not needing drugs to potentially share with this program. That did result in one program sharing product, and eventually on June 8<sup>th</sup> the product was received by the program. During this period, however, the program and NTCA reached out to DTBE colleagues as this drug is also used as part of a regimen for those coinfecting with HIV.

Ms. Wegener ended with a quote from this TB controller, that read as follows: “I continue to learn quite a bit of the pharmacy process and addressing medication shortages, and it has become very clear that our pharmacy is at the mercy of the distributor. Specific issues impacting medication supply are either not known or shared by the distributor, therefore programs cannot be as proactive in planning for these shortages. Our experience has been that the pharmacy may receive word to expect to reduce supply, but the reality is that such orders may not be filled. I do remain concerned that as quickly as the shortage started, it has now ended without any visibility regarding what may have created and subsequently ended the shortage. I think this greatly underscores the need for greater visibility as changes such as these directly impact our ability to care for our patients.”

To conclude, Ms. Wegener hoped they all agree that we have continued to have challenges with TB drug supply. The reports appear to have accelerated in frequency, complexity and impact for TB programs and patients. She noted that it does appear that TB programs would love to see a centralized national supply, but recognized the challenges associated with this solution. She also said that additional patient assistance programs would be helpful, but more easily obtained would be a national TB drug website, better more proactive communication re drug shortages and supply disruptions. She thanked those who contributed to the slides and opened to questions.

Ms. Cole brought up questions and feedback on advice requested before asking for general questions.

### ***ADVICE REQUESTED FROM ACET***

1. What are the highest priority questions for discussion with FDA?
2. Is there value in a single point of contact for communications with manufacturers and distributors? Who best, or which organization, best positioned to assume this role?

No questions taken from the phone, so they proceeded to the chat.



Dr. Kline asked: *“can you describe where the problem in supply lines is localized?”* Ms. Wegener replied that she cannot, she knows they are more frequently that these challenges appear to be in the distribution pipeline, but at the same time some programs report challenges in distribution but other programs in different geographic locations do not report these problems. As such, it is difficult to pinpoint where the problem is placed.

Ms. Marks added that the VA website might be a model for a "national TB drug website", and she shared the VA website is: <https://www.vendorportal.ecms.va.gov/nac/Pharma/List>

Dr. Neela Goswami asked: *“Have you identified any best practices for sharing TB drugs between programs when there are regional differences in supply?”* Ms. Wegener replied that, again, it is very complicated. They were fortunate in the case of rifabutin that there were adequate drugs in one program and they were willing to share, but oftentimes the sharing of product is challenged around the contractual process within a program and it really is on an ad-hoc basis. Ms. Wegener added that they are very bound by the contractual arrangements with specific distributors. The ability and agility to move and secure a contract with a distributor was not something that their programs could do as readily.

Dr. Suraj Madoori asked: *“could a cooperative agreement be set-up between Indian Health Service (IHS) for TB drug supply, since it seems they are not seeing supply challenges?”* Ms. Wegener replied that she would not know. Ms. Cole referred to Dr. LoBue and he asked if the question was about CDC serving as a central drug provider. Dr. Madoori did not clarify but Ms. Wegener referred to Dr. Iralu to see if IHS has some protective factor around these kinds of challenges. Dr. Iralu then clarified that IHS can secure medications from the VA/DOD drug sources, so they have a different supply chain. He does not think CDC has access to that. Ms. Cole called on Dr. Jennifer Flood to comment, who added that the IHS and the VA should be investigated to determine if there are parts of those programs that could be helpful in finding a nationwide solution. Her second comment was that she thinks we should consider a central website and a national point of contact in exchange of drug supply challenges. This is something ACET members may view as a potential recommendation later in the meeting. Dr. LoBue addressed this saying he thinks they have already estimated that if they were to purchase drug for the entire country then it would consume the entire budget. Also, they have tried this already and failed miserably. If the country were dependent on CDC for rifampin right now, they have none. Large organizations like the VA that purchase large amounts of medications have a large amount of staff and budget to do so. For CDC it is not a practical solution. Another question was asked if all public health programs have access to the 340B program, and Dr. LoBue replied that yes, they do, but mentioned it is a pricing issue and the 340B program does not address the supply issue. He broke down the supply issue into 3: first is when the manufacture is not producing drug. Second, the manufacturer may be producing enough drugs, but the distribution process is too complex and even the same distributor can have challenges in one part of the country while not in another. The third is a price issue, where prices can go up quite a lot and 340B addresses some of that, but they have seen these increases in 340B as well. The person also asked if the WHO have had experiences in this regard that might be helpful for us. Dr. LoBue replied once again stating two issues with the



global drug facility. One is that they cannot get drugs that do not have FDA approval, and the second has to do with the long lead time associated with purchasing drugs. During an acute shortage, you cannot just request for more drugs. When this alternative of reaching out to the global drug facility has been brought up in the past during an acute drug shortage, the speed with which that could be turned around was not quick enough.

Ms. Cole finished the questions and transitioned to Dr. Jennifer Flood for her presentation.

## Update on ACET Workgroups

### 1. TB Elimination Roadmap Update

#### **Jennifer Flood, MD, MPH**

Chief, Tuberculosis Control Branch  
Division of Communicable Disease Control  
Center for Infectious Diseases  
California Department of Health Services

Dr. Flood stated that she had a brief report. She reiterated the importance of the NTCA presentation on survey findings and that it really serves to demonstrate widespread impacts and suggests some ways they might mitigate them. She recommended they can start picking on lower hanging fruit, like a national drug website or point of contact for exchange so at least communication flows and some of the troubleshooting can be done in a more streamlined fashion. She finds this could be a good recommendation for CDC from ACET. She noted that the workgroup has not met in 2020, but they did want to bring the FDA into the conversation following the letter ACET sent over a year ago, in part to check in whether there are new opportunities or strategies that could improve the TB drug supply and strategies that could optimize price or expedite approvals/importation. She finds that an action item for the workgroup and ACET includes outreach to FDA. She thinks this outreach was started but following the pandemic there has not been further movements. She also believed that by the December 2020 meeting, it would be good for the workgroup to meet with the FDA and invite them to the upcoming meeting.

