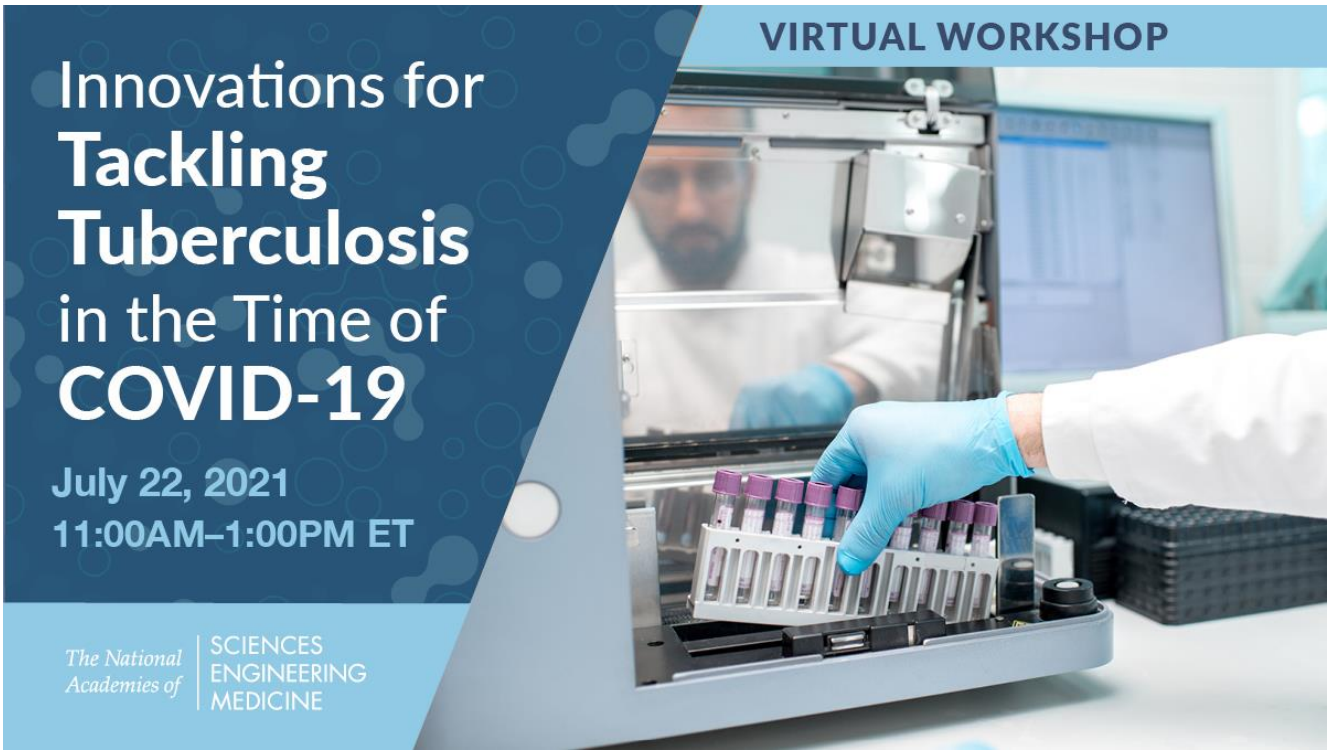
Forum on Microbial Threats

Innovations for Tackling Tuberculosis in the Time of COVID-19

Part One of a Two-Part Virtual Workshop
July 22, 2021



The National Academies of
SCIENCES • ENGINEERING • MEDICINE

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

INNOVATIONS FOR TACKLING TUBERCULOSIS IN THE TIME OF COVID-19

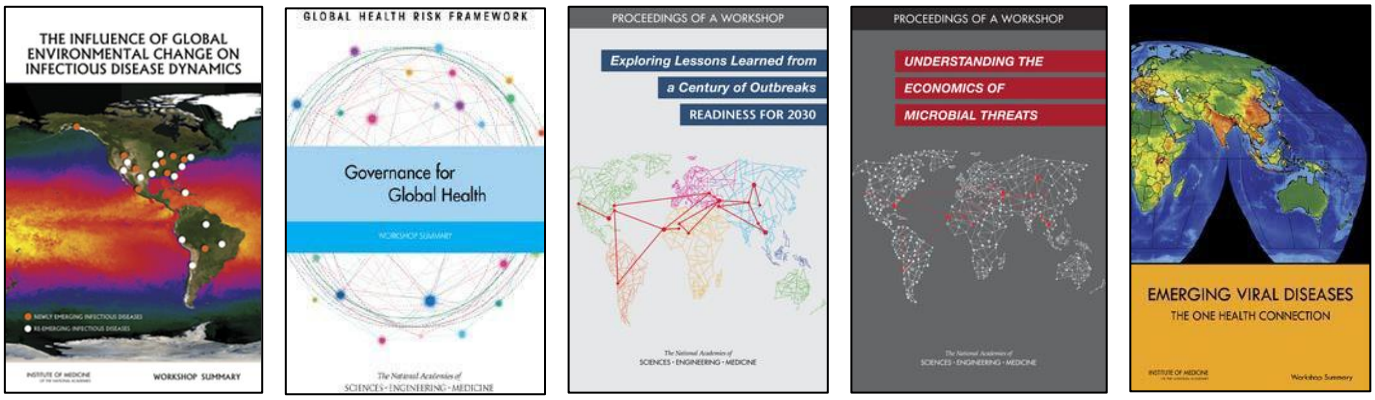
Part One of a Two-Part Virtual Workshop
July 22, 2021

TABLE OF CONTENTS

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

BOARD ON GLOBAL HEALTH

THE FORUM ON MICROBIAL THREATS



ABOUT THE FORUM

The Forum on Microbial Threats of the National Academies of Sciences, Engineering, and Medicine (National Academies) was created in 1996 at the request of the Centers for Disease Control and Prevention and the National Institutes of Health to provide a structured opportunity for discussion and scrutiny of critical, and possibly contentious, scientific and policy issues related to research on and the prevention, detection, surveillance, and responses to emerging and reemerging infectious diseases in humans, plants and animals as well as the microbiome in health and disease. The Forum brings together leaders from government agencies, industry, academia, and nonprofit and philanthropic organizations to facilitate cross-sector dialogue and collaboration through public debate and private consultation to stimulate original thinking about the most pressing issues across the spectrum of microbial threats.

Despite decades of progress, the need for the Forum on Microbial Threats remains. Problems such as MERS, Ebola, Chikungunya, Zika, yellow fever, and antibiotic resistance demonstrate how the issue of emerging infections is global and unrelenting. The drivers are ever more pervasive, and the consequences—human, social, and economic—loom larger than ever.

The Forum convenes several times each year to identify and discuss key problems and strategies in the area of microbial threats. To supplement the perspectives and expertise of its members, the Forum also holds public workshops to engage a wide range of experts, members of the public, and the policy community. All workshops are summarized in high quality scholarly workshop proceedings that are available for free download from the National Academies Press.

The Forum on Microbial Threats is part of the National Academies' Board on Global Health. For more information about the Forum, please visit our website: www.nationalacademies.org/microbialthreats.

SPONSORS

Financial support for the Forum is derived from the following government agencies, industries, and nonprofit and philanthropic associations:

- American Society of Tropical Medicine and Hygiene
- Burroughs Wellcome Fund
- EcoHealth Alliance
- Infectious Diseases Society of America
- Johnson & Johnson
- Merck & Co., Inc.
- New Venture Fund
- Sanofi Pasteur
- Biomedical Advanced Research and Development Authority
- U.S. Agency for International Development
- U.S. Centers for Disease Control and Prevention
- U.S. Department of Homeland Security
- U.S. Department of Veterans Affairs
- U.S. Food and Drug Administration
- U.S. National Institute of Allergy and Infectious Diseases
- Uniformed Services University of the Health Sciences

The Forum greatly appreciates our sponsors that make intellectual and financial contributions to the Forum's work.

HIGHLIGHTS OF RECENT WORKSHOP PROCEEDINGS

- The Critical Public Health Value of Vaccines: Tackling Issues of Access and Hesitancy: Proceedings of a Workshop (2021)
- Vaccine Access and Hesitancy: Part One of a Workshop Series: Proceedings of a Workshop—in Brief (2020)
- Exploring the Frontiers of Innovation to Tackle Microbial Threats: Proceedings of a Workshop (2020)
- The Convergence of Infectious Diseases and Noncommunicable Diseases: Proceedings of a Workshop (2019)
- Exploring Lessons Learned from a Century of Outbreaks: Readiness for 2030: Proceedings of a Workshop (2019)
- Understanding the Economics of Microbial Threats: Proceedings of a Workshop (2018)
- Urbanization and Slums: Infectious Diseases in the Built Environment: Proceedings of a Workshop (2018)
- Combating Antimicrobial Resistance: A One Health Approach to a Global Threat: Proceedings of a Workshop (2017)
- Building Communication Capacity to Counter Infectious Disease Threats: Proceedings of a Workshop (2017)

FORUM'S ACTION COLLABORATIVE – ONE HEALTH

The Forum's One Health Action Collaborative (OHAC), led by Gail Hansen, D.V.M., is an ad hoc activity that engages a community of participants who are interested in contributing to ongoing exploration and information sharing related to One Health topics. OHAC is committed to accelerating the implementation of a One Health approach in the field to counter microbial threats. Members include a subset of Forum members and a diverse range of external stakeholders from multiple sectors and disciplines such as public health, animal health, plant pathology, agriculture, environment, biotechnology, and others. Drawing from the dynamic discussions over regular conference calls, OHAC advises on One Health efforts that are internal and external to the National Academies, through the publication of papers and the hosting of seminars. For more info, click here.

FORUM MEMBERSHIP

Membership in the Forum includes a diverse range of stakeholders from multiple sectors.

Peter Daszak, Ph.D. *(Chair)*
EcoHealth Alliance

Kent E. Kester, M.D. *(Vice Chair)*
Sanofi Pasteur

Rima F. Khabbaz, M.D. *(Vice Chair)*
U.S. Centers for Disease Control and Prevention

Emily Abraham, Dr.PH.
Johnson & Johnson

Kevin Anderson, Ph.D.
U.S. Department of Homeland Security

Cristina Cassetti, Ph.D.
National Institute of Allergy and Infectious Diseases

Andrew Clements, Ph.D.
U.S. Agency for International Development

Scott F. Dowell, M.D., M.P.H.
Bill and Melinda Gates Foundation

Marcos A. Espinal, M.D., Dr.P.H., M.P.H.
Pan American Health Organization

Eva Harris, Ph.D.
University of California, Berkeley

Elizabeth D. Hermsen, Pharm.D., M.B.A.
Merck & Co., Inc.

Christopher R. Houchens, Ph.D.
Biomedical Advanced Research and Development Authority

Chandy C. John, M.D., M.S.
American Society of Tropical Medicine and Hygiene

Mark G. Kortepeter, M.D., M.P.H.
Uniformed Services University of Health Sciences

Michael Mair, M.P.H.
U.S. Food and Drug Administration

Jonna A. K. Mazet, D.V.M., M.P.V.M., Ph.D.
University of California, Davis

Victoria McGovern, Ph.D.
Burroughts Wellcome Fund

Sally A. Miller, Ph.D.
The Ohio State University

Suerie Moon, Ph.D., M.P.A.
The Graduate Institute, Geneva

Rafael Obregon, Ph.D., M.A.
United Nations Children's Fund

Kumanan Rasanathan, M.B.Ch.B., M.P.H
Health Systems Global

Gary A. Roselle, M.D.
U.S. Department of Veterans Affairs

Peter A. Sands, M.P.A.
The Global Fund to Fight AIDS, Tuberculosis & Malaria

Thomas W. Scott, Ph.D.
University of California, Davis

Matthew Zahn, M.D.
Orange County Health Care Agency

FORUM STAFF

Julie Liao, Ph.D.
Director, Forum on Microbial Threats
(202)-334-2191
JLiao@nas.edu

Charles Minicucci
Research Assistant
(202)-334-2157
CMinicucci@nas.edu

Claire Biffl
Senior Program Assistant
CBiffl@nas.edu

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

Innovations for Tackling Tuberculosis in the Time of COVID-19

Part One of a Two-Part Virtual Workshop
July 22, 2021

AGENDA

Objectives:

This two-part public workshop will examine future innovations required to meet the United Nations High-Level Meeting (UNHLM) on Tuberculosis targets in 2022 and the WHO END TB Strategy targets by 2030.

Despite being preventable and curable, tuberculosis (TB) has long been the world's deadliest infectious disease and continues to kill 1.4 million and sicken 10 million new people each and every year, mostly the poorest and most vulnerable people in the world. Unfortunately, COVID-19 and its mitigation efforts have taken a devastating toll on countries with the highest burden of TB disease and the global TB response, threatening to reverse up to eight years of progress. Recent modeling exercises project that between 2020 and 2025, the initial impact in 2020 of the COVID-19 pandemic will result in an additional 1.4 million TB deaths. The webinar series will consider the science behind the innovations required to bring TB diagnosis, treatment, prevention, and political commitment to the 21st century and achieve the ambitious targets set by the UNHLM and WHO.

