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

Hybrid Meeting of the
Advisory Council for the Elimination of Tuberculosis
December 12-13, 2023

Record of the Proceedings

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ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS
December 12-13, 2023

Minutes of the 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, Viral Hepatitis, STD, and TB Prevention (NCHHSTP, the Center), Division of Tuberculosis Elimination (DTBE) convened a hybrid meeting of the Advisory Council for the Elimination of Tuberculosis (ACET). The proceedings were held on December 12-13, 2023 beginning at 9:30 AM Eastern Time (ET) on December 12, 2023 and 10:00 AM on December 13, 2023.

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 the 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 of CDC's TB Prevention Research portfolio and program priorities; and review the extent to which progress has been made toward TB elimination.

Information for the public to attend the hybrid ACET meeting via webinar or teleconference was published in the *Federal Register* in accordance with FACA regulations and rules. All sessions of the meeting were open to the public.

December 12, 2023 Opening Session

Robert Belknap, MD
Medical Director, Denver Metro Tuberculosis Clinic
Public Health Institute at Denver Health
ACET Chair

Deron Burton, MD, JD, MPH (CAPT, USPHS)
Deputy Director, National Center for HIV, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control & Prevention
ACET Designated Federal Officer (DFO)

Marah E. Condit, MS
Public Health Analyst, Advisory Committee Management
Office of Policy, Planning, and Partnerships
National Center for HIV, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control and Prevention

Dr. Belknap called the meeting to order at 9:30 AM ET on December 12, 2023. Marah Condit provided meeting instructions. She noted that members of the public would have an opportunity to provide comment during the second day of the meeting at 10:15 AM ET. CAPT Burton welcomed participants and conducted a roll call to confirm the attendance of ACET voting members, ex-officio members, and liaison representatives. He explained that ACET meetings are open to the public and all comments made during the proceedings are a matter of public record. He reminded ACET voting members of their responsibility to disclose any potential individual and/or institutional conflicts of interest (COI) for the public record and recuse themselves from voting or participating in these matters.

ACET Voting Member Institution/Organization	Potential Conflict of Interest
Amina Ahmed, MD Levine Children's Hospital at Carolina Medical Center	No conflicts
Robert Belknap, MD Denver Metro Tuberculosis Tuberculosis Clinic	No conflicts
Adithya Cattamanchi, MD University of California, San Francisco	No conflicts
Lisa Chen, MD University of California, San Francisco	No conflicts
William Glover, PhD, D(ABMM), MT(ASCP) North Carolina State Laboratory of Public Health	No conflicts
Ann Loeffler, MD Multnomah County Oregon	No conflicts
Lynn Sosa-Bergeron, MD Connecticut Department of Public Health	No conflicts
Kristine Steward-East Advocate for Tuberculosis	No conflicts
Jason Stout, MD, MHS Duke University Medical Center	No conflicts

The roll call confirmed that the 21 voting and *ex-officio* members in attendance constituted a quorum for ACET to conduct its business on December 12, 2023. The roll was called subsequent to each break and lunch, with a quorum established each time throughout the day.

CAPT Burton thanked Dr. Robert Belknap and Ms. Kristine Steward-East for extending their terms by 180 days to allow the ACET to have full membership. He welcomed new National Tuberculosis Controllers Association (NTCA) liaison member, and Dr. Joseph Burzynski, from the Bureau of Tuberculosis Control at the NYC Department of Health and Mental Hygiene (NYC Health) and reported that CDR Misty Carlson was appointed as the Ex Officio representative from United States Immigration and Customs Enforcement (ICE). In addition, he announced that the 2024 ACET meeting dates have been set for June 25-26, 2024 and December 3-4, 2024.

Dr. Belknap extended his welcome to everyone. He expressed gratitude to Dr. Lynn Sosa-Bergeron, who was instrumental in helping to organize the outstanding agenda for this meeting; Ms. Condit, who makes all of this run smoothly; and CAPT Burton for his support in the role of ACET's Designated Federal Officer (DFO), who is moving on from his role as Deputy Director of NCHHSTP to become a Division Director in another center.

NCHHSTP Director's Report

Jonathan Mermin, MD, MPH
RADM and Assistant Surgeon General, United States Public Health Service (USPHS)
Director, National Center for HIV, Viral Hepatitis, STD and TB Prevention
Centers for Disease Control & Prevention

RADM Mermin provided the NCHHSTP Director's Report, beginning with CDC priorities. The new CDC Director has identified three focus areas, which are to: 1) prioritize efforts to rapidly identify and respond to health threats, which includes the agency's work on the Fall/Winter viral respiratory season; 2) continue to address and get upstream of the mental health and overdose crises; and 3) break down silos to support young families, so that children thrive no matter where they live. In addition, she intends to continue the efforts the agency has undertaken in terms of the "Moving Forward" initiative.

During the last ACET meeting, there was discussion about the syndemic framework for prevention. NCHHSTP continues this work and expects over the next year to identify priorities related to administrative changes, flexible funding announcements, and multi-pathogen screening conducted within the same populations to ensure support NCHHSTP is trying to determine what efforts make the biggest public health difference, being cost-saving, and ensuring effective implementation over time. While still working on this internally, the plan is to engage with external partners as well.

In terms of NCHHSTP leadership and reorganization, RADM Mermin made the following announcements:

- CAPT Deron Burton has accepted the position of Division Director for the newly formed Division of Blood Disorders and Public Health Genomics (DBDPHG) in the National Center on Birth Defects and Developmental Disabilities (NCBDDD), which begins on December 15, 2023. Dr. Winston agreed to serve as Acting DFO for the ACET for the time being.

- CAPT Robyn Neblett Fanfair is the Acting Division Director of the Division of HIV Prevention (DHP).

- Dr. Leandro Mena retired in November 2023. Dr. Laura Bachmann is the Acting Division Director of the Division of STD Prevention (DSTDP).

- In October 2023, the Division of Adolescent and School Health (DASH) moved back to the National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP) where it was housed 10 years ago. DASH is still receiving some HIV resources from NCHHSTP, so NCHHSTP will continue to be involved in DASH's sexual health for youth activities.

The Division of Viral Hepatitis (DVH) issued 2 new screening recommendations for hepatitis C for infants and pregnant people who have hepatitis C, and new screening recommendations for hepatitis B.[1] In August 2023 CDC announced the availability of the 2021 Viral Hepatitis Surveillance Report and the 2023 Viral Hepatitis National Progress Report. Because the number of viral hepatitis cases reported to CDC in 2020 and in 2021 may be lower than in years before the COVID-19 pandemic began, findings in these reports should be interpreted with caution. The Council of State and Territorial Epidemiologists voted in June 2023 to approve a new case definition of hepatitis B. The new definition will 1) Improve sensitivity and specificity of acute case definition; 2) Improve criteria to more accurately confirm chronic hepatitis B cases; and 3) Specify that all cases (confirmed and probable) be publicly reported, which will substantially increase the number of cases reported annually. CDC will update its surveillance guidance online to align with the new case definition and will go live with the update in 2024.

There has been some success in lowering acute hepatitis B incidence. However, lowering hepatitis C incidence has not had the same success. CDC published a report that suggests the majority of people with hepatitis C still have not been cured nearly a decade after DAAs were first approved in the United States.[2] Only about a third of people in the US who have known they have had hepatitis C for about 10 years have been cured.[3] Although this varies somewhat by age and the type of insurance, no group has over half of people having been cured. The treatment as prevention approach to hepatitis C is not working very well in the US, so NCCDPHP is thinking a lot about what it means to try to move upstream to change policies among insurers. They have been working with Commissioners of Insurance, Commissioners of Health, Centers for Medicare & Medicaid Services (CMS), and others who have some ability to leverage an environment from which people normally suffer.

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[1] https://www.cdc.gov/hepatitis/statistics/surveillanceguidance/index.htm
[2] Wester et al., MMWR; 2023; https://www.cdc.gov/nchhstp/newsroom/2023/viral-hepatitis-cure-cascade.htm
[3] Wester et al., MMWR; 2023; https://www.cdc.gov/nchhstp/newsroom/2023/viral-hepatitis-cure-cascade.htm

CDC released new recommendations for perinatal hepatitis C screening in November 2023[4] These new CDC recommendations will introduce: 1) HCV testing of all perinatally exposed infants with a nucleic acid test (NAT) for detection of HCV ribonucleic acid (RNA) at age 2–6 months, 2) consultation with a health care provider with expertise in pediatric hepatitis C management for all infants and children with detectable HCV RNA, 3) Perinatally exposed infants and children with an undetectable HCV RNA result at or after age 2 months do not require further follow-up unless clinically warranted. Furthermore, a NAT for HCV RNA is recommended for perinatally exposed infants and children aged 7–17 months who have previously not been tested, and a hepatitis C virus antibody (anti-HCV) test followed by a reflex NAT for HCV RNA (when anti-HCV is reactive) for perinatally exposed children aged ≥18 months who have not previously been tested. Proper identification of perinatally infected children, referral to care, and curative treatment are critical to achieving the goal of hepatitis C elimination.

CDC has partnered with NIH to contribute $6M in funding to NIH's Independent Test Assessment Program (ITAP) to rapidly facilitate the regulatory review and availability of high-quality, accurate, and reliable diagnostic test for hepatitis C. Since approximately one-third of patients have incomplete hepatitis C testing, CDC published in July 2023 updated operational guidance recommending complete HCV testing. This means that all sites performing HCV screening should ensure single-visit sample collection which allows for automatic HCV RNA testing when an HCV antibody test is reactive to avoid incomplete testing. It is expected that automatic HCV RNA testing on all HCV antibody reactive samples will increase the percentage of patients with current HCV infection who are linked to care and receive curative antiviral therapy. CDC is supporting the FDA in its effort to down-classify hepatitis B diagnostics from Class III to Class II. With the recent changes to vaccination and screening recommendations, it is all the more critical to develop new technologies that can simplify and expedite HBV testing.

The Division of STD Prevention (DSTDP) continues to try to tackle rising sexually transmitted disease (STD) rates for the past decade. Some of that is being done through a syndemic approach from the Component C of Ending HIV Epidemic (EHE). EHE resources support sexually transmitted infections (STI) clinics to incorporate pre-exposure prophylaxis (PrEP) and do a better job of STI screening. From July 2021 to December 2022 there was a 36% increase in the proportion of the clinics that offer PrEP onsite, with 72% of clinics now offering this service. The concept is that someone who has an STI is twice as likely to transmit or acquire HIV. Some of the HIV prevention services that were scaled up in 26 STD specialty clinics in 16 states included extragenital (pharynx and rectum) NAAT for GC/CT, STD express visits, risk assessment and education for PrEP, linkage for PrEP, referral for PrEP, and onsite PrEP Treatment (starter or 3-months).[5]

DSTDP also established a research consortium, the Sexually Transmitted Infections Impact Research Consortium (STIIRC),[6] that is modeled in many ways after the Tuberculosis Trials Consortium (TBTC). In addition, on October 2nd draft guidelines for doxycycline as post-exposure prophylaxis (PEP) for bacterial STIs[7] were posted in the Federal Register for public comment Taking 200 mg of doxycycline once orally within 72 hours of oral, vaginal, or anal sex is really the most exciting STI interventions since human papillomavirus (HPV) vaccine. This protocol

[4] https://www.cdc.gov/mmwr/volumes/72/rr/pdfs/rr7204a1-H.pdf
[5] Data submitted by 26 EHE-Funded STD clinics for the reporting period of July 2021 – June 2022, and 25 STD clinics for the reporting period of July – December 2022: https://www.grants.gov/web/grants/view-opportunity.html?oppId=349237
[6] https://www.cdc.gov/std/dstdp/dcl/cdc-finalizes-new-sti-research-consortium.htm
[7] https://www.cdc.gov/std/treatment/guidelines-for-doxycycline.htm

decreased gonorrhea, chlamydia, and syphilis by about two-thirds in multiple studies. The studies were successful in Gay, bisexual, and other men who have sex with men (MSM) and transgender women. Therefore, the strength of that recommendation and quality of evidence recommendations are A1.

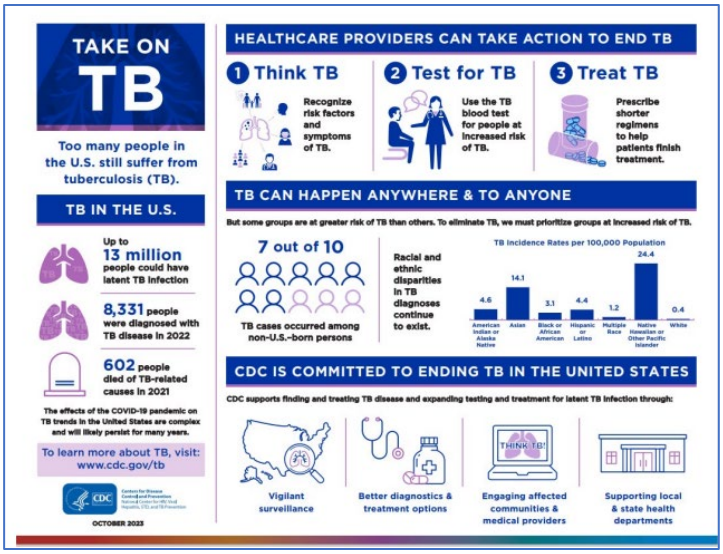
DHP's 2023 prevention priorities include better weaving health equity approaches into the entire HIV prevention portfolio, including by engaging partners and people with lived experience to help identify and develop strategies to effectively overcome the systemic barriers facing the communities we serve, which include racism, homophobia, transphobia and other stigmas that exacerbate health disparities. DHPs will focus on adopting holistic, whole person care approaches and strengthening collaborations that place HIV prevention and treatment in the context of other diseases; these approaches and collaborations can help broaden our reach among key populations and create efficiencies in delivering integrated care for multiple health conditions. Holistic, coordinated care is essential for addressing overlapping epidemics, like HIV, STIs, and substance use. CDC is committed to providing or connecting a person to all the services that meet their needs wherever they seek care. Focus on models of care improve efficiency and reduce stigma by supporting jurisdictions to develop and provide integrated, status neutral approaches to HIV care, which recognize the shared needs of people with HIV and those seeking prevention services. Deepening and broadening our engagement with communities and people with lived experiences whose perspectives are needed to tailor solutions and increase the effectiveness of prevention and treatment efforts at the local level. Data were published earlier in 2023 showing that there was a 12% reduction in HIV incidence from 2017-2021, the highest level of people ever (87%) knowing their HIV status, a 13% increase in PrEP coverage in 2017 to 30% in 2022, and an increase in viral suppression from 63% in 2017 to 66% in 2021. In addition, the US met the goal of eliminating perinatal transmission in 2018.

DTBE Director's Update

Philip LoBue, MD, FACP, FCCP
Director, Division of Tuberculosis Elimination
National Center for HIV, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control and Prevention

Dr. LoBue updated ACET on the Fiscal Year (FY) 2024 budget; release of the 2022 final surveillance report; TBTC, Tuberculosis Epidemiologic Studies Consortium (TBESC); the *Think. Test. Treat TB* campaign; and laboratory activities. In November, a continuing resolution was passed that will fund CDC through February 2, 2024. The continuing resolution maintains funding at the FY 2023 levels and pushes back the deadline to pass all 12 appropriations bills to April 30, 2024 before a 1% sequester would take effect, meaning that the budget would be reduced by 1%. This is all up in the air depending upon what Congress and the President decide to do. Therefore, DTBE is still operating with a good deal of uncertainty.

With regard to the final 2022 US TB surveillance report, *Reported Tuberculosis in the United States, 2022* was released exclusively online on November 15, 2022. In terms of key highlights, the reported number of TB cases in the US increased from 7,870 TB cases in 2021 to 8,331 TB cases in 2022—a 5.9% increase. National TB incidence rate increased from 2.4 cases per 100,000 persons in 2021 to 2.5 cases per 100,000 persons in 2022. A total of 8 states reported incidence rates higher than the national incidence rate. A slide set and this infographic were created to highlight findings from the report:



Turning to the TBTC update, Study 35 is a Phase 1/2 open-label, single arm, exposure-controlled study to determine the appropriate dosing of a novel water-dispersible, child-friendly formulation of rifapentine with isoniazid in children 0—12 years of age. This trial also aims to assess the safety of this formulation in HIV-infected and HIV-uninfected children. A Data Safety Monitoring Board (DSMB) review was completed successfully in November 2023. The trial reached its final interim analysis, not exceeding pharmacokinetic and safety targets. Qualitative findings were presented at the Union Conference in Paris in November 2023. Since this slide was created, this trial completed full enrollment in the various phases of the study.

TBTC Study 37, Assessment of the Safety, Tolerability, and Effectiveness of Rifapentine given Daily for Latent Tuberculosis Infection (LTBI) (ASTERoiD), is an open-label, Phase 3 randomized controlled trial (RCT) that compares the safety and effectiveness of a 6-week regimen of daily rifapentine against the current standard of 12 to 16 weeks of rifamycin-based treatment for LTBI. A total of 14 sites are enrolling participants thus far, with 455 participants enrolled as of November 15, 2023. Unfortunately, this study was paused for a period of time during COVID. The good news is that the study is now onboarding 8 medium- and high-incidence sites to open for enrollment during the first and second quarters of 2024. An additional 3 domestic sites are being onboarded to open for enrollment during the first and second quarters of 2024. Preparation is underway for the first interim analysis, which is anticipated in the first quarter of 2024.

TBTC Study 38, Combination Regimens for Shortening Tuberculosis Treatment (CRUSH-TB), compares the effectiveness and safety of a new 4-month bedaquiline, moxifloxacin, and pyrazinamide-based (+ rifabutin or + delamanid) regimens to the standard of care 6-month regimen among patients with drug-susceptible pulmonary TB disease. This trial aims to enroll at least 288 participants over the next year. It uses an adaptive design that allows addition of other study arms to the trial to assess new TB treatment regimens. The first 2 sites opened at the end of November 2023, and the first 2 participants were enrolled in Uganda. Since that time, at least 6 people have been enrolled and at least 2 sites are up. This study is moving along nicely, with confidence that it will be possible to achieve the goal of enrolling 288 participants over the next year.

Regarding the TBESC update, this is a single large project as opposed to multiple studies. The TBESC-III objectives are to: 1) identify primary care settings that serve non-US–born persons at elevated risk for TB infection; 2) collect retrospective and prospective electronic medical record data; 3) design and implement primary-care–based interventions to improve performance measures across the LTBI care cascade; 4) monitor and evaluate intervention performance over time to identify efficient and effective strategies to prevent TB disease; and 5) estimate the potential health and economic impacts of TBESC-III clinical care-based interventions. In terms of TBESC-III progress, baseline data collection has been closed out and final baseline and interim intervention cascades of care were generated along with dashboards to monitor intervention impacts. As of November 2023, the accepted dataset contains data on over 650,000 patients and 17,000,000 unique records. This is orders of magnitude of anything that has been collected before. Sites have implemented interventions designed to increase testing and treatment of LTBI following the latest CDC guidelines. Data collection on the effects of the interventions is ongoing.

The *Think. Test. Treat TB.* communications campaign was expanded, with a focus on raising latent TB infection awareness among healthcare providers (HCP). The campaign was distributed and amplified across digital channels, consistently exceeding industry benchmarks and the 2022 metrics among HCP. This yielded an estimated 8.79 million impressions (a 532% increase from 2022), over 18,000 clicks (a 921% increase from 2022), an average click-through rate of 0.21% (a 62% increase from 2022), and an average engagement rate of over 3%. Project staff engaged 7 new partners with professional medical and public health organizations and conducted an outcome evaluation that includes finalizing and sharing a written report of findings and recommendations with health department partners who implemented the campaign. The provider page has information about TB risk factors, latent TB testing and treatment, and resources for providers.

Moving to the laboratory update, some exciting new services are being offered. First, a new Clinical Laboratory Improvement Amendments of 1988 (CLIA)-compliant targeted next generation sequencing (tNGS) assay was implemented. This new assay allows for detection of resistance to new and repurposed antituberculosis drugs in addition to the previously tested first- and second-line drugs and improves the ability to detect emerging resistance. Second, rapid fluoroquinolone testing was implemented to support public health submitters during an isoniazid drug shortage and to offer testing for the 4-month rifapentine/moxifloxacin regimen for drug-susceptible TB. The Reference Laboratory received a total of 1,211 patient samples in FY 2023, of which 980 were tested by a rapid molecular detection of drug resistance method and 1,036 by growth-based drug-susceptibility testing (DST) methods.

ACET Discussion (RADM Mermin & Dr. LoBue)

Dr. Loeffler inquired about the potential for continued expansion of the *Think. Test. Treat TB.* communications campaign. In addition, she asked about the uptick in the incidence of HIV and congenital syphilis.

Dr. LoBue pointed out that what happens in the future in terms of expansion will depend upon the appropriation. This will be problematic if the 1% sequestration occurs. Even if continued expansion is not possible, the team has produced a large number of products that have been downloaded across the country well beyond the sites that are participating in this program. A lot has been accomplished thus far and that legacy will continue regardless of the funding for the campaign. Materials can be downloaded and customized for programming.