### 2. LTBI

Ms. Cole asked Dr. Flood to provide an update on the TB Elimination Roadmap as part of the LTBI Workgroup update.

Dr. Flood noted that this will also be a brief update. She restated that the purpose of the workgroup is to describe what needs to occur for LTBI TTT of those with risk to become routine in US and then make recommendations to CDC and HHS on strategies and approaches to support successful scale-up of LTBI testing and treatment. In terms of progress and products, Dr. Flood mentioned they met regularly and delivered a report for the Roadmap to scale up LTBI testing and treatment in the US that was accepted by ACET vote in the December 2019 meeting. They are currently waiting for the submission response from HHS on that report and hope for publication, such as through the MMWR.

Dr. Flood stated some key issues for action, including selecting and proposing 10 concrete steps for 5-year implementation priorities, noting the activities already occurring and planned by DTBE, but the purpose would be to engage ACET and DTBE in a conversation over what concrete steps can be prioritized. She also added the importance of looking at different ways doors could be opened during the pandemic. There are so many tools used in the pandemic, many of which were repurposed from TB, so it is important to consider what ways we can sustain these tools. There are a multitude of activities and investments that have occurred, and she suggest they should think of how to sustain them for

synergistic use for TB and other diseases.

### **ADVICE REQUESTED FROM ACET**

1. Clarify how ACET workgroup can take steps needed for an independent publication or publication with companion CDC editorial or collaboration with DTBE.
  - a. Dr. LoBue addressed this by using the process of submitting the Essential Components document as an example. He mentioned that, in that case, the document had to go through CDC clearance given the presence of an internal CDC author. He deferred to Dr. Winston to see she had anything to add, and she mentioned that the letter to the HHS Secretary would still have to go through approval, while the roadmap manuscript would go through CDC clearance and approval after HHS approves the letter. The letter and recommendations must be approved in order to then be considered for publication in MMWR.

Ms. Cole did not take further questions and moved forward to review the draft letters. The letter prepared by ACET to be sent to the HHS Secretary to request submission of the “Roadmap for Advancing TB Elimination in the United States through Scale Up of Testing and Treatment of Latent TB Infection” was reviewed to solicit comments and edits. Dr. Flood sought clarification regarding the MMWR submission process, which Dr. LoBue clarified stating that the letter is requesting first to accept the recommendations and then MMWR submission. Dr. Flood then suggested additional wording to include “other journals”, in addition to MMWR, as part of the submission in order to have other options should it not be accepted for publication in MMWR. Dr. Robert Benjamin suggested adding wording that addresses the impact of COVID-19. The edit was agreed to be included in the conclusion. Dr. Flood moved to accept the document with the proposed edits. Dr. Robert Horsburgh seconded it. The motion was accepted with no abstentions or oppositions.

Ms. Cole asked for any further comments. Dr. Flood mentioned that ACET needs to find a substitute for her in the workgroup, as she would be rotating off ACET after her four-year tenure. She thanked them for their work in the workgroup and Ms. Cole thanked Dr. Flood for her time and work.

### **ACET Business Session**

#### **Barbara Cole, RN, MSN, PHN**

TB Controller

Riverside County (California) Department of Public Health

ACET Chair and Workgroup Chair

Ms. Barbara Cole, ACET Chair, opened the Business Session and facilitated a review of old and current business items that warranted ACET’s formal action. Ms. Cole allowed time for additional discussion and/or requests for future agenda items.

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Minutes of the Meeting:

*Advisory Council for the Elimination of Tuberculosis*

June 16, 2020 • Page 31

## Business Item 1: Approval of Previous ACET Meeting Minutes

Ms. Cole inquired whether there was a motion to accept the December 10-11<sup>th</sup>, 2019 ACET meeting minutes; Dr. Ana Alvarez moved to accept the minutes, seconded by Dr. Robert Horsburgh Jr. With no further discussion or corrections, the motion to accept the minutes carried unanimously with no abstentions or oppositions.

## Business Item 2: Advice Requested from ACET

Ms. Cole reminded the quorum that one of ACET's responsibilities is to provide advice to the Department of Human Health Services (HHS) and the CDC; hence, the dedicated segment within the meeting.

	Topic	Discussion from Minutes	Action
I.	What service should Centers of Excellence (COE) prioritize if resources limited/some activities need to be limited during the rest of this or the next funding cycle?	See page 17-18	COE Team to provide a list of COE points of contact to ACET members.  This list has yet to be provided. Ms. Cole will follow-up to get this list.
II.	How can COEs provide optimal coordination and support to Tuberculosis (TB) programs beyond the current efforts?		
III.	Are there any partners or stakeholders that the COEs should be working with beyond their current partnership?		
IV.	What populations or sectors in the US do you think are in need of, and may not be benefiting from, COE services and how could we better target them?		
I.	General comments in reaction to presentation	See page 22-23	Discuss having a representative from the TB Community Network assigned to ACET, would require a change in ACET charter.
II.	Any feedback on the proposed Latent TB Infection (LTBI) campaign and community engagement network?		
III.	Any suggestion for the provider component of the campaign?		There were no comments around this action. Ms. Margie Scott-Cseh clarified that charter renewal is on March 15, 2021.
IV.	Any suggestions for the evaluation component of the campaign?		

- V. Any suggestions of key partners to brief and include in this effort?
- VI. Does ACET have any additional guidance on how they would like to engage with TB Community Network in the future?
- I. Suggestions for how to address the challenges associated with distribution or drug supply shortages See page 39-40

**Business Item 3: Report to HHS Secretary**

Ms. Cole stated there was not enough new information to warrant a new report but wanted to revisit the priorities for 2021 outlined from the previous report given the information presented during the meeting. No priorities were removed, but Dr. Julie Higashi suggested adding verbiage about the potential loss to TB infrastructure due to the impact of COVID-19, which Ms. Cole agreed to add in the infrastructure section. Regarding the section *Assistance from the HHS Secretary*, Ms. Cole suggested adding a bullet around the general impact of the pandemic on TB. Dr. Jennifer Flood also suggested including a bullet that addresses disparities which had not been previously included. There were no objections to the remaining items in this section. When inquiring about further accomplishments to include in this report, Dr. David Horne suggested including content about the synergies between TB and COVID-19 in the research piece of the report, while Dr. Julie Higashi added that they should also discuss vaccine development. Ms. Cole finished by stating that the goal is to have the letter approved and a draft report for review prior to the next meeting in December.