This public webinar series will feature invited presentations and discussions to consider:

- How can we accelerate the development of affordable point-of-care tests for TB? What barriers or challenges have prevented the development of accessible point-of-care tests for TB for low and middle income countries?
- Improvements in the usual care for TB: Can we achieve a two-week, non-toxic treatment for drug-sensitive and drug-resistant TB?
- How can we rapidly use the TB platform, such as contact investigation, in low- to middle-income countries to address COVID-19 and other airborne infections to prevent future pandemics?
- How can we ensure increased and sustained commitments to reach the UNHLM TB targets in high burden countries, despite the challenges from COVID-19?

A proceedings of the presentations and discussions at the webinar will be prepared by a designated rapporteur in accordance with institutional guidelines. For more information on this virtual workshop, please visit the main project page.

WORKSHOP PART 1

Thursday, 22 July, 2021
11:00 AM – 1:00 PM ET

Current State of Tuberculosis Elimination and Impact of COVID-19

11:00 AM **Welcome Remarks, Workshop Overview and Goals**
Workshop Co-Chairs

GAIL H. CASSELL
Harvard Medical School

KENNETH G. CASTRO
Rollins School of Public Health & School of Medicine
Emory University

11:05 AM **Opening Addresses: Current Status and Urgency of Ending TB Around the Globe**

JIM YONG KIM
Global Infrastructure Partners

SALMAAN KESHAVJEE
Harvard Medical School

ERIC RUBIN
New England Journal of Medicine

Challenges and Innovations

Moderator: Lucica Ditiu

11:30 AM **Diagnostics**
SOUMYA SWAMINATHAN
World Health Organization

11:40 AM **Vaccines and Therapeutics**
EMILIO EMINI
Bill & Melinda Gates Foundation

11:50 AM **Critical Need for New Business Models**
KEVIN OUTTERSON
Boston University School of Law

12:00 PM **Discussion**
Moderator: LUCICA DITIU
STOP TB Partnership / UNOPS

12:55 PM **Wrap-up and Adjourn**
GAIL H. CASSELL, *workshop co-chair*
KENNETH G. CASTRO, *workshop co-chair*

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

Innovations for Tackling Tuberculosis in the Time of COVID-19

A Two-Part Virtual Workshop

PLANNING COMMITTEE

Gail H. Cassell, Ph.D. *(Co-Chair)*
Senior Lecturer on Global Health and Social Medicine
Harvard Medical School

Kenneth G. Castro, M.D. *(Co-Chair)*
Senior TB Scientific Advisor
TB Division, Office of Infectious Diseases
Bureau for Global Health, USAID
Professor of Global Health, Epidemiology, and Infectious Diseases
Rollins School of Public Health and School of Medicine
Emory University

Emily Abraham, Dr.P.H.†
Member, Forum on Microbial Threats
Director, External Affairs and Policy
Global Public Health at Johnson & Johnson

Andrew Clements, Ph.D.†
Member, Forum on Microbial Threats
Senior Technical Advisor, Emerging Threats Division
U.S. Agency for International Development

Lucica Ditiu, M.D.
Executive Director
STOP TB Partnership

Marcos A. Espinal, M.D., Dr.P.H., M.P.H.†
Member, Forum on Microbial Threats
Director, Department of Communicable Diseases and Health Analysis
Pan American Health Organization

Hamidah Hussain, MBBS, MSC, Ph.D.
Global Technical Lead
Interactive Research & Development

Tereza Kasaeva, M.D., Ph.D., M.S.
Director, Global Tuberculosis Programme
World Health Organization

Kent E. Kester, M.D.†
Vice-Chair, Forum on Microbial Threats
Vice President and Head
Translational Science and Biomarkers
Sanofi Pasteur

Monique Mansoura, Ph.D., M.S., M.B.A.
Executive Director
Global Health Security and Biotechnology
MITRE

Peter Sands, M.P.A.†
Member, Forum on Microbial Threats
Executive Director
The Global Fund to Fight AIDS, Tuberculosis and Malaria

Charles Wells, M.D.
Head of Therapeutics Development
Bill & Melinda Gates Medical Research Institute

† Member, Forum on Microbial Threats

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

Innovations for Tackling Tuberculosis in the Time of COVID-19

A Two-Part Virtual Workshop

PLANNING COMMITTEE BIOGRAPHIES

Gail H. Cassell, Ph.D., D.Sc. (Hon.), *(Co-Chair)* is Senior Lecturer, Department of Global Health and Social Medicine, Harvard Medical School. She is a member of the National Academy of Medicine [formerly the Institute of Medicine (IOM)] of the National Academy of Sciences and served two terms on the IOM Council, the governing board. She is a former member of the Health Sciences Policy Board and was an inaugural member of the Emerging Infectious Disease Forum. She founded the IOM Forum on Drug Discovery, Development and Translation and she was the inaugural Co-Chair of the Forum during which time she organized 6 IOM workshops in South Africa, Russia, India, and China in collaboration with the National Academy of Sciences in these countries to assess the realities of Drug Resistant TB and to develop a blue print for action. She is former Vice President for Scientific Affairs and Distinguished Lilly Research Scholar of Infectious Diseases and former Vice President for Infectious Diseases Drug Discovery and Development of Eli Lilly and Company Indianapolis, Indiana. In this capacity among other things, she was responsible for initiating and leading the not-for-profit Lilly TB Drug Discovery Initiative launched in 2007. In 2003, she was one of two individuals at Lilly who initiated and developed the Lilly Multidrug Resistant Tuberculosis (MDRTB) Partnership. The partnership has resulted in company support to date exceeding $170 million dollars. Prior to moving to Lilly in 1997, Dr. Cassell was the former Charles H. McCauley Professor and Chairman of the Department of Microbiology at the University of Alabama Schools of Medicine and Dentistry at Birmingham, a department which ranked first in research funding from the National Institutes of Health (NIH) during the decade of her leadership. She obtained her B.S. from the University of Alabama in Tuscaloosa and in 1993 was selected by that institution as one of the top 31 female graduates of the Centennial following the admission of the first female to the University in 1893. She obtained her Ph.D. in Microbiology from the University of Alabama at Birmingham and was selected as its 2003 Distinguished Alumnus. She is a past President of the American Society for Microbiology and is currently serving her second elected term on the Board of Governors of the American Academy of Microbiology. Dr. Cassell is an elected life time member of the U.S Council on Foreign Relations. She was named to the original Board of Scientific Councilors of the Center for Infectious Diseases, Centers for Disease Control (CDC) and served as Chair of the Board. She has served on the Advisory Board of the of the Director of NIH, Director of CDC, and the Secretary of Health and Human Services Advisory Council of Public Health Preparedness, the Food and Drug Administration's (FDA) Science Board, the Advisory Committee to the Commissioner. She was a member of the NIH Science Management Board and Advisory Councils of the National Institute of Allergy and Infectious Diseases and the Fogarty International Center of NIH. For two decades she was a member of the Steering Committee of the U.S.-Japan Cooperative Medical Sciences Program responsible for advising the respective governments on joint research agendas, (U.S. State Department/Japan Ministry of Foreign Affairs). She was instrumental in establishment of the U.S./Russia Cooperative Medical Sciences and Training Program under the Bilateral Presidential Commission in 2009 which was a collaboration involving NIH, the US National Academy of Sciences, the Russian Academy of Sciences, and the Russian Academy of Medical Sciences. In 2012, the American Society for Microbiology and the Federation of European Microbiology Societies established the Mäkelä–Cassell Exchange Program for pioneering international engagement for young scientists. She has served on several editorial boards of scientific journals and has authored over 350 articles and book chapters. She has received national and international awards for her research in infectious diseases, including: two honorary degrees; the CDC Honor Award in Public Health for exceptional leadership and contributions in the development and implementation of CDC's Emerging Infectious Disease Plan 1997; a Citation from the FDA Commissioner for her role as Chair of the review of science and technology at the FDA and the Report FDA: Science and Mission at Risk 2008."

Kenneth G. Castro, M.D., *(Co-Chair)* Physician-scientist trained in epidemiology, with a specialty in internal medicine and subspecialty in infectious diseases. An award-winning author of more than 175 scholarly and evidence-based policy

publications; serves as a peer reviewer for numerous scientific journals and is an associate editor for the journals *International Journal of Tuberculosis and Lung Disease* and *Emerging Infectious Diseases*. A native Puerto Rican, Dr. Castro speaks fluent Spanish, and has frequently served as advisor to the Puerto Rico Department of Health, the Pan American Health Organization, World Health Organization, and several Ministries of Health in countries where TB and HIV constitute major public health problems. In 2008 Dr. Castro was recognized by the Hispanic Officers Advisory Committee, U.S. Public Health Service Commissioned Corps with the prestigious Juan Carlos Finlay award. In October 22, 2011, he was profiled in The Lancet as a "Public Health Hero" by Associate Editor Pamela Das. In March 2014 he received the Lifetime Achievement Award from the International Union Against Tuberculosis and Lung Diseases, North America Region, and the Lifetime Achievement Award conferred by the U.S. Agency for International Development. In June 2016 he received the prestigious CDC Charles C. Shepard Lifetime Science Achievement Award. "This award recognizes individuals for a body of work contributing to public health."

Emily Abraham, Dr.P.H., is Director of External Affairs and Policy for Johnson & Johnson Global Public Health, where she focuses on tuberculosis, HIV, antimicrobial resistance, and non-communicable diseases. Her background is in the intersection of global/domestic public health and business, with expertise in policy, management, research, health economics, market access, and digital health across multiple disease areas.

Andrew Clements, Ph.D. is a Senior Scientific Advisor for the Emerging Threats Division in the U.S. Agency for International Development's Bureau for Global Health. He received his Ph.D. in Anaerobic Microbiology from Virginia Tech and completed his post-doctoral training in biochemistry at the National Institutes of Health. Between 1997 and 2005, he served as an infectious disease advisor at USAID focusing on the development, management, and monitoring of international programs to address malaria, tuberculosis, antimicrobial resistance, and infectious disease surveillance. Since 2005, he has managed a number of projects (PREDICT, PREVENT) and partnerships with the Food and Agriculture Organization of the UN and the World Health Organization that support prevention, detection, and response to emerging zoonotic threats in developing countries. He also analyzes trends for emerging zoonotic threats and has participated in USAID's responses to new diseases, including H5N1 and H7N9 avian influenza, H1N1 pandemic influenza, MERS-CoV, and Ebola.

Lucica Ditiu, M.D., Executive Director of the Stop TB Partnership, is a Romanian pulmonologist, accomplished professional and leader in the global fight against tuberculosis (TB) and other communicable diseases. Dr. Ditiu graduated from the University of Medicine and Pharmacy in Bucharest, Romania in 1992 and has the specialization on Lung Diseases Specialist acquired in 1998. Dr. Ditiu is UN staff since 2000 and in this capacity she led emergency and preparedness and TB related work in Albania, Macedonia and Kosovo; she was the head of WHO Balkan Office, a TB and TB/HIV Medical Officer in WHO Regional Office for Europe and the lead of the TB REACH of Stop TB Partnership. Over her more than 20 years international career in public health, Dr. Ditiu published numerous articles, research papers, op-eds and interviews and served in different Boards and committees, including the Global Fund. Dr. Ditiu's work is driven by the firm belief that we should "leave no one behind" and is one of the strongest advocates within the international community in the fight for ensuring unrestricted access to quality diagnosis, treatment and care for all people, especially the most marginalized. A firm believer in innovation, flexibility, change, breaking the rules and thinking out of the box, Dr. Ditiu is dedicated to driving political commitment and engagement to accelerate the efforts to End TB. Dr. Ditiu participated in MDR TB related meetings of the National Academy.

Marcos A. Espinal, M.D., Dr.P.H., M.P.H., is the director of the Department of Communicable Diseases and Health Analysis at the Pan American Health Organization (PAHO), Regional Office of the World Health Organization (WHO) for the Americas. Dr. Espinal, a national of the Dominican Republic, holds a medical degree from the Universidad Autónoma de Santo Domingo, Dominican Republic (1985). He has an M.P.H. (1990) and a Dr.P.H. (1995) from the University of California at Berkeley School of Public Health. His work experience includes positions in the Ministry of Health of the Dominican Republic and the National Center for Research on Maternal and Child Health; the New York City Public Health Department; and the WHO where he worked for 13 years. Before joining PAHO, Dr. Espinal served as Executive Secretary of the WHO Stop TB Partnership, a global movement aiming at the elimination of TB as a public health problem. Dr. Espinal has published more than 100 peer-reviewed publications in the field of communicable diseases. He is a recipient of the Scientific Prize of the International Union against Tuberculosis and Lung Diseases, the Walter and Elise A. Hass

International Award by the University of California at Berkeley for a distinguished record of service in international health, and the Princess Chichibu Memorial Tuberculosis Global Award by the Japan Anti-Tuberculosis Association.

Hamidah Hussain, MBBS, M.Sc., Ph.D., is a public health professional with over two decades of experience in designing, implementing, and evaluating global health service delivery programs and epidemiological research in Pakistan, Bangladesh, Tajikistan, Indonesia, Philippines and South Africa. Her portfolio includes work on active case finding for susceptible and drug resistant TB, childhood TB, TB preventive services, childhood vaccines, and preventable diseases, Malaria control programs along with costing and cost effectiveness of these interventions.