RADM Mermin clarified that the uptick in the incidence of HIV has not been observed. Some states have had increases and some have had decreases, and there is variance by jurisdiction as well. Incidence for HIV is modeled because the estimated median time between infection and diagnosis is 3 years. Because HIV is a chronic infection when diagnosed, CD4 counts at the time of diagnosis and mathematical modeling are used to estimate when the infection occurred. That also relies on diagnoses. Due to the disruption in diagnoses from COVID-19, the modeling results should be taken with more caution during that timeframe. Everyone is eager to see what the situation will be for 2023. Thus far, it appears that the model has a fairly steady decrease. There is a congenital syphilis crisis, which has been a big issue. The Assistant Secretary for Health (ASH) established the National Syphilis and Congenital Syphilis Syndemic (NSCSS) Federal Task Force, which is pulling together various agencies to try to respond rapidly and more robustly than has been possible over the past 2 years. The increase has been occurring for several years. Syphilis has now become a self-sustaining epidemic among the heterosexual population in a way that it had not been for a few years. That means that women are now more susceptible to getting infected and rates are higher in women of reproductive age. That has resulted in an increase in the rates of perinatal transmission of syphilis. Assessment of missed opportunities for preventing congenital syphilis shows that about a third of the cases are among those who have had no prenatal care, which probably would be less likely for someone with HIV. About two-thirds of people have experienced some sort of gap in that process. Some of that may be due to social or economic determinants of health and/or that more could be done at the healthcare setting level. While not insurmountable, the challenge is great.

Dr. Tomkins asked whether the partnerships mentioned with medical and professional organizations are diverse in participation.

Dr. LoBue indicated that they have definitely been trying to ensure diversity. The TB Elimination Alliance (TEA) has been focused on engaging diverse partners who work with people who are at risk for TB. It is known that Asian Americans, Hispanic Americans, and African Americans have had a disproportionately high incidence of TB.

Ms. Steward-East asked about how medical providers would access the website and advertisement. For instance, is the information being pushed or is there a way for HCP to access pediatric information?

Dr. LoBue indicated that there is a *Think. Test. Treat TB*. Campaign website where medical providers can obtain information, which is available through the internet. There also is a focused part of the campaign specifically to work with the partner sites CDC has been working with for specific outreach in those areas. The campaign initially focused on the community and was not a national campaign. The early work was primarily with Seattle and Los Angeles and the partners they work within their communities to reach community clinics and providers who deal with populations to get them to expand LTBI testing and treatment. There are 2 different aspects. One is the general information that anyone can access on the website and the other is the specific campaign working in those sites.

Dr. Deluca indicated that they were able to do paid advertising through a variety of channels to try to reach HCP, but that piece has stopped because there is no additional funding. However, they are continuing to work with medical associations and other partners with whom relationships have been established. All of the materials are available free of charge on the CDC ordering system. Over 60,000 materials have been distributed across the country. While proactive advertising is no longer being done, there is still great demand. He provided the link for the *Think. Test. Treat TB*. website for providers: https://www.cdc.gov/thinktesttreattb/healthcare-

providers.html. Specific images can be downloaded and shared as part of the Partners Toolkit, which can be located by scrolling to the end of the page once accessed: https://www.cdc.gov/thinktesttreattb/partnerToolkit.html#Sample-SocialMedia.

Dr. Narita asked whether in addition to awareness of HIV status there also is an interest in awareness of TB infection status. In the past, mention was made that a decision to test is a decision to treat. Perhaps awareness needs to be elevated.

Dr. LoBue said that, at least among clinicians, there may be a hesitancy to test due to lack of being up-to-date on current treatments or even not having good knowledge about toxicity and how to prevent it. There is the bigger challenge of getting this on clinicians' radar in addition to everything else they have to do, especially in the primary care setting, which TBESC is working on ways to build this into the system such that it is automatic. Thought must be given to the context in which clinicians are working. If someone is in a risk group for TB, testing should be part of their routine primary care. Getting testing and treatment added at the system level is related largely to the measures upon which they are graded. This does not exist for TB and is extremely hard to add, given that there is not much appetite for doing so.

RADM Mermin added that essentially, the idea is to make the healthy choice an easy choice, even for clinicians, so that ultimately it is automatic. Everyone in America does not need to be screened for LTBI, but there are populations for whom there is an increased chance of people having undiagnosed LTBI. Once the test is done, it gives the clinician time to work with the patient to help them be ready for treatment. That takes time because there are a variety of steps along the pathway toward treatment that are not as easy as for some other infections, such as the need for a chest x-ray. A better and more specific test would allow for a reduction of the overall number of people who need to be treated, which also could concentrate efforts. The intervention of a simpler and safer treatment also would be beneficial, given that it is a time-consuming treatment for LTBI and only about 5% to 10% of people will benefit and the others will not. However, that number needed to treat (NNT) is not awful. For example, many more mammograms must be performed to identify malignancy, but it has become routine in the healthcare setting to do those routine exams. Continuing down this path is one of the benefits of the TBESC.

Dr. Ahmed asked whether pediatric and family medicine practices have been part of the TBESC from the outset and inquired as to what the plan is for sustainability once this is implemented. Even if it is part of the electronic medical record (EMR), education has to be provided.

Dr. LoBue responded that the practices included are broad. For example, Kaiser includes the whole Kaiser system and broad testing is encouraged across the population. While he did not have specifics about each site and the number of pediatric patients involved readily available, he can find out. Sustainability is a major issue. First, a determination must be made about what to maintain. Until recently, the focus has been almost completely on the health department to do this in terms of finding LTBI related to contact tracing or setting up a screening program in the health department. For many reasons, that is not a feasible approach to this. The focus needs to shift to community and primary care. Initial interactions with professional societies and others raised issues about this being a lot of work amongst the many other things HCP must do. For that reason, before going back to them to push, it is better to have a proof of principle to be able to say what is needed, that it will not be easy, that it may require some resources, but it can be done. The 4 sites and areas are very different. The first pilot was conducted in one small place and then was expanded to multiple sites to get a broader perspective in different parts of the country. This is a major lift and they will have to see what happens. Going forward, the hope is

that they will be able to say that it will need support but it has been tried in multiple places and found that certain things appear to work in terms of LTBI cascading. Uptake will depend upon the leadership in facilities. Some places have champions who recognize that this is an issue for the people who they serve. The studies will help because it will be possible to offer more specific guidance about what seems to work. This is a very big country with many facilities, it will be a struggle moving forward without champions.

Mr. Watts observed that the TBESC looked very promising, given that they are based in communities and primary care practices. He requested additional information about prospective EMR data.

Dr. LoBue explained that this means that at a certain point going forward, they did not have these interventions and baseline information was collected about what goes on in terms of their normal practices. There is some retrospective information, but prospective information is collected at the baseline day. At a certain point when interventions are implemented, additional prospective data will be collected beyond those interventions to determine what effect those interventions have compared to baseline normal practice performance related to the various steps in the LTBI care cascade.

Dr. Thanassi proposed a paradigm shift as opposed to primary care physicians who, as pointed out, are so difficult to reach and change in terms of the way they practice primary and community care. There are 150 million employed Americans and thousands of occupational health medical doctors (MDs) who are experts in training and testing employees when they are hired. Not all occupations test for TB. The focus is on healthcare workers (HCW), but she has started to think that there could be a focus on TB testing in other high-risk occupations and allowing occupational health MDs, who are protecting the workforce, to test and treat people at the sites of their workforce and at the time of hire. This could make a big impact on TB elimination if occupational health professionals are engaged, as well as the primary care professionals. In addition, corporations are invested in keeping their workforce safe.

Dr. LoBue said this would be great if they could be reached but lamented that even in various TB outbreaks, corporations will not implement this. Therefore, he is not as optimistic about corporations and employers getting behind this—particularly given the cost involved.

Dr. Stout thought it seemed pretty clear that the future of screening for LTBI is probably very much tied to large EMRs and the ability to leverage them, such as TBESC is examining, and probably artificial intelligence (AI). The key data element on which that rests is country of birth, which often is not routinely captured in the clinical setting. He expressed an interest in hearing what the current TBESC has in setting in which that variable was not captured previously and interventions to obtain those data. Obviously, there are sociopolitical ramifications to capturing birthplace.

Dr. LoBue said he would have to review some of the modeling papers because he believes these are addressed. He thinks this is very population-specific. Foreign-born and non-US-born are very country- and risk factor-dependent. This has been a sticky point. The capture of that critical risk factor is basically a surrogate for likely exposure to TB in the past. While he did not know the specifics for each site offhand, in this case, the 2 options that have been considered thus far are places that are willing to add/capture birthplace or using some other type of surrogates. The variable that is assumed to be helpful, though not perfect, is primary language spoken. They will have to wait to see what comes out of the sites with this.

Dr. Chen said she felt like they need to keep echoing that *Think. Test. Treat TB.* is a great campaign and the best practices and lessons learned will come out of this. Follow-through must be emphasized, which is the case with all studies. There is a lot of great data in this space, but getting that into practice has been the rate-limiting step globally. She asked how ACET members could help the agency with that. Many of the liaisons and *ex officio* represent professional societies and advocacy groups, so consideration should be given to how to help members mobilize to help move this along. Finding better regimens, new diagnostics, and/or a vaccine is tough. The answer is to push. A lot of this boils down to insurance company payments and incentives for groups to jump in, such as occupational health professionals as Dr. Thanassi proposed. That could be an easy venue, but work must be done on the hard element of incentives. Getting something on the prevention list or grading list is difficult. She recognized that the agency is working on this, but she asked RADM Mermin and Dr. LoBue how to turn the dial. She stressed that ACET members would work on this and they now have the tools and evidence that CDC has funded, but follow-through is needed.

RADM Mermin pointed out that a fair amount of this pertains to putting resources where the epidemic is and recognizing that everywhere is not equal and populations are not equal. Some community health centers know that TB is a problem because they have had active cases and if they screened their population, they probably would get 20% positive for LTBI. While those community centers would have high outcomes for screening, other places would not be recommended to engage in routine LTBI screening for everyone or where it would be a second or third step in the foci. It is important to find the places where the biggest difference can be made, because the community and clinicians will be more sensitive to it and will care more about it. He loved the idea about systems that could be put into place. Kaiser, the VA, most state prisons, and the federal Bureau of Prisons (BOP) have tackled TB pretty well. That was not always the case. There is the idea that a policy change or other efforts would result in fruitful outcomes in some of the community centers or healthcare systems. Technological solutions do matter. A 4-month regimen is better than a 9-month regimen. Shrinking the treatment time to be more palatable will make it easier for people to adopt treatment, along with the communication campaigns. Many people still have the sense that LTBI treatment is toxic, which is a leftover from 9 months of isoniazid (INH). It will be necessary to change the communication ethos to emphasize that the benefits of new treatments outweigh the risks. That will happen over time, but there is a strange contradiction occurring in that the new number of cases of TB is slowly decreasing every year at the same time there are efforts to expand LTBI screening, which makes more people worried. This is a conflict almost always with TB in the US. Overseas is a different story where people are much more concerned for a variety of reasons. A lot of the information that the TBESC is uncovering could help answer some of the questions and concerns of clinicians, societies, and healthcare centers.

Dr. Chen suggested targeted grants or funding for which groups could apply in close partnership with their local TB programs, because local programs are key to making things happen. That is done globally now. All of the funds are going to local programs to make sure this happens. The tools are available. There are not enough funds to give to everyone, but not everyone needs them. For instance, perhaps occupational health organizations could apply for funding as long as they could demonstrate partnerships with local TB groups.

Dr. LoBue agreed that this has to be a partnership between a local TB program and whatever community clinical or facility, especially at the start when they need their “hand held” by people who have the expertise in how to do this. The TB Elimination Alliance mini-grants are focused on these types of efforts. The problem is that there is a lack of large funds that could be spread widely across the US. This is not unique to TB. Hepatitis C treatment was terrible when he was

going through medical training. It involved intravenous (IV) therapy that made people sick and did not work. Now there is a great short-course all oral therapy such that one would think everyone is getting treated and cured, but this is not the case.

Dr. Chen stressed that it is sad and should not be this way that TB and hepatitis both have curable treatments and they should not be where they are. That can be changed, but they are a small voice. ACET knows that CDC would do what they could if they had the funds, but all of the members need to know how to help with visibility and awareness. The Test to Treat campaign has done that in a targeted way.

RADM Mermin said he very much appreciated the perspective. They would not be there if they had succeeded. Public health demands a problem to solve. He thinks they can keep learning from examples because everything is not all going to be equally effective or equally efficient. Screening and changing practice requires a champion, regardless of the disease. Sometimes champions are free because there is an organization in a community that cares that is willing to help do this. Having success in the local environment by pulling in the community, implementing something routinely, and showing that can help expand to the broader local environment (e.g., county or state).

Dr. LoBue added that the program must be focused on the entire cascade. They have seen examples of people doing a lot of testing but not doing a good job of treatment. He recalled someone saying to him before the interferon-γ release assay (IGRA) that the tuberculin skin test is not therapeutic.

Dr. Belknap noted that regarding the work with the FDA and downgrading of testing, one of the things the ACET discussed previously is the need for access in the US to all of the best available tests. He wondered whether there were any thoughts on opportunities for ways to move forward in terms of access to various polymerase chain reaction (PCR) platforms that are being used globally but to which the US does not have access.

Dr. LoBue said he thought most TB tests are Class 2, so the bigger problem is more about collecting adequate data for the FDA to approve the test. In addition, even when not extraordinarily costly, manufacturers do not see the market for these tests in the US. This is true even with some tests that already are approved, such as GeneXpert®. Even the older version, though not optimal, still works. However, it is unclear whether the US will have access to a test that already has been approved due to the market issue.

RADM Mermin added that one option is to care about the platform. For example, they are working with GeneXpert® for point-of-care (POC) hepatitis C. Having a machine available that just needs the cartridge could be easier. Facilities would not be required to buy the machine. That already is being done by another aspect of the healthcare system. The other thing would be that while there are only 8,333 annual cases of TB, there probably are over 8 million cases of LTBI. For diagnostic purposes, there probably would be a market for an improved LTBI screen because that would require testing probably tens of millions of people to find those cases. That becomes more profitable, so thinking about that could help.

Dr. Belknap pointed out that the NNT for active TB to diagnose that 8,000+ is a much higher number, which is left out at times. Using the default, which is a 100+ year old test of an acid-fast bacillus (AFB) smear, use of NAAT has been a recommendation from CDC for a decade plus. Yet, they still are not used fully. This gets back to levers and incentives. What would it take to say this is not a recommendation or option, but NAAT is the test that should be done as part of

the preferred work-up for suspected active TB and also moving beyond sputum because these tests are needed for the work-up and evaluation of extrapulmonary and pediatric TB.

Dr. LoBue agreed that there is the question of whether people will use the test even if it is available. Unfortunately, if 10 people are suspected, it would still be only 80,000 tests. That will not entice a manufacturer. It has to be in the millions, so it would still be problematic in terms of getting something to market. That is why some places have adopted NAAT and others have not despite the recommendation having been out for a long time. Usually, it comes down to one of two things. One is providers who are not knowledgeable of the recommendations and the second is access. In places that do not see a lot of TB, the diagnostic laboratories are not likely to invest in those.

Dr. Belknap emphasized that anything that can be done to make it easier and take it out of the clinician's realm of decision-making, as with testing for TB infection, is the key. People are being missed and this is causing preventable deaths because people do not think of it.

RADM Mermin said he thought AI probably could help with this. The other concept in terms of making it happen without thought is the idea of routine screening for infectious disease. When someone presents to the hospital right now, BIOFIRE® could be used to determine whether they have certain infections. Tests that use a respiratory sample should automatically be screening for nucleic acid for TB so that this is assessed even for the clinician whose mind it never crossed that the patient could have TB. While multiplex screening processes need to be expanded, this is not cheap, but taking it out of the hands of doctors could be one of the solutions.

Dr. Belknap said he thinks it is great that the laboratory has integrated rapid testing for fluoroquinolones. There is seemingly an increasing need across the board to know about that because of INH resistance. If they want and expect people to move toward using the 4-month regimen, this information is needed. He wondered what it would take to make fluroquinolones part of first-line testing.

Dr. LoBue said he thought they would need to talk to their laboratory personnel about writing the guidelines and having laboratory testing for TB. Not being a laboratorian, he was not sure how difficult it would be for local county health laboratories to add this and do it in a way that is feasible and proficient such that the results would be reliable.

Dr. Belknap commented that it was amazing to hear about providing care and the work of the TBTC; TBESC; and the *Think. Test. Treat.* Campaign work. He recognized that DTBE has done amazing things to advance TB despite funding having been flat or effectively cut by 40%. He wondered and worries about what the tipping point at which these things cannot continue to be done. It makes him uncomfortable to compare TB to other under-funded public health diseases, and he does not think that is the right mindset. In some jurisdictions, the only funding is what is provided by the DTBE. Some states and local counties provide some funding. He knows how much gets done with very little and how thin things are stretched, but there will be a point at which they cannot stretch any further, which concerns him. He does not think that Dr. LoBue can continue to cut an ever-shrinking pie in more creative ways to support all of the efforts that impressively have been done.

RADM Mermin said that they agree and whenever they conduct site visits, they find that health departments are feeling the same squeeze. COVID was an interesting time during which resources were available in a way that have not occurred in a long time. Now there are budget cuts almost everywhere, which is following the severe reductions in both budgets and personnel

that were experienced 8 to 10 years ago . The entire agency is feeling it along with everyone else in public and even clinical medicine. The job is tough for anyone managing their health department TB program, as well as for DTBE, in terms of getting the job done in a way that makes the biggest difference. There is always an interest in expressing how important areas of public health deserve resources.

Dr. LoBue added that he appreciated and dreaded Dr. Belknap's point because it is something he thinks about all of the time. If things continue the way they are, they will reach a point where the decision will have to be made to stop one thing to preserve everything else. That will be very hard because much of DTBE's work is exciting, innovative, and the staff loves doing the work. That will be a loss for them, but the reality and driving factor are that they do it because no one else is doing it. DTBE is not duplicating other people's work, so when they stop whatever they have to stop, it probably is not going to get done.

Dr. Loeffler shared this link https://www.cdc.gov/thinktesttreattb/index.html and reminded everyone that just moving the needle of medical homes to be positively inclined to LTBI treatment is good. Even if folks do not have time to incorporate the care cascade, a positive inclination during conversations with patients is good. In terms of next steps, it is important to address re-exposure, poor adherence of prior LTBI treatment, drug resistance, immunologic tests that reflect current infection versus treated infection versus innate/acquired immunity. There are many opportunities.

Dr. Benjamin asked how to deal with inconsistent supply/shortage of TB drugs once someone is screened and found infected.

Dr. Ahmed asked whether for *Think.Test.Treat.* ob-gyn organizations are engaged. This is a captive audience, at least those who show up for prenatal care, and they can complete treatment in the time they are engaged in medical follow-up.

Dr. Ray emphasized the need to be able to identify the people who are most likely to develop disease.

Dr. Deluca (CDC) shared that DTBE's Communications, Education, and Behavioral Studies Branch (CEBSB) conducts consistent survey research with a national representative sample of HCP. He also suggested reviewing the most recent *MMWR* on the latest survey results at the following link: https://www.cdc.gov/mmwr/volumes/72/wr/ mm7244a2.htm?s_cid=mm7244a2_w&ACSTrackingID=USCDCNPIN_2014-DM116621&ACSTrackingLabel=New%20CDC%20Analysis%20of%20U.S.%20Health%20Care%20Providers%E2%80%99%20TB%20Practices&deliveryName=USCDCNPIN_2014-DM116621. Also, DTBE's key findings were that: 1) among 3,647 health care providers surveyed, approximately one half (53%) reported routinely testing non–US-born patients for TB infection; 2) more than one half (59%) reported prescribing any treatment for LTBI, but only 33% reported prescribing the preferred short-course regimens. In addition, 41% referred patients to a health department for LTBI infection treatment; and 3) further efforts are needed to address barriers for HCP to test for and treat LTBI in persons at risk. Dr. Deluca indicated that he would be happy to present on this national research during a future ACET meeting. NNT reference: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6553715/

Dr. Loeffler pointed out that budget cuts lead to a vicious cycle of burnout and loss of the most knowledgeable and efficient staff. It is harder to recruit and there is a long on-boarding process.

Dr. Chen said she thought the pulse across many TB health programs is that the tipping point has been reached, as mentioned by Dr. Belknap. Programs are making tough decisions, prioritizing efforts, and consequentially needing to drop other activities.

