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Title:

Tuberculosis Research and Development: Seeding the Future

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World Tuberculosis (TB) Day commemorates the discovery of *Mycobacterium tuberculosis* as the cause of tuberculosis by Dr. Robert Koch in 1882. It reminds the global community that 136 years later, TB remains the deadliest infectious disease globally, responsible for a staggering 1.7 million deaths in 2016 (1). Given the persisting burden TB imposes on humanity, innovative and concerted approaches to its control are required. In May 2014, ministers at the 67th World Health Assembly in Geneva, endorsed the World Health Organization (WHO) End TB Strategy which envisions a world without TB (2). In line with the Sustainable Development Goals (SDGs) framework adopted by United Nations (UN) member states, governments called for ambitious targets to end the TB epidemic - a 90% reduction in deaths and 80% reduction in incidence by 2030 compared to 2015 (3). As a disease that disproportionately affects the poorest and most vulnerable populations, TB sits at the intersection of health and socio-economic development. Tackling the epidemic will therefore bolster and reflect efforts in achieving a number of other SDG targets, such as eradicating poverty and malnutrition, ending the HIV/AIDS epidemic, reducing mortality among women and children, and strengthening health systems.

The act of placing research and innovation at the heart of the End TB strategy, alongside patient-centered care and prevention, in tandem with bold policies and supportive systems, recognizes that achieving substantial reductions in TB incidence and mortality requires innovations, starting with development of new tools and accelerating universal access to new and existing technologies. Priorities include a rapid, affordable, easy to use point-of-care test for diagnosis and simultaneous detection of drug resistance; safer, shorter treatment regimens for drug-sensitive-, drug resistant- and latent forms of the disease; and a new universally applicable, effective vaccine for pre- and post-exposure prophylaxis.

TB research remains, however, grossly underfunded. The 'Global Plan to End TB' estimates that US\$ 9 billion needs to be invested on research between 2016 and 2020 to address the most urgent gaps in diagnosis, treatment and prevention (4). The current level of research and development (R&D) expenditure (between 600 and 700 million US\$ per year) constitutes a fraction of this amount, and is not commensurate to the global burden of TB. Based on

recent analyses, TB is responsible for nearly 2% of disability-adjusted life-years (DALYs) and 2% of deaths globally, but receives a paltry 0.25% of the estimated US\$ 265 billion spent on medical research annually (5). In addition, drug-resistant forms of TB account for a quarter of annual deaths due to antimicrobial resistance (AMR), and TB is projected to be one of the three biggest drivers of the economic toll from AMR (6). TB receives less funding for research than other global health problems such as HIV and malaria, both in absolute terms and relative to its share of DALYs and premature mortality. Declining investments by industry over the past 5 years, coupled with flat expenditures from major public and philanthropic funders, point to the need to bring fresh resources into the TB research field and the imperative to develop innovative, flexible and collaborative mechanisms for advancing the science needed to end TB (5, 7).

The past, present and future threat that TB poses to human health and global health security reflects the continuing gross neglect in funder and political commitment into the TB research field over the past half century. A decisive action by all governments working in concert with the private and philanthropic sectors, civil society and communities affected by TB is necessary to make research a real priority. Funding for TB R&D must increase substantially over past levels, and regulatory and other institutional barriers to research need to be resolved with urgency (8).

New hope comes from the first WHO Global Ministerial Conference on 'Ending TB in the sustainable development era: a multisectoral response', convened in Moscow in November 2017, where governments committed to pursuing a series of actions at the national and international levels. (9)

At the *national level*, governments agreed to take steps, together with all stakeholders, to create research-enabling environments that nurture and facilitate TB R&D. This entails:

- developing country-specific strategic plans for TB research through capacity-building and multisectoral partnerships;
- activating domestic financing mechanisms to increase funding for TB R&D, including for applied health and social science research,

- establishing/strengthening national TB research networks and reducing research- and implementation-related regulatory impediments.

At the *international level*, governments agreed to work together and in collaboration with WHO and global partners to develop a new *Global Strategy for TB research* to unite and guide the TB R&D community on the development of new tools and innovative strategies for delivering patient-centered services grounded on human rights and health equity principles. This global strategy should have several aims, including:

- enhancing the cooperation and coordination of research to promote efficient use of available resources;
- mobilizing resources for TB research, including through innovative financing mechanisms and incentive strategies, and through a more diverse funding base;
- promoting the sharing of data and information to rapidly advance the implementation of research priorities related to the end TB response.

To concretize these objectives, countries recommended drawing on new and existing R&D initiatives, such as the AMR R&D Collaboration Hub proposed in the 2017 G20 Leaders' Declaration (10), and the TB Research Network stated in the BRICS Leaders Xiamen Declaration (11), formally announced at the WHO Ministerial Conference in Moscow. TB R&D is on the brink of a new era with opportunities commencing from the Moscow declaration to end TB and the forthcoming United Nations General Assembly high-level meeting on TB. This offers a unique window to redirect and refocus national, regional and global actors towards a closer solidarity in TB R&D efforts. Research is not a luxury - it is a necessity that no government, funder and global public health fraternity committed to working towards achieving the SDG vision of a healthier, more prosperous and secure world can afford to ignore.

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