She led the IRD's flagship TB program based at the Indus Hospital in Karachi and was instrumental in scaling DR-TB treatment services in two provinces of Pakistan. She was also part of the team that received The Global Fund grant on TB and Malaria as Principal Recipient. Dr. Hussain is currently the Global Technical Lead for IRD's TB Preventive treatment programs and have assisted Pakistan and Afghanistan to draft their national TB preventive treatment guidelines.

She is the founding country director for IRD Bangladesh where she also served as the senior strategy advisor to the National TB Control Program providing leadership in establishing vision and technical direction of USAID funded Challenge TB project. Previously Dr. Hussain worked at the Johns Hopkins Bloomberg School of Public Health in Baltimore and BRAC in Bangladesh. Dr. Hussain received medical degree from The Aga Khan University, Master in Health Policy, Planning and Financing from London School of Hygiene and Tropical Medicine and PhD in health economics from University of Bergen, Norway.

Tereza Kasaeva, M.D., Ph.D., M.S., is the Director of the World Health Organization's Global TB Programme. As Director of the WHO Global TB Programme, she is responsible for setting norms, policies and standards on global TB prevention, control and care including on tackling drug resistance, coordinating technical support, monitoring the global situation, developing innovative interventions through translation of new evidence into policies & practice, promoting research & development and through addressing system challenges such as community and private sector engagement.

Dr. Kasaeva was previously the Deputy Director of the Department of Medical Care in the Ministry of Health of the Russian Federation. In this role, she conceived the concept of, and co-led the organisation of the First WHO Global Ministerial Conference on Ending TB in the Sustainable Development Era which took place on 16-17 November 2017 in Moscow. This landmark event brought together 75 Ministers of Health and other sectors from 120 country delegations overall, among over 1000 participants including civil society, partners, academia and the corporate sector. The Moscow Declaration to End TB, adopted at the conference, includes commitments and calls to action to accelerate efforts to end the TB epidemic, and will inform Heads-of-State participating in the first-ever United Nations General Assembly high-level meeting on TB in 2018. She also co-led efforts among BRICS Member States to set up and launch the BRICS TB Research Network to advance collaboration, mobilize resources and catalyse TB R&D.

As a leading health expert, Dr. Kasaeva has over 25 years of experience in public health, with over ten years at the Ministry of Health of the Russian Federation. She has worked closely with numerous stakeholders including Member States, civil society, as well as national and international partners. For the past decade, she coordinated the national TB programme in the Russian Federation. She facilitated and directed the cooperation between former Soviet Union countries, EUROZEU, BRICS and other countries on problems related to TB, HIV and migration. Since 2013, she has been the co-chair of the Secretariat of the High-Level Working Group of the Russian Ministry of Health and WHO on TB. In 2017, she was a member of the WHO Strategic and Technical Advisory Group for TB (STAG-TB). In addition, Dr. Kasaeva has been instrumental in leading efforts to, modernize the health system in the country, prevent and control socially significant diseases, as well as promote outpatient care for TB patients.

Dr. Kasaeva graduated from the North Ossetian State Medical Academy in the Russian Federation in 1992 as a Medical Doctor and specialized in Cardiology at the same Academy. She has a PhD in Public Health focusing on the perfection of outpatient technologies for the treatment of the TB patients from the I.M. Sechenov First Moscow State Medical University. She also has a Master's degree in International Relations with a focus on politics and governance from the European Studies Institute in Moscow, Russia. She is certified as a healthcare organization specialist by the Russian Medical Academy of Postgraduate Education. In 2015, she was awarded the prestigious Breastplate "Excellence in Public Health", and the Honorary Diploma of the Ministry of Health and Social Development of the Russian Federation in 2009.

Kent E. Kester, M.D., is currently Vice President and Head, Translational Science and Biomarkers at Sanofi Pasteur. In this capacity, he leads a team of over 200 research and clinical professionals in the US and France focused on the translational development of new vaccines.

During a 24-year career in the U.S. Army, he worked extensively in clinical vaccine development and led multiple research platforms at the Walter Reed Army Institute of Research, the U.S. Department of Defense's largest and most diverse biomedical research laboratory with a major emphasis on emerging infectious diseases, an institution he later led as its Commander. His final military assignment was as the Associate Dean for Clinical Research in the School of Medicine at the Uniformed Services University of the Health Sciences (USUHS).

Dr. Kester holds an undergraduate degree from Bucknell University and an M.D. from Jefferson Medical College, completing his internship and residency in internal medicine at the University of Maryland and a research fellowship in infectious diseases at the Walter Reed Army Medical Center. Currently a member of the US Government Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) and the Department of Veterans Affairs Health Services Research & Development Service Merit Review Board, he previously chaired the Steering Committee of the NIAID/USUHS Infectious Disease Clinical Research Program, and has served as a member of the FDA Vaccines & Related Biologics Products Advisory Committee (VRBPAC), the NIAID Advisory Council, and the CDC Office of Infectious Diseases Board of Scientific Counselors. He is the Vice Chair of the National Academy of Medicine Forum on Microbial Threats and is also a member of the Standing Committee on Emerging Infectious Diseases and 21st Century Health Threats. Board-certified in both internal medicine and infectious diseases, Dr. Kester holds faculty appointments at USUHS and the University of Maryland; and is a fellow of the American College of Physicians, the Royal College of Physicians of Edinburgh, the Infectious Disease Society of America, and the American Society of Tropical Medicine and Hygiene. He is a member of the clinical faculty at the University of Maryland Shock Trauma Center in Baltimore and the Wilkes-Barre VA Medical Center.

Monique Mansoura, Ph.D., M.S., M.B.A., joined The MITRE Corporation as the Executive Director for Global Health Security and Biotechnology in September 2017. She brings technical, policy and business expertise from both the public and private sectors. For twenty years she has been a trailblazer on the development and sustainability of the industrial base and resilient supply chains central to the public-private partnerships that are vital to global health security, the bioeconomy and healthcare. She was a leader of the COVID-19 Healthcare Coalition, led by MITRE and the Mayo Cl and received the MITRE President's Award in recognition of that work.

During a recent sabbatical, Monique explored new business models and financial vehicles for raising and deploying funds to enhance global health security as a Research Affiliate of the MIT Laboratory for Financial Engineering (LFE), led by Professor Andrew Lo.

She serves on the Board of the International Cancer Expert Corps (ICEC) and is dedicated to capacity and capability building for the provision of cancer care in low- and middle-income countries and in doing so, bridging the investment dichotomy between infectious diseases and cancer.

Monique earned a PhD in Bioengineering and a M.S. in Human Genetics from the University of Michigan, a B.S. in Chemical Engineering from Wayne State University, and an MBA in the Sloan Fellows Program in Innovation and Global Leadership at MIT.

Monique co-chaired (with Richard Hatchett) the 2015 IOM Workshop Planning Committee "Enabling Rapid Response and Sustained Capability with Medical Countermeasures to Mitigate Risk of Emerging Infectious Diseases" and served on the 2009-2010 workshop planning committee for "The Public Health Emergency Medical Countermeasures Enterprise - Innovative Strategies to Enhance Products from Discovery through Approval."

Peter Sands, M.P.A., is the executive director of The Global Fund to Fight AIDS, Tuberculosis, and Malaria. Since June 2015, Mr. Sands has been a research fellow at Harvard University, dividing his time between the Mossavar-Rahmani Center for Business and Government at Harvard Kennedy School and the Harvard Global Health Institute, part of the Harvard T.H. Chan School of Public Health, and working on a range of research projects in financial markets and regulation, fintech, and

global health. Mr. Sands' engagement with global health issues includes: chairing the U.S. National Academy of Medicine's Commission on a Global Health Risk Framework for the Future, which in January 2016 produced the highly influential report The Neglected Dimension of Global Security: A Framework to Counter Infectious Disease Threats; chairing the World Bank's International Working Group on financing preparedness, which in May 2017 published From Panic and Neglect to Investing in Health Security: Financing Preparedness at a National Level; authoring several papers on infectious disease crises in the New England Journal of Medicine, The Lancet, and British Medical Journal; being the lead non-executive director between 2011-2017 on the Board of the UK's Department of Health, which provides oversight and policy direction to the UK's National Health Service; and being an active member on both the U.S. National Academy of Science's Committee on Ensuring Access to Affordable Drugs and the Forum on Microbial Threats. Mr. Sands is a board member or advisor to several startups in the fintech and meditech arenas, such as Noble Markets (US) and Cera (UK). He was group chief executive of Standard Chartered PLC from November 2006 to June 2015. He joined the Board of Standard Chartered PLC as group finance director in May 2002, responsible for finance, strategy, risk and technology, and operations. Prior to this, Mr. Sands was a senior partner at worldwide consultants McKinsey & Co. Before joining McKinsey, he worked for the UK's Foreign and Commonwealth Office. He has served on various boards and commissions, including as a director of the World Economic Forum and co-chairman of Davos, governor of the UK's National Institute for Economic and Social Research, member of the International Advisory Board of the Monetary Authority of Singapore, member of the Browne Commission on Higher Education Funding in the UK, member of the China People's Association for Friendship with Foreign People's Global CEO Council, co-chair of the UK-India CEO Forum, board director of the Institute of International Finance, chairman of the International Monetary Conference, member of the International Advisory Board of Lingnan University, China, and trustee of the Camden Roundhouse, London. Mr. Sands graduated from Brasenose College, Oxford University with a first class degree in politics, philosophy, and economics. He also received a Master in Public Administration from Harvard University, where he was a Harkness Fellow. Mr. Sands, who grew up in Singapore and Malaysia, is married to author and bookshop owner, Betsy Tobin and has four children.

Charles Wells, M.D., currently serves as Head of Therapeutics Development at the Bill & Melinda Gates Medical Research Institute in Cambridge, Massachusetts, where he joined in May 2019. Previously he served as Executive VP for Global Health and Development for Infectious Diseases at Evotec carrying forward in this role with the transfer of the Infectious Diseases Therapeutics R&D group from Sanofi to Evotec in July 2018. His work in this role included overseeing development activities for new therapeutic agents for malaria, bacterial diseases and biologics development for HIV, chikungunyan virus and viral hepatitis among other diseases. Prior to joining Sanofi in late 2015, he served as Senior Medical Director for the development and initial registration of delamanid (Deltyba) for treatment of multidrug resistant tuberculosis at Otsuka Pharmaceuticals, during 2007-2015. Before Otsuka, he served as Chief of the International Research and Programs Branch of the Division of Tuberculosis Elimination at the U.S. Centers for Disease Control and Prevention (CDC) during 2000-2007. He is a native of North Carolina where he completed his medical studies at the University of North Carolina at Chapel Hill in 1992 and then his post-graduate medical training in internal medicine and infectious diseases at Emory University, as well as the Epidemic Intelligence Service at CDC.

Charles previously served as a member in the role of industry representative for the National Academies of Science, Engineering, and Medicine, Committee on Clinical Trials during the 2014-2015 Ebola Outbreak in West Africa during Jan – Nov 2016.

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

Innovations for Tackling Tuberculosis in the Time of COVID-19

Part One of A Two-Part Virtual Workshop
July 22, 2021

SPEAKER BIOGRAPHIES

Emilio A. Emini, Ph.D., is the Director of the Tuberculosis and HIV Program at the Bill & Melinda Gates Foundation. He joined the foundation in 2015 following a greater than 30-year career in the biopharmaceutical industry during which he held multiple senior positions in anti-infectives and vaccines R&D. At the Merck Research Laboratories, from 1983 to 2004, Emilio led the biological research that developed the first of the highly active antiretroviral therapies for HIV and led multiple vaccine research teams that participated in the successful development of a number of vaccines, including vaccines for human papillomavirus and rotavirus. Following a two-year leave from the industry at the International AIDS Vaccine Initiative, Emilio joined Wyeth/Pfizer as the Senior Vice President of Vaccine R&D where he led the development of the Prevnar 13 vaccine for prevention of pneumococcal disease.

Emilio is a recipient of the Distinguished Alumnus Award from the Cornell University Graduate School of Medical Sciences. He is an elected Fellow of the American Academy of Microbiology, and the College of Physicians of Philadelphia. He is a former Trustee of the National Foundation for Infectious Diseases and served as a member of the National Preparedness & Response Science Board, an advisory committee to the U.S. Secretary of Health and Human Services.

Until recently, Emilio served on the Board of the Gates Medical Research Institute. As of August 1st, 2021, he will join the Institute as its CEO.

Salmaan Keshavjee M.D., Ph.D., ScM, is Professor of Global Health and Social Medicine at Harvard Medical School and the Director of Harvard Medical School's Center for Global Health Delivery. He is also a physician in the Division of Global Health Equity at Boston's Brigham and Women's Hospital, where he is Associate Professor of Medicine.

Dr. Keshavjee is a leading expert in tuberculosis treatment and the anthropology of health policy. He is the author of Blind Spot: How neoliberalism infiltrated global health¬. He has worked extensively with the Boston-based non-profit Partners In Health (PIH) on the treatment of multidrug-resistant tuberculosis (MDR-TB). Over the last 20 years, Dr. Keshavjee has conducted clinical and implementation research on MDR-TB in Russia, both in the prison and civilian sectors. He was Deputy-Director for the Partners In Health's health programs in Lesotho (2006-2008), launching one of the first community-based treatment programs for multi-drug resistant tuberculosis/HIV co-infection in sub-Saharan Africa. More recently, he has been working with Advance Access & Delivery, a non-governmental organization for which he is a co-founder and clinical advisor for projects in India and South Africa. His research has resulted in a number of clinical and policy manuscripts on TB and MDR-TB, which have had significant clinical and policy impact.