**Business Item 4: Status of Essential Component Document**

Ms. Cole provided an update on the Essential Component document stating it has been submitted and the team is working with the editor on minor edits. She is hopeful that it will be completed within the next couple of months.

**Business Item 5: Impact of Public Charge Executive Order**

Ms. Cole reminded the committee that the Public Charge Executive Order is in effect. She inquired whether there are any major issues that stemmed from this order. There were no comments from the group.

**Future Agenda Items**

Ms. Cole, ACET Chair, noted the Agenda Setting Workgroup would further develop the initial suggestions presented herein. The following topics were suggested:

Presenter	Agenda Item
Representative from Food and Drug Administration (FDA)	Discussion/presentation on drug supply and drug shortage concerns

Dr. Julie Higashi	Presentation on latest bacille Calmette-Guerin (BCG) vaccine guidelines for local programs for ACIP consideration
Dr. Nick DeLuca	Provide update on Latent TB Infection Community Engagement Network and communications campaign rollout
TBD	Presentation on COVID-19 & TB impacts and opportunities
TBD	Updates from the Tuberculosis Epidemiology Studies Consortium (TBESC) and the Tuberculosis Trials Consortium (TBTC)

**Public Comment Session**

No public comments were provided during this meeting.

**Closing Session**

The next ACET meeting will be convened on December 8 and 9, 2020. It is yet to be determined whether the meeting will be conducted in-person or virtually.

With no further discussion or business brought before ACET, Dr. Armitage moved to adjourn the meeting and was seconded by Dr. Belknap. The motion was accepted unanimously. Ms. Cole adjourned the meeting at 3:38pm on June 16, 2020.

**CHAIR’S CERTIFICATION**

I hereby certify that to the best of my knowledge, the foregoing minutes of the proceedings are accurate and complete.

Date

Barbara Cole, RN, MSN, PHN  
 Chair, Advisory Council for the  
 Elimination of Tuberculosis

# Attachment 1: Day 1 Participants' Directory

## ACET Members Present

Dr. Ana Alvarez  
Ms. Barbara Cole, Chair  
Dr. Robert Belknap  
Dr. Jennifer Flood  
Dr. David Horne  
Dr. Robert Horsburgh, Jr.  
Dr. Lixia Liu  
Ms. Kristine Stewart-East  
Dr. Zelalem Temesgen  
Dr. Lisa Armitage

## ACET Members Absent

### ACET Ex-Officio Members Present

Dr. Naomi Aronson  
US Department of Defense

Dr. Robert Benjamin  
STOP TB USA

Dr. Amy Bloom  
US Agency for International Development

Dr. Ulana Bodnar  
US Department of Justice

Dr. Laura Cheever  
HIV/AIDS Bureau (HAB)

Dr. Karen Elkins  
US Food and Drug Administration

Dr. Jonathan Iralu  
Indian Health Service

Dr. Lawrence Kline  
US Section, US-Mexico Border Health  
Commission

Dr. David Weissman for Mr. Stephen Martin  
National Institute for Occupational Safety  
and Health

Dr. Gary Roselle  
US Department of Veteran Affairs

### ACET Ex-Officio Members Absent

Ms. Sarah Bur  
Federal Bureau of Prisons

Dr. Mamodikoe Makhene  
National Institute of Allergy and Infection  
Diseases, National Institutes of Health

Dr. Thomas Nerard  
US Department of Labor/Occupational  
Safety and Health Administration

### ACET Liaison Representatives Present

Dr. Shama Ahuja  
Council State and Territorial  
Epidemiologists

Dr. David Bryden  
RESULTS

Dr. Julie Higashi  
National Tuberculosis Controllers  
Association Treatment Action

Mr. Surajkumar Madoori  
Treatment Action Group

Dr. Robert Morris  
National Commission on Correctional  
Health

Dr. Howard Njoo  
Public Health Agency of Canada

Dr. Ameer Patrawalla  
Global Tuberculosis Institute



Ms. Susan Rappaport  
American Lung Association

Dr. Randall Reves  
International Union Against TB and Lung  
Disease

Dr. Kathleen Ritger  
National Association of County and City  
Health Officials

Ms. Susan Ruwe  
Association for Professionals in Infection  
Control and Epidemiology

Dr. Lornel Tompkins  
National Medical Association

Dr. Ameer Patrawalla  
American College of Chest Physicians

### **ACET Liaison Representatives Absent**

Dr. Charles Daley  
American Thoracic Society

Mayleen Ekiek  
Pacific Island Health Officers Association

Dr. John Hellerstedt  
Association of State and Territorial Health  
Officials

Dr. Ilse Levin  
American Medical Association

Ms. Nuala Moore  
American Thoracic Society

Dr. Gudelia Rangel  
Mexico Section, US-Mexico Border Health  
Commission

Ms. Susan Ray  
Infectious Disease Society of America

Dr. Michael Tapper  
Society for Healthcare Epidemiology of  
America

Mr. Bobby Watts  
National Health Care for the Homeless  
Council

Dr. Daphne Ware  
Association of Public Health Laboratories

### **CDC Representatives**

Dr. Terence Chorba  
Mr. Justin Davis  
Dr. Tracy Dalton  
Dr. Nick DeLuca  
Mr. Bruce Everett  
Ms. Vanessa Fong  
Dr. Neela Goswami  
Dr. Maryam Haddad  
Ms. Stephanie Johnston  
Ms. Jasmine Kenney  
Ms. Allison Kline  
Ms. Maureen Kolasa  
Ms. Kathryn Koski  
Dr. Philip LoBue  
Ms. Allison Maiuri  
Ms. Suzanne Marks  
Dr. Jonathan Mermin  
Ms. Staci Morris  
Dr. Thomas Navin  
Dr. Scott Nabity  
Dr. Subhadra Nandakumar  
Dr. Drew Posey  
Mr. Bob Pratt  
Dr. Joanna Regan  
Dr. Amber Robinson  
Ms. Annie Rossetti  
Dr. Suraj Sable  
Ms. Margie Scott-Cseh  
Ms. Sarah Segerlind  
Ms. Maria Sessions  
Ms. Rebekah Stewart  
Ms. Eva Trinh  
Ms. Dawn Tuckey  
Dr. Andrew Vernon  
Dr. Carla Winston