Current ACET Recommendations Update

Philip LoBue, MD, FACP, FCCP
Director, Division of Tuberculosis Elimination
National Center for HIV, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control and Prevention

Dr. LoBue focused on ACET recommendations from December 2022 through June 2023. During the June 2023 meeting, further discussion on the TB workforce recommendation included pursuing working with an outside organization, such as the Council of State and Territorial Epidemiologists (CSTE), to conduct an assessment; and incorporation of an assessment as part of the next CDC TB prevention and control cooperative agreement. These recommendations have been added to the table below:

Topic	Recommendation	Actions
Topic: TB Workforce Item #: 2022-4 Date: 12/14/2022	ACET recommends that CDC define the key components of an effective public health TB workforce in the US. ACET recommends CDC: 1) Develop a standard process for evaluation and periodic assessment of the US PH TB workforce 2) Consider a cost analysis to sustain the current TB workforce to achieve TB elimination 3) Pursue working with an outside organization, such as the Council of State and Territorial Epidemiologists (CSTE), to conduct an assessment 4) Incorporate an assessment as part of the next CDC TB prevention and control cooperative agreement	• With regard to the 3rd recommendation pertaining to conducting an assessment: – Working with NTCA, CDC identified a participant for the upcoming CSTE Epidemiology Capacity Assessment (ECA) Workgroup, which will develop and pilot the survey tool • In terms of the 4th recommendation regarding the cooperative agreement: – Details of the cooperative agreement cannot be made public until the official funding opportunity announcement in 2024 – Any information about TB workforce assessment in the cooperative agreement will be presented to ACET during the first meeting after the official announcement
Topic: DMI/PHDS Item #: 2023-4 Date: 6/21/23	ACET recommends CDC to work with partners to identify TB data modernization priorities focusing on interoperability between data sources and automating collection and sharing of high-quality data.	• Roque Miramontes presented on current efforts in this area during this meeting for ACET's consideration
Topic: DMI/PHDS Item #: 2023-5 Date: 6/21/23	ACET recommends CDC explore a common dataset across NCHHSTP and the specific variables that are high value for TB care that could be shared across the Center.	• Michelle Van Handle presented on current efforts in this area during this meeting for ACET's consideration

ACET Discussion

No questions or comments were raised.

Data Modernization Initiative (DMI): DTBE Priorities and Activities

CAPT Roque Miramontes, PA-C, MPH
Division of Tuberculosis Elimination
National Center for HIV, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control and Prevention

CAPT Miramontes provided an update that included information about the DMI background and direction, DTBE's data management ecosystem and processes, current DTBE DMI projects and status, challenges, and future direction. He acknowledged that the DTBE program is just one program at CDC and that there are many programs within CDC that all are working on DMI. In addition to the staff within DTBE and NCHHSTP, there are staff within other agency programs, the Office of the Chief Information Officer (OCIO), and other state and local partners. The DMI is a 5-priority initiative at CDC that has the potential to touch every electronic system that comes in contact with an agency system. At first glance, it looks like a system of tools, which it is. This system helps select, store, analyze, and share data. It also is designed to provide a new way of thinking.

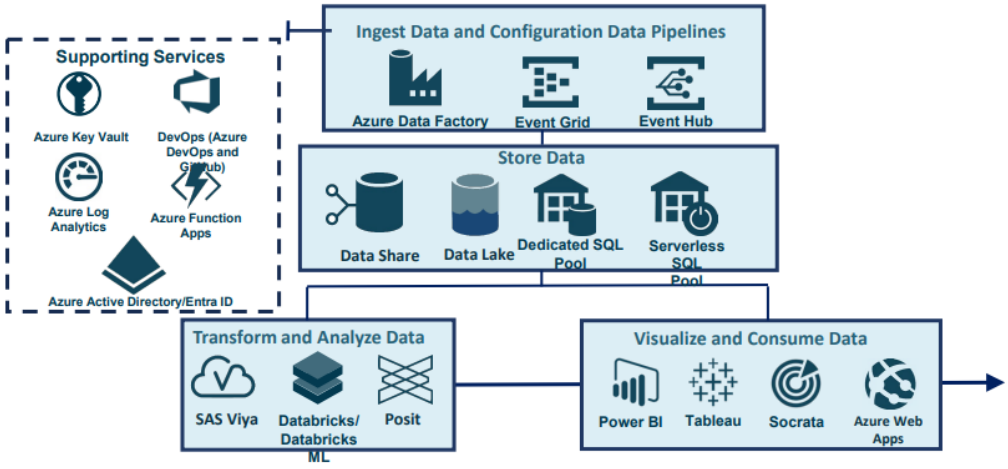
As a result of some of the complex emergencies that have occurred over the past decade, critical gaps were identified in public health capacity and infrastructure. Critical partners such as the Council of State and Territorial Epidemiologists (CSTE), the Association of Public Health Laboratories (APHL), the Healthcare Information and Management Systems Society (HIMMS), the Association of State and Territorial Health Officials (ASTHO), the National Association of County and City Health Officials (NACCO), and many others began sounding the alarm to Congress that were essentially for making the case for a major sustained investment in data modernization. One of the major concerns was that siloed systems complicated and slowed reporting. One anecdote CAPT Miramontes shared was that when he visited a city/county health department a few years back, he watched an epidemiologist enter data into 3 systems—one for the state, one for CDC, and one they used for case management. Funding in FY2020 amounted to $50 million in appropriations and $500 million in Coronavirus Aid, Relief, and Economic Security Act (CARES Act) funding. $50 million in FY2021; $100 million in FY2022; and $175 million in FY2023 also came from appropriations. This was a new initiative, so a multi-year plan was put in place that required staff, new tools, and partnerships.

DMI is a unified and comprehensive effort to modernize core data and surveillance capabilities across the federal and state public health landscape. The strategy lays out 5 key priorities which are to: 1) build the right foundation and strengthen and unify critical infrastructure for a response-ready public health ecosystem; 2) accelerate data into action to improve decision-making and protect health; 3) develop a state-of-the-art workforce; 4) support and extend partnerships; and 5) manage change and governance to support new ways of thinking and working.

CAPT Miramontes focused on 2 projects that DTBE believes fall under the priority of building the right foundation. The first used Enterprise Data Analytics and Visualization Platform (EDAV) tools that are available enterprise-wide and are intended to improve and modernize data capabilities at CDC. DTBE's data management group took advantage of 2 of the tools recently made available in the EDAV to work out a way to modernize the National Tuberculosis Surveillance System

(NTSS) reports. DTBE created NTSS reports a few years ago for all TB reporting partners that allowed them to see exactly what DTBE sees when their data arrive. EDAV is cloud-based in its data management and processing ecosystem. Keeping data in the cloud expands the ability to store data effectively, which is a benefit since the electronic data go back to 1993. It also is helpful for resource-intensive data and analysis tools that continue to come online. EDAV users can integrate, transform, analyze, visualize, and share data with both internal and external audiences. EDAV includes secure data storage and transformation and analysis tools such as Power BI, Tableau, Socrata, and Azure Web Apps . EDAV allows DTBE to use its normal Secure Access Management Services (SAMS) authentication methods to provide Power BI reports and visuals to external partners in TB programs.

The EDAV platform currently has 11 services that brings together powerful data management and processing tools to help users more efficiently accomplish discrete tasks within their technical workflows. Although this is a basic architectural flow, this diagram illustrates these services:



SAS Viya is only available to DTBE at this time in the EDAV platform. DTBE is just now getting an opportunity to work with this product that is described as a high-performing AI and analytics product or platform.

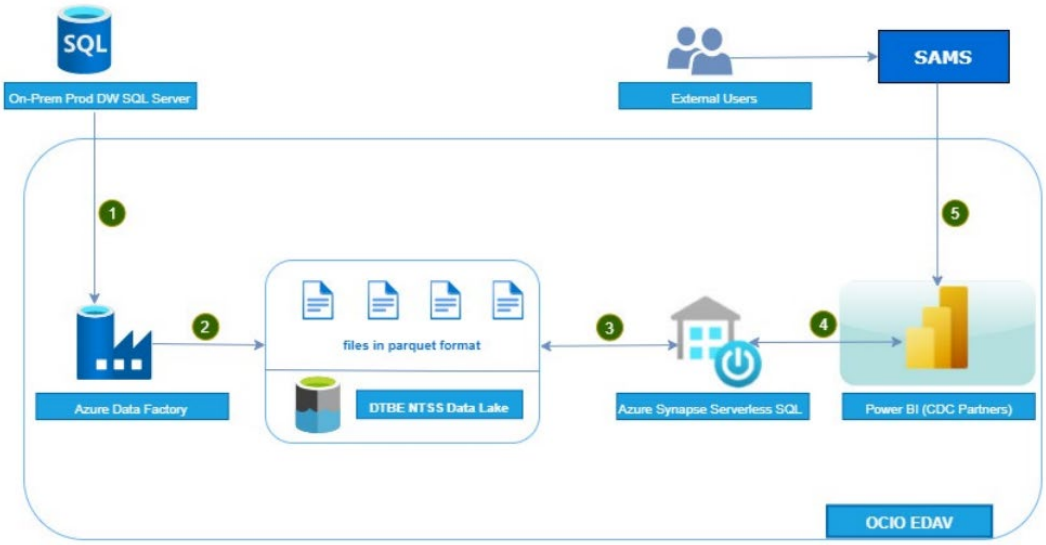
In terms of DTBE's current surveillance and reporting system, TB is among the early diseases reported at the state level. There are data that go back to the late 1880s in at least one state. At the national level, DTBE has been collecting TB data with a consistently applied definition since 1952, although they have some data that go back to the 1930s. DTBE is among the first CDC programs to implement the National Notifiable Disease Surveillance System (NEDSS). With NEDSS, DTBE's data management and surveillance group is able to receive electronic data using tools such as Health Level Seven (HL7) and the Public Health Information Network (PHIN), which are still used today. Of course, nothing in this realm is possible without strong partnerships with states. Together, DTBE and internal and external partners built and tested much of the current ecosystem that is applied each year to national reporting.

There are areas for which improvements can be made, which relates to where DTBE's projects touch on the second DMI priority to accelerate data into action to improve decision-making and protect health. DTBE understands the need for state and local partners to have rapid access to actionable data with the least amount of reporting redundancies. To do this, DTBE must integrate

the data into its current system, do any transformation of the data needed to ensure that it is uniform, analyze it, and make it available for visualization by partners.

To provide more details about the projects DTBE is implementing that are using DMI tools, the EDAV / NTSS Reports Tool is a pilot project that is pretty far along using EDAV tools to build out the quality assurance (QA) reports that are currently in the NTSS reports application that DTBE will be displaying for external users in Power BI. The goal is to replace the current NTSS reports application case listing with the addition of Power BI visuals that better inform the national tuberculosis surveillance quality states. Project development has been completed and tested internally and externally among 8 pilot sites. DTBE is using EDAV to provide access to the Power BI portal in SAMS for state users. The tool has the ability to automatically refresh the reports daily from the TB Data Warehouse where DTBE currently stores all surveillance data. DTBE is currently in the process of reviewing feedback from the external pilot and making updates to the reports, along with adding help and documentation for this system. This tool will be available to all partners by the end of the year and was introduced during the December TB Data Users Group call that occurred earlier in the week. The process of giving reports to partners is less complicated with fewer steps than previously, which is a positive. The fewer steps, the fewer components that can break. The plan is to run in parallel to the current system by which NTSS reports are made available; however, it should be possible to retire the older system in 2024.

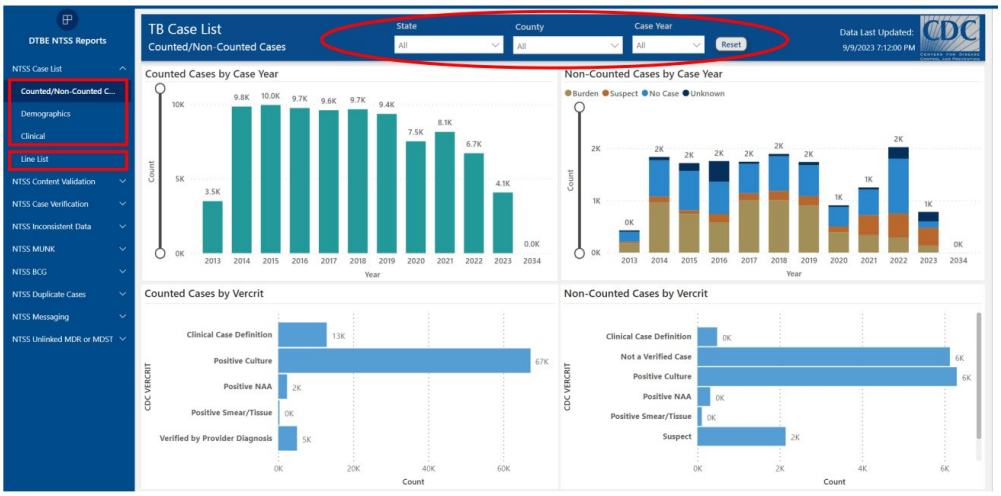
CAPT Miramontes shared this diagram to illustrate what the back-end of the system looks like in terms of data flow:



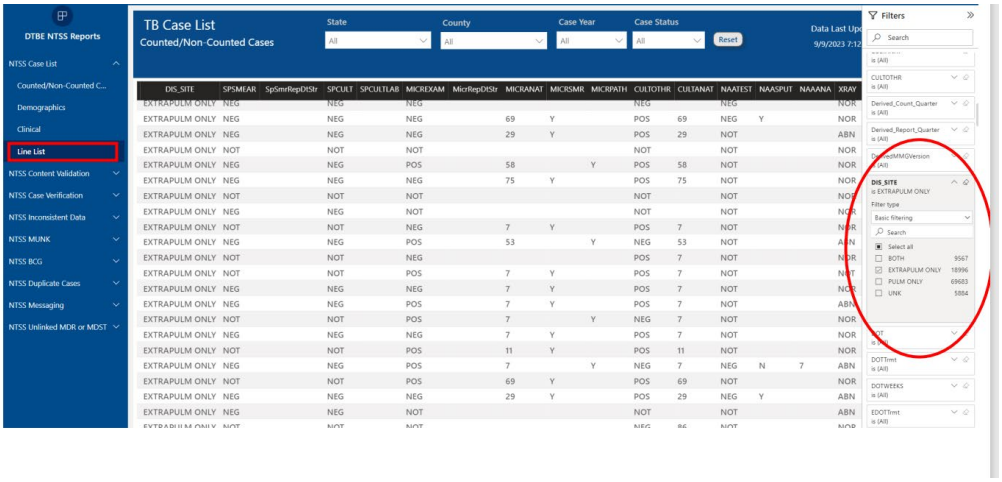
He explained that the process starts by moving data from DTBE on premises servers to the Azure Data Factory in the cloud. The Azure Data Factory is a fully managed serverless data integration service that orchestrates and automates movement and transformation of data. DTBE does not currently host surveillance data reported to them in the cloud, but that is coming. The process that DTBE uses to examine and share the data are already in the cloud. The DTBE NTSS Data Lake is an Azure Data Factory lake storage area that is a secure cloud-based enterprise that is a centralized repository to store large amounts of structure, unstructured, semi-structured data in any format and facilitates big data analytic workloads, which is where DTBE's surveillance data will land. Access to the project folders is restricted to project personnel and is

controlled via Azure Active Directory Groups. Azure sends out serverless SQL that enables DTBE to query files stored in Azure storage. It does not have local storage or ingestion capabilities. CDC partner Power BI enables this tool to share reports and dashboards with internal and external users. SAMS acts as a gateway to allow users to access the Partners Power BI. SAMS access is available to anyone a state gives access to that DTBE then adds as a user. However, users can view only the data from their jurisdiction. The only other needed access for that user is the internet.

These 2 diagrams show what external users will see when they log in with respect to the report design:



This is a dashboard view, but there is a capability to drill down to see additional reports in the query prompt at the top, circled in red. Also in red along the left side is the view that users see in the larger window of the display. This one is displaying cases based on whether they are verified using the verification criteria applied to the system to count cases. DTBE has used this same type of display to monitor case counts internally for the last couple of years, which has been helpful internally and with external partners. There are a number of other queries along the left side as well, including a Line List of cases illustrated below:



This option allows states to see exactly what DTBE sees, which allows for troubleshooting of any reporting issues that arise. This tool allows sorting and filtering by any column provided with just a few simple clicks. Clicking on any column will allow sorting by that variable, either ascending or descending. The panel on the right circled in red allows the user to select the column to filter further for more analysis across the line listed information.

The next project focuses on laboratory data. One of the databases that DTBE houses and maintains for the DTBE Laboratory Branch is the Drug Resistance Research Database. This is where the laboratory team is storing whole genome sequencing (WGS) results data so that they can perform analyses as needed. The actual WGS sequence data is stored elsewhere and is expected to grow quite large with regular imports of new data files. DTBE is exploring EDAV as a possible solution for the future of these data in order to begin moving TB data, including warehouse data, into the Azure platform. Currently, DTBE is testing the EDAV data importing capabilities in order to produce a similar process of file drop-off and uploading into the database. EDAV also offers many analytic options. The next step will be to understand how these tools can better help with the storage and analysis processes.

There is a third project on which DTBE is working, which was introduced during the last ACET meeting. At a high level, EMR data will be mapped by the sites onto the TBESC-III data dictionary. The data will then be submitted to CDC and moved into EDAP where data QA/QC will be performed. Once the submission passes Q/QC, it is called the “Bronze” data. Standardized cleaning rules will then be applied to create the “Silver” dataset. Finally, logic will be used to create analytically derived variables that will result in a “Gold” dataset that can be used for analysis, including generating LTBI care cascades that will allow for comparison of baseline and host intervention results.

In terms of some of the challenges to organizing and prioritizing data management activities, there are a number of challenges to data modernization in general. These include the constant introduction of new software and analysis capabilities. Consideration also must be given to how AI fits into DTBE’s plans, specifically with regard to predictive machine learning (ML) and generative AI, which has been in the news cycle regularly over the last year. There also are the complexities of data harmonization. It is challenging when programs value specific epidemiologic data differently. For instance, TB control programs collect and display data and pay close attention to TB in the 0—5 year age cohort, while the DHP might be more focused on displaying data in those who are ≥15 years of age. There always is a risk to privacy when merging electronic health data (EHR), which can serve as an analysis limitation. The sheer amount of EHR data that are collected and stored are growing exponentially. By some estimates, hospital data alone is expanding by 40% on a compounded annual growth rate—faster than any other sector, including media and financial services. With so much data being created, it is increasingly difficult to decide what to put in front of decision-makers. Finally, standing up all DMI services will take time and flexibility on the part of implementers and their stakeholders.

With regard to future direction, DTBE is in the process of preparing for a competition of the informatics contract that helps devise and update TB data systems. As part of the updated requirement, DTBE is including specific language supporting the modernization of TB data systems and the use of CDC’s EDAV platform. On the horizon for NTSS is moving the TB Data Warehouse into the Azure Cloud for faster deployments and updates to reports, exploring future NTSS data access and analytics, and using data to best inform leadership and external partners. In terms of analysis, AI workgroups are being formed to help think through the growing and changing slate of tools. EDAV training is available through the EDAV Data Academy at CDC.

Supporting states' training needs is an important consideration for DMI. DTBE is looking at tools that will help with analyses such as SAS Viya, Python, and R Packages.

CDC is committed to the support of public health departments in terms of implementing data modernization. Funding is provided through CDC's Strengthening US Public Health Infrastructure, Workforce, and Data Systems Grant for which the web link is: https://www.cdc.gov/infrastructure/phig/index.html. The DMI group also has provided technical assistance (TA) to public health PH departments in 49 states and large jurisdictions with connecting to electronic case reporting infrastructure to receive COVID-19 data. In addition, DMI staff are collaborating with national partners to facilitate learning networks and provide opportunities for increased knowledge and skill development.

CAPT Miramontes closed by saying that none of this is straightforward or easy. There are many challenges. He once heard a public health leader refer to siloed systems as "little pillars of excellence." Although he said this partially in jest, there is truth to that statement. Each program understands their disease best, including epidemiologic trends and how and when to pivot what is collected and reported. It is important to stay true to that expertise while also meeting DMI priorities.

ACET Discussion

Dr. Thanassi reported that the Veterans Health Administration (VHA) has recently announced their use of Enterprise Health, which they are calling eSure, to develop an EHR for its 400,000 HCW. In that will be a TB module. She wondered what the collaboration might be between the DBTE program and other government agencies, such as the VHA.

CAPT Miramontes responded that as it pertains to surveillance data, the VA is not a mandatory reporter to CDC. Most of the surveillance data come from local and state health departments. While he did not know offhand what is occurring at the agency level regarding collaborations, but here are many moving parts and many stakeholders with an interest in DMI. It is not an easy task, but it is important to continue to work on this so that epidemiologists are not having to enter data into 3 separate systems.

In terms of the example CAPT Miramontes shared at the beginning of his presentation, Dr. Belknap asked whether he envisioned this as replacing those 3 systems in order to manage the receipt of epidemiological data and the case management aspects of work. Often when there are 2 systems, they are at odds.

CAPT Miramontes answered that there is certainly the potential for that, but EMR data are a big piece of this. The toolset is flexible and will allow for collaboration in a number of areas. At least DTBE is now thinking about case management. It is national reporting, which is what DTBE is focused on, but a number of other groups are working on this. The OCIO is leading DMI and a number of workgroups have convened over the last year to year and a half that are still meeting to ensure that they are covering topics that are of importance to state and local jurisdictions.

RADM Mermin suggested that one of the major areas of potential opportunities for public health, especially its intersection with clinical medicine, is AI—particularly ML. AI already has revolutionized the concept of imaging and reading of images. In the TB world, there are at least some preliminary studies that are pretty good at x-rays. He asked whether CAPT Miramontes feels that there is any space in the near future for the work that he is doing to pull in AI or if it is a "wait and see" situation.

CAPT Miramontes replied that predictive ML certainly is an area that they could apply. A fair amount of the modeling is led by the Center level to help NCHHSTP use its resources in the best manner possible. Generative AI is part of predictive ML that, for instance, could be applied to the data that go back to 1930.