Dr. Keshavjee is the Chair of the Steering Committee for the Zero TB Initiative, a global coalition of implementers, policy-makers and activists working to create islands of tuberculosis elimination in a number of countries worldwide. He was the Chair of the World Health Organization/Stop TB Partnership's Green Light Committee for Multidrug-resistant TB from 2007-2010. He has been involved in a number of global guidelines for tuberculosis treatment including at the World Health Organization and the American Thoracic Society. During the Covid-19 epidemic he has been involved with the work of the START coalition, committed to using layered technologies to keep public spaces safe from airborne disease transmission.

Jim Yong Kim (@JimYongKim), M.D., Ph.D., is Vice Chairman and Partner at Global Infrastructure Partners, a fund that invests in infrastructure projects across several sectors around the world.

From July 2012 to February 2019, Kim served as the 12th President of the World Bank Group. Soon after he assumed that position, the organization established two goals to guide its work: to end extreme poverty by 2030; and to boost shared prosperity, focusing on the bottom 40 percent of the population in developing countries.

During Kim's tenure, the World Bank Group supported the development priorities of countries at levels never seen outside of a financial crisis. Along with partners, the World Bank achieved two successive, record replenishments of the institution's fund for the poorest countries. The World Bank Group also launched several innovative financial instruments, including facilities to address infrastructure needs, prevent pandemics, and help the millions of people forcibly displaced from their homes by climate shocks, conflict, and violence.

A physician and anthropologist, Kim's career has revolved around health, education, and improving the lives of the poor. Before joining the World Bank Group, he served as the President of Dartmouth College and held professorships at Harvard Medical School and the Harvard School of Public Health. From 2003 to 2005, Kim served as Director of the World Health Organization's HIV/AIDS department. He led WHO's "3 by 5" initiative, the first-ever global goal for AIDS treatment, which greatly expanded access to antiretroviral medication in developing countries. In 1987, Kim co-founded Partners In Health, a non-profit medical organization that now works in poor communities on four continents.

Kim received a MacArthur "Genius" Fellowship, was recognized as one of America's "25 Best Leaders" by *U.S. News & World Report,* and was named one of *TIME* magazine's "100 Most Influential People in the World."

Kevin Outterson, J.D., LL.M., teaches health care law at Boston University, where he co-directs the Health Law Program. He serves as the founding Executive Director and Principal Investigator for CARB-X, a $480M international public-private partnership to accelerate global antibacterial innovation. Key partners in CARB-X include the US Government (BARDA & NIAID), the Wellcome Trust, the German Federal Ministry of Education and Research (BMBF), the UK Government (GAMRIF), and the Bill & Melinda Gates Foundation.

Professor Outterson's research work focuses on the law and economics of antimicrobial resistance. He served as a senior author on many key research reports on antibiotic innovation, including Chatham House, ERG, DRIVE-AB, and the Lancet Commission. Professor Outterson was given the 2015 Leadership Award by the Alliance for the Prudent Use of Antibiotics for his research and advocacy work. He has testified before Congress, Parliamentary working groups, WHO, and state legislatures. Since August 2016, he leads CARB-X, the world's largest and most innovative antibiotic accelerator.

Eric Rubin, M.D., Ph.D., is an Associate Physician specializing in infectious disease at Brigham and Women's Hospital and is a Professor in the Department of Immunology and Infectious Diseases at the Harvard T.H. Chan School of Public Health. He serves on several scientific advisory boards to groups interested in infectious disease therapeutics. Dr. Rubin has also previously served as the Associate Editor for Infectious Disease at the New England Journal of Medicine as well as an editor for several basic science journals including PLoS Pathogens, Tuberculosis, and mBio.

Soumya Swaminathan, M.D., was appointed WHO's first Chief Scientist in March 2019. A paediatrician from India and a globally recognized researcher on tuberculosis and HIV, she brings with her 30 years of experience in clinical care and research and has worked throughout her career to translate research into impactful programmes. Dr Swaminathan was Secretary to the Government of India for Health Research and Director General of the Indian Council of Medical Research from 2015 to 2017. In that position, she focused on bringing science and evidence into health policy making, building research capacity in Indian medical schools and forging south-south partnerships in health sciences. From 2009 to 2011, she also served as Coordinator of the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases in Geneva.

She received her academic training in India, the United Kingdom, and the United States of America, and has published more than 350 peer-reviewed publications and book chapters. She is an elected Foreign Fellow of the US National Academy of Medicine and a Fellow of all three science academies in India. The Science division's role is to ensure that WHO stays ahead of the curve and leverages advances in science and technology for public health and clinical care, as well as ensuring that the norms, standards and guidelines produced by WHO are scientifically excellent, relevant and timely. Her vision is to ensure that WHO is at the cutting edge of science and is able to translate new knowledge into meaningful impact on population health worldwide.

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

Background Material

1. World Health Organization's End TB Strategy – information sheet

2. United Nations High-Level Meeting on Tuberculosis

a. Key Targets and Commitments for 2022
b. 2020 Progress Report

3. Perspectives on the future of tuberculosis research

a. Reimagining the Research Approach to Tuberculosis
b. 2019: A Banner Year for Tuberculosis Research

THE END TB STRATEGY

World Health Organization

Global strategy and targets for tuberculosis prevention, care and control after 2015

VISION	**A world free of tuberculosis** – zero deaths, disease and suffering due to tuberculosis			
GOAL	**End the global tuberculosis epidemic**			
INDICATORS	**MILESTONES**		**TARGETS**	
	2020	**2025**	**SDG 2030**	**END TB 2035**
Reduction in number of TB deaths compared with 2015 (%)	35%	75%	**90%**	**95%**
Reduction in TB incidence rate compared with 2015 (%)	20% (<85/100 000)	50% (<55/100 000)	**80% (<20/100 000)**	**90% (<10/100 000)**
TB-affected families facing catastrophic costs due to TB (%)	Zero	Zero	**Zero**	**Zero**

PRINCIPLES

1. *Government stewardship and accountability, with monitoring and evaluation*
2. *Strong coalition with civil society organizations and communities*
3. *Protection and promotion of human rights, ethics and equity*
4. *Adaptation of the strategy and targets at country level, with global collaboration*

PILLARS AND COMPONENTS

1. INTEGRATED, PATIENT-CENTRED CARE AND PREVENTION

A. Early diagnosis of tuberculosis including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups
B. Treatment of all people with tuberculosis including drug-resistant tuberculosis, and patient support
C. Collaborative tuberculosis/HIV activities, and management of co-morbidities
D. Preventive treatment of persons at high risk, and vaccination against tuberculosis

2. BOLD POLICIES AND SUPPORTIVE SYSTEMS

A. Political commitment with adequate resources for tuberculosis care and prevention
B. Engagement of communities, civil society organizations, and public and private care providers
C. Universal health coverage policy, and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control
D. Social protection, poverty alleviation and actions on other determinants of tuberculosis

3. INTENSIFIED RESEARCH AND INNOVATION

A. Discovery, development and rapid uptake of new tools, interventions and strategies
B. Research to optimize implementation and impact, and promote innovations

THE GLOBAL STRATEGY AND TARGETS FOR TUBERCULOSIS PREVENTION, CARE AND CONTROL AFTER 2015, WERE ENDORSED BY ALL MEMBER STATES AT THE 2014 WORLD HEALTH ASSEMBLY.

ENDING THE TB EPIDEMIC

Ending the global TB epidemic is feasible with dramatic decline in TB deaths and cases, and elimination of economic and social burden of TB. Failure to do so will carry serious individual and global public health consequences.

Achievement of this goal by 2030 requires:

1. **Expanding the scope and reach of interventions** for TB care and prevention, with a focus on high-impact, integrated and patient-centered approaches;
2. **Eliciting full benefits of health and development policies and systems,** through engaging a much wider set of collaborators across government, communities and the private sector;
3. **Pursuing new scientific knowledge and innovations** that can dramatically change TB prevention and care.

To ensure full impact, these actions must build on principles of government stewardship, engagement of civil society, human rights and equity, and adaptation to the unique context of diverse epidemics and settings**.**

IMPLEMENTING THE END TB STRATEGY: THE ESSENTIALS

For more information on implementing the END TB Strategy: http://www.who.int/tb/publications/2015/The_Essentials_to_End_TB/en/

TOP-TEN PRIORITY INDICATORS FOR MONITORING IMPLEMENTATION OF THE END TB STRATEGY AT GLOBAL AND NATIONAL LEVELS

INDICATOR	RECOMMENDED TARGET LEVEL
TB TREATMENT COVERAGE	≥ 90%
TB TREATMENT SUCCESS RATE	≥ 90%
PERCENTAGE OF TB-AFFECTED HOUSEHOLDS THAT EXPERIENCE CATASTROPHIC COSTS DUE TO TB	0%
PERCENTAGE OF NEW AND RELAPSE TB PATIENTS TESTED USING A WHO-RECOMMENDED RAPID TESTS AT THE TIME OF DIAGNOSIS	≥ 90%
LATENT TB INFECTION TREATMENT COVERAGE	≥ 90%
CONTACT INVESTIGATION COVERAGE	≥ 90%
DRUG SUSCEPTIBILITY TESTING (DST) COVERAGE FOR TB PATIENTS	100%
TREATMENT COVERAGE, NEW TB DRUGS	≥ 90%
DOCUMENTATION OF HIV STATUS AMONG TB PATIENTS	100%
CASE FATALITY RATIO (CFR)	≤ 5%

KEY TB FACTS

- 10 million people fell ill with TB in 2017, including 0.9 million among people living with HIV.
- TB was one of the top 10 causes of death worldwide in 2017, and was responsible for more deaths than HIV.
  In 2017, 1.6 million people died from TB*, including 0.3 million among people with HIV.
- Globally in 2017, an estimated 558 000 people developed TB that was resistant to rifampicin (RR-TB), the most effective first-line drug, and of these, 82% had multidrug-resistant TB (MDR-TB).

ACHIEVEMENTS

54 million
lives saved between 2000 and 2017

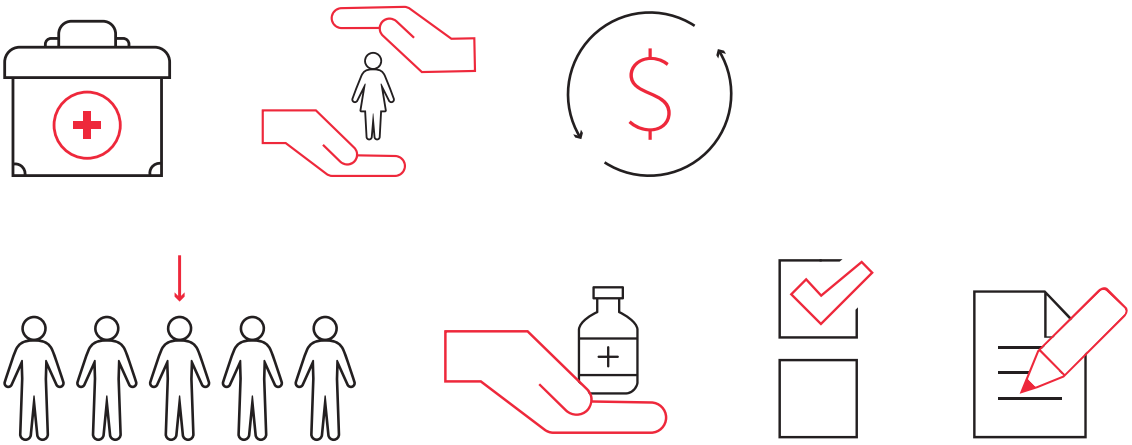
33% drop
in TB deaths between 2000 and 2017

CHALLENGES

MDR-TB crisis
Gaps in detection and treatment. Only one in four people needing MDR-TB treatment were enrolled on it

Funding gap
US$3.5 billion funding shortfall for TB implementation in 2018, and over US$2.0 billion per year for TB research

UN HIGH-LEVEL MEETING ON TB
KEY TARGETS & COMMITMENTS
FOR 2022



Stop TB Partnership hosted by UNOPS

UNHLM ON TB KEY TARGETS FOR 2022

'WE, HEADS OF STATE AND GOVERNMENT AND REPRESENTATIVES OF STATES AND GOVERNMENTS ASSEMBLED AT THE UNITED NATIONS IN NEW YORK ON 26 SEPTEMBER 2018':

1.
COMMIT TO PROVIDE **DIAGNOSIS AND TREATMENT**

with the aim of successfully treating 40 million people with tuberculosis by 2022.

2.
COMMIT TO PROVIDE **DIAGNOSIS AND TREATMENT**

with the aim of successfully treating 3.5 million children with tuberculosis by 2022.

3.
COMMIT TO PROVIDE **DIAGNOSIS AND TREATMENT**

with the aim of successfully treating 1.5 million people with drug-resistant tuberculosis, including 115 000 children with drug-resistant tuberculosis, by 2022.

4.
COMMIT TO **PREVENT TUBERCULOSIS**

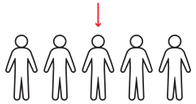
for those most at risk of falling ill so that at least 30 million people, including 4 million children under five years of age, 20 million other household contacts of people affected by tuberculosis, and 6 million people living with HIV, receive preventive treatment by 2022.