## **Guest Presenters**

Dr. Susan Maloney  
Global TB Branch, Division of Global  
HIV & TB  
Center for Global Health

Ms. Suzanne Marks  
Division of TB Elimination

Ms. Michelle Van Handel  
Program Performance Improvement  
Office, NCHHSTP

Ms. Donna Wegener  
National Tuberculosis Controllers  
Association

## **Members of the Public**

Mr. Pete Dupree  
Dr. Brent Gibson  
Dr. Barbara Laughon  
Dr. Lakshmi Ramachandra  
Ms. Lindsey Trischler  
Mr. Joseph Yumul

## Attachment 2: Glossary of Acronyms

Acronym	Definition
<b>ACET</b>	Advisory Council for the Elimination of Tuberculosis
<b>ATS</b>	American Thoracic Society
<b>BASICS</b>	Building and Strengthening Infection Control Strategies
<b>BCG</b>	Bacille Calmette-Guerine
<b>CAMP</b>	Coalition for Applied Modeling for Prevention
<b>CAPE</b>	Consortium to Accept Prevention Economics
<b>CDC</b>	Centers for Disease Control and Prevention
<b>CLINT</b>	Cluster Investigation Tool
<b>COI</b>	Conflict of Interest
<b>COE</b>	Centers of Excellence
<b>DASH</b>	Division of Adolescent and School Health
<b>DFO</b>	Designated Federal Officer
<b>DGMQ</b>	Division of Global Migration and Quarantine
<b>DGHT</b>	Division of Global HIV & Tuberculosis
<b>DOPT</b>	Directly Observed Preventive Therapy
<b>DPH</b>	Department of Public Health
<b>DTBE</b>	Division of Tuberculosis Elimination
<b>ECHO</b>	Extension for Community Healthcare Outcomes
<b>eDOT</b>	Electronic Directly Observed Treatment
<b>ELEVATE</b>	Engaging Local Experts to Validate and Analyze TB data to End TB
<b>FACA</b>	Federal Advisory Committee Act
<b>FDA</b>	(United States) Food and Drug Administration
<b>GDF</b>	Global Drug Facility
<b>HAV</b>	Hepatitis A Virus
<b>HBV</b>	Hepatitis B Virus
<b>HCV</b>	Hepatitis C Virus
<b>HHS</b>	(United States) Department of Health and Human Services
<b>HRSA</b>	Health Resources and Services Administration
<b>IDSA</b>	Infectious Disease Society of America
<b>IGRA</b>	Interferon Gamma Release Assay
<b>IHS</b>	Indian Health Service
<b>INH</b>	Isoniazid
<b>LATTE</b>	Location and Time to Epi
<b>LITT</b>	Logically Inferred Tuberculosis Transmission
<b>LTBI</b>	Latent Tuberculosis Infection
<b>MDR-TB</b>	Multidrug-Resistant Tuberculosis
<b>MMWR</b>	Morbidity and Mortality Weekly Report
<b>MSM</b>	Men Who Have Sex with Men
<b>MTB</b>	Mycobacterium Tuberculosis
<b>NAP</b>	National Action Plan
<b>NCHHSTP</b>	National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention
<b>NEEMA</b>	NCHHSTP Epidemiologic and Economic Modeling Agreement
<b>NIH</b>	National Institutes of Health

<b>NTCA</b>	National Tuberculosis Controllers Association
<b>PEPFAR</b>	<b>A President's Emergency Plan for AIDS Relief</b>
<b>PERCH</b>	Pneumonia Etiology Research for Child Health
<b>PrEP</b>	Pre-exposure Prophylaxis
<b>PLHIV</b>	People Living with HIV
<b>POC</b>	Point of Contact
<b>PPD</b>	Purified Protein Derivative
<b>PPE</b>	Personal Protective Equipment
<b>PPML</b>	The Prevention Policy Modeling Lab
<b>RIF</b>	Rifapentine
<b>SAT</b>	Simultaneous Amplification Testing
<b>SETC</b>	Society for Epidemiology in Tuberculosis Control
<b>SLIPTA</b>	Stepwise Laboratory Improvement Process Toward Accreditation
<b>SLMTA</b>	Strengthening Laboratory Management Toward Accreditation
<b>SMS</b>	Short Message Service
<b>SNP</b>	Single Nucleotide Polymorphism
<b>SSP</b>	Syringe Services Program
<b>STD</b>	Sexually Transmitted Disease
<b>TB</b>	Tuberculosis
<b>TBESC</b>	Tuberculosis Epidemiologic Studies Consortium
<b>TBTC</b>	Tuberculosis Trials Consortium
<b>TPT</b>	TB Preventive Treatment
<b>TST</b>	Tuberculin Skin Test
<b>TTT</b>	Targeted Testing and Treatment
<b>UNHLM</b>	United Nations High Level Meeting
<b>US</b>	United States
<b>USPSTF</b>	US Preventive Services Task Force
<b>WG</b>	Working Group
<b>WHO</b>	World Health Organization
<b>3HP</b>	12-dose Regimen of Isoniazid-Rifapentine
<b>4R</b>	4-month Regimen of Rifapentine

## **ADDENDUM 1: Roadmap for Advancing TB Elimination in the United States through Scale up of Testing and Treatment of Latent TB Infection**

### **Recommendations of the Advisory Council for the Elimination of Tuberculosis (ACET)**

**Prepared by:** ACET Latent Tuberculosis Infection Workgroup

#### **Summary**

This statement from the Advisory Council for the Elimination of Tuberculosis updates the strategy to eliminate tuberculosis (TB) in the United States (2, 7). The report provides new recommendations to prevent TB, specifically through focus on identifying individuals at risk and testing and treating latent TB infection (LTBI). To scale up testing and treatment of latent TB infection, recommendations include: 1) identifying and engaging individuals at risk and their providers, 2) encouraging prevention using focused, effective testing and treatment strategies, 3) developing streamlined LTBI surveillance and monitoring systems to measure and optimize outcomes and 4) securing new funding to support these new activities. Effective communication strategies and outreach to affected communities and healthcare providers are crucial components for success of each strategy. Research to improve diagnostics and treatment and advance vaccine development will also be essential to reach TB elimination.