Dr. Sosa-Bergeron said she is very interested in the EDAV platform and appreciates the focus on interaction and exchange between CDC and public health. It seemed to her that the next logical step would be to use these data for public consumption, so she was curious to know what the thinking is about that. Along those lines, even though TB is a low incidence disease compared to STDs, she wondered how those data could be used by public health at the local or state level to create infographics so that there is not duplication of efforts. In addition, she expressed interest in hearing more about the goals of the recompete of the informatics contracts.

CAPT Miramontes indicated that for the recompete of the informatics contracts, DTBE is including specific language supporting the modernization of TB data systems and the use of CDC's EDAV platform and DMI in general. In terms of the question regarding data for public consumption, the goal is always to provide or display data as quickly as possible in all instances. They are limited somewhat in that they have to wait until the data arrives before it can be reported. The dashboard view has been used over the last couple of years to monitor data arrival. In some cases, data did not arrive until early January for some reporting areas. Some states submitted data quickly as soon as they received it and counted the cases locally. DTBE is able to turn data around immediately and put it back out for consumption at the local and state levels.

Dr. Stout said that as he was listening, it seemed to him that the key bottleneck in public health surveillance probably is not at the federal level. The issue is that the cases occur at the local level and tedious and manual processes are needed to collect data from various EHRs, the data must then be processed into some standardized form, perhaps enter the data into several systems, one of which is the state system that eventually transmits to CDC. With that in mind, he inquired as to what investments CDC is making to improve the efficiency of that part of the process. Especially with the declining public health workforce and declining funds, it is imperative to work smarter rather than harder.

CAPT Miramontes indicated that there are a number of tools. NTSS reports did not exist 10 years ago. When they first moved to a NEDSS-based system, it was opened up to all reporting areas to use whatever tools they felt worked for them, with the understanding that TB is not the only disease of interest. States and counties wanted to use systems that work for all diseases. When the NTSS reports were created, it was done with an eye toward making the data visible immediately because cases were being lost electronically. There had to be a way to track where cases were lost, so the reports were created so that states could find the breakdown. It is challenging to report data that are coming in in pieces. Verification criteria are applied to all cases that come in.

Dr. Stout clarified that he was asking about the part of the process before all of that happens. For example, the process of getting data directly from EHRs into reportable form occurs at the county, district, or state level before going to CDC is the rate-limiting step. Some large EHRs have a large market share, such as Epic. Investing in a system that automatically would pull data from Epic for surveillance purposes that could be standardized across states for reportable diseases would be a huge boon and seems like it would be a good investment of federal resources.

CAPT Miramontes indicated that DTBE has worked with EHRs to help answer certain questions, such as working with pharmacy data. This particular product is focused on the surveillance data that comes to them from the states because there typically is only one person at states who counts a case. Working with EHRs would provide a potential source of states getting data quicker and in turn getting it to DTBE quicker. With DMI, there is potential for activities in that area.

Dr. LoBue added that having started his TB career at CDC in a county health department, he understood exactly what Dr. Stout was talking about. At the DTBE level, it starts to get complicated. From a CDC standpoint, DTBE's relationship is with the states. Their funding goes to the states and a few large county/city programs, but they generally do not work directly with most of the 3000 counties or municipalities in the US that are on the frontlines collecting these data. Each of the 50 states have many counties and the relationships between the counties in each of these states differ. There is Home Rule versus non-Home Rule. The data systems used are very different and what each state wants differs. It would not be simple to do this on a large scale very quickly. If a particular state with a particular locality approached DTBE with an interest in trying to conduct a pilot to determine what could be done, perhaps through CAPT Miramontes DTBE could go to the DMI leadership to ask whether there is something they could do to start looking at this at least on a pilot level. From DTBE's perspective, it is hugely complicated to deal with 3 levels since they do not work directly with a locality without the state being involved as a rule. States ultimately have the public health and reporting authority and determining cases, with the understanding that the critical part is where this starts, which sometimes is the most complicated and least resourced part.

Ms. Van Handel indicated that she would be sharing some of the interoperability and standardization aspects during the next presentation.

Regarding Epidemiology and Laboratory Capacity (ELC) funding, Dr. Sosa-Bergeron indicated that a lot of funds have been allocated to states to focus on electronic case reporting in particular. While it is very complicated, that work is ongoing.

Dr. Narita emphasized that while state programs play a crucial role, in order to address TB, urban sites have to be addressed.

Mr. Watts inquired about the promise of DMI to advance equity or reduce inequity. Data are not neutral, so he wondered how that is being addressed.

CAPT Miramontes indicated that DTBE is certainly very interested in collecting data, and does collect data, related to health equity. The Health Equity Workgroup (HEW) is looking carefully at the data that are collected. He did not have information offhand about what is being done at the agency level in terms of what is being done specifically regarding some of the workgroups that have met.

Mr. Watts recalled that Dr. LoBue mentioned the disparity of localities and jurisdictions, but that the extent to which certain data can be mandated or incentivized to be collected, especially regarding race, ethnicity, and language, varies. Some localities and jurisdictions collect it well and some do not, but this is a very valuable tool to the extent that collecting it at least could be incentivized. Race, ethnicity, and language data could be used to help drive out disparities because if not collected, the disparities are not seen and are then just overlooked.

NCHHSTP Datasets and Standardized Variables

Michelle Van Handel, MPH
National Center for HIV, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control and Prevention

Ms. Van Handel provided information on NCHHSTP-led and other data sources commonly used, as well as data standardization efforts. NCHHSTP has case surveillance data across its divisions that includes the following:

- Adult and pediatric HIV case surveillance led by the DHP
- Acute hepatitis A, B, C and E and chronic HBV and HCV infection, perinatal HBV infection, acute hepatitis E led by the DVH
- Congenital syphilis, syphilis, chlamydia, gonorrhea, and chancroid case surveillance led by the DSTDP
- TB case surveillance led by the DTBE

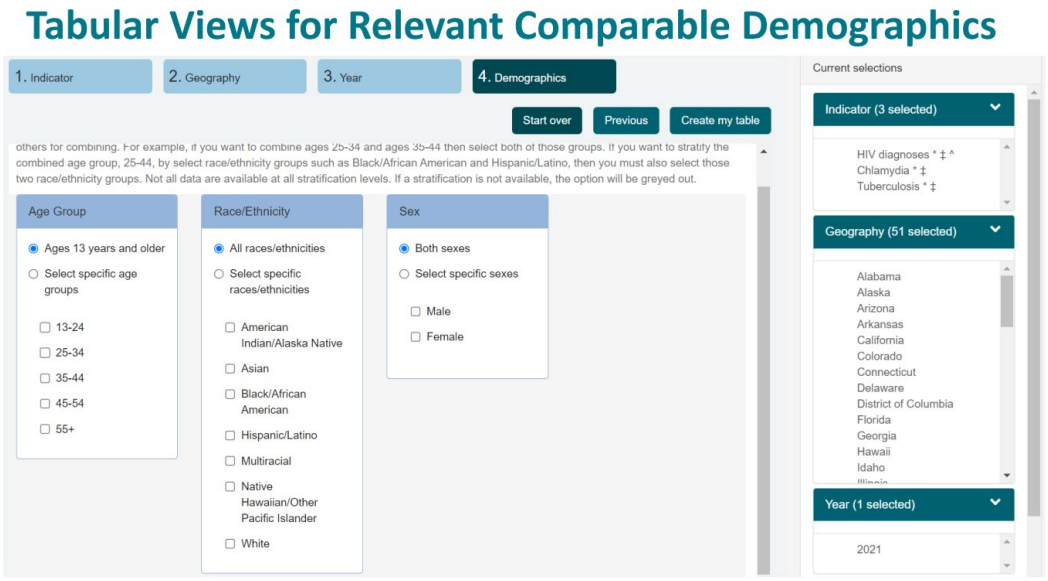
Across these surveillance systems, there is strong consistency in several demographic variables as shown in this table:

	HIV	VH	STD	TB
Age	X	X	X	X
Sex	X	X	X	X
Gender	X			
Race/ethnicity	X	X	X	X
U.S.-born / non-U.S.-born				X
Transmission risk group	X			

This consistency in demographics facilitated the development of NCHHSTP's AtlasPlus,[8] which is an interactive tool that allows users to create customized tables, maps, and charts. It includes about 20 years of CDC's surveillance data on HIV, viral hepatitis, STDs, and TB and indicators on social determinants of health (SDOH). The indicators that are included are expanded regularly. Users can view diseases by year, geography, and demographics and can stratify data by age group, race/ethnicity, sex, transmission category (HIV), country of birth (TB), and geography, Geography includes national and state levels available for all indicators, region available when all state data are complete for a region, metropolitan statistical area (MSA) available for select HIV indicators, and county available for all but 6 indicators.

[8] https://www.cdc.gov/nchhstp/atlas/index.htm

Ms. Van Handel shared several screenshots to illustrate the state and county level data and side-by-side visuals that can be generated. Each of the visuals available on AtlasPlus can be downloaded as a PowerPoint (PPT) or the underlying data can be downloaded as a comma-separated values (CSV) file. Users also can look at the data in a tabular view and can select multiple indicators at the same time, as shown in this example:



There are other variables in the case surveillance data that are not currently standardized across diseases for epidemiologic and scientific reasoning. For example, a user might want to look at the timing of exposure earlier, later, or for a longer timeframe depending upon the disease or outcome. NCHHSTP is exploring when and where it could be more standardized and understand what those differences mean from an interpretation perspective. Some examples of co-morbidities that NCHHSTP looks at across disease areas include pregnancy, diabetes, end-stage renal disease (ESRD), viral hepatitis, and immunocompromised. Another area is drug and alcohol use for cigarette smoking, injection drug use, non-injecting drug use, and alcohol use. Here the timing varies quite a bit across the disease areas. For example, injection drug use for HIV is asked more historically “any injection drug use after 1977.” For viral hepatitis, the range is between “during 2-6 weeks” or any time “before symptom onset.” Another area involves questions related to living conditions and travel. These variables include homeless in past 12 months or ever, correctional facility, resident of long-term care facility, hospitalized, ever lived outside the US, and travel or lived outside US or Canada. The timing and question vary on correctional facility. Another area relates to occupation and includes the variables of correctional facility employee; food handler; free text industry/occupation; healthcare worker, clinical lab, dental; migrant/seasonal worker; and public safety. Again, the timing and question differ for various health areas.

Despite the differences in the exact wording or timing, a lot of overlap is seen between exposures, experiences, and occupations of interest across NCHHSTP. They have the opportunity to assess the variables across these data sources to look at overlapping pictures if not the exact same picture, so they are able to gain insights by looking at these in similar ways. At the state and local health departments, there also are opportunities given that there might be more access to identification or name to look at some of the linkages across.

To highlight a few of the other surveillance systems within NCHHSTP, the DHP has the Medical Monitoring Project (MMP). This is a cross-sectional, representative, complex sample survey that assesses behavioral and clinical characteristics of adults with diagnosed HIV infection in the US. The DPH also has the National HIV Behavioral Surveillance (NHBS) system. This is a comprehensive system for bio-behavioral surveillance conducted since 2003 in populations with high burden of HIV. The NHBS system collects data on behavioral risk factors for HIV, HIV testing behaviors, receipt of prevention services, and use of prevention strategies.

The DSTDP has the STD Surveillance Network (SSuN). The SSuN provides enhanced behavioral, demographic, and clinical information on gonorrhea cases reported to state and local health departments and on patients presenting for care in specialty STD clinical settings, and explores innovative strategies to improve STD surveillance. The DSTDP also has the Gonococcal Isolate Surveillance Project (GISP). This project monitors antimicrobial resistance (AR) trends in Neisseria gonorrhoeae in the US through a collaborative project among selected STD clinics and their state or local public health authorities, and regional laboratories participating in the Antibiotic Resistance Laboratory Network (ARLN), and CDC.

Moving on to a few of the other data sources[9] that are led out of CDC more generally. The Behavioral Risk Factor Surveillance System (BRFSS) conducts telephone surveys that collect state data about US residents regarding health-related behaviors, chronic conditions, and preventive service use. The National Health and Nutrition Examination Survey (NHANES) assesses the health and nutritional status of adults and children in the US and combines interviews and physical examinations. The National Health Interview Survey (NHIS) collects information on the health of the US civilian non-institutionalized population. The National Survey of Family Growth (NSFG) collects information on pregnancy and births, marriage and cohabitation, infertility, use of contraception, family life, and general and reproductive health.

There also are laboratory, claims, EMR, and pharmacy-based data sources to triangulate or supplement data that are not represented in the other surveillance sources. Some of these can be found at data.cdc.gov, which is a consolidated resource to access data from across CDC including data for injury and violence, other National Notifiable Diseases Surveillance System (NNDSS) data, vaccinations, smoking and tobacco use, pregnancy and vaccination, disability and health, chronic disease data, and more. Internally, CDC also analyzes data for laboratory tests and claims data such as CMS Transformed Medicaid Statistical Information System (T-MSIS)[10], EMRs, and pharmacy. More information is available in the Center for Surveillance, Epidemiology, and Laboratory Services (CSELS) Data Hub.[11]

Regarding data standardization efforts, given all of the internal and external data sources, gaps, and alignments (though some are purposeful based on need for a specific disease or condition), data standardization is a priority area across CDC, HHS, and other organizations. The United States Core Data for Interoperability (USCDI) is part of the Office of the National Coordinator for Health Information Technology (ONC). The ONC coordinates identification, assessment, and public awareness of interoperability standards and implementation specifications that can be used by the US healthcare industry to address specific interoperability needs, including those for clinical, public health, and research purposes. They do this through the Interoperability Standards Advisory (ISA) process. ISA is designed to provide clarity, consistency, and

[9] More information: https://data.cdc.gov/
[10] https://www.medicaid.gov/medicaid/data -systems/macbis/transformed-medicaid-statistical-information -system-t-msis/index.html
[11] https://www.hhs.gov/sites/default/files/cdc-csels-data-hub.pdf

predictability regarding the standards and implementation classifications that could be used for a given clinical health information technology (IT) interoperability purpose. The USCDI is part of that process and is a standardized set of health data classes and constituent data elements for nationwide, interoperable health information exchange. USCDI version 1 was first released in February 2020 and version 4 was published in July 2023, so this is evolving quickly. The intent is to provide a common core of standardized data to support treatment, payment, healthcare operations, and requests for patient, public, and other authorized uses. Increased standard of patient care information could feed into other case reporting and analyses.

CDC works in the same space but at the higher DMI level. The ultimate goal of CDC's DMI is to get better, faster, actionable insights for decision-making and to do so by developing and deploying world-class data and analytics to meet today's and tomorrow's needs. There are 5 priorities, which are to: 1) build the right foundation 2) accelerate data into action; 3) develop a state-of-the-art workforce; 4) support and extend external partnerships; and 5) manage change and governance. Foundational to this is the work to advance interoperability for public health. Effective public health relies on getting data where it needs to be to protect health. Modern data exchange is needed, with coordinated standardized data. CDC is working closely with partners like ONC through a number of initiatives leveraging newer policies and modern standards with the hope to make data more interoperable. This includes work with ONC on the USCDI, HL7, and Fast Healthcare Interoperability Resources® (FHIR®) to access and exchange information using FHIR® that is not readily available now.

Not only is the government working in this space, but also the public health surveillance community identified the need to develop consensus on common definitions for core surveillance data elements to address variations in how jurisdictions or programs define and populate data elements. CSTE convened a workgroup to improve data quality through the development and application of consensus definitions for core data elements that are used for national notifiable conditions surveillance. Similar to CDC, CSTE is aligning with USCDI and recently recommended definitions, implementation, and actions for a suite of dates-related data elements such as *Illness (Symptom) Onset Date, Report Dates, and Laboratory-related Dates, and (Clinical) Diagnosis Date*.[12]

The last effort Ms. Van Handel highlighted was HHS's work to collect sexual orientation and gender identity (SOGI) and SDOH data. The National Science and Technology Council (NSTC) published the *Federal Evidence Agenda on LGBTQI+ Equity*[13] to provide a roadmap for opportunities for the federal government to continue to build evidence and leverage data to advance equity for lesbian, gay, bisexual, transgender, queer, and intersex (LGBTQI+) people. The aim is to better understand the needs, care, and services of people of all identities and the extent to which there may be disparities in health services and access to care across these populations by expanding SOGI data collection in surveys, research, clinical, medical, and administrative sources in a standardized manner.

In closing, Ms. Van Handel expressed her hope that this was a helpful snapshot of the different data sources available across CDC and resources leveraged outside CDC to gain insights to inform public health action, as well as the work that is underway to increase data standards and interoperability. These are enormous efforts and probably each one of them could be their own

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[12] https://cdn.ymaws.com/www.cste.org/resource/resmgr/briefs/DSWG_Dates_of_PH_Importance_.pdf
[13] https://www.whitehouse.gov/wp-content/uploads/2023/01/Federal-Evidence-Agenda-on-LGBTQI-Equity.pdf; and https://ncvhs.hhs.gov/subcommittees-work-groups/sogi-sdoh-data-workgroup/

presentation. There also are many people behind each of these projects. Notably, this work is grounded in the day in and day out work at the state, local, and territorial health departments that collect, clean, interpret, and provide surveillance data to CDC and others.

ACET Discussion

Regarding a question about whether any variables or groups of variables are being prioritized for standardization where it does not exist and a comment that not only do definitions have to be standardized, but also formats have to be standardized, Ms. Van Handel indicated that Erin Sizemore, previously the Data Modernization Implementation Lead for NCHHSTP, built the tables that she used in the presentation and she believes that the discussions are ongoing. Across the agency, there is a lot of discussion regarding standardizing the pregnancy status variables so that those are more consistent within NCHHSTP and across CDC.

In terms of the USCDI, Dr. Belknap asked whether there was any sense with each new versions whether it was mostly refinements in the cross work that is happening with the CSTE and if it would get to a place of relative stability and where she saw that heading.

Ms. Van Handel said that her take is that the process is pretty iterative. They are refinements versus major revamps. The ONC highlights what has been updated last on each of these and the USCDI is just part of their efforts around data standardization and interoperability.

Dr. Ahmed asked why perinatal hepatitis B but not hepatitis C and whether not getting the country of birth of the parents under demographics is because it is too difficult to obtain.

Ms. Van Handel said that they might consider moving in the direction of collecting perinatal hepatitis C, but it differs from hepatitis B, which has a long historical program around the vaccination. As of yet, there is not a treatment before or for hepatitis C during pregnancy. While she did not know the answer to the demographic question offhand, she could follow up on that.

Dr. LoBue added that while it has changed over time, at one point they collected whether the parents were non-US-born. However, he did not know how much detail beyond that was collected. A lot of this pertains to practicality from the standpoint of the collector. CDC would be happy to accept pretty much whatever anyone would give them. The variables in the TB cases were somewhat of a negotiation between those who receive the data and the state and local representatives on the group that put it together. From a practical standpoint, as Dr. Stout pointed out earlier, data collection originates at the local level and that is where the bulk of the work is.

Dr. Ahmed added that for perinatal hepatitis B if the vaccination data are being collected, that is very helpful. She is surprised at how many mothers are refusing the vaccination for their babies at birth.

Ms. Van Handel said that while she did not have the latest data handy, they do collect that.

TB Elimination Alliance (TEA): Community Engagement

TEA Background and Overview

Leeanna Allen, MPH
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Communications, Education, & Behavioral Studies Branch
Division of Tuberculosis Elimination
National Center for HIV, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control and Prevention

Ms. Allen indicated that she and the representatives from the TEA Steering Committee, Jeffrey Caballero from the Association of Asian Pacific Community Health Organizations (AAPCHO) and Jamila Shipp from the Asian & Pacific Islander American Health Forum (APIAHF), would be providing an update on TEA activities. To provide some background on why TEA exists, it is known that achieving elimination requires expanding testing and treatment for people with LTBI. It also is known that in the US, many of the populations at risk for TB receive their medical care from private HCP, community health centers, and other providers outside of the public health system. Therefore, it is important to engage and educate the HCP, health care agencies, and organizations who serve communities at risk so that they can meet populations with the TB preventive treatments that they need.

TEA is a national partnership of community leaders who are dedicated to increasing knowledge, testing, and treatment of TB and LTBI, particularly among communities especially at risk for TB. The goals of TEA are to:1) conduct outreach to communities most affected by TB; 2) increase awareness and understanding of LTBI testing and treatment strategies, especially among primary care providers and community health centers; 3) share resources and best practices among providers, providing opportunities to network; and 4) develop partnerships to scale existing initiatives to benefit other communities.

TEA[14] was launched in October 2019 by CDC's National Center for State, Tribal, Local, and Territorial Public Health Infrastructure and Workforce's cooperative agreement titled, "Strengthening Public Health Systems and Services Through National Partnerships to Improve and Protect the Nation's Health." TEA is led by the APIAHF, with support from the AAPCHO, Hepatitis B Foundation, and Stop TB USA. The 15 current members represent a diverse set of organizations that includes community health centers, community-based organizations (CBOs), public health agencies, academic institutions, and other partners. Many other local CBOs and health clinics were involved and engaged with TEA through many of their other activities.