5.
COMMIT TO MOBILIZE **SUFFICIENT AND SUSTAINABLE FINANCING**

for universal access to quality prevention, diagnosis, treatment and care of tuberculosis, from all sources, with the aim of increasing overall global investments for ending tuberculosis reaching at least US$13 billion a year by 2022.

6.
COMMIT TO MOBILIZE **SUFFICIENT AND SUSTAINABLE FINANCING FOR R&D**

with the aim of increasing overall global investments to US$2 billion, in order to close the estimated US$1.3 billion gap in funding annually for tuberculosis research, ensuring all countries contribute appropriately to research and development.



7.
PROMOTE AND SUPPORT **AN END TO STIGMA AND ALL FORMS OF DISCRIMINATION,**

including by removing discriminatory laws, policies and programmes against people with tuberculosis, and through the protection and promotion of human rights and dignity.

Recognize the various sociocultural barriers to tuberculosis prevention, diagnosis and treatment services, especially for those who are vulnerable or in vulnerable situations, and the need to develop integrated, people-centred, community-based and gender-responsive health services based on human rights.

8.
COMMIT TO DELIVERING, AS SOON AS POSSIBLE, **NEW, SAFE, EFFECTIVE, EQUITABLE, AFFORDABLE, AVAILABLE VACCINES,**

point-of-care and child-friendly diagnostics, drug susceptibility tests and safer and more effective drugs and shorter treatment regimens for adults, adolescents and children for all forms of tuberculosis and infection, as well as innovation to strengthen health systems such as information and communication tools and delivery systems for new and existing technologies, to enable integrated people-centred prevention, diagnosis, treatment and care of tuberculosis.

9.
REQUEST THE DIRECTOR-GENERAL OF THE WORLD HEALTH ORGANIZATION TO **CONTINUE TO DEVELOP THE MULTISECTORAL ACCOUNTABILITY FRAMEWORK**

and ensure its timely implementation no later than 2019.

10.
FURTHER REQUEST THE SECRETARY GENERAL, WITH THE SUPPORT OF THE WORLD HEALTH ORGANIZATION, TO **PROVIDE A PROGRESS REPORT IN 2020**

on global and national progress, across sectors, in accelerating efforts to achieve agreed tuberculosis goals, which will serve to inform preparations for **a comprehensive review by Heads of State and Government at a high-level meeting in 2023.**

UNHLM ON TB KEY COMMITMENTS

'WE, HEADS OF STATE AND GOVERNMENT AND REPRESENTATIVES OF STATES AND GOVERNMENTS ASSEMBLED AT THE UNITED NATIONS IN NEW YORK ON 26 SEPTEMBER 2018':

In addition to the ten headline targets, these are some of the key commitments in the Political Declaration, grouped according to the Key Asks (**https://bit.ly/2AixuCY**) proposed by the TB community.
The full Declaration can be viewed here: **https://bit.ly/2OylPnA**

END TB

REACH ALL PEOPLE BY CLOSING THE GAPS ON TB DIAGNOSIS, TREATMENT AND PREVENTION

P24: 'Commit to providing diagnosis and treatment with the aim of successfully treating 40 million people with tuberculosis from 2018 to 2022, including 3.5 million children, and 1.5 million people with drug-resistant tuberculosis including 115,000 children...'
P25: 'Commit to preventing tuberculosis for those most at risk of falling ill through the rapid scaling up of access to testing for tuberculosis infection, according to the domestic situation, and provision of preventive treatment, with a focus on high-burden countries, so that at least 30 million people, including 4 million children under 5 years of age, 20 million other household contacts of people affected by tuberculosis, and 6 million people living with HIV, receive preventive treatment by 2022...'

TRANSFORM THE TB RESPONSE TO BE EQUITABLE, RIGHTS-BASED AND PEOPLE-CENTERED

P14: '...affirm that all these people [affected by TB] require integrated people-centred prevention, diagnosis, treatment, management of side effects, and care, as well as psychosocial, nutritional and socioeconomic support for successful treatment, including to reduce stigma and discrimination.'
P17: '...in order to make the elimination of tuberculosis possible, prioritizing, as appropriate, notably through the involvement of communities and civil society and in a non-discriminatory manner, high-risk groups and other people who are vulnerable or in vulnerable situations, such as women and children, indigenous peoples, health-care workers, migrants, refugees, internally displaced people, people living in situations of complex emergencies, prisoners, people living with HIV, people who use drugs, in particular those who inject drugs, miners and others exposed to silica, the urban and rural poor, underserved populations, undernourished people, individuals who face food insecurity, ethnic minorities, people and communities at risk of exposure to bovine tuberculosis, people living with diabetes, people with mental and physical disabilities, people with alcohol use disorders, and people who use tobacco, recognizing the higher prevalence of tuberculosis among men.'
P18: 'Recognize the various sociocultural barriers to tuberculosis prevention, diagnosis and treatment services, especially for those who are vulnerable or in vulnerable situations, and the need to develop integrated, people-centred, community-based and gender-responsive health services based on human rights.'
P19: 'Commit to promoting access to affordable medicines, including generics, for scaling up access to affordable tuberculosis treatment, including the treatment of multidrug-resistant and extensively drug-resistant tuberculosis, reaffirming the World Trade Organization Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement), as amended, and also reaffirming the 2001 World Trade Organization Doha Declaration on the TRIPS Agreement and Public Health...'
P25: 'Commit to... enacting measures to prevent tuberculosis transmission in workplaces, schools, transportation systems, incarceration systems and other congregate settings.'
P33: 'Commit to developing community-based health services through approaches that protect and promote equity, ethics, gender equality and human rights in addressing tuberculosis...'
P34: 'Commit to related improvements in policies and systems on each country's path towards achieving and sustaining universal health coverage, such that all people with tuberculosis or at risk of developing tuberculosis receive the quality, accessible and affordable prevention, diagnosis, treatment and care services they need without suffering financial hardship, with stewardship of antimicrobials and prevention and infection control, within public and community, including faith-based organizations, and private sector services.'
P37: 'Commit to... promote and support an end to stigma and all forms of discrimination, including by removing discriminatory laws, policies and programmes against people with tuberculosis...'
P38: 'Commit to providing special attention to the poor, those who are vulnerable, including infants, young children and adolescents, as well as elderly people and communities especially at risk of and affected by tuberculosis, in accordance with the principle of social inclusion, especially through ensuring strong and meaningful engagement of civil society and affected communities in the planning, implementation, monitoring and evaluation of the tuberculosis response...'

ACCELERATE DEVELOPMENT OF ESSENTIAL NEW TOOLS TO END TB

P42: 'Commit to advancing research for basic science, public health research and the development of innovative products and approaches... including towards delivering, as soon as possible, new, safe, effective, equitable, affordable, available vaccines, point-of-care and child-friendly diagnostics, drug susceptibility tests and safer and more effective drugs and shorter treatment regimens for adults, adolescents and children for all forms of tuberculosis and infection...'
P43: 'Commit to create an environment conducive to research and development of new tools for tuberculosis, and to enable timely and effective innovation and affordable and available access to existing and new tools and delivery strategies and promote their proper use, by promoting competition and collaboration...'
P45: 'Promote tuberculosis research and development efforts aiming to be needs-driven, evidence-based and guided by the principles of affordability, effectiveness, efficiency and equity and which should be considered as a shared responsibility. In this regard, we encourage the development of new product development partnership models and, for multidrug-resistant tuberculosis, continue to support existing voluntary initiatives and incentive mechanisms that separate the cost of investment in research and development from the price and volume of sales, to facilitate equitable and affordable access to new tools and other results to be gained through research and development...'

INVEST THE FUNDS NECESSARY TO END TB

P46: 'Commit to mobilize sufficient and sustainable financing for universal access to quality prevention, diagnosis, treatment and care of tuberculosis, from all sources, with the aim of increasing overall global investments for ending tuberculosis and reaching at least 13 billion United States dollars a year by 2022...'
P47: 'Commit to mobilize sufficient and sustainable financing, with the aim of increasing overall global investments to 2 billion dollars, in order to close the estimated 1.3 billion dollar gap in funding annually for tuberculosis research, ensuring that all countries contribute appropriately to research and development...'

COMMIT TO DECISIVE AND ACCOUNTABLE GLOBAL LEADERSHIP INCLUDING REGULAR UN REPORTING AND REVIEW

P48: 'Commit to develop or strengthen, as appropriate, national tuberculosis strategic plans to include all necessary measures to deliver the commitments in the present political declaration, including through national multisectoral mechanisms to monitor and review progress achieved towards ending the tuberculosis epidemic, with high-level leadership, preferably under the direction of the Head of State or Government, and with the active involvement of civil society and affected communities, as well as parliamentarians, local governments, academia, private sector and other stakeholders within and beyond the health sector...'
P49: 'Request the Director General of the WHO to continue to develop the multisectoral accountability framework in line with World Health Assembly resolution 71.3 and ensure its timely implementation no later than 2019.'
P53: 'Also request the Secretary-General, with the support of the WHO, to provide a progress report in 2020 on global and national progress, across sectors... which will serve to inform preparations for a comprehensive review by Heads of State and Government at a high-level meeting in 2023.'

On 26 September 2018 at the UN General Assembly in New York, Member States held the first high-level meeting on TB, the world's deadliest infectious disease.

The meeting resulted in a political declaration endorsed by Heads of State and Government outlining the key commitments that must be met for the world to end the TB epidemic by 2030, as called for in the UN Sustainable Development Goals. In 2023 UN Member States will convene a follow-up high-level meeting for a comprehensive review of their progress.

Stop TB Partnership hosted by UNOPS

UNHLM on TB Key Targets & Commitments for 2022

Global Health Campus
Chemin du Pommier 40
1218 Le Grand-Saconnex
Geneva, Switzerland

A digital version of this publication is available on stoptb.org/resources

END TB

Stop TB Partnership

END TB

It's Time

to play my part

to achieve the targets in the UN Political Declaration on TB by 2022.

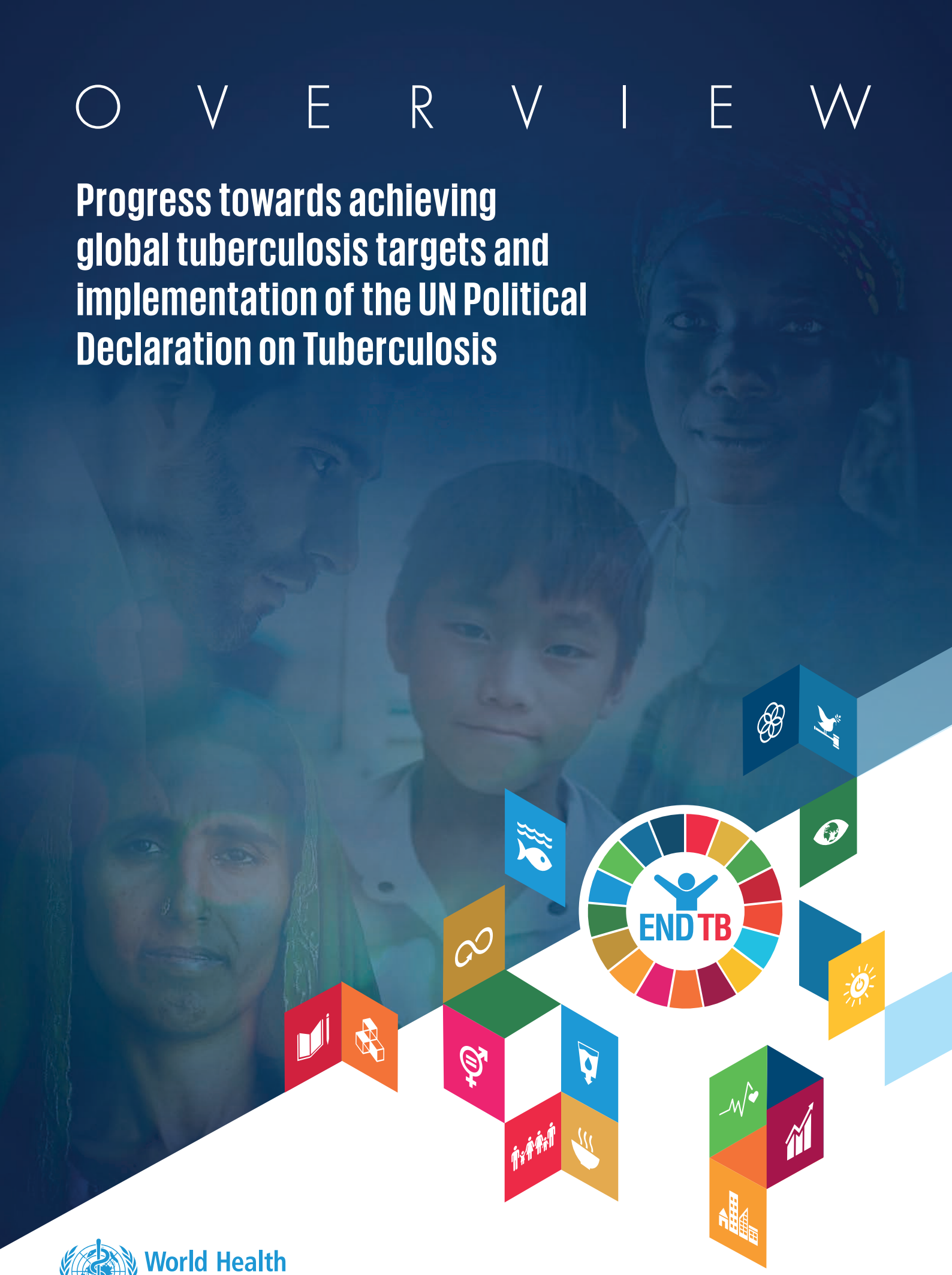
#EndTB

Signed by:

Take a photo of yourself holding this page with your signature and post on social media using #EndTB

O V E R V I E W

Progress towards achieving global tuberculosis targets and implementation of the UN Political Declaration on Tuberculosis



World Health Organization

This is a summary review of progress towards global TB targets, and in implementation of the political declaration of the UN High Level Meeting on TB declaration. Overall the report shows that high-level commitments and targets have galvanized global and national progress towards ending TB, but that urgent and more ambitious investments and actions are required to put the world on track to reach targets, especially in the context of the COVID-19 pandemic.