#### **BACKGROUND/INTRODUCTION**

The Advisory Council for the Elimination of Tuberculosis (ACET) provides advice and recommendations regarding the elimination of tuberculosis to the Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC). The ACET Latent Tuberculosis Infection (LTBI) Workgroup was established to develop a strategy document with concrete recommendations to address latent tuberculosis infection (LTBI) with the goal of ultimately eliminating tuberculosis (TB) within the United States.

This report provides a major update to the 1989 Strategic Plan publication (7). In the past 2 decades, the epidemiology of TB in the US has changed. To date, strategies to control TB in the United States have focused on rapidly finding and treating patients with active TB disease and testing and treating their contacts with minimal focus on the larger reservoir of persons with latent TB infection.

Today untreated LTBI is the main generator of new TB cases in the US and is responsible for a significant slowing in the decline of TB disease. Persons with LTBI are not ill and have no clinical evidence compatible with TB disease, but can become sick in the future and develop active disease. In 2014, the World Health Organization published guidance for the scale up of LTBI testing and treatment in low incidence countries. In addition, in 2016, the US Preventive Services Task Force (USPSTF) released findings calling for routine LTBI testing and treatment of non-US-born (non-USB) adults and those residing in congregate settings (27), yet these recommendations are only slowly being adopted. These recent recommendations emerged in tandem with the introduction of a more accurate test for LTBI (the interferon- $\gamma$  release assays [IGRAs]) and shorter, safer treatment regimens for LTBI (9, 16). In addition, expansion of healthcare access has created new opportunities for care of populations at high-risk for LTBI and development of TB disease. While these opportunities can help us advance to TB elimination,

the need for strategies to promote widespread adoption of LTBI testing and treatment requires update of the TB elimination roadmap. Scaling up prevention efforts by improving our ability to conduct LTBI testing and treatment and measure LTBI outcomes is the focus of this strategy document.

While modeling studies have suggested we cannot make substantial progress toward eliminating TB without an LTBI-focused approach (10), the barriers to LTBI scale-up must first be addressed. Individuals with LTBI feel well and may be unaware of their risk of developing TB disease and the benefit of testing and treatment, resulting in minimal patient-driven demand for testing and treatment. Although many non-USB persons are in routine care, LTBI risk assessment and testing are often overlooked by clinicians because of competing health priorities and a knowledge gap related to TB/LTBI. Many healthcare providers are unaware of the USPSTF LTBI recommendations and are unclear about who to test and treat; they also are unfamiliar with the new and better tests, and the shorter and safer drug regimens for treating LTBI. Across healthcare settings, there are currently few systems to help busy physicians with LTBI testing and treatment; most electronic health records do not include TB risk factor questions as a part of routine health maintenance screening and changing electronic health records (EHRs) to include elements important for TB risk assessment, such as country of birth, is not straightforward. Public health department resources for LTBI testing and treatment are often meager, and there has been no unified effort to promote LTBI testing and treatment scale-up to community providers who care for large volumes of high-risk patients. Lack of designated funding and effective local, regional and national TB prevention initiatives and LTBI awareness campaigns have impeded public health department action. Finally, the complementary roles of public health departments and primary care providers in TB prevention have not been well-articulated. As a result, many national and community-based organizations that support high-risk patients are not yet fully focused on the need for, and benefits of, TB prevention.

Most patient and provider education about LTBI and TB disease has come from health departments and academia. While these sources have provided valuable information, they have not always been effective. New active strategies are needed that reach out to the target populations, address the needs and concerns of high-risk individuals and their healthcare providers and provide practical action steps that will lead to engagement in LTBI care. It will be essential to engage key community partners both to design new strategies, produce culturally tailored materials and motivate at-risk individuals to seek appropriate testing and treatment. Community-based and medical professional organizations play an important role in this process. Providers in all settings need to be empowered to identify and evaluate their clients at risk for LTBI (22). Finally, while education is necessary, it also important to develop a marketing approach tailored to specific high-risk groups of patients and providers to encourage engagement and action.

Healthcare access poses an additional barrier for many individuals who would benefit from TB prevention services. Patients who are at risk for TB may not be in care or may experience prohibitive out-of-pocket costs for LTBI assessment and treatment (e.g., IGRA testing, medical evaluation, chest radiograph, and medications). Most public and private healthcare settings have limited budgets for LTBI diagnostics and treatment. Although many healthcare settings routinely screen patients for infections such as HIV and Hepatitis B and C, many fewer routinely assess for LTBI and there usually is no synergy between these screening activities even though many patients are at risk for all of these infections. Many Federally Qualified Health Centers (FQHCs) that provide care to high-risk clients do not have



adequate funding for LTBI testing and treatment. Health departments have been unable to focus on LTBI because of the absence of designated funding and the need to prioritize attention on TB disease. With TB disease waning in much of the country, many healthcare providers lack experience and knowledge about TB and LTBI, especially of the newer tests and treatment regimens, and the essential step of excluding TB disease prior to LTBI treatment. Systems for supporting adherence of patients throughout treatment, particularly in community healthcare settings, are typically undeveloped. Finally, the return on investment and future savings incurred by LTBI testing and treatment by reducing future costly disease has not yet ignited activity.