Some of the important milestones in the development of TEA since its October 2019 inception have included recruiting member organizations that serve Asian American, Native Hawaiian, and Pacific Islander communities; funding a first round of mini-grants; sponsoring a summit; and training and TA. This was all done during a global pandemic, which meant that a lot of adjustments had to be made in the original project plan to which TEA partners responded beautifully. CDC originally funded TEA at about $310,000 per year. In 2022, CDC increased the funding to expanding the populations at risk for TB that TEA focuses on to include non-US-born

[14] www.tbeliminationalliance.org

Hispanic and Latino communities and US-born African American communities. In 2023, the work to expand TEA has continued. Partnership building is not a fast process. It takes time to build trust strategically, which TEA has been building on the successes that they have had to continue to expand this membership. TEA also has been working to build partnerships and inroads with the TB community. This year during the National TB Conference, TEA showcased some of the mini-grantees. The also will be conducting an evaluation this year.

Looking ahead, the current cooperative agreement is set to end on July 31, 2024. While it is anticipated that there will be a new cooperative agreement to support this type of work, details were not available on the timeline at this point. Though the DTBE understands that this will bring some uncertainties, the Division is committed to supporting the important work and contributions of TEA.

Additional Background, Strategies, and National Partnerships

Jeffrey B. Caballero, MPH
Executive Director, Association of Asian Pacific Community Health Organizations
Co-Lead, TB Elimination Alliance

Mr. Caballero expressed gratitude to the ACET members for inviting TEA to provide an update for a second time. TEA has 4 Steering Committee members, each of whom makes a unique contribution to this national partnership. AAPCHO is a national association of community health centers that primarily serve under-served Asian American and Native Hawaiian/Pacific Islander populations. The APIAHF is a national advocacy organization working with Asian American and Native Hawaiian/Pacific Islander communities across the country. The Hepatitis B Foundation is a critical part of this partnership because they are the lead organization for Hep B United, which served as a model for the TEA program. Stop TB USA provides TB subject matter experts (SMEs) and ensures that TEA is grounded in advocacy for TB.

In terms of its mission, TEA is a national partnership of community leaders dedicated to eliminating TB and LTBI inequities among Asian American and Native Hawaiian/ Pacific Islander populations through education, raising awareness, and innovation. While TEA started with Asian American and Native Hawaiian/Pacific Islander and then expanded to include the Latino and African American communities over the last 2 years, its vision of healthy communities free of TB remains unchanged.

As Ms. Allen noted, the pandemic impacted program launch in 2019. However, the partnership conducted a 2-year planning process that helped to recalibrate TEA's plans and develop a roadmap for the next several years. In 2020, TEA reached out to recruit local partners and convened its first virtual summit. From 2021-2022, TEA repeated these efforts to continue growing partnerships and increasing the number of mini-grantees with a focus on best practices and cultivating TB champions. In 2023, TEA convened its 4th virtual summit and increased the number of mini-grantees and expansion of TEA populations. TEA membership has grown, the number of mini-grantees has increased, community leadership has been enhanced across the country, and partnership contributions have expanded.

Over the last 2 years, with community reflections during the pandemic experience, TEA developed Health Equity Expansion Goals to guide the program's expansion efforts, which are to: 1) improve capacity for state and local healthcare programs to provide culturally and linguistically competent TB/LTBI services to high-risk priority populations; 2) support TB/LTBI outreach and education to underserved A/AA and NH/PI, Non-U.S Born Latinos, and African

American communities; 3) uplift and empower the voices of non-US born Latino and African American communities facing TB/LTBI disparities in the US; 4) establish mutual accountability and ownership with non-AA and NH/PI-serving communities to achieve TB elimination priorities; and 5) forge long-lasting partnerships with TB programs and healthcare settings focused on health equity initiatives serving A/AA and NH/PI communities and expansion populations. These new goals coincided with additional resources from CDC.

To provide a few examples of Tea's engagement and integration in national LTBI and TB spaces, the TEA Steering Committee members, member organizations, and mini-grantees proactively engaged in World TB Day with TB survivors' networks and Stop TB on Capitol Hill and have been engaged at local events and its social media networks. TEA has partnered with the TB Training Centers to conduct learning collaboratives and a number of webinars to target medical providers from community organizations. TEA Steering Committee members and mini-grantees also have been engaged in the NTCA conference, which has grown over the last few years, including participating in the planning committee for next year. Particularly noteworthy, TEA has partnered with NTCA to establish an NTCA Workgroup with a special focus on Pacific Islanders in the Pacific Basin, Hawaii, and the Continental US (CONUS).

Collectively, TEA has strategically integrated in LTBI and TB spaces to mutually leverage existing resources and new opportunities, such as partnerships with the training centers and community health convenings United Nations General Assembly (UNGA) TB event in September 2023. There also are examples of individual leadership at the national and local levels. AAPCHO staff are serving in Stop TB USA's board and also are actively engaged in NTCA efforts on the West Coast. Mr. Caballero also has been participating in another CDC public health advisory group that is working on creating models to improve public health decision-making at the national, state, and local levels that include enhanced TB community engagement and testing strategies. In addition, he began participating as an ACET liaison in 2023. He expressed his hope that the ACET was as impressed as he is in how TEA has integrated in key national LTBI and TB spaces in the short time that it has existed.

Local Partnerships and Mini-Grantees

Jamila Shipp, MPH
Managing Director of Capacity Building, Asian & Pacific Islander American Health Forum
Co-Lead, TB Elimination Alliance

Ms. Shipp shared examples to illustrate the breadth and depth of TEA's local partnerships. TEA recently convened its TB Elimination Alliance Summit on November 8-9, 2023 that was focused on the theme "Healthy Communities Free of TB." The summit drew 185 participants from 18 states, which demonstrated how TEA is growing and touching different communities in various places. Notably, over 67% of attendees were first-time participants who came to engage with TEA's community partners. This summit focused on highlighting the amount of work the mini-grantees have been doing. Participants included individuals from state and local public health departments (25%), CBOs (20.1%), community health centers (9.5%), TB Controllers (7.4%), and TB Centers of Excellence (6.7%). This varied representation emphasizes the shared commitment to building healthier communities together free of TB.

TEA is very proud of the summit's growth over the past few years. In 2020, the TB summit was conducted online. It started small with 18 sessions and 135 participants. In 2021, TEA decided to have a partnership with Hep B and conducted a TB Hep B summit. There were 237 attendees, 133 organizations, 34 states and US territories, and 6 counties. In 2022, TEA again collaborated with Hep B and doubled the number of attendees to 449 with 26 panels and 14 sessions. The 2023 summit focused on TB without the Hep B partnerships. This summit had 285 registrants, 32 speakers, 185 participants, and 18 states and US territories. Most of the speakers were mini-grantees from either the present or years past.

Over the last few years, TEA has been able to award over $800,000 to 36 organizations. Grantees have been located in Washington State, Oregon, California, Nevada, Alaska, Colorado, Texas, Arkansas, Illinois, Minnesota, Wisconsin, Michigan, Ohio, New York, Massachusetts, Georgia, Florida, Guam, and the Marshall Islands. The 3 new states awarded in 2023-2024 include Washington, Illinois, and Florida based on case data and understanding where the disease burden is. This year, TEA allocated $232,000 to the following 11 organizations:

Arkansas Coalition of Marshallese (Springdale, AR)
- Priority Populations: Marshallese, NH/PI
- CBO - TEA funded since 2020.
- Focus Areas: Community Engagement, Provider Education

Asian Pacific Health Foundation (San Diego, CA)
- Priority Populations: A/AA, NH/PI, non-U.S. born Latino American, and/or U.S. born African American communities, youth
- CBO - TEA funded since 2021
- Focus Area: Community Engagement

EthnoMed (Seattle, WA)
- Priority Populations: A/AA, Marshallese, NH/PI, U.S. born African American communities, non-U.S. born African communities
- CHC - New 2023-2024 TEA Grantee
- Focus Areas: Community Engagement, Provider Education

Jericho Road Community Health Center (Buffalo, NY)
- Priority Populations: US born African American communities, non-US-born African communities, A/AA (Burmese, Nepali) communities
- FQHC - New 2023-2024 TEA Grantee
- Focus Area: Community Engagement

Midwest Asian Health Association (Chicago, IL)
- Priority Populations: /AA, NH/PI, non-U.S. born Latino American, and US born African American communities
- CBO - New 2023-2024 TEA Grantee
- Focus Areas: Community Engagement, Provider Education

Mission Neighborhood Health Center (San Francisco, CA)
- Priority Populations: A/AA, non-U.S. born Latino American communities
- FQHC - New 2023-2024 TEA Grantee
- Focus Area: Community Engagement

Regional Pacific Islander Taskforce (San Francisco, CA)
- Priority Populations: NH/PIs (Fijians)
- CBO - New 2023-2024 TEA Grantee
- Focus Area: Community Engagement

Rural Women's Health Project (Gainesville, FL)
- Priority Populations: non-U.S. born Latino/Latino American communities
- CHC - New 2023-2024 TEA Grantee
- Focus Area: Community Engagement

San Diego County Medical Society Foundation, dba Champions for Health (San Diego, CA)
- Priority Populations: A/AA, NH/PI, non-U.S. born Latino American, and/or U.S. born African American communities
- CHC - TEA funded since 2020
- Focus Area: Community Engagement

Todu Guam Foundation, Ltd. (Tamuning, Guam)
- Priority Populations: Pacific Islanders, TB Centers of Excellence
- CBO - TEA funded since 2022
- Focus Areas: Community Engagement, Provider Education, Quality Improvement

We Are TB / Somos TB (National)
- Priority Populations: TB Survivors, non-U.S. born Latino/Latino American communities
- CBO - TEA funded in 2020-2021; first time funding Somos TB
- Focus Areas: Community Engagement

Another project to highlight is the Rural Women's health Project (RWHP) in Central Florida. The RWHP uses promotores, which are community health workers (CHWs) who are trained in TB and TB education. They speak Spanish and go to churches, nurseries, worksites, and other areas to talk to community members. They have engaged in 360 direct education sessions, distribute flyers and posters, use a WhatsApp circle, have delivered over 1500 messages through their health education text services, and more. This is just a highlight of one program that has used its funding to think of different ways to reach out to communities to stop TB. TEA is excited to be working on evaluation and evaluation tools to assess how the strategic goals have been met in terms of the outcomes achieved in the mini-grant sites.

In closing, Ms. Shipp shared some upcoming announcements and events, including the 4th Annual TEA Summit, AAPCHO's 2023 TB webinar and publication, TEA's 2023-2024 mini-grant recipient press release, TEA's 2025 annual TB webinar with Ebeye Ministry of Health, the 2024 World TB Day and UCSF World TB Day Symposium, and the 2024 NAR/NTCA Tuberculosis conference. She also extended a gracious "thank you" to all of the organizations that have been doing innovative work on the ground. Without them, it would not be possible to eliminate TB.

ACET Discussion

In terms of the mini-grants, Dr. Loeffler asked how much of the work is volunteer and how much is paid.

Ms. Shipp indicated that some of the work is volunteer and sometimes small stipends are provided.

Dr. Belknap asked whether any of the mini-grants have led to the ability to apply for and receive additional funding outside of the original mini-grant. He emphasized the impressive amount of work that has been accomplished and the growth that has occurred, particularly given having to work through a pandemic.

Mr. Caballero clarified that the intent of the mini-grant program is first and foremost to help establish the relationship between the CBOs, the communities, and the local health department TB programs. From the beginning, the mini-grants were never intended to support the sustainability of these programs. The intention is to highlight the unique contributions that these community organizations can contribute to these efforts and engage them to take some ownership of health inequity in their communities. There are efforts to look at and support the pursuit of additional funding opportunities. As shown by the list, esteemed institutions are working in partnership with community partners. These types of partnerships are continuing to cultivate and have demonstrated effectiveness in their communities. TEA is hoping to soon start seeing additional granting available to them. He also acknowledged their CDC partners, who have been incredible in guiding them along the way, helping them navigate the TB space, and making sure they are connecting with the right people at the state and local levels so that this work can continue to prosper.

Dr. Belknap asked whether the TEA Co-Leads had any questions for ACET.

Mr. Caballero said that because this is his first year as a liaison for ACET, he is still in the learning phase in terms of the various entities and roles that participants have played. AAPCHO is involved in many efforts, so he still needs to work with CDC and other partners to figure out how to best navigate the limited resources and time that folks have. This is the first time that he has been involved in the public health advisory group that is looking at modeling of different prevention programs. In terms of the models being proposed through the relationship with Emory University and modeling institutions throughout the country, very innovative community engagement strategies and testing strategies have been identified. He wished more people knew about this.

Thinking about the advisory role that ACET has, Dr. Chen asked what TEA thought would be needed for the long-game now that they have lived through the preliminary stage, established partnerships, shown that this works, and are evaluating the outcomes.

Mr. Caballero said that he wanted to “take baby steps” here as far as where they are in their success, given that they have 2 years of experience. In terms of engaging under-served, high-risk Asian American and Native Hawaiian/Pacific Islander populations, both his and Ms. Shipp’s organizations have decades of relationships. While they have experience in how to cultivate these relationships, the expansion opportunities through TEA have been very exciting. The engagement and partnerships with CBOs who are serving non-US-born Latino and African American communities have been very promising. He feels the big challenge now in building community ownership is looking for national partners for those respective folks similar to the AAPCHO and APIAHF that can help support the national advocacy that is needed for such organizations to remain engaged. AAPCHO’s and TEA’s resources are going to be limited and they will need those other national partners to be working with them to develop a more robust support system for CBOs across the communities of color that are in need of this type of support. He wants to ensure that they reach out to those respective communities appropriately, engage their national support structures, and cultivate what needs to happen for those local communities to continue the great partnerships in which they are involved.

ATS/CDC/IDSA/ERS Treatment Guidelines Updates

Carla Winston, PhD, MA
Associate Director for Science
Division of Tuberculosis Elimination
National Center for HIV, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control and Prevention

Dr. Winston presented *Clinical Practice Guideline* draft updates for the treatment of drug-susceptible and drug-resistant TB, which is sponsored by the American Thoracic Society (ATS) with participation from the CDC, the European Respiratory Society (ERS), and the Infectious Diseases Society of America (IDSA). She presented the background, methodology, and current status of the draft updates. In terms of background, the updates they are seeking to make for the treatment of drug-susceptible TB treatment were based on the 2016 *Official American Thoracic Society/Centers for Disease Control and Prevention/European Respiratory Society/Infectious Diseases Society of America Clinical Practice Guideline.*[15]

Prior to 2016, the guideline was issued in 2003. For now, this guideline serves as the current routine *Clinical Practice Guideline* for all of the US and has been endorsed by the ERS. The 2016 *Clinical Practice Guideline* focused predominantly on the 6-month treatment regimen with which everyone is familiar with isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB) as the mainstays of standard drug therapy. It focused on daily dosing being optimal for completion of treatment and the best outcomes. It also focused on special situations such as treatment for HIV, treatment in pregnancy, and treatment of pericarditis and TB meningitis. There was mention in this guideline of a shorter regimen for smear-negative and culture-negative TB of 4 months using the same drugs as for the 6-month regimen.

In 2019, the *Clinical Practice Guideline* was updated to include treatment of drug-resistant TB. The 4 organizations (ATS, CDC, ERS, IDSA) currently participating in updates to the *Clinical Practice Guideline* also were part of the 2019 guideline.[16] In 2019, there were 25 recommendations for drug-resistant TB. Dr. Winston focused on a few of these, which were to start with 5 drugs in the intensive phase for drug-resistant TB and at least 4 effective drugs in the continuation phase; recommend consultation with an expert in drug-resistant TB, such as through the CDC-funded Centers of Excellence (CoEs); ensure that molecular and phenotypic testing occurred for any drugs that were proposed to be used in the regimen; a duration of 15 to 21 months after culture conversion; and a preference for all oral regimens being recommended.

In 2021, the *New England Journal of Medicine* (*NEJM*) published the results of a Phase 3 trial sponsored by CDC's TBTC with collaboration from the National Institutes of Health (NIH) AIDS Clinical Trials Group (ACTG). This trial showed that a 4-month regimen containing INH, rifapentine (RPT), PZA, and moxifloxacin (MOX) was as effective as the standard 6-month regimen. Following on this, CDC published *Interim Guidance: 4-Month Rifapentine-Moxifloxacin Regimen for the*

[15] https://academic.oup.com/cid/article/63/7/e147/2196792?login=false
[16] https://www.atsjournals.org/doi/10.1164/rccm.201909-1874ST

Treatment of Drug-Susceptible Pulmonary Tuberculosis — United States, 2022 in the *Morbidity and Mortality Weekly Report* (*MMWR*)[17] recommending that the 4-month RPT/MOX-containing regimen was an option in addition to the standard regimen for persons with drug-susceptible pulmonary TB.

In early 2022, in reaction to the 2019 FDA approval of bedaquiline, pretomanid, and linezolid (BPaL) as a regimen to treat drug-resistant TB based on the original trial that was used to undergird the FDA approval, CDC issued *Provisional CDC Guidance for the Use of Pretomanid as part of a Regimen [Bedaquiline, Pretomanid, and Linezolid (BPaL)] to Treat Drug-Resistant Tuberculosis Disease*[18] and updated that guidance in 2023 following publication of the ZeNix trial that showed that lower dosing of linezolid was effective with fewer adverse events (AEs) and the Pragmatic Clinical Trial for a More Effective Concise and Less Toxic MDR-TB Treatment Regimen(s) (TB-PRACTECAL) study[19] results having been published, which added MOX to the BPaL regimen. Similar to the CDC recommendations, the World Health Organization (WHO) published the *WHO Consolidated Guidelines on Tuberculosis, Module 4: Treatment - Drug-Susceptible Tuberculosis Treatment*[20] updated guideline in May 2022 and the *WHO Consolidated Guidelines on Tuberculosis, Module 4: Treatment - Drug-Susceptible Tuberculosis Treatment*[21] in December 2022. These were based on a Grading of Recommendations, Assessment, Development, and Evaluations (GRADE)-based guidelines group.

The May 2022 WHO guideline mentioned not only a recommendation for the 4-month regimen using RPT/MOX-containing shortening treatment to 4 months as a regimen, but also recommended that children with non-severe TB could receive a shorter 4-month regimen based on the standard regimen being a short 2-month intensive phase followed by a 2-month continuation phase with the standard 4 drugs for children with non-severe TB based on the Shorter Treatment for Nonsevere Tuberculosis in African and Indian Children (SHINE) trial. It is known that about two-thirds of children have non-severe disease, so this guideline essentially was recommending shorter treatment for children and adults.

Since 2003, 2016, 2019 there have been multiple clinical trials that indicate effective shorter treatment and focus on shorter treatments that already are known to be effective, such as those for non-severe TB. Based on these trial results, ATS/CDC/ERS/IDSA sought to update clinical practice guidelines in order to support shorter treatments that have effective outcomes.

Moving to the methods, ATS organized a Memorandum of Understanding (MOU) in May 2022 between the 4 organizations (ATS, CDC, ERS, IDSA) based on a request to ATS in 2021 to initiate a clinical practice update. This MOU established a collaborative agreement for the joint preparation, review, approval, publication, and dissemination of an updated clinical practice guideline, *Update on the Treatment of Drug-susceptible and Drug-resistant Tuberculosis: An ATS/CDC/ERS/IDSA Clinical Practice Guideline*. ATS is the lead organization for this effort and has administrative responsibility, including administrative support for the project (e.g., scheduling calls, meetings, facilitating the document development, liaising between the organizations, and conducting the review and approval processes). ATS, CDC, ERS, and IDSA each appointed 6 representatives (1 Co-Chair and 5 Content Experts) with clinical, epidemiological, and laboratory

[17] https://stacks.cdc.gov/view/cdc/114844
[18] https://www.cdc.gov/tb/topic/drtb/bpal/default.htm
[19] https://pubmed.ncbi.nlm.nih.gov/35698158/
[20] https://www.who.int/publications/i/item/9789240048126
[21] https://www.who.int/publications/i/item/9789240063129

expertise in TB. ATS provided the methodologists, which was a team of 3 more senior methodologists and 2 more junior methodologists. They also were able to recruit a patient representative from We Are TB.

ATS is responsible for managing the COI and confidentiality policies associated with review of the guidelines, including collecting, vetting, and maintaining all of the updated disclosures of the guideline participants and overseeing and constructing a management plan to mitigate any potential conflicts. All members who were on the guidelines panel who had a potential COI were asked to abstain from recommendations related to their conflict. The guidelines panel Co-Chairs finalized the written recommendations for review and submitted them first to the panel members and then to ATS Scholar One, which is their online publication portal for review. After comments and concerns from that review are addressed, each organization will review the guideline and consider approving the final guideline for publication. There were 25 subject matter voting members. Dr. Winston stressed how much she enjoyed working with this phenomenal group and recognized and appreciated all of the effort they put forward to bring this *Clinical Practice Guideline* to its current stage. More importantly, many of these people participated as well in the WHO guideline development process and potentially will contribute again either as data contributors or as reviewers.

Guideline recommendations were developed using the GRADE methodology. The GRADE-ADOLOPMENT (Adoption, Adaptation, or Development) guidelines process was employed to utilize Evidence-to-Decision (EtD) frameworks based on existing guidelines and evidence. This group took advantage of the WHO guidelines issued in 2022 in that all of the analytic work to piece out the evidence from the clinical trials had already been done by WHO in the process of assessing these questions. Rather than having to undertake a systematic review, meta-analysis, or individual patient data meta-analysis, in this case the group relied on the WHO published EtD frameworks and then evaluated specific questions of interest for updating US and European contexts based on the status of the current 2016 and 2019 guideline and the new evidence that has come to light since those guidelines were published. The group of methodologists also conducted a targeted literature search in 3 databases (Medline, Embase, Cochrane central register of clinical trials) using a “tuberculosis” and randomized clinical trial filter to confirm whether there were any new clinical trial data. They did include and review observational data and studies of experiential effects; however, the basic methodology was focused on RCT outcomes.