INTRODUCTION

Tuberculosis (TB) is a severe global threat that disproportionally affects the poorest and most vulnerable. In 2019 about 10 million people fell sick with the disease and 1.4 million died, making TB the leading infectious killer worldwide and one of the top ten causes of death overall. One-third of deaths among people living with HIV are due to TB. With close to half a million people developing drug-resistant TB annually, it is also a major contributor to antimicrobial resistance. A quarter of the world's population is infected with Mycobacterium tuberculosis. This is an enormous human and societal toll for a curable and preventable disease.

In 2014 and 2015, all Member States committed to ending the TB epidemic by 2030, through their adoption of the World Health Organization's (WHO) End TB Strategy and the United Nations (UN) Sustainable Development Goals (SDGs). Efforts to further galvanize political commitment to the fight against TB intensified in 2017 and 2018. The first WHO global ministerial conference on TB was held in 2017. The resulting Moscow Declaration included commitments to key drivers of faster progress, which were subsequently endorsed at the World Health Assembly in 2018: universal access to health care, multisectoral action and accountability, financing and research.

With universal access to health care, almost everyone who develops TB can be successfully treated and preventive treatment offered to those most at risk. Since 2000, TB treatment has averted more than 60 million deaths, but many people have missed out on diagnosis and care. Multisectoral action is needed to eliminate the economic distress, vulnerability, marginalization, stigma and discrimination often faced by those affected by TB, and to drive down the number of people developing TB infection and disease by addressing determinants including poverty, undernutrition and the prevalence of HIV infection, diabetes, mental health and smoking. Research breakthroughs such as a new vaccine are needed to rapidly reduce TB incidence worldwide to the levels already achieved in low-burden countries.

The General Assembly held its first high-level meeting on TB, titled *United to End TB: An Urgent Global Response to a Global Epidemic*, on 26 September 2018. This brought together heads of state and government as well as other leaders and was preceded by a civil society hearing. The political declaration[2] reaffirmed commitments to the SDGs and End TB Strategy and established new global targets and commitments to action.

As requested in the political declaration, a 2020 progress report to the General Assembly has been developed with the support of the WHO Director-General.[2] It covers:

- Progress towards global TB targets;
- Progress in translating commitments into action;
- The COVID-19 pandemic and TB - impact and implications;
- Recommendations.

Overall, the report shows that high-level commitments and targets have galvanized global and national progress towards ending TB, but that urgent and more ambitious investments and actions are required to put the world on track to reach targets, especially in the context of the COVID-19 pandemic. It will inform a comprehensive review at a high-level meeting on TB in 2023.

GLOBAL COMMITMENTS TO END TB

1 United Nations General Assembly. Resolution 73/3: Political declaration of the high-level meeting of the General Assembly on the fight against tuberculosis. United Nations; 2018 (www.un.org/en/ga/search/view_doc.asp?symbol=A/RES/73/3)

2 Further details about the topics covered in this report, including country case studies, are provided in the annual WHO *Global Tuberculosis Report*. The 2020 edition will be published in October.

TB IS THE TOP INFECTIOUS DISEASE KILLER WORLDWIDE

IN 2019

1.4 MILLION PEOPLE DIED FROM TB

INCLUDING 208 000 DEATHS AMONG PEOPLE WITH HIV

TB IS THE LEADING KILLER OF PEOPLE WITH HIV

AND A MAJOR CAUSE OF DEATH DUE TO ANTIMICROBIAL RESISTANCE

10 MILLION PEOPLE FELL ILL WITH TB

5.6 MILLION MEN

3.2 MILLION WOMEN

1.2 MILLION CHILDREN

OVERVIEW OF PROGRESS TOWARDS GLOBAL TB TARGETS

A) SDGs AND END TB STRATEGY: TARGETS

TB INCIDENCE

9% REDUCTION 2015-2019

TB DEATHS

14% REDUCTION 2015-2019

% OF PEOPLE WITH TB FACING CATASTROPHIC COSTS

49% OF PEOPLE WITH TB FACE CATASTROPHIC COSTS

B) UN HIGH-LEVEL MEETING ON TB: TREATMENT TARGETS

TB TREATMENT

14.1 million TREATED IN 2018 & 2019

TB PREVENTIVE TREATMENT

6.3 million TREATED IN 2018 & 2019

C) UN HIGH-LEVEL MEETING ON TB: TARGETS FOR INCREASED FUNDING

UNIVERSAL ACCESS TO TB PREVENTION, DIAGNOSIS, TREATMENT AND CARE

US$ 6.5 billion IN 2020

TB RESEARCH

US$ 906 million IN 2018

THE COVID-19 PANDEMIC AND TB – IMPACT AND IMPLICATIONS

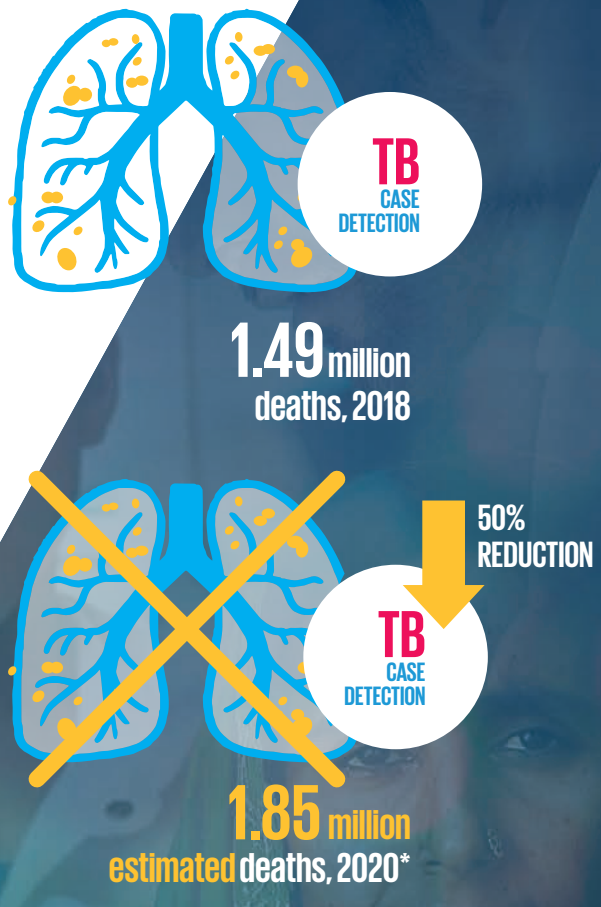
Since the end of 2019, the COVID-19 pandemic has caused enormous health, social and economic impacts. Even after some of these are mitigated or contained, there will be medium and longer-term consequences. In the context of the global TB epidemic, COVID-19 threatens to reverse recent progress towards global TB targets.

The WHO analysis assessed the additional number of TB deaths that could occur globally in 2020, for different combinations of a decrease in case detection (compared with levels prior to the pandemic) and the number of months for which this decrease occurs (Fig. 17). If the number of people with TB detected and treated falls by 25–50% over a period of 3 months, a range considered plausible based on data from several high TB burden countries including India and Indonesia, there could be approximately 200–400 thousand excess TB deaths in 2020, bringing the total to around 1.7–1.9 million. An increase of 200 thousand would take the world back to 2015 levels and an increase of 400 thousand to 2012 levels.

Since WHO declared COVID-19 a Public Health Emergency of International Concern in January 2020, the WHO Global TB Programme is monitoring the impact and providing guidance and support to Member States, in close collaboration with Regional and Country Offices, civil society and partners including the Stop TB Partnership and Global Fund.

WHO recommends that TB services are maintained and strengthened as essential during the current pandemic and other outbreaks. This includes, ensuring access to people-centered prevention and care services; effective infection prevention and control measures; proactive planning for procurement, supply and risk management and leveraging the expertise and experience of national TB programmes especially in rapid testing and contact tracing, for the COVID-19 response.

DRAMATIC SETBACK TO PROGRESS PREDICTED IF CONTINUITY OF ESSENTIAL TB SERVICES NOT ENSURED



If TB detection drops by 50% over three months, the number of TB deaths worldwide would increase by nearly 400 000.

(* These estimates include TB deaths among HIV-positive individuals.)

3 It is also possible that TB could worsen COVID-related outcomes.

4 WHO. Information note on ensuring continuity of TB services during the COVID-19 pandemic

RECOMMENDATIONS

High-level commitments and targets have galvanized global and national progress towards ending TB, yet urgent and more ambitious investments and actions are required to end TB. These are especially critical in the context of the COVID-19 pandemic, which has already impacted the TB response, and threatens to reverse recent progress.

Member States are urged to implement the following 10 priority recommendations to put the world on track to reach agreed targets by 2022 and beyond; and reduce the enormous human and societal toll caused by TB.

1. Fully activate high-level leadership to urgently reduce TB deaths and drive multisectoral action to end TB

Given that TB is the world's top infectious killer, that it is a preventable and curable disease, that progress is too slow to reach global targets;
and
that TB incidence is declining far too slowly, the key drivers of the TB epidemic include social and economic determinants such as poverty and under-nutrition as well as health-related risk factors, that half of people with TB and their households face catastrophic costs;
and
that the COVID-19 pandemic poses a major risk that TB deaths, TB incidence and the number of people with TB facing catastrophic costs will significantly increase.

Ensure that high-level multisectoral collaboration and accountability under the leadership of Heads of State or Government, including regular reviews of progress, is in place in all countries - especially those with a high TB burden.

Ensure that progress towards national targets for reductions in TB deaths and TB incidence is regularly monitored and reviewed at the highest level, and findings acted upon, especially in countries with a high burden of TB.

Strengthen national notification and vital registration systems so that they meet quality and coverage standards, to ensure robust measurement of trends in TB incidence and deaths.

Ensure social protection measures including essential benefit packages and subsidization schemes are fit-for-purpose, so that no one affected by TB faces catastrophic costs.

2. Urgently increase funding for essential TB services including for the health workforce

Given that funding for universal access to TB prevention, diagnosis, treatment and care is vital to achieve a substantial reduction in TB deaths, that funding needs to double to reach the global target of at least US$ 13 billion per year by 2022 and that spending on TB offers one of the best returns on investment in health and development:

Increase domestic funding to combat TB, especially in middle-income countries with a high TB burden, while also building synergies in the response to both TB and COVID-19.

Increase international donor funding for the TB response, from both existing or new innovative funding mechanisms, so that funding levels are commensurate with the burden of disease.

3. Advance universal health coverage to ensure all people with TB have access to affordable quality care and resolve under-reporting challenges

Given that Member States have committed to reach an additional one billion people with essential health services by 2023, that access to TB treatment is increasing but not yet enough to reach the target of 40 million between 2018 and 2022, and that there is an annual gap of about 3 million people, including half a million children, who miss out on access to care or are not reported:

Ensure that TB services are maintained and strengthened as an essential component of sustainable health systems and progress towards universal health coverage. This includes as recommended by WHO, expanded access to:

- rapid molecular diagnostics as the initial test to diagnose TB including resistance to key drugs
- treatment with new effective drugs and regimens
- psychosocial, nutritional and other support
- systematic screening for TB and TB preventive treatment

Improve financial protection for people affected by TB and drug-resistant TB through relevant mechanisms, such as national health insurance systems or other pooled pre-payment schemes, across public and private health sectors.

Scale up engagement and leverage the capacity of private and other unlinked public health care providers in the delivery of TB prevention, diagnosis and care services to reach the missing people with TB including children, especially in countries with a large private sector.

Ensure mandatory notification of all people diagnosed with TB, covering public, private and community-based providers, facilitated by expanded use of electronic case-based reporting and digital technologies.

4. Address the drug-resistant TB crisis to close persistent gaps in care

Given that drug-resistant TB is a major contributor to antimicrobial resistance and is a threat to global health security; that close to half a million people develop drug-resistant TB every year, of which less than half are diagnosed and only around 100 000 successfully treated; and that progress towards the target of treating 1.5 million people with drug-resistant TB including 115000 children between 2018 and 2022 is therefore far too slow.

Expand use of rapid molecular TB diagnostics and test all those diagnosed with TB and rifampicin resistance for susceptibility to the fluoroquinolone class of drugs.

Expand access to WHO-recommended all-oral treatments for adults and children diagnosed with drug-resistant TB.