To measure progress in expanding LTBI testing and treatment, LTBI monitoring and surveillance are critical activities to target and evaluate the success of public health interventions. Local and nationwide LTBI surveillance and monitoring systems are needed that support data flow among varied healthcare settings, local and state health departments, and the CDC. LTBI is an asymptomatic condition that can be detected only through diagnostic testing (the tuberculin skin test [TST] or IGRA) and through the exclusion of active disease via chest imaging. Ironically, while many high-risk individuals go unevaluated, much of the testing for LTBI in the US currently is done through administrative or employment testing of low-risk populations. Although LTBI is reported in some areas, public health agency resource constraints limit the proportion of LTBI reports that can be investigated.

At both local and national levels, monitoring the success of interventions is critical. A major impediment to adoption of LTBI testing and treatment in healthcare settings is that there is no national requirement for quality improvement of LTBI testing and treatment or no required national LTBI performance metrics. There is a clear need for measuring LTBI burden over time and establishing a system for monitoring LTBI practices and outcomes. Several first steps that will allow better measurement of LTBI testing and treatment have occurred in the U.S: 1) minimum data elements for LTBI surveillance (26, 19) have been established, 2) informatics infrastructure (Tuberculosis Latent Infection Surveillance System [TBLISS]) has been developed and 3) a growing number of states now mandate LTBI reporting and 4) the National Health and Nutrition Examination Survey (NHANES) LTBI testing has also provided key estimates of LTBI in the US. Establishing national metrics for federally funded clinical settings, disseminating tools for tracking LTBI care steps, and supporting data exchange will help spur further progress.

## **METHODS**

In January 2018, ACET convened a workgroup comprised of ACET members and subject matter experts to review existing evidence on strategies to achieve TB elimination and approaches for LTBI testing and treatment scale-up. A review of both program experience and the published literature was synthesized on strategies to accelerate the decline of TB cases in the US. The most recently published LTBI testing and treatment recommendations of the Institute of Medicine, USPSTF and CDC were considered. Experiences of US health departments in TB elimination planning and successful LTBI testing and treatment programs were analyzed.

Both current epidemiology and published modeling studies forecasting results of specific interventions were reviewed. Published reports on the facilitators and barriers for identifying and engaging high-risk populations and establishing systems for successful testing and treatment were examined.

While prior US TB strategic plans have emphasized diagnosis, treatment and contact investigation for individuals with TB disease as the top priorities for TB elimination, these ACET recommendations highlight the new, additional priority of LTBI testing and treatment in high-risk persons to prevent TB disease as an equally important and necessary strategy to achieve further TB case decline. Building on USPSTF recommendations published in 2016 (27), the recommendations in this document can be applied by the CDC and state and local health departments in partnership with medical care settings, industry, and community organizations.

## **FINDINGS/RECOMMENDATIONS**

There are four major activities required for scaling up LTBI testing and treatment in the United States: 1) identify and engage individuals at-risk and their providers; 2) increase testing of at-risk individuals and increase treatment of infected individuals; 3) measure outcomes of LTBI testing and treatment scale-up, and 4) secure funding for these TB disease prevention activities. Effective outreach, communication, education and partnership are crucial cross-cutting components for implementing these activities. Two additional high-priority interventions include research to improve diagnosis and treatment of LTBI and policies that implement targeted testing and treatment of LTBI in adult migrants before arrival in the US. To support each activity, ACET recommends the actions described below:

### **Identify and engage individuals at risk and their providers**

#### *Community outreach*

1) Launch a marketing strategy targeted at public and community-based organizations to raise awareness about who is at risk for LTBI and TB disease and who needs testing, and to create demand for testing in healthcare settings:

- Engage community organizations to endorse/encourage TB screening
- Provide web-based tools for the public to determine individual risk (“Know Your TB Status/Risk”), to locate testing sites by zip code and to generate a risk assessment record for individuals to keep and to trigger testing by their healthcare provider
- Develop community-specific and culturally competent messages and education tools for specific patient groups at risk for TB

2) Use evidence-based strategies tailored to settings and risk groups to bring people at risk into care for testing and treatment

3) Build on and HIV/Hepatitis B and C/Sexually Transmitted Disease screening initiatives to replicate successful models of how to motivate patients and providers through engagement, linkage to care, testing (e.g., blood draw/chest radiograph) and treatment

4) Work with homeless organizations to implement risk-based testing and treatment

#### *Provider outreach*

5) Engage medical professional organizations to endorse/encourage TB screening

6) Identify and disseminate a list of provider groups and health plans serving large numbers of non-USB individuals to local health departments so they can focus their LTBI testing and treatment scale-up efforts

7) Encourage LHDs to engage with providers to communicate with local high-risk groups and give them the tools to do this effectively; as an example, academic detailing has been successful and used to outreach to clinicians on focused topics

8) Disseminate efficient models of LTBI risk-based testing and treatment work flows and protocols to clinics serving high risk patients

### **Increase LTBI testing and treatment with the most effective tools**

- 1) Initiate an awareness campaign to educate and disseminate effective tools for providers including:
  - Methods for effectively communicating to patients about the need for LTBI testing and treatment
  - Simple educational products about risk assessment (including who to test among non-USB populations), testing and treatment
  - Recommendations about additional key risk groups warranting testing (e.g., immunocompromised, contacts)
  - Messages that explain the USPSTF recommendation
  - Information about use of new short-course regimens
  - Steps for ruling out TB disease before beginning LTBI treatment
  - Steps for reporting LTBI to their jurisdiction, if mandated
- 2) Disseminate adherence strategies, for example, treatment support networks for patients, tailored case management strategies for specific patient groups, electronic Directly Observed Therapy (eDOT) strategies and electronic telemedicine follow-up models
- 3) Support documentation of treatment completion within healthcare systems, including adding an ICD-11 code for treatment completion documentation and ensure that patients have these records as they move across health systems and locations
- 4) Incentivize healthcare providers and plans to perform routine risk assessment to identify high-risk patients, including simple EHR tools to determine individual risk, including test order sets
  - Engage companies that provide EHRs to develop capacity for recording, using and analyzing TB risk factors including country of birth
  - Disseminate standardized elements for TB risk assessment, testing, and treatment for EHR systems and support EHR user networks for systematic changes
- 5) Facilitate outreach to and provide incentives for populations and their providers undergoing required testing (status adjusters) to promote linkage to and completion of treatment
- 6) Initiate a program for pre-departure LTBI testing and treatment for adults who are migrating to the US
- 7) Describe roles of local, state, federal, health department and health care providers for TB prevention
- 8) Build consultative capacity within public health departments, regional centers and the CDC Centers of Excellence for access by community providers and organizations