The key trial outcomes that both the WHO and this guideline panel evaluated included treatment success, failure and recurrence, death, loss to follow-up, AEs, and amplification of drug resistance. For each question, the panel clarified the specific PICO questions of interest (Population, Intervention, Comparison, Outcomes) that were going to be evaluated. Using the GRADE approach, each adopted or adapted recommendation was rated as either “strong” or “conditional” based on quality of evidence, balance between benefits and harms, certainty of evidence, and assessment factors such as equity, feasibility, resources, and acceptability. All panel members without a declared COI reviewed the EtD tables and recommendations and voted on the recommendations.

In terms of “strong” and “conditional” recommendations, “strong” implies “should” and “conditional” is more similar to “suggested” or “may receive.” Of course, no recommendation can take into account all of the unique and individual features of individual people or clinical circumstances. The implications of “strong” or “conditional” recommendations are more particularly described in the following table:

Audience	Strong	Conditional
Patients	The overwhelming majority of individuals in this situation would want the recommended course of action, and only a small minority would not.	The majority of individuals in this situation would want the suggested course of action, but a sizeable minority would not.
Clinicians	The overwhelming majority of individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Different choices will be appropriate for different patients, and you must help each patient arrive at a management decision consistent with her or his values and preferences. Decision aids may be useful to help individuals make decisions consistent with their values and preferences.
Policy-Makers	The recommendation can be adapted as policy in most situations, including for the use as performance indicators.	Policy making will require substantial debates and involvement of many stakeholders. Policies are also more likely to vary between regions. Performance indicators would have to focus on the fact that adequate deliberation about the management options has taken place.

The PICO questions, panel's draft recommendations, and comments follow:

PICO 1

Should the four-month regimen composed of two months of Isoniazid, Rifapentine, Pyrazinamide, Moxifloxacin (2HPZM) followed by two months Isoniazid, Rifapentine, Moxifloxacin (2HPM) vs. standard six-month drug-susceptible TB regimen of two months of Isoniazid, Rifampin, Pyrazinamide, Ethambutol (2HRZE) followed by four months of Isoniazid, Rifampin (4HR) endorsed by the ATS/CDC/IDSA guidelines be used for adolescents and adults with drug-susceptible pulmonary TB?

Recommendation (conditional recommendation)
In people aged 12 years or older with drug susceptible pulmonary tuberculosis, we conditionally recommend the use of a 4-month regimen of isoniazid, rifapentine, moxifloxacin and pyrazinamide.

Comments

This is the same recommendation that WHO promulgated in 2022, as well as the same recommendation that CDC independently promulgated in 2022 in the *MMWR*. There was moderate certainty for evidence, the evidence for benefits was high, and the evidence for resistance was low—mainly based on a low number of observed events. The certainty was found to be high for cure and retention in treatment, moderate for AEs, and low for drug resistance based on a low number of events.

PICO 2

Should four-month regimen composed of standard-dose two months of Isoniazid, Rifampin, Pyrazinamide, Ethambutol (2HRZE) followed by two months of Isoniazid, Rifampin(2HR) vs. standard six-month drug-susceptible TB regimen of two months of Isoniazid, Rifampin, Pyrazinamide, Ethambutol (2HRZE) followed by four months of Isoniazid, Rifampin (4HR) endorsed by the ATS/CDC/ERS/IDSA guidelines be used for children and adolescents with non-severe drug-susceptible pulmonary TB?

Recommendation (strong recommendation)
In children and adolescents between 3 months and 16 years of age with non-severe TB (without suspicion or evidence of MDR/RR-TB), we recommend the use of a 4-month treatment regimen 2HRZ(E)/2HR rather than the 6-month drug-susceptible TB regimen of 2HRZ(E)/4HR.

Comments
There was moderate certainty of evidence, with high levels of evidence for treatment success and moderate for all-cause mortality and AEs based primarily on imprecision of the events based on a low number of events.

PICO 3
Should six-month regimen composed of bedaquiline, pretomanid and linezolid vs. the 15 months or longer drug-resistant TB regimens composed according to current ATS/CDC/ERS/IDSA drug-resistant TB treatment guidelines be used in adolescents and adults with rifampin-resistant pulmonary TB?

Recommendation (strong recommendation)
In adolescents, aged 14 years and older, and adults with rifampin-resistant pulmonary TB with resistance or patient intolerance to fluoroquinolones, who have either had no previous exposure to bedaquiline and linezolid or have been exposed for less than 1 month, we recommend the use of the 6-month treatment regimen, composed of bedaquiline, pretomanid and linezolid (BPaL), rather than more than 15-month regimens.

Comments
The panel made this strong recommendation based on very low quality of evidence, which is the same quality assessment as WHO's. However, this was upgraded by the panel from being a conditional recommendation as WHO released in 2022 to a strong recommendation for the intervention in US and European settings based on considerations for persons with TB that shorter treatment would be preferred. The other difference from this panel's approach and the WHO's is that WHO was comparing to all oral 9-month regimens and this panel compared back to the 2019 guideline for drug-resistant TB that were inclusive of 15-month and longer regimens.

PICO 4
Should a six-month regimen composed of bedaquiline, pretomanid, linezolid and moxifloxacin vs. the 15 months or longer drug-resistant TB regimens composed according to current ATS/CDC/ERS/IDSA drug-resistant TB treatment guidelines be used in adolescents and adults with rifampin-resistant, fluoroquinolone-susceptible pulmonary TB?

Recommendation (strong recommendation)
In adolescents, aged 14 years and older, and adults with rifampin-resistant, fluoroquinolone-susceptible pulmonary TB, we recommend the use of a 6-month treatment regimen, composed of bedaquiline, pretomanid, linezolid (600 mg), and moxifloxacin (BPALm), rather than the 15-month or longer regimens.

Comments
This was upgraded to a strong recommendation from the WHO recommendation, which was conditional. The panel felt that the strong recommendations were justified favorably by the profile of BPALm relative to standard of care. However, the quality of the evidence was considered very low in part because there were very small numbers of patients treated with BPALm. For the most part, the panel was looking at TB-PRACTECAL data, so there was an N of about 62 people for

comparison. Therefore, there was a small number of events, potential for confounding, and indirectness in the comparison.

The panel also highlighted research gaps, such as the analysis of cross-resistance that is needed between drugs such as bedaquiline and clofazimine or other drugs used to examine outcomes to which the panel did not have access in terms of their evaluation of the evidence. The panel also wanted to enhance and highlight the need for additional expansion of methods, including molecular drug susceptibility for moxifloxacin, newer drug susceptibilities and combinations of drugs, and antibiotic stewardship associated with use of drugs that previously were held for second line such as moxifloxacin that are now being used more as frontline treatment. Data are needed for longer term outcomes since most outcomes are for a maximum of 30 days past the end of a trial or relapse or recurrence. The panel did not have outcomes beyond 1 year for the studies they were evaluating. Data are needed for use of these regimens for extrapulmonary TB and populations who were not included (e.g., pregnant women, older adults, and younger children for some of the regimens). Data are needed for other shorter regimens. Several have been published and there are more to come. Costs and cost-effectiveness data are needed in terms of maintaining treatment completion and how to use therapeutic drug monitoring over time, and how all of those factors would play into costs and outcomes over time. The panel also highlighted health equity and access concerns as part of the research gaps as these recommendations are taken up.

Regarding next steps, the documents have been submitted to ATS for review. ATS will conduct a review of documents with external peer reviewers. The documents will then come back to the guideline panel to make revisions. The organizations (ATS, CDC, ERS, IDSA) will review for their own internal approvals. Dr. Winston anticipates that they will see recommendations for shorter TB regimens in the US and European contexts in 2024. After those recommendations are published, the panel will continue to assess programmatic implementation, gaps, and uptake. As the lead organization, ATS typically would lead new review process generally at about 3 years after publication.

In closing, Dr. Winston invited ACET's questions, wish list, feedback, and contributions to thinking about what people would need to hear specific to the US and European context. She acknowledged that this context of the recommendations is unlikely to be a huge surprise, given that people have seen the WHO recommendations.

ACET Discussion

Ms. O'Brien observed that with a lot of the newer medications and shorter regimens, people may be taking other medication such as blood pressure medication. She wondered when these regimens are being used outside of studies "out in the wild" clinicians are documenting reactions and if that information will feed into the update in 3 years.

Dr. Winston said that one aspect is general post-marketing surveillance. Once a drug or regimen is on the market, there are a couple of ways that post-marketing surveillance occurs for unusual AEs. One is through routine FDA reporting for AEs. The other specifically for TB would be through national surveillance for which there would not be something as direct as, "My patient was on X/Y drug and had an effect that I think was related to some combination of drugs." That would tend to go to FDA. National surveillance will allow for assessment of uptake of regimens. There is some delay in that and there are limitations because what people are asked to report on a report of a verified case of TB is their initial drug regimen, but drug regimens may change over time. The update may not be known until the end of someone's specific treatment that they

actually completed. In terms of the potential for how that information is obtained, one example is that New York City (NYC) has looked at and published some preliminary information through abstracts on their experience with the 4-month RPT/MOX-containing regimen. CDC has the BPaL Advanced Monitoring Project that has published on their first 20 patients' experience with BPaL and will publish a close-out letter. There was not a specific drug or condition that came out of that reporting that gave some indication of a safety signal that had not been previously picked up. CDC will now be reporting their BPaL and BPALm patients in the US. The BPaL Implementation Group (BIG) that included people from the CoE and others published in *Clinical Infectious Diseases* (*CID*) on their experience with BPaL. If a very rare outcome probably would be difficult to pick up in TB surveillance, but these tend to be identified through the network of clinicians who are involved in expert TB treatment or through publications of things like case reports and additional experience in the field.

Dr. Burzynski said he was somewhat surprised to see the conditional recommendation for the 4-month regimen and wondered how the panel reached that recommendation. That was a large trial with high quality evidence.

Dr. Winston responded that the question being asked pertained to the 4-month RPT/MOX-containing regimen, which was non-inferior in the clinical trial and was ranked by WHO and this Guidelines Panel as a conditional recommendation, meaning that one may receive either this regimen or the 6-month regimen as opposed to saying someone "should" in almost every case receive the 4-month RPT/MOX-containing regimen. Part of why panelist did not feel that they were ready to go to a "should" on that was the design of the trial being a non-inferiority trial and also because there may be some subgroups of people with whom a provider would like to make a different decision. For example, a provider may not want to change someone over to the 4-month regimen who already was started on treatment in the hospital on the standard drug regimen. If a practice does not have a program workflow that includes MOX up front, the provider may not want to start that contains MOX without knowing the fluoroquinolone susceptibility. Another example would be that the individual is an older person, and the provider has some concerns about use of the fluoroquinolone in an extreme of age or based on some comorbidity. Those were the types of considerations that made panelists feel that this recommendation should be conditional. It is not that there is something wrong with the regimen, but rather that there may be individual or programmatic circumstances that lead people to choose the standard regimen, which is equally effective.

Dr. Stout pointed out that the truth is, no one in the US in 2023 is asking whether 15-month regimens should be used for MDR-TB versus 6-month regimens based on BPaL. The pertinent clinical question now regards whether BPaL should be used as the standard for people with fluroquinolone-susceptible TB or BPALm. He asked whether the panel addressed that question or BPALc or if that also was studied. In terms of process, guideline revisions are more frequent than they used to be, but now it is every 3 years. Given the wonderful increase in new TB drugs, trials, advances in treatment, and hopefully more published studies in the future, he wondered why they were sticking with a somewhat antiquated model of formal guideline committees that meet every so many years and by the time the guidelines are published they often are out of data, versus a more continuous model analogous to what UpToDate does with their period rapid reviews of data that are published online quickly.

Dr. Winston indicated that in the case of treating a person with RIF-resistant fluroquinolone-susceptible TB, the panel recommended starting with BPALm. BPaL versus BPALm is in the text in the sense that PICO 4 adds a notation about fluroquinolone-susceptible pulmonary TB.

Dr. Chen, who was a member of the panel, added that they talked about this a great deal. At the time, in the consideration of even the wording of the PICO questions, the panel had to look at the evidence that was available at that moment. They did receive some backdoor data before publication and the WHO EtD tables early before publication. In the studies, there was not a direct comparison between BPaL and BPALm. There were 4 study arms assessed initially, by study design, they pulled forward the arms that looked most likely to have success. That was not something about which they felt they could make a strong statement. She is most excited about the new stratified design trials that are coming up that are looking at the evidence base for the kinds of decisions practitioners make at the bedside. They took into consideration what the people taking the pills are thinking as well.

In terms of Dr. Stout's process question, Dr. Winston said it is exciting to be in a place in which there are many new regimens are being tested, a lot of combinations, and a lot of work. The timeline was 2003, 2016, and 2019. CDC published the interim guidelines for the 4-month regimen, BPaL, and BPALm because they were able to develop a publication based on the evidence that they had and chose methodology that was somewhat less intensive. The GRADE methodology is very intensive. CDC's interim publications were well-received though they did not use GRADE. For the collaboration with ATS, CDC gratefully and delightedly accepted being part of this panel. In terms of launching living guidelines, the issue is mostly one of finances. It takes a lot of money, literally millions of dollars, to support online platforms such as UpToDate. Obviously, UpToDate has a revenue model in which they are getting money in. Every member on this guideline panel was a volunteer for every part of this process other than the methodologists who received payment from ATS.

Ms. O'Brien pointed out that there is the ongoing Active TB Drug-Safety Monitoring and Management (aDSM) system and suggested that data should be collected from other countries.

Dr. Winston said that she has not personally worked with aDSM for BPaL and BPALm. The CDC medical officers and CDC-funded CoEs probably have seen the overwhelming majority of people treated in the US with those drug combinations. However, she could not speak for other countries. Every PICO needs a population, intervention, comparison, and an outcome. That would be the one place where a drug reporting AE system might have some limitations in that there would not necessarily be a comparison group. The comparison group for the BPaL and BPALm questions, the panel used the same WHO EtD tables from the trials and that is unchanged from what WHO published in 2022. Therefore, she does not have a way to incorporate that without a comparator, which would be a highly varied standard of care across different RIF-resistant mechanisms. That does sound like something to add to the research gaps.

Dr. Loeffler asked whether the structure of the document would be focused mostly on answering the PICO questions or if an effort would be made to be more comprehensive. She also pointed out that there are jurisdictions that use 9 months of standard treatment, and said she is somewhat concerned about how people are going to use these regimens. She wondered if there could be discussion of a registry to monitor uptake in the post-marketing/post-licensure setting, which she thought would give people a lot of confidence in using a 4-month regimen.

Dr. Winston indicated that it is a short manuscript addressing these 4 PICO questions. The manuscript does have a number of appendixes, including the EtD tables, which include all of the factors being weighed, including the assessments for equity, balance of effects, and costs. The other aspects of the document that may be helpful and are novel are things like monitoring suggestions, such as what clinical or laboratory tests one might want to have along the way for people on different regimens and a flowchart for defining non-severe TB in children.

RADM Mermin emphasized that these updated draft recommendations represented an enormous amount of structured thought process and bringing people together. It was highlighted that a lot of new interventions/treatments are becoming available. It takes a while to conduct studies, so some of the special situations get dropped off such as for pregnant women, young children, children at all. Yet, they do not want to conduct a study to answer a question that is current because the current questions will be answered in the 3 to 5 years it takes to run the study. Instead, they want to answer the questions that will be relevant 5 years from now. He asked how the TB community sets priorities for the most important research questions that need to be answered, such as the side questions so that people can be treated from populations who essentially are neglected because they are not part of the first trials of a new intervention.

Dr. Winston said that some of the things that are underway now are pharmacokinetic studies in young children, including and overlapping with researchers who are conducting pharmacokinetic studies in pregnant women and people with HIV. One specific example is with RIF water dispersible tablet among children. That will get them to a bridging study to be able to evaluate the 4-month regimen in children, which is still a question in terms of best dosing. Those are highly collaborative studies in terms of work with NIH and other funders.

Dr. LoBue added that these are the kinds of things that a TBTC core science group go through all of the time. There are a lot of factors such as the capacity of the consortium given its current workload, the feasibility of answering a specific question given the make-up of the consortium, et cetera. The bigger issue, which he thinks is finally being addressed, is coordination among the various research groups. NIH is now taking a more normal leadership role in bringing the major trials groups together in order to determine the questions, who is addressing what, and who is best able to address what.

Dr. Cattamanchi asked for additional insight into uptake and availability of BPaL, BPALm, and the 4-month regimen for drug-susceptible TB and what more can be done to have these guidelines used in practice.

Dr. Winston said that they are working closely with their partners to understand uptake for the 4-month regimen. They are aware of and have been getting information about certain programs that have started to implement the 4-month regimen quite aggressively and consistently. She anticipates that they will hear more during the April North American Region meeting and National TB Coalition of America meeting with people reporting that out. BPaL and BPALm have been strongly organized through the CoEs and the CDC Field Services Branch (FSB). The Project Officers and Medical Officers are working closely with people in the field to collect additional information. For the new Report of Verified Case of Tuberculosis (RVCT) that is coming online in 2023, there is detailed information collection for drug-resistant TB specifically. For the first time, there will be detailed data collection that enables them to look at changes in regimens over time, which is not currently included in the surveillance data. Only the initial drug regimen that a person is started on is collected, but that could change very quickly, so the completion regimen is not known until 2 years later when the case follow-up report is due.

Dr. Chen said that she would be remiss if she did not give voice to what she is hearing in their region, which is that the TBTC is going to be enrolling subjects from high burden global areas where they can recruit and complete in a timely way. In terms of comorbidities, the US population has many folks with all of the comorbidities for which the drug-drug combinations are not going to be reflected in the side effects from the larger trials. Programs are struggling with very difficult cases, older cases, severe comorbidities, extensive extrapulmonary disease, et cetera. The

complexity is never going to make it to one of the TBTC trials, yet these are the burning issues that people struggle with every day in programs. In terms of implementation is that probably, the 4-month regimen is not rolling out like one would expect because of the US's older population and all of the side effects. Yet, the 6-month drug-resistant TB rollout is rolling out in a much more robust way. From the clinical standpoint, it is not just straight MDR. It is the people who cannot take the old regimen. There are reasons why BPaL is easier.

Dr. LoBue said that since DTBE is funding TBTC, one of the rules is that if a study does not have relevance in the US, it is not going to get done. The second problem is that with 8,300 TB patients in the US, they are extremely limited in how many of those they will be able to enroll in clinical trials. They enroll as many as they can, but to get the numbers needed for statistical significance, they have to enroll internationally. They also cannot possibly enroll enough people to study individual situations. This is one reason he has questioned a lot of the data that have been used previously for MDR-TB with meta-analyses of single patients. Each of those patients is so different in terms of how their regimens are being changed and individualized, he questioned how they could be lumped together as a group and say this is the outcome that applies to all of those patients. This is the problem with patients who have comorbidities or age, given that so many changes in the regimen are made over 6 or 9 months, there are gaps in time. This relates to something someone said to him a long time ago about trying to use guidelines and data and then actually treating patients being about the art of medicine and that sometimes, one just has to be a doctor and use the art of medicine. There is only so much that can be applied from these studies and guidelines.

Dr. Chen agreed that there is no way they ever could enroll enough patients, but it does mean that they could be a little creative in funding groups that can look across disciplines across these issues. What are some best practice recommendations? If they had hepatologists, transplant folks, et cetera it would help them to problem-solve through some of these issues. While there will not be one answer for everyone, some guidance is needed. She thinks they can be creative and engage in more focused efforts on the issues that are most troubling to help make the best decisions possible. It takes effort, will, and time.

Dr. Belknap agreed that it is not something that would fit into the TBTC in terms of capacity and funds required, but he thinks that there is something in between the rigorously conducted, highly controlled, randomized clinical trial and nothing. If they were easy, they would have been done by now. Dr. Loeffler mentioned having a registry, which is a way to capture observational data over time that is not already captured through TBTC like regimen changes that captures the initial regimen and nothing else. Studies could be designed simplistically to allow easy enrollment and broad criteria, but that requires resources. Unless there is some large influx of dollars to DTBE that did not need to offset all of the losses everywhere else, and, and, and—outside sources of funding would be required to design a network to do something that might be similar to what was done without funding for the BIG study and the collection of information. That was non-randomized. A large, randomized trial could be done to answer some simple questions about how best to manage INH-resistant TB or intolerance to medications, for example. There are possible ways and he supports creativity, but it will not be easy.