Increase access to affordable high-quality drugs and diagnostics for populations in need, using effective mechanisms such as the Stop TB Partnership Global Drug Facility.

Include actions to address drug-resistant TB explicitly within national antimicrobial resistance strategies and plans.

5. Dramatically scale up provision of TB preventive treatment

Given that access to TB preventive treatment is increasing far too slowly to reach the target of 30 million people between 2018 and 2022, due to very low coverage among household contacts of people diagnosed with TB:

Massively expand household contact investigation including for children and people with drug-resistant TB, by updating national policies and strategies for TB preventive treatment in line with WHO recommendations, increasing investments and building synergies with contact tracing efforts for the COVID-19 response.

Promote and expand access to testing for TB infection and TB preventive treatment with new medicines and shorter regimens, with adherence support.

Continue to expand the coverage of TB preventive treatment for people living with HIV alongside antiretroviral treatment.

6. Promote human rights and combat stigma and discrimination

Given that promotion and protection of the human rights of people affected by TB is a legal, ethical and moral imperative, and that people affected by TB continue to be subjected to human rights violations which together with stigma and discrimination impede access to care and add to the suffering caused by the disease:

Review and update laws, policies and programmes to combat inequalities and eliminate stigma and discriminatory practices in the TB response, working together with civil society and affected communities and with particular attention to vulnerable populations.

Ensure that national TB strategies, plans, policies and other documentation avoid stigmatizing language.

7. Ensure meaningful engagement of civil society, communities and people affected by TB

Given that engagement of civil society, communities and people affected by TB is essential to the TB response, and that while this has grown since the UN high-level meeting on TB accelerated efforts are needed to ensure more extensive engagement:

Actively invest in building the capacity of civil society, representatives of affected communities including TB survivors, to ensure their meaningful engagement in all aspects of the TB response, including in policy making forums, planning, care delivery, monitoring and review.

8. Substantially increase investments in TB research to drive technological breakthroughs and rapid uptake of innovations

Given that global funding for TB research needs to more than double to reach the annual target of US$ 2 billion, that chronic underfunding of TB research means there are still no point of care tests, treatments remain long, the only licensed vaccine is over 100 years old and provides limited protection, and that ending TB depends on the development and rapid uptake of new tools and innovation:

Increase investment in TB research and innovation to at least US$ 2 billion per year from national governments, bilateral and multilateral financing sources as well as development and private sector institutions.

Develop and implement actionable, fully-funded and well-resourced national strategies for TB research and innovation, building on the WHO Global Strategy for TB Research and Innovation, in collaboration with research networks, relevant non-state actors, international agencies and TB community advisory boards.

As a matter of urgency, support the implementation of Phase II and Phase III trials for the most promising TB vaccine and drug candidates.

Ensure that TB diagnostics and drugs are prioritized for fast-track review by national regulatory authorities and considered for inclusion in essential lists.

Rapidly adopt and implement innovations including digital technologies related to the different aspects of TB prevention and care.

9. Ensure that TB prevention and care are safeguarded in the context of COVID-19 and other emerging threats

Given the enormous health, social and economic impact of the COVID-19 pandemic, which in 2020 alone may cause hundreds of thousands of excess TB deaths due to disruptions of essential TB services and access to care, that national TB programmes are already heavily engaged in the COVID-19 response, and that there are obvious similarities in the responses needed for both TB and COVID-19:

Ensure that TB prevention, diagnosis and treatment are maintained as essential health services in the context of health emergencies, with infection prevention and control measures in place for health facilities and affected households.

Monitor and review the impact of the COVID-19 pandemic on the TB response including with the engagement of civil society and affected communities, to inform timely action.

Build back stronger by learning lessons from the COVID-19 pandemic, including by enhancing the resilience of TB programmes during emergencies, implementing catch-up recovery plans to reach targets, and harnessing innovations such as digital technologies.

10. Request WHO to continue to provide global leadership for the TB response, working in close collaboration with Member States and other stakeholders, including to prepare for a High-Level Meeting on TB in 2023

Given that WHO as the UN specialized agency for health provides global leadership and coordination for the TB response, in collaboration with stakeholders such as the Global Fund, Stop TB Partnership, Unitaid, civil society and other entities, and that as requested in the political declaration has finalized the Multisectoral Accountability Framework for TB and is supporting its adaptation and use, WHO is requested to:

Continue to provide leadership and coordination to accelerate progress, including through political dialogue and multisectoral engagement; normative guidance and technical support to Member States; monitoring, reporting and review; and shaping of the TB research and innovation agenda.

Continue to support Member States to adapt and use the Multisectoral Accountability Framework for TB in collaboration with partners, civil society and affected communities, and lead periodic global reviews of the TB response.

Support the Office of the UN Secretary-General to prepare a comprehensive review by Heads of State and Government at a UN high level meeting on TB in 2023, informed by WHO's Global TB Report, global, regional and national high-level reviews and preceded by an interactive civil society hearing.

Am. J. Trop. Med. Hyg., 98(3), 2018, pp. 650–652
doi:10.4269/ajtmh.17-0999

Perspective Piece

Reimagining the Research Approach to Tuberculosis†

Anthony S. Fauci* and Robert W. Eisinger

Office of the Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland

Abstract. Controlling and ultimately ending tuberculosis (TB) as a public health scourge will require a multifaceted and comprehensive approach involving the intensification of public health efforts, including scaling-up the delivery of current diagnostic, preventive, and therapeutic tools. However, a critically important element in the effort to end TB is an accelerated biomedical research effort to address the many unanswered questions about the disease process itself and to develop improved and innovative countermeasures. An intensive effort toward these research goals will facilitate the achievement of the aspirational goal of ending TB.

Tuberculosis (TB) is a disease of historical importance, accounting for at least 1 billion deaths over the past two centuries, more than the combined number of deaths from malaria, smallpox, human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS), cholera, plague, and influenza.[1] More than 2 billion people are estimated to be latently infected with *Mycobacterium tuberculosis* (*Mtb*), and TB is the leading cause of death among infectious diseases and one of the top 10 causes of death worldwide. In 2016, an estimated 1.7 million TB deaths occurred. There were an estimated 10.4 million new TB cases in 2016, 10% of which were among individuals living with HIV infection. About 490,000 of the new cases were multidrug-resistant TB (MDR-TB), with 6.2% of those cases identified as extensively drug-resistant TB (XDR-TB).[2]

The first World Health Organization (WHO) Global Ministerial Conference on Ending TB in the Sustainable Development Era: A Multisectoral Response (Moscow, November 16–17, 2017) was an historical event that brought attention to the compelling need to reassess the global effort to end this historic scourge. The conference highlighted the importance of implementing effectively the tools that we already have for preventing TB and diagnosing and treating/caring for people infected with *Mtb*, and it underscored the need for additional, improved tools for this purpose, with the latter resulting from biomedical research.[3] At the conference, one of us (A.S.F.) outlined how we might "reimagine" our research response to TB and bring TB research into the twenty first century with the application of new diagnostic, therapeutic, and vaccine platforms.

The increasing incidence of MDR-TB and XDR-TB during the past few years has sparked heightened attention to the urgent need for a comprehensive "tool kit" of new and better strategies to prevent, diagnose, treat, and control TB and drug-resistant TB.[4] We must not take just an incremental approach to another drug or another diagnostic. TB is an ancient disease; however, we need to understand it in modern terms and use cutting-edge technologies to ask and answer questions that were never addressed in the first place because years ago, we felt that we had effective drugs that could cure the disease. It is true that elegant research has been conducted in the field of TB over the past few years; however, because of the complexity of this disease, critical questions remain unanswered regarding the pathogenesis of TB. In addition, there remains a paucity of innovative and highly effective interventions. We must change our mind-set about our end game in the approach to TB research. Our goal should be to transform the entire field.

The current situation with TB research contrasts dramatically with the unprecedented advances in HIV/AIDS research made in the > 36 years since HIV was first reported.[5,6] We now have a robust HIV/AIDS tool kit that includes techniques to detect as few as one to two copies of HIV RNA in the blood with a simple and widely available test[7]; more than 30 FDA-approved antiretroviral drugs, which when used in combination, result in a substantial projected life-expectancy and a return to normal daily activities in the vast majority of treated individuals[8]; and safe and highly effective prevention strategies including preexposure prophylaxis to prevent acquisition of HIV.[9] In addition, several promising vaccine candidates are presently being tested in large-scale, international Phase 2 clinical trials.[10–12] We should not settle for any less when it comes to TB.

Recently, efforts have been made to emulate the HIV research model in the fight against TB. In this regard, the U.S. Government's Global Tuberculosis Strategy is closely aligned with the WHO's End TB Strategy, "A World Free of TB." Both place a high priority on intensified research and innovation to successfully achieve an end to TB.[13,14] Various aspects of the TB research agenda involving pathogenesis, diagnostics, therapeutics, and vaccines were presented by A.S.F. at the Moscow conference.

PATHOGENESIS RESEARCH

More than 130 years after the discovery of *Mtb* as the etiologic agent of TB, we still know surprisingly little about the precise mechanisms of TB disease pathogenesis. Generations of research advances and technologies applied to other diseases have bypassed the field of TB research. Key questions remain unanswered, particularly regarding the complex interactions between the pathogen and the host. This gap in our knowledge will benefit greatly from interdisciplinary, systems biology approaches to TB pathogenesis that include

* Address correspondence to Anthony S. Fauci, National Institute of Allergy and Infectious Diseases, National Institutes of Health, 9000 Rockville Pike, Building 31, Room 7A03, Bethesda, MD 20892. E-mail: afauci@niaid.nih.gov

† This article is based on a lecture given by Anthony S. Fauci, MD on November 17, 2017, in Moscow, Russia, at the First World Health Organization Global Ministerial Conference on Ending Tuberculosis in the Sustainable Development Era: A Multisectoral Response.

computational and mathematical modeling of the complex biological interactions between pathogen and host. Such efforts will contribute greatly to enlightening the still opaque areas of maintenance of latency, escape from latency, disease activation, and correlates of immunity.[15] In addition, key research challenges in pathogenesis must be addressed with regard to TB/HIV co-infection, including the factors associated with higher rates of progression to active TB and the accelerated course of HIV in coinfected individuals; different clinical/radiographic manifestations of pulmonary TB; and reduced immune control and a greater degree of extrapulmonary TB dissemination.[16] Limitations of animal models of dual infection are also an impediment that must be addressed.

DIAGNOSTICS

The GeneXpert MTB/rifampicin resistant diagnostic (Cepheid, Sunnyvale, CA) has been a welcome addition to the TB diagnostic armamentarium.[2] However, there is still a need for improved and transformative TB diagnostics to overcome the severe limitations of antiquated, nonstandardized, and imprecise techniques which are used presently in most settings. In addition, the application of twenty first century diagnostic technologies that can detect *Mtb* in a variety of clinical specimens from multiple body sites in addition to sputum, as well as advanced approaches for monitoring and predicting treatment outcomes are a priority. If we can detect a single copy of HIV RNA in the blood of an HIV-infected individual and track disease progression with viral load testing, we should be able to develop a comparable diagnostic and disease monitoring capability for TB, as far-fetched as this might seem at present.

The diagnosis of TB in coinfected individuals is complicated because extrapulmonary and paucibacillary pulmonary disease is more common with HIV infection, and these forms of the disease require greater test sensitivity. Yet, TB diagnosis is still focused predominantly on sputum specimens, which can be difficult to obtain in HIV-infected people, particularly children.[17,18] For all TB patients, there is a critical need for rapid, inexpensive, and accurate "point-of-care" molecular diagnostics that can rapidly differentiate between drug-sensitive and drug-resistant forms of *Mtb*, such that appropriate drug regimens can be prescribed, based on the molecular profile of the pathogen. Although an extensive data bank of genomic sequences from numerous *Mtb* strains is available, additional basic research is needed on gene mutations resulting in drug resistance to help inform treatment decisions.[19]

THERAPEUTICS

World Health Organization's recent report *Antibacterial Agents in Clinical Development: An Analysis of the Antibacterial Clinical Development Pipeline, including Tuberculosis* noted the critical need for additional support for basic science on *Mtb*, drug discovery, and clinical development of better TB treatment strategies.[20] Current treatment regimens recommended by WHO include up to four drugs for 6 months, but result in an insufficient ~83% cure rate globally in newly diagnosed individuals. World Health Organization also has cited the desperate need for newer, non-toxic drugs and shorter regimens for treatment of MDR-TB because the current regimens include four to seven drugs for 9–20 months, with only a ~54% cure rate globally.[2]

Approximately half of MDR-TB patients have resistance to second-line drugs, and XDR-TB treatment is effective in only about 30% of these individuals.[2] Despite the urgent need for better treatments, only a few new drugs and lead agents are in the drug pipeline.[2,21] There remain numerous hurdles that must be overcome in the successful development of safe and effective TB therapeutics, including the length and complexity of treatment regimens, challenges to adherence, toxic side effects, drug–drug interactions, and drug resistance. There also are unique challenges for TB treatment in HIV-coinfected individuals, including drug–drug interactions between TB therapy and antiretroviral therapy, which can result in additive toxicities, risk of immune reconstitution inflammatory syndrome, and the limited availability of pediatric drug formulations.[22]

One initiative to address these challenges is the TB drug accelerator, an innovative international collaboration between seven pharmaceutical companies and six research institutions. The project is designed to address the shortage of new TB drugs by funding early-stage TB drug discovery.[23] In an effort to boost clinical research on TB, the National Institutes of Health (NIH) has used the infrastructure and capacity of its extensive HIV clinical trials networks to conduct critical studies of potential TB treatment regimens, including a 1-month short-course of rifapentine/isoniazid to prevent active TB in HIV-infected patients with latent TB. These networks have also conducted MDR-TB treatment studies of bedaquiline and delamanid, alone and in combination, as well as studies of optimized and individualized MDR-TB therapy for HIV-infected and HIV-uninfected children.[24]

We should not despair of the possibility of achieving the goal of a combination of drugs directed at multiple targets administered for a substantially shorter period of time than is presently required and that will cure an individual infected with any strain of *Mtb*. We never would have imagined 25 years ago that we could durably suppress HIV replication to undetectable levels with three antiretroviral drugs given as a single pill once per day. Our goals for the ultimate therapy of TB should be no less aspirational.