### **Measure success and outcomes of LTBI testing and treatment scale-up**

- 1) Establish national, state and local LTBI surveillance systems that, to the extent feasible, exchange data among healthcare settings, state and local health departments, and the CDC to measure and improve outcomes of LTBI testing and treatment
  - Define the core elements and approaches for simple effective LTBI surveillance and monitoring systems
  - Determine and incorporate the needs and capabilities of local/state health departments for successful surveillance
  - Engage public health and community providers in the system design and implementation
  - Create systems that respond to healthcare setting, local and state needs and feasibility constraints

- Implement laboratory reporting of the TB blood test results (IGRAs) for surveillance purposes as an important first step
- 2) Establish and track simple national, state and local quality improvement and performance metrics that measure (1) the percent of non-USB tested for LTBI, (2) the percent of LTBI treatment completion for those who test positive and (3) the percentage of active TB cases meeting criteria for potentially being preventable (e.g. were at known risk and not tested and/or not offered treatment)
- Work with the Health Resources and Services Administration (HRSA) and Centers for Medicare and Medicaid Services (CMS) to establish national performance measures
  - Include these measures in the CMS Adult and Child Core Set and Medicare Quality Improvement requirements
  - Assess whether risk criteria were met for testing
- 3) Work with state and local health departments to launch rigorous evaluation and improvement of newcomer testing and treatment (status adjusters and persons with TB B-notification)

### **Secure TB prevention funding for education, testing, treatment, surveillance and research**

- 1) Establish private and public partnerships involving philanthropy, industry, governmental, and nongovernmental health organizations for a national TB prevention/elimination initiative
- 2) Identify new funding streams to offset patient financial burden for the uninsured, as well as those insured with high co-pays
- Recommended strategies include making testing available for free, supporting a USPSTF review of LTBI treatment as prevention activity so that both testing and treatment have cost-sharing removed, and dissemination of financial analyses of the return on investment of LTBI testing and treatment to policymakers and health plans
  - Ancillary actions that could remove financial barriers for programs and patients include allowing use of federal cooperative agreement funds for LTBI treatment and stimulating drug manufacturers to lower costs
- 3) Create a budget and secure funding for LTBI surveillance system
- Funding support should include electronic DOT/telemedicine adherence and follow-up to ensure treatment completion and create efficiency through electronic case reporting directly from electronic health records
- 4) Support research to advance needed tools
- While intensifying TB prevention through increased LTBI testing and treatment is an important step toward TB elimination, ending TB will require novel interventions; even though LTBI diagnostics and treatment regimens and our understanding of LTBI have improved, they are far from perfect
  - Ongoing investment in research is critical to reach elimination and the workgroup identified five of the eight research priorities articulated by WHO (28) as the most critical to advance our ability to prevent TB in the US

### **Recommended Priorities for Research**

1. Define the rate of progression to active TB among those with LTBI generally and for specific subgroups to inform the risk/benefit ratio of LTBI testing and treatment to aid clinical decision-making
2. Develop more predictive diagnostics to identify those with LTBI who will progress to TB disease
3. Conduct trials to assess effective shorter treatment options
4. Identify interventions that promote treatment adherence and prevent attrition during the LTBI care cascade
5. Identify the most cost-effective approaches and populations to focus screening testing and treatment

### **DISCUSSION**

The expected impact of these new policy recommendations, if fully adopted, will be a successful expansion of LTBI testing and treatment and prevention of TB disease for those at risk. Modeling results have predicted that with a 4-fold to 8-fold increase in targeted testing and treatment using the most effective tools (e.g., IGRA and short course treatment regimens) (11), we can realize a substantial reduction of TB cases in the US and achieve pre-elimination targets (10). These tools provide us with the opportunity to save lives and reduce TB-related costs, morbidity, and deaths.

Useful lessons can be gleaned from the successful national “Know Hepatitis B Campaign” developed by CDC and the Hep B United coalition (14). The challenges for hepatitis B prevention were addressed by reaching Asian Americans for testing in their communities, in their language and with trusted leaders. The plan for accomplishing this was through partnerships with Asian American organizations, CDC funding of a cooperative agreement and providing linkage to care and integrating hepatitis B with other important conditions. Similarly, progress in ending HIV has occurred through federal commitment and funding. The national LTBI initiative can build on and learn from these successes.

In addition to domestic expansion of LTBI testing and treatment, advancing policy and action outside the US in parallel is crucial. Successfully addressing and reducing TB globally in high-burden countries is a critical component for elimination of this disease. In addition, policies should promote testing and encourage referral for LTBI treatment of immigrants applying for permanent residency during health examinations done before US entry and at the time of visa status change in the US. The current overseas requirement for pre-departure screening of immigrants should be expanded to include those requesting student, worker, and extended tourist visas with the goals of TB case detection as well as diagnosis for LTBI with encouragement of LTBI treatment (22). LTBI diagnosis and treatment can be successful and efficient with new tests and short-course treatment. While many activities must occur in parallel, prioritizing and staging actions to advance TB elimination may be needed in the context of limited resources. The workgroup recommended tackling the following high-priority interventions first, shown in the following graphic.