Dr. Sosa-Bergron said she thought they all were recognizing the huge shift in how TB is being treated, whether it is drug-sensitive or drug-resistant, in a pretty short period of time. Given the relatively small number of TB patients in the US, it is still going to be the public health programs that are responsible for making sure clinicians know about the latest guidelines. In order to maintain credibility, they need the tools to be able to tell people what to do and how to do it. Dr. Belknap mentioned the critical importance of sensitivity testing for the drugs that they want to

use. Fluroquinolones are at the top of that list, such as WGS at the local level. Another issue is that they are substituting cheap drugs for very expensive drugs that the US cannot get due to shortages. For example, it has to be easier to get bedaquiline (BDQ) if that is going to be the mainstay of every regimen used, let alone the other drugs that are easier to get but are still really expensive—even for people with average insurance. These things must be tackled simultaneously. Otherwise, they can have all of the guidelines in the world, but if they cannot actually make them happen, public health will lose credibility.

Regarding the registry suggestion, Ms. O'Brien observed that very few people are followed around and watched as much as a TB patient. All of that is an opportunity. If someone had told her and a lot of others with TB that when they are finished with treatment, they would like to stay in touch to see what happens in the long-run, many of them would have done it. She would have done it forever. A lot of it is so invasive already, there are many ways to get information. While she understands the lack of funding, ACET was not there to talk about the reasons they are not doing this. They are there to talk about doing things to make this better. There is a way to establish a registry. There is real human suffering, time, energy, emotion, and loss that could be counted to help other people. That could be so valuable.

Dr. Loeffler said the other thing she wanted folks to think about is that many people receiving BPaL(M) in the US are drug intolerant rather than resistant. They may have received weeks or months of standard treatment first (killing a large part of the burden of MTb) and it is important to be careful about extrapolating treatment success for those individuals.

Dr. Ritger asked whether Dr. Loeffler meant by "intolerant" that the person is unable to take the medications even though they kill their TB.

Dr. Loeffler said that this is what she meant. A particular drug or regimen makes some people feel terrible or causes dangerous toxicity in that individual.

Dr. Ritger comment that it seems important to capture relapse, but this is not captured very well. If it is less than a year, it is not counted as a case, so there is no incentives for programs to submit enter all of those data into a surveillance system and submit them again. If it is more than a year, it is not clear that there is an easy way for CDC to capture that. It is a key evaluation point for all of the new regimens. It could just be a checkbox for "Is this is relapse case? Yes, No, Unknown" or something like that. She would be all for that.

Dr. Goswami asked whether anyone foresaw NIH partnering on these kinds of guidelines with CDC, such as happens for COVID treatments et cetera, given their increased roles in TB clinical trials. She said she also was curious about how the guidelines document may address results from RIFASHORT (4 months) given that the regimen uses rifampin rather than the more expensive and scarcer rifapentine.

Dr. Winston reiterated that there are 4 organizations on the ATS guidelines on which they are now working. Otherwise, she did not have any information on NIH participation of lack thereof in these guidelines. RIFASHORT was published after the WHO EtD tables were created. Her personal interpretation of the RIFASHORT outcomes was that they were somewhat disappointing, and some have advocated for testing higher doses of RIF to enhance those outcomes. The group who has been working with RIFASHORT, which included CDC, they plan to retool and look at that. The other trial that first came out and also had some less optimistic results was the Clofazimine- and Rifapentine-Containing Treatment Shortening Regimens in Drug-Susceptible Tuberculosis (CLO-FAST) Study. The panel dealt with the evidence that was

within the decision framework of publication through 2022. She was not aware of any other trials specific to these questions that would change the outcome of the panel's recommendations. As she mentioned with regard to the methods, there was a look for any additional clinical trials that were specifically relevant to this.

Dr. Stout pointed out that the 4-month regimen also may not be rolling out because of cost and the fact that it was microbiologically "inferior-noninferior."

Dr. Ray said that the change in how TB is treated has rocked her world over the last 3 years compared to the previous 20 years.

Ms. Condit provided the links to WHO and evidence annexes:
WHO Consolidated Guidelines on Tuberculosis (TB), Module 4: Treatment - Drug-Resistant Tuberculosis Treatment 2022:
https://iris.who.int/bitstream/handle/10665/365308/9789240063129-eng.pdf?sequence=1
Web annexes for drug-resistant TB treatment evidence:
https://apps.who.int/iris/bitstream/handle/10665/365284/9789240063983-eng.pdf
https://www.who.int/publications/i/item/9789240063129
9789240048140-eng.pdf (who.int)

Dr. Belknap indicated that the final *Bedaquiline, pretomanid, and linezolid with or without moxifloxacin for tuberculosis* report has been published in *Lancet RM* and thanked Dr. Goswami for sharing the link: https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(23)00426-5/fulltext

Business Session 1

Robert Belknap, MD
Medical Director, Denver Metro Tuberculosis Clinic
Public Health Institute at Denver Health
ACET Chair

During this session, Dr. Belknap first called for approval of the minutes from the June 2023 ACET meeting and then opened the floor for general input about topics or discussions ACET heard throughout the day, topics or issues that require follow-up, and/or any potential recommendations that ACET may want to make to CDC.

Business Item 1: Approval of Previous ACET Meeting Minutes

A motion was properly placed on the floor by Dr. Loeffler and seconded by Dr. Sosa-Bergeron to accept the minutes from the June 2023 ACET meeting. With no further discussion or changes, the motion to accept the minutes as written carried unanimously with no abstentions or opposition.

Business Item 2: ACET General Input

- Perhaps there is something that ACET can do to support advocacy regarding the ongoing problem of false positives.

- Better access to molecular testing for diagnostics, removing isolation, et cetera. When the test first became available, every corner of India had GeneXpert®. Perhaps there is something that ACET can do to help get this more widely available and more widely used, and perhaps Cepheid or someone else from industry could be brought into the discussion about lowering the cost.
  - Dr. Belknap indicated that they did have Cepheid at ACET last year, and he made a note to follow up with them. One thing they learned in that discussion from a representative from Cepheid and a representative from the FDA was that it is not the FDA's responsibility to approach Cepheid to submit data. It is up to Cepheid to approach the FDA to understand what data are required to get some of the tests approved. Dr. Belknap will follow up with Cepheid again.
  - Dr. LoBue indicated that Cepheid started this technology in the post office to look for anthrax, which was funded by the US taxpayers, they still wanted TBTC to go back to the taxpayers to get more US GeneXpert® data to go for FDA approval. There is no legal provision that requires any company that has technology funded by US taxpayers to have them get FDA approval for a test.
  - RADM Mermin added that there are 2 potential options. The first is that the Center has recently funded companies to submit tests to the FDA for consideration. The second is that if collaborative research is done, it can be patented.

- The FDA's new Proposed Rule will significantly harm not only CDC laboratories, but also public health laboratories that are trying to fill the void with locally developed tests. While the comment period closed on 12-4-23, perhaps there is an opportunity for the ACET to write in support of allowing a public health exemption or allowing the continuation of some drugs and diagnostics to be protected, which would take this up to the HHS level.

- What can ACET do to address the TB drug shortage issue and possibly recommend that first- and second-line TB drugs be placed on the National Essential Drug Formulary?
  - Dr. LoBue emphasized that ACET has tried many things to address drug shortages, so he did not know what else possibly could be done. ACET has written numerous letters, established a Drug Shortage Working Group, had FDA present, et cetera.
  - RADM Mermin noted that FDA is currently considering a way of importing Bicillin because of the shortage. That does not need ACET support. The Center continues its effort to ensure that they are communicating effectively with CDC's sister agency and others within HHS. The hope is that precedents will set up a certain situation. ACET has never provided advice on laboratory-developed tests.

- There has been a large influx of new arrivals in New York this year of people coming from countries with high rates of TB, which is affecting their situation. There was a great desire of people wanting to get tested a couple of years ago with the influx of people from the Ukraine. There does not appear to be any push to increase testing now of new arrivals. Sometimes people have bottles of 4 TB medicines that they say their doctor put them on, but there is no information about their cultures. Perhaps something could be done to help with these issues.

- Dr. LoBue said he was not aware of any current requirement related to TB testing or screening. The only requirement for TB testing and screening that he is aware of is when permanent immigrants or refugees request a status adjustment.
- During the last ACET meeting, there was discussion about IGRA testing but no provision of LTBI treatment. Dr. LoBue indicated that the recommendations are still being finalized on this. The requirement is going to be for the IGRA component and consideration is being given to a provision for voluntary treatment at sites that can feasibly do that. The test results would be provided to the US, but it would be a huge burden for programs in the US to offer treatment. There is not going to be a requirement to offer overseas treatment. He did not know what, if anything, ACET actually could do about it. ACET does have an ICE *Ex Officio* member who they could invite to present on this during a future meeting.
- CDR Misty Carlson from ICE indicated that she is a physician on the Infectious Disease Team for Immigration and Customs and would be happy to discuss this situation. A lot of what they do, for whatever reason, is not in the public domain. She is happy to provide an email to their Tasking Services to obtain information regarding the guidelines.[22] Furthermore, she has been cleared in other talks to give the number of their Infection Prevention Officers at each ICE facility throughout the nation. Almost all facilities have Infection Prevention Officers who report to the local health department. She will share that information and hopefully, that will build communication between ICE and those in the field who are helping detainees.

Day 1 Wrap-Up

With no further business posed, the meeting was adjourned at 4:40 PM ET. The ACET stood in recess until 10:00 am ET on December 13, 2023.

[22] For questions about ICE Health Service Corps Clinical Guidelines or questions about a non-citizen's healthcare, please email IHSCTaskings@ice.dhs.gov and question will be addressed.

December 13, 2023 Opening Session

Robert Belknap, MD
Medical Director, Denver Metro Tuberculosis Clinic
Public Health Institute at Denver Health
ACET Chair

Deron Burton, MD, JD, MPH (CAPT, USPHS)
Deputy Director, National Center for HIV, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control & Prevention
ACET Designated Federal Officer (DFO)

Marah E. Condit, MS
Public Health Analyst | Advisory Committee Management
Office of Policy, Planning, and Partnerships
National Center for HIV, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control and Prevention

Dr. Belknap called the meeting to order at 10:00 AM ET on December 13, 2023. Marah Condit provided meeting instructions. CAPT Burton conducted a roll call to confirm attendance of the ACET voting members, *ex-officio* members, and liaison representatives. He reminded everyone that ACET meetings are open to the public and that all comments made during proceedings are a matter of public record. He informed the ACET members to be mindful of their responsibility to disclose any potential COI, as identified by the CDC Committee Management Office, and to recuse themselves from voting or participating in discussions for which they have a conflict. The roll call confirmed that the 18 voting members and *ex-officio* members in attendance constituted a quorum for ACET to conduct its business on December 13, 2023. No additional COIs were declared and quorum was maintained throughout the meeting.

Public Comment

Jester Jersey
Vaccine Advocate

Good morning to the members of the Advisory Council for the Elimination of Tuberculosis. My name is Jester Jersey. Thank you for allowing me to speak to you today. I have worked with various vaccine national messaging organizations that have been active before and through the COVID pandemic and continue their health advocacy today. The reason I am addressing you is because tuberculosis has recently made news headlines in the US as global vaccination rates have dropped. Reasons for this may vary, but among the top factors cited by the literature are the COVID pandemic, the abundance of disinformation, and the lack of trust in the science keeping us safe. This applies both internationally and domestically. Although TB is well-controlled within the US, there is always a concern due to its contagious nature. Not only have other vaccine-preventable diseases like measles and polio seen regional outbreaks, but continued concerns that low vaccine rates for seasonal illnesses like flu, RSV, and COVID could add further strains on already scarce health resources. As a vaccine advocate and a first generation Filipino-American born in the United States, my parents often shared stories about growing up in the Philippines where vaccine access was difficult, particularly against TB. I grew

up fortunate that I was born in America where I have been free from any vaccine-preventable diseases thanks to regularly available immunizations. Unfortunately, according to the World Health Organization, we are currently seeing the largest global incidence of TB since 1995. We also saw the lowest global vaccine rates in 30 years. Although there has been a slight recovery in the past year, global immunizations are still down by 20 million. The same goes for vaccinations domestically. If it happens outside the US, it might eventually affect the US as well.

There is a gap between the science and the people that has yet to be bridged to increase vaccination rates. The longer that gap exists, the more pain, disease, and casualties will result if diseases remain unchecked. Yesterday there was mention about better community engagement to address domestic health concerns. My advice to ACET today is to work with fraternal service organizations, such as Kiwanis and Rotary, who have addressed diseases globally such as eliminating tetanus and polio respectively in the last few years. While we may not be using vaccines much to address TB like other vaccine-preventable disease, we could still use a boost in trusted messaging. Messaging is as much medicine as medicine itself. Therefore, I urge the Advisory Council for the Elimination of Tuberculosis, the CDC, the HHS, and President Joe Biden's Administration to incorporate fraternal service organizations in their health and messaging strategies to keep Americans safe and emphasize the importance of the science keeping us safe. Thank you, stay safe, and have a nice day.

Julie Higashi, MD, PhD
TB Control Program Director
Los Angeles County Department of Public Health

Thank you very much for a great session. I wanted to touch on the discussion related to NAAT testing and the GeneExpert® platform. We know that the Ultra version of the test is not available in the US and there are no plans to actually seek FDA approval, but I thought I heard something about the actual current Expert® test not being available in the US. I just wanted to make sure that I was hearing correctly because this is a really important test for us in the local programs because it is so accessible. It has allowed at least LA County to really have access at almost all of its 88 hospitals to a NAAT test. If we do not have access to that test, it is really going to threaten our ability to make timely diagnoses. There was discussion about volume of testing and the limitations of the business case for the test in the US. I had heard the number 80,000. I would like to comment on the fact that this test not only helps us make diagnoses for TB but also exclude other diagnoses like NTM. In the US, that is particularly important. I think the volume of tests that are being done is grossly underestimated and we have an opportunity with our electronic lab reporting to assess the volume. As far as trying to address the concern that there is not a business case to use this test in the US is something that California and LA County would be interested in pursuing to make sure that they have access to this test. The company's headquarters, I believe, are in California so that is something that at an advocacy level California can help out with. I think we can have influence because we are finding that the ability to exclude a diagnosis is just as important. We have done some work on looking at smear grade. I think it is not just diagnoses. It is also making decisions that these have impact on program capacity and who we are spending our time on. Thank you.

ACET Discussion

In terms of NAAT testing, Dr. LoBue said he would address what they know. The company has not said anything publicly or that he has heard specifically saying that they are going to discontinue the test in the US. The potential issue about why people might be concerned about that possibility is that the newer version of the test is basically what they use everyplace else.

The older version is only being used in the US. That leaves people concerned that at some point, the company may decide to discontinue that test. He clarified that he just threw out the number 80,000 10 to 1 for cases, but it could be substantially more than that. Ultimately, it does not matter what numbers they find. It is the company that makes the business decision. They know how many tests they sell in the US and they know what their threshold is and he does not think that they have a lot of influence over that.

Dr. Chen thanked Mr. Jersey for joining the meeting and sharing his ideas. In terms of vaccine advocacy across the board, as public health people, they do appreciate the efforts of the public. She thought that the suggestion to engage with fraternal organizations was a good idea. Looking across the table, there were representatives from NTCA and We Are TB that engage in a lot of civil society outreach and coordination, and she appreciates those efforts. In TB, advocacy is needed for a good vaccine, which they do not have yet. That is the key to moving on prevention goals at some points. If there are vaccine advocacy groups who are looking for messaging for TB, it is that they want to push research forward and they are hoping that is the future. She thanked the commenters for joining the ACET in the public forum and stressed that it was wonderful to hear more voices.

Ms. O'Brien from We Are TB invited Mr. Jersey to contact We Are TB, there are tuberculosis advocacy actions that she can include him in. At wearetb.com, there is a place for advocacy and she would be happy to connect him for TB vaccine advocacy.

Business Session 2

Robert Belknap, MD
Medical Director, Denver Metro Tuberculosis Clinic
Public Health Institute at Denver Health
ACET Chair

Dr. Belknap opened Business Session 2 and facilitated a review of old and current business items that warranted ACET's formal action and allowed time for additional discussion and/or requests for future agenda items.

Business Item 1: Dates for 2024 ACET Meetings

The dates for the 2024 ACET meetings are June 25-26, 2024 and December 3-4, 2024.

Business Item 2: FDA Proposed Rule on Laboratory-Developed Tests (LDTs)

There was extensive discussion and concern about how ACET could comment on the LDT issue. A lot of the FDA approved tests in the US are focused on the Cepheid's test that it is only approved for people 18 or older or sputum specimens only. From a laboratory perspective, there is no choice but to develop a laboratory-test for alternative specimen types for alternative patient demographic or age categories. Having this FDA Rule target LDTs in the laboratory is going to affect the ability to target and develop those tests where there is a gap from the FDA-approved tests. There was strong sentiment that ACET should comment on that. Given that the FDA public comment period opened after the June ACET meeting and closed before the December ACET meeting, there was not an opportunity for ACET to develop an independent letter. The understanding is that if the Proposed Rule becomes a Rule, it will not be implemented immediately. There will be a phased period of time over 4 years during which the implementation

of the rule is worked out, so it is possible that there still will be several decision points for FDA about how to implement this Rule. Therefore, it is likely that there will be other opportunities for ACET to provide input on how the Rule is implemented with respect to TB, even if it becomes Rule between now and the next ACET meeting. Perhaps ACET needs to put forth a statement or collective idea about the anticipated impact of the loss of LDTs. Laboratories must make decisions now. Even prior to the new Rule being implemented over a 4-year implementation period probably will impact what laboratories decide today about whether to pursue something. The uncertainty itself will halt progress, which could result in delays 4 to 5 years in terms of what is seen at the bedside. With all of these and other potential issues in mind, ACET supported the formation of a working group (WG), the scope of which would cover up to the June ACET meeting. DTBE can provide the WG with survey data and APHL potentially could provide the same survey data from public health laboratories that they provided to the NTCA when they prepared their letter of response. Ms. Condit shared a link for Tuberculosis Laboratory Aggregate Reports.[23]

Vote: Establish an ACET WG to Address the FDA Proposed Rule on LDTs
A motion was properly placed on the floor by Dr. Sosa-Bergeron and seconded by Dr. Ahmed to establish an ACET WG to evaluate the current landscape of LDT development and usage in the diagnosis of TB and potential impacts from the FDA Proposed Rule. With no further discussion or changes, the motion carried unanimously with no opposition. Dr. Cattamanchi abstained, given that he arrived after the predominance of the discussion had been completed.

Business Item 3: Establishment of the Drug Shortages WG

A request was made for ACET to consider advising CDC and HHS to request adoption of the WHO Preferred List of Medications, which includes TB medications, to the Essential Medication List. There is a new proposal from the White House to use the Defense Production Act to incentivize the production of medications in shortage. The ACET submitted a letter to Secretary Becerra on May 30, 2023 pertaining to drug shortages that referred to the United States Senate Committee on Homeland Security and Government Affairs published report titled *Short Supply: The Health and National Security Risks of Drug Shortages* that outlines the current problems and gives recommendations to address them. The letter asks that HHS work with FDA to review and update the essential medications list. It is the NTCA's understanding is that with the new White House initiative, that is not in their purview, and they have been further advised by advocates that rather than asking specifically for TB medications to be included in that essential medicines list that they ask for WHO-approved medicines to be included, given that it is already vetted and approved and could be embraced with this initiative. Perhaps the ACET could refer to the May 2023 letter to indicate that the timing of raising this issue again could be impactful for the new White House initiative, or could add an amendment could be made to the existing letter.

Vote: Establish the Drug Shortages WG
A motion was properly placed on the floor by Dr. Chen and seconded by Dr. Ahmed to form the ACET Drug Shortages WG, with a charge to review the letter submitted to HHS in May 2023 and to bring updated information for ACET to discuss. The focus of the workgroup is to evaluate the current actions of the federal government to address and mitigate drug shortages and ensure tuberculosis medications are included in discussions and plans to consider and vote on during the June ACET meeting. With no further discussion or changes, the motion carried unanimously

[23] https://www.cdc.gov/tb/publications/reportsarticles/labreports.htm

as written with no abstentions or opposition.

December 2023 ACET Recommendations	Action
1) **Establish the LDT WG**	• ACET voted unanimously to establish an ACET WG to evaluate the current landscape of LDT development and usage in the diagnosis of TB and potential impacts from the FDA Proposed Rule.
2) **Establish the Drug Shortages WG**	• ACET voted unanimously to establish an ACET Drug Shortages WG, with a charge to use the scope to review the letter submitted to HHS in May 2023 and to bring updated information for ACET to discuss. The focus of the workgroup is to evaluate the current actions of the federal government to address and mitigate drug shortages and ensure tuberculosis medications are included in discussions and plansto consider and vote on during the June ACET meeting.