VACCINES

A safe and effective TB vaccine is urgently needed to protect against all forms of TB in adults and adolescents.[25,26] Recent modeling exercises underscore that a new TB-preventive vaccine that is 60% efficacious and provided to 20% of adults and adolescents globally could avert ~60–70 million cases in its first 25 years of use, and an infant vaccine could potentially avert 6–7 million new TB cases.[26]

However, it appears that we are far from our goal of a useful TB vaccine. The BCG vaccine is not effective in preventing adult pulmonary TB, which is the major transmissible form of the disease, and the vaccine is no longer recommended for HIV-coinfected children.[27] With regard to the development of new vaccine platforms to prevent TB, there remain many challenges. These include unanswered questions about the pathogenesis of TB infection and disease as mentioned previously; gaps in our knowledge of the precise nature of protective immunity; a lack of reliable and sensitive correlates of immune protection; limited understanding of the precise nature and effectiveness of pulmonary host defenses to *Mtb*, whether innate and/or

adaptive; and limited predictive value of effectiveness in animal models.[28] Clearly, the development of a safe and effective vaccine remains one of the most formidable TB biomedical research challenges, but a challenge that we must vigorously undertake.

In summary, we cannot adequately address the broad issue of infectious diseases in global health without directly addressing TB, the greatest infectious killer. Now is the time to reinvigorate our response to TB by building on the momentum of the successful November 2017 Ministerial Conference in Moscow. It is critical to reimagine what is possible with innovative biomedical research and to accelerate our multifaceted research programs with increased and sustained resources, including critical support for training the cadre of the next generation of TB researchers. With robust, creative, and aggressive research efforts and by rapidly translating research results into TB control strategies that can be implemented globally, we can reach the aspirational goal of ending TB.

Received December 21, 2017. Accepted for publication December 21, 2017.

Published online January 22, 2018.

Authors' addresses: Anthony S. Fauci and Robert W. Eisinger, Office of the Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, E-mails: afauci@niaid.nih.gov and robert.eisinger@nih.gov.

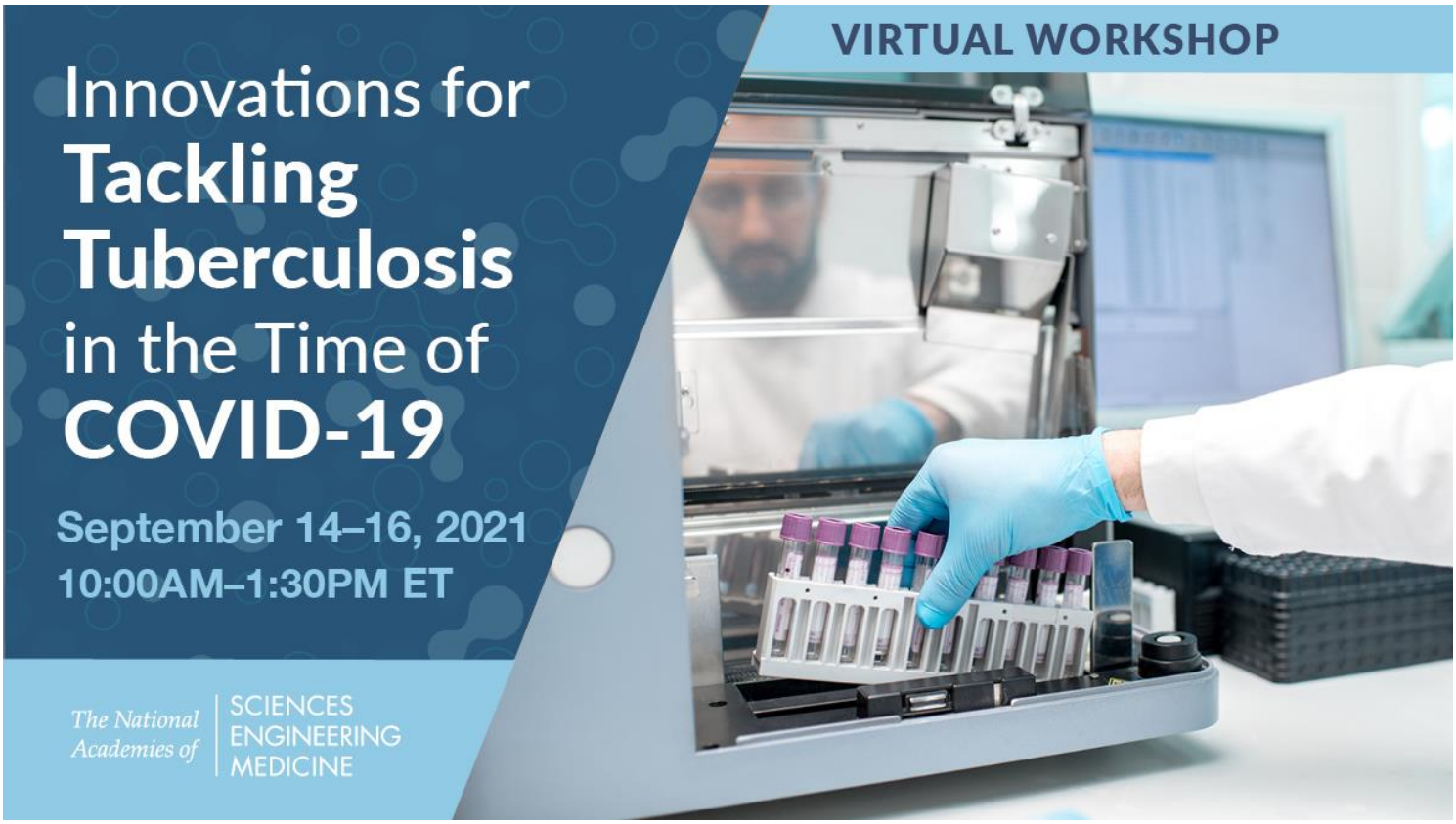
REFERENCES

1. Paulson T, 2013. Epidemiology: a mortal foe. *Nature 502:* S2–S3.
2. World Health Organization, 2017. *Global Tuberculosis Report 2017*. Geneva, Switzerland: WHO.
3. World Health Organization, 2017. *Moscow Declaration to End TB.* First WHO Ministerial Conference to Ending TB in the Sustainable Development Era: A Multisectoral Response, Moscow, Russia, November 16–17, 2017.
4. Fauci AS; NIAID Tuberculosis Working Group, 2008. Multidrug-resistant and extensively drug-resistant tuberculosis: the National Institute of Allergy and Infectious Diseases Research agenda and recommendations for priority research. *J Infect Dis 197:* 1493–1498.
5. Centers for Disease Control and Prevention, 1981. Kaposi's sarcoma and pneumocystis pneumonia among homosexual men—New York City and California. *MMWR Morb Mortal Wkly Rep 30:* 305–308.
6. Centers for Disease Control and Prevention, 1981. Pneumocystis pneumonia—Los Angeles. *MMWR Morb Mortal Wkly Rep 30:* 250–252.
7. Palmer S et al., 2003. New real-time reverse transcriptase-initiated PCR assay with single-copy sensitivity for human immunodeficiency virus type 1 RNA in plasma. *J Clin Microbiol 41:* 4531–4536.
8. Marcus JL, Chao CR, Leyden WA, Xu L, Quesenberry CP Jr, Klein DB, Towner WJ, Horberg MA, Silverberg MJ, 2016. Narrowing the gap in life expectancy between HIV-infected and HIV-uninfected individuals with access to care. *J Acquir Immune Defic Syndr 73:* 39–46.
9. Centers for Disease Control and Prevention, 2016. *Pre-Exposure Prophylaxis*. Available at: https://www.cdc.gov/hiv/risk/prep/index.html. Accessed December 2, 2017.
10. Fauci AS, 2017. An HIV vaccine is essential for ending the HIV/AIDS pandemic. *JAMA 318:* 1535–1536.
11. National Institute of Allergy and Infectious Diseases, 2016. *First New HIV Vaccine Efficacy Study in Seven Years Has Begun.* Bethesda, MD: NIAID.
12. National Institute of Allergy and Infectious Diseases, 2017. *NIH and Partners Launch HIV Vaccine Efficacy Study*. Bethesda, MD: NIAID.
13. U.S. Agency for International Development, 2015. *United States Government Global Tuberculosis Strategy 2015–2019.* Washington, DC: USAID.
14. World Health Organization, 2015. *The End TB Strategy—Global Strategy and Targets for Tuberculosis Prevention, Care, and Control after 2015.* Geneva, Switzerland: WHO.
15. Flynn JL, Chan J, 2001. Tuberculosis: latency and reactivation. *Infect Immun 69:* 4195–4201.
16. Pawlowski A, Jansson M, Skold M, Rottenberg ME, Kallenius G, 2012. Tuberculosis and HIV co-infection. *PLoS Pathog 8:* e1002464.
17. Mendez-Samperio P, 2017. Diagnosis of tuberculosis in HIV co-infected individuals: current status, challenges and opportunities for the future. *Scand J Immunol 86:* 76–82.
18. Venturini E, Turkova A, Chiappini E, Galli L, de Martino M, Thorne C, 2014. Tuberculosis and HIV co-infection in children. *BMC Infect Dis 14 (Suppl 1):* S5.
19. The Broad Institute, 2017. *TB-ARC Project (Tuberculosis Antibiotic Resistance Catalog Project).* Available at: https://www.broadinstitute.org/genome-sequencing-and-analysis/tb-arc-project-tuberculosis-antibiotic-resistance-catalog-project. Accessed December 4, 2017.
20. World Health Organization, 2017. *Antibacterial Agents in Clinical Development—An Analysis of the Antibacterial Clinical Development Pipeline, Including Tuberculosis.* Geneva, Switzerland: WHO.
21. Stop TB, Partnership, 2017. *2017 Global New TB Drug Pipeline.* Available at: http://www.newtbdrugs.org/pipeline/clinical. Accessed December 2, 2017.
22. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents, 2017. *Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents.* Available at: https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-opportunistic-infection/325/tb. Accessed December 5, 2017.
23. International Federation of Pharmaceutical Manufacturers, 2017. *TB Drug Accelerator Program.* Available at: http://partnerships.ifpma.org/partnership/tb-drug-accelerator-program. Accessed December 2, 2017.
24. Sizemore CF, Hafner R, Fauci AS, 2017. *NIH Statement on World Tuberculosis Day.* Bethesda, MD: NIAID.
25. Stop TB Partnership Working Group on New TB Vaccines, 2017. *TB Vaccine Pipeline.* Available at: http://www.newtbvaccines.org/tb-vaccine-pipeline/. Accessed December 5, 2017.
26. World Health Organization, 2016/2017. *Global Investments in Tuberculosis Research and Development: Past, Present, and Future.* Geneva, Switzerland: WHO.
27. Centers for Disease Control and Prevention, 2016. *BCG Vaccine.* Available at: https://www.cdc.gov/tb/publications/factsheets/prevention/bcg.htm. Accessed December 4, 2017.
28. Brennan MJ, Thole J, 2012. Tuberculosis vaccines: a strategic blueprint for the next decade. *Tuberculosis (Edinb) 92 (Suppl 1):* S6–S13.

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

STAY TUNED

FOR PART TWO OF THIS WORKSHOP ON SEP 14-16



We are exploring the possibility of providing translation services to the workshop in September.

If you are interested in attending the second part of the workshop in September and have a preference for translation, please let us know by filling out this brief survey

The event will be posted on the main project page here. You can also sign up for our listserv to receive a "Save the Date" announcement for all of our future events: www.nationalacademies.org/microbialthreats

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

UPCOMING FROM THE FORUM ON MICROBIAL THREATS

TOWARDS A POST-PANDEMIC WORLD: LESSONS LEARNED FROM COVID-19 FOR NOW AND THE FUTURE

Free live webcast!

The Forum on Microbial Threats will host a multi-day public workshop that will broadly examine the response to COVID-19 in the US and abroad. These virtual events will host retrospective and prospective discussions on the broad impacts of the rapidly-evolving pandemic on human health and society. Events will explore new understandings, challenges, and emerging data for leaders in governments, public health systems, the private sector, and communities to consider in the ongoing pandemic responses with a view towards enhancing resilience and preparedness for future outbreaks.

Stay tuned for more details!

To receive a "Save the Date" announcement for our events, sign up for our listserv on our website: www.nationalacademies.org/microbialthreats