### **High-Priority Interventions**

1. Create a visible national TB prevention and elimination plan focused on LTBI testing and treatment
2. Secure funding and partnerships for CDC and health department-led activities and stimulatesupport needed by community organizations and persons at risk and healthcare providers
3. Launch marketing strategy targeted at public and community-based organizations to raise awareness of who is at risk for LTBI and TB disease and to create demand for testing in healthcare settings public and community based organizations
4. Disseminate evidence-based strategies tailored to risk groups and settings to bring people at risk into care for testing and treatment
5. Disseminate efficient models and tools for LTBI risk-based testing and treatment in clinical settings (e.g., template for systematic approach to LTBI care cascade steps, workflows, protocols, EHR triggers)
6. Facilitate outreach to and provide incentives for newcomers (status adjusters and those with B-notification) who test positive to promote linkage to and completion of treatment
7. Establish and track simple national state and local quality improvement and performance metrics to stimulate improvement
8. Specifically, establish measure in CMS Child and Adult Core set which will be required of federally funded providers/clinics (FQHCs, Medicaid, and Medicare healthcare providers)
9. Work with state and local health departments to launch rigorous evaluation and improvement of new comer testing and treatment (e.g., status adjusters and TB B-notifications)
10. Support a prioritized LTBI research agenda advancing 2-3 high impact studies in next 5 years

### **High-Priority Interventions: Future Steps**

1. Create streamlined exchange of LTBI data for monitoring and action across healthcare settings, local and state health departments and CDC.
2. Initiate a program for adult pre-departure LTBI testing and treatment building on the Vietnam pilot experience
3. Implement new research findings that can lead to faster adoption of best practices and speed TB decline

## **CONCLUSION**

Substantial progress has been made in reducing tuberculosis in the United States, but the decline has stalled, with persistent morbidity, cost and transmission of TB. A commitment to achieve TB elimination is crucial for progress and requires effective partnerships across diverse organizations and health system components. TB decline can be accelerated by a robust investment in targeted testing and treatment of latent TB infection added to strong core TB infrastructure for TB disease diagnosis and treatment. In parallel, global TB prevention efforts and research are vital to realizing TB elimination.

### **Summary Recommendations**

- Resource and commit to a national TB elimination plan
- Engage and motivate providers and health systems
- Outreach to high-risk populations
- Conduct research to advance tools for LTBI testing and treatment
- Measure and improve outcomes of the LTBI care cascade

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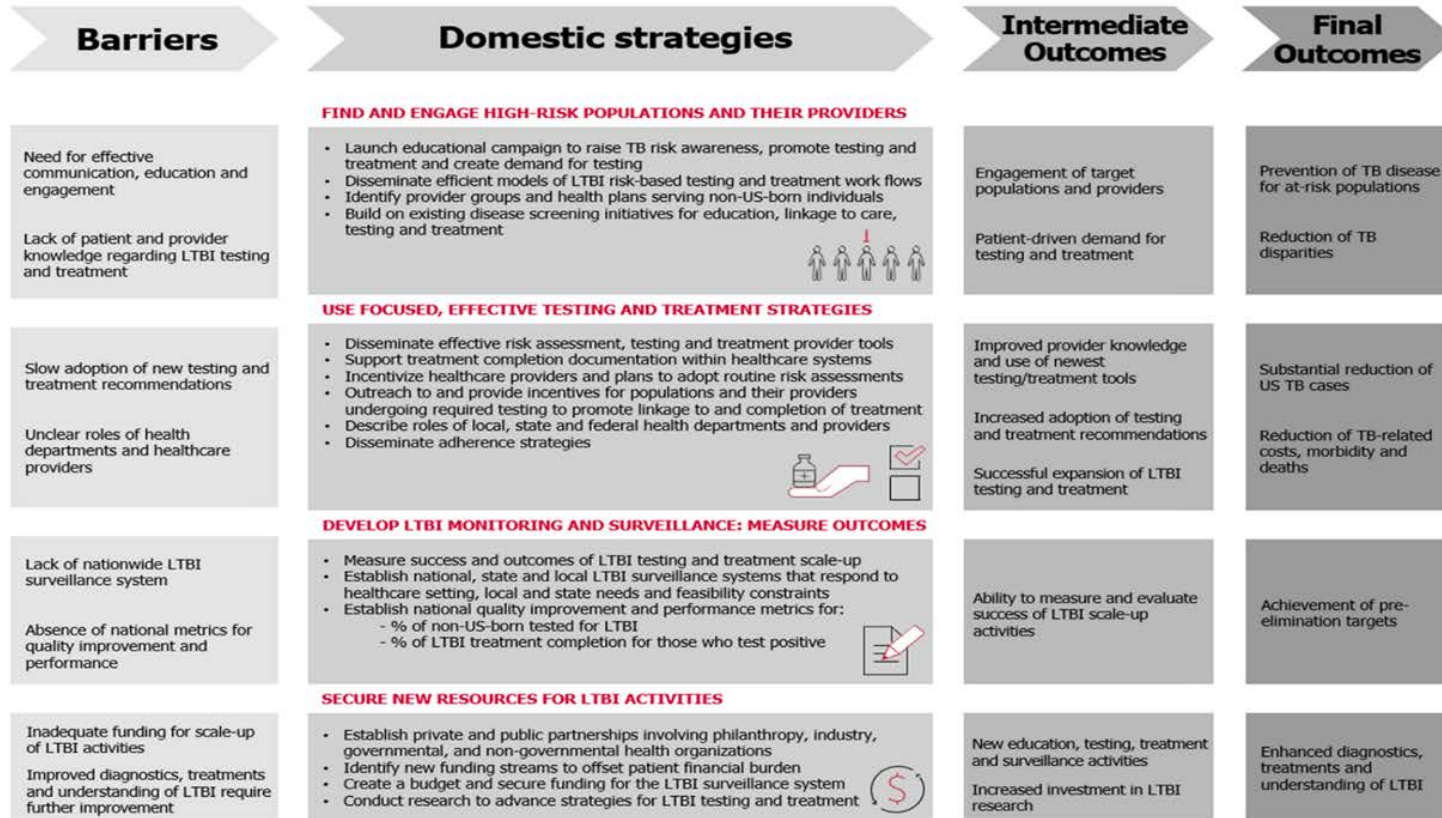
Minutes of the Meeting:

*Advisory Council for the Elimination of Tuberculosis*

June 16, 2020 • Page 49

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# LTBI TESTING AND TREATMENT SCALE-UP ROADMAP



12