Business Item 4: Future Agenda Items

Dr. Belknap reminded everyone that agenda-setting should refer back to the priorities set forth in the Biennial Letter submitted to HHS in June 2023 in terms of what information ACET needs and who they need hear from to advance those priorities, the members were provided with a copy of the letter. He emphasized that they were merely posing topics during this session as opposed to actually deciding the agenda. The following topics were put forth for consideration:

- Presentation from ICE regarding TB testing and treatment
- Update on 340b and waiver for sharing drugs across jurisdictions
- What CLIA and FDA can require for laboratory test reporting
- FDA presentation/discussions specifically on how they foresee the Proposed Rule regarding LDTs working, and possibly include presentations from the DTBE laboratory and APHL who understand the possible implications and to determine whether ACET could make recommendations to HHS regarding the potential to influence implantation of the FDA Rule with regard to TB
- Possibly invite Cepheid back to follow up on the previous discussion from last year when they presented[24]
- Update on TBESC-III of the analyzed baseline data and discussion of challenges/successes in automated extraction of data from EMRs for TB public health purposes
- Review prior work and recommendations from ACET related to TB prevention and control in congregate settings
- CDC presentation on *Think. Test. Treat.* to hear conclusion and next steps
- Consider inviting the Association of College Physicians to discuss administrative testing for TB, LTBI, and over-diagnosis/over-treatment
- Ukraine evaluation and TB impact and perhaps expanding that to recent arrivers largely from Central and South America

[24] When the question about possible discontinuation of Xpert in the US in the future has come up previously, prior Cepheid contacts include: Devasena Gnanashanmugam, M.D. Vice President, Medical Affairs MOBILE +1 404 450 4597 EMAIL devasena.gnanashanmugam@cepheid.com

- Pregnancy severe disease/female genital urinary TB
- Migrant situation in NYC, which is very interesting and relevant
- Personal stories/comments about how delays in diagnosis causes damage to people's lives in terms of dying, long-term lung damage, risk of infecting family members and communities, et cetera
- It would be fascinating to get a global view of how TB affects various agencies
- Impacts on the public health infrastructure in terms of staffing, early retirements, cuts, and downsizing
- Update on PHIGs
- Post-TB sequelae, burden of problem in the US, services provided beyond TB in the US to minimize TB related disability
- How to increase the involvement of local pharmacists in the screening and treatment of TB
- Mental Health/Therapy during and after treatment to help with the stigma
- Increasing the involvement of pharmacists in the screening and treatment of TB

Closing & Adjourn

Robert Belknap, MD
Medical Director, Denver Metro Tuberculosis Clinic
Public Health Institute at Denver Health
ACET Chair

Philip LoBue, MD, FACP, FCCP
Director, Division of Tuberculosis Elimination
National Center for HIV, Viral Hepatitis, STD, and TB Prevention
Centers for Disease Control and Prevention

Dr. Belknap expressed appreciation to the ACET members for their time and discussion during this productive meeting, emphasizing how fantastic it was to see some people in person and have others join via Zoom who could not travel. He emphasized what a pleasure and honor it was to have served as the ACET Chair for the last couple of years and to have been an ACET member for 5 years. He values what everyone brings to the discussions and the hard work that the ACET is trying to do in terms of advancing TB elimination.

CAPT Burton added his thanks for this excellent ACET meeting and everyone's thoughtful input, for being a vibrant group, and for supporting TB elimination efforts. He said he very much enjoyed his time at the ACET DFO where he learned a ton, was inspired by the members, and looked forward to the great work coming out of ACET in the future.

With no further discussion or business brought before ACET, the meeting was officially adjourned at 11:48 am on December 13, 2023.

Chair's Certification

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

Date	**Robert Belknap, MD, Chair** **Advisory Council for the Elimination of Tuberculosis**

Attachment 1: Participant Directory

ACET Members Present

Dr. Robert Belknap, Chair
Dr. Amina Ahmed
Dr. Adithya Cattamanchi
Dr. Lisa Chen
Dr. William Glover
Dr. Ann Loeffler
Dr. Kathleen Ritger
Dr. Lynn Sosa-Bergeron
Ms. Kristine Steward-East
Dr. Jason Stout

ACET *Ex-Officio* Members Present

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

Dr. Amy Bloom
US Agency for International Development

Dr. Kevin Taylor
Department of Defense

CDR Misty Carlson
Department of Homeland Security

Dr. Karen Elkins
Food and Drug Administration

Dr. Sheena Harris
Agency for Healthcare Research and Quality

Dr. Jonathan Iralu
Indian Health Service

Dr. Mamodikoe Makhene
National Institutes of Health

Mr. Stephen Martin
National Institute for Occupational Safety and Health

CDR Tara Rhodes
Bureau of Prisons

CAPT David Wong
Office of Minority Health

ACET *Ex-Officio* Members Absent

Dr. Gary Roselle
Department of Veteran Affairs

ACET Liaison Representatives Present

Dr. Susan Ray
Infectious Disease Society of America

Dr. Joseph Burzynski
National Tuberculosis Controllers Association

Ms. Valerie Adelson
American Thoracic Society

Dr. Natasha Bagdasarian
Association of State and Territorial Health Officials

Dr. Robert Benjamin
Stop TB USA

Mr. Jeffrey Caballero
Association of Asian Pacific Community Health Organizations

Dr. Jonathon Golub
International Union Against TB and Lung Disease

Ms. Elizabeth Lovinger
Treatment Action Group

Dr. Masahiro Narita
National Association of County and City Health Officials

Ms. Kate O'Brien
We are TB

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

Dr. Sylvie Stacy
National Commission on Correctional Health

Dr. Wendy Thanassi
American College of Occupational and Environmental Medicine

Mr. Andrew Tibbs
Council of State and Territorial Epidemiologists

Dr. Lornel Tompkins
National Medical Association

Mr. Bobby Watts
National Healthcare for the Homeless Council

ACET Liaison Representatives Absent

Ms. Susan Rappaport
American Lung Association

Dr. Amee Patrawalla
American College of Chest Physicians

Dr. Mayleen Ekiek
Pacific Island Health Officers Association

Dr. Charles Daley
American Thoracic Society

Mr. Colin Puzo Smith
RESULTS

Dr. Daphne Ware
Association of Public Health Laboratories

Dr. David Weber
Society for Healthcare Epidemiology of America

ACET Designated Federal Officer

CAPT Deron Burton
NCHHSTP Deputy Director

Federal Representatives

David Weissman
Kathleen Deroos
Naomi Aronson
Leeanna Allen
Carissa Bisnath
Kevin Borden
Deron Burton
Marah Condit
Nick Deluca
Annelise Doney
Erica Figueroa
Neela Goswami
Kay H
Megan Harbour
Savannah Harrelson
Nicholas Jarboe
Awal Khan
Adam Langer
Philip LoBue
Suzanne Marks
Jonathan Mermin
Roque Miramontes
Selma Moore
Caitlin Reed
Maria Sessions
Angela Starks
Michelle Van Handel
Jennifer Whitmon
Carla Winston
Reid Hogan Yarbro

Guest Presenters

Jeffrey B. Caballero, MPH
Jamila Shipp, MPH

Members of the Public

Linda Ashkin
Rajita Bhavaraju
Andrea Cruz
Maryam Haddad
Julie Higashi
Jester Jersey
Steve Kammerer
Claire Leback
Andrea Liptak
Tanya Liscio
John Nguyen-Yap
Mary Pulchinski
Sara Stokes
Wes Stubblefield
Alexander Tin
Gary Trentman
Stephanie Wallace
Shu-Hua (Sue) Wang

Attachment 2: Glossary of Acronyms

Acronym	Definition
AAPCHO	Association of the Asian Pacific Community Health Organizations
ACET	Advisory Council for the Elimination of Tuberculosis
ACOEM	American College of Occupational and Environmental Medicine
ACTG	AIDS Clinical Trials Group
aDSM	Active TB Drug-Safety Monitoring and Management
AE	Adverse Event
AHRQ	Agency for Healthcare Research and Quality
AI	Artificial Intelligence
AI/AN	American Indian/Alaskan Native
AIDS	Acquired Immunodeficiency Syndrome
AMA	American Medical Association
AMR	Antimicrobial Resistance
APHL	Association of Public Health Laboratories
APIAHF	Asian and Pacific Islander American Health Forum
AR	Antimicrobial Resistance
ARLN	Antibiotic Resistance Laboratory Network
ARPE	Aggregate Reports for TB Program Evaluation
AFB	Acid-Fast Bacillus
ASH	Assistant Secretary for Health
ASTERoiD	Assessment of the Safety, Tolerability, and Effectiveness of Rifapentine given Daily for LTBI
ASTHO	Association of State and Territorial Health Officials
ATS	American Thoracic Society
BDQ	Bedaquiline
BIG	BPaL Implementation Group
BOP	Federal Bureau of Prisons
BPaL	Bedaquiline, Pretomanid, and Linezolid
BRFSS	Behavioral Risk Factor Surveillance System
CARES Act	Coronavirus Aid, Relief, and Economic Security Act
CBO	Community-Based Organization
CID	*Clinical Infectious Diseases*
CSELS	Center for Surveillance, Epidemiology, and Laboratory Services

Acronym	Definition
CDC	Centers for Disease Control and Prevention
CDPH	Chicago Department of Public Health
CEBSB	Communications, Education, and Behavioral Studies Branch
CFA	Center for Forecasting and Outbreak Analytics
CHWs	Community Health Workers
CITC	Curry International TB Center
CLIA	Clinical Laboratory Improvement Amendments of 1988
CLO-FAST	Clofazimine- and Rifapentine-Containing Treatment Shortening Regimens in Drug-Susceptible Tuberculosis
CMS	Centers for Medicare & Medicaid Services
CoE	Centers of Excellence
COI	Conflict of Interest
CONUS	Continental US
CRUSH-TB	Combination Regimens for Shortening Tuberculosis Treatment
CSTE	Council of State and Territorial Epidemiologists
CSTLTS	Center for State, Tribal, Local, and Territorial Support
CSV	Comma-Separated Values
DASH	Division of Adolescent and School Health
DBDPHG	Division of Blood Disorders and Public Health Genomics
DFO	Designated Federal Official
DHP	Division of HIV Prevention
DHS	Department of Homeland Security
DMI	Data Modernization Initiative
DSMB	Data Safety Monitoring Board
DST	Drug-Susceptibility Testing
DSTDP	Division of STD Prevention
DTBE	Division of Tuberculosis Elimination
DVA	Department of Veterans Affairs
DVH	Division of Viral Hepatitis
ECA	Epidemiology Capacity Assessment
EDAV	Enterprise Data Analytics and Visualization
EHE	Ending the HIV Epidemic
EHR	Electronic Health Record
ELC	Epidemiology and Laboratory Capacity for Prevention and Control of Emerging Infectious Diseases Cooperative Agreement
EMB	Ethambutol
EMR	Electronic Medical Record
ERS	European Respiratory Society
ESRD	End-Stage Renal Disease
ET	Eastern Time
EtD	Evidence-to-Decision
FACA	Federal Advisory Committee Act

Acronym	Definition
FDA	(United States) Food and Drug Administration
FHIR®	Fast Healthcare Interoperability Resources®
FSB	Field Services Branch
GISP	Gonococcal Isolate Surveillance Project
GRADE	Grading of Recommendations, Assessment, Development, and Evaluations
GRADE-ADOLOPMENT	GRADE-Adoption, Adaptation, or Development
HBV	Hepatitis B Virus
HCP	Healthcare Providers/Professionals
HCV	Hepatitis C Virus
Hep	Hepatitis
HHS	(United States) Department of Health and Human Services
HIMSS	Healthcare Information and Management Systems Society
HIV	Human Immunodeficiency Virus
HL7	Health Level Seven
HPV	Human Papillomavirus
HRSA	Health Resources and Services
ICE	(United States) Immigration and Customs Enforcement
IDSA	Infectious Diseases Society of America
IGRA	Interferon-γ Release Assay
INH	Isoniazid
ISA	Interoperability Standards Advisory
IT	Information Technology
ITAP	Independent Test Assessment Program
IV	Intravenous
LGBTQI+	Lesbian, Gay, Bisexual, Transgender, Queer, and Intersex+
LTBI	Latent Tuberculosis Infection
MDR-TB	Multidrug-Resistant Tuberculosis
ML	Machine Learning
MMP	Medical Monitoring Project
MMWR	*Morbidity and Mortality Weekly Report*
MOU	Memorandum of Understanding
MOX	Moxifloxacin
MSA	Metropolitan Statistical Area
MSM	Men Who Have Sex with Men
NAAT	Nucleic-Acid Amplification Test
NACCHO	National Association of County and City Health Officials
NASTAD	National Alliance of State and Territorial AIDS Directors
NCBDDD	National Center on Birth Defects and Developmental Disabilities
NCCDPHP	National Center for Chronic Disease Prevention and Health Promotion
NCHHSTP	National Center for HIV, Viral Hepatitis, STD and TB Prevention
NEDSS	National Notifiable Disease Surveillance System

Acronym	Definition
NEMS	North East Medical Services
NEJM	*New England Journal of Medicine*
NH/PI	Native Hawaiian and Pacific Islander
NHANES	National Health and Nutrition Examination Survey
NHBS	National HIV Behavioral Surveillance
NHCHC	National Health Care for the Homeless Council
NHIS	National Health Interview Survey
NIH	National Institutes of Health
NMA	National Medical Association
NNDSS	National Notifiable Diseases Surveillance System
NNPHI	National Network of Public Health Institutes
NNT	Number Needed to Treat
NSCSS Federal Task Force	National Syphilis and Congenital Syphilis Syndemic Federal Task Force
NSFG	National Survey of Family Growth
NSTC	National Science and Technology Council
NSTC	National Society of TB Clinicians
NTCA	National Tuberculosis Controllers Association
NTSS	National Tuberculosis Surveillance System
NYC	New York City
OCIO	Office of the Chief Information Officer
ONC	Office of the National Coordinator for Health Information Technology
PCP	Primary Care Providers
PCR	Polymerase Chain Reaction
PEP	Post-Exposure Prophylaxis
PHAC	Public Health Agency of Canada
PHIG	Public Health Infrastructure Grant
PHIN	Public Health Information Network
PHLs	Public Health Laboratories
PICO	Population, Intervention, Comparison, Outcomes
POC	Point-of-Care
PPT	PowerPoint
PrEP	Pre-Exposure Prophylaxis
PZA	Pyrazinamide
QA/QC	Quality Assurance/Quality Control
RCT	Randomized Controlled Trial
RIF	Rifampin
RNA	Ribonucleic Acid
RPT	Rifapentine
RWHP	Rural Women's health Project
RVCT	Report of Verified Case of Tuberculosis

Acronym	Definition
SAMS	Secure Access Management Services
SDOH	Social Determinants of Health
SHINE Trial	Shorter Treatment for Nonsevere Tuberculosis in African and Indian Children
SME	Subject Matter Expert
SOGI	Sexual Orientation and Gender Identity
SSP	Syringe Services Program
SSuN	STD Surveillance Network
STD	Sexually Transmitted Diseases
STI	Sexually Transmitted Infections
STIIRC	Sexually Transmitted Infections Impact Research Consortium
T-MSIS	Transformed Medicaid Statistical Information System
TA	Technical Assistance
TB	Tuberculosis
TB-PRACTECAL	Pragmatic Clinical Trial for a More Effective Concise and Less Toxic MDR-TB Treatment Regimen(s)
TBCB	California Tuberculosis Control Branch
TBESC	Tuberculosis Epidemiologic Studies Consortium
TBTC	Tuberculosis Trials Consortium
TEA	Tuberculosis Elimination Alliance
tNGS	Targeted Next Generation Sequencing
UNGA	United Nations General Assembly
US	United States
USCDI	United States Core Data for Interoperability
USPHS	United States Public Health Service
VA	Veterans Administration
VHA	Veterans Health Administration
WG	Working Group
WHO	World Health Organization
WGS	Whole Genome Sequencing
XDR-TB	Extensively Drug-Resistant TB

Attachment 3: Letter From May 30, 2023

ACET

Advisory Council for the Elimination of Tuberculosis

May 30, 2023

The Honorable Xavier Becerra
Secretary
Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Mister Secretary:

The Advisory Council for the Elimination of Tuberculosis (ACET) provides advice and recommendations regarding the elimination of tuberculosis (TB) in the United States to the Secretary of HHS, the Assistant Secretary of HHS, and the director of CDC. The members of ACET are writing to you regarding the increasing frequency of drug shortages in the United States (US).

Intermittent shortages of critical medications for treating TB, syphilis, cancer and other medical conditions have become increasingly common in the US. As an example, rifampin has been the cornerstone of treatment for most patients with TB for the past 50 years. It is also one of the preferred medications for treating latent TB infection (LTBI). In recent years, the US has experienced intermittent disruptions in rifampin supplies, putting people and communities at risk. One reason for this has been a decline in medication suppliers to the US market from five to two, which is inadequate to sustain supplies if one of them has a problem with either manufacturing or distribution. We are now experiencing critical shortages of other first line TB medications including isoniazid, pyrazinamide and ethambutol that severely impacts our ability to not only treat TB disease but also prevent future cases of TB.[i]

Recent advances in the treatment of drug-resistant TB have been made. Historically this required 18–24 months of treatment using a combination of medications with frequent and sometimes severe toxic side effects. Newer treatment regimens that are highly effective at curing drug-resistant TB in 6 months [ii] are now available. Realizing their full benefit requires that providers have timely and predictable access to the medications for the patients that need them.

Equitable access to TB medications and other medications for life-threatening diseases should be a priority. TB affects persons in all fifty states and US territories but access to these newer and effective treatment regimens for TB is not the same across the US. Recent trends in shortages across a wide range of medications elevates our concern about the short and long-term stability of the US drug supply and the US supply chains even more. Ensuring access to essential medicines is also a national security issue. The United

States Senate Committee on Homeland Security and Government Affairs recently published a report titled *Short Supply: The Health and National Security Risks of Drug Shortages* [iii] that outlines the current problems and gives recommendations to address them.

We recognize that this is a complex problem that cannot be solved by HHS or any single governmental agency. We respectfully ask that HHS:

1. **Prioritize working with appropriate stakeholders**, including CMS, the pharmaceutical industry, and others involved in contracting practices to address the root causes of drug shortages, as outlined in the 2019 FDA Report. [iv]

2. **Work with FDA to review and update the essential medications list** which currently does not include all first-line medications for treating drug-sensitive and drug-resistant TB

The inability to acquire and distribute essential medications in the US is both a public health and national security risk and needs to be a top priority for HHS.

Sincerely,

Robert Belknap, MD
Chair, Advisory Council for the Elimination of Tuberculosis

Cc:
Jonathan H. Mermin, MD, MPH, RADM and Assistant Surgeon General USPHS, Director, National Center for HIV, Viral Hepatitis, STD and TB Prevention
Philip LoBue, MD, Division of Tuberculosis Elimination Director, National Center for HIV, Viral Hepatitis, STD and TB Prevention
ACET Members

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[i] https://www.cdc.gov/tb/publications/letters/2023/tb-drug-shortage.htm 1
[ii] https://www.cdc.gov/tb/topic/drtb/bpal/default.htm
[iii] https://www.documentcloud.org/documents/23719898-2023-03-20-hsgac-majority-draft-drug-shortages-report9
[iv] https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions

Attachment 4: Written Public Comments

Dear Advisory Council for the Elimination of Tuberculosis (ACET),

My name is Jester Jersey. I am a first-generation born American after my family moved here to the United States from the Philippines. Today, I am an influencer and vaccine advocate who promotes the efficacy, safety and importance of vaccines.

Today, I address the council regarding the concerns of low vaccine rates. I understand the council's agenda and purpose is to consider strategies to address tuberculosis. I would like to suggest the strategy to work with community-based fraternal service organizations, such as Kiwanis International and Rotary International among others.

Fraternal service organizations have been an instrumental force in decreasing the incidence of vaccine-preventable diseases in several third-world nations globally while at the same time doing good service in their local communities. Prior to COVID, Kiwanis and Rotary have been responsible for addressing tetanus and polio, respectively, around the world.

However, fraternal organizations had been largely absent from any appreciable involvement during the COVID pandemic on a national level. This resulted in many casualties due to a lack of trust in the science, the vaccine and health authorities in general. This in turn may have possibly contributed to greater hesitancy to get vaccinated, and the subsequent lack of demand for the current schedule of vaccines, including the new COVID boosters and RSV vaccines. Even at the time of this writing, vaccine rates for most immunizations remain low.

However, perhaps the most damaging legacy of this lack of engagement with communities through messaging and trusted messengers are the diseases that were preventable before the pandemic, such as measles, the flu, and now, the growing U.S. cases of tuberculosis.

Vaccines may be the greatest tools we have in the fight against vaccine-preventable disease. Unfortunately, just like COVID, we aren't using one of our best resources wisely- community-based organizations, particularly fraternal service organizations, who have shown they've done incredible work abroad and could also do the same for communities in the United States. As a child, my parents often told me about the threat of disease when they were growing up, with tuberculosis being among them. I am fortunate to have grown up in the United States, where vaccines are more easily accessible. That is why I wanted to be a voice for vaccines- so others don't need to live in fear of vaccine-preventable diseases.

While vaccine rates have somewhat improved since the World Health Organization's report last summer of low global vaccine rates, this was prior to an RSV vaccine being approved. At the same time, COVID, despite the end of the Pandemic Health Emergency(PHE) in May, continues to seesaw like the flu, while other vaccine preventable diseases like measles and polio routinely resurface on news reports. The same occurred with tuberculosis recently. It will only be a matter

of time before more diseases join that list- ones we've already been close to eliminating yet occasionally resurface due to a lack of enthusiasm for vaccines.

We've seen the human toll vaccine-preventable diseases and low vaccine rates have taken. By not working with fraternal service organizations like Kiwanis, Rotary and other local organizations with national networks and community roots, it is only an open invitation to experiencing more of the same in the future- more ill and more casualties. I urge the Advisory Council for the Elimination of Tuberculosis, the CDC, HHS and president Joe Biden's administration to work with fraternal service organizations to help with vaccine efforts here in the United States like they have with vaccine-preventable disease worldwide.