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World TB Day 2016: reflections on the global TB emergency

The theme for this year's World TB Day is *Unite to End TB*, and now is the time to reflect on international efforts to control tuberculosis, which was declared a global emergency by WHO in 1993.[1] Since then, the disease has remained an indicator of poverty related diseases, neglect by donors and funders, and inequity.

Although the 2015 WHO Global TB Report[2] highlights notable achievements in global tuberculosis control efforts,[3] tuberculosis claimed more lives worldwide than any other infectious disease in 2014. Consequently, much more needs to be done (table) in this era of Sustainable Development Goals[4] if the target of the WHO End TB Strategy[5] to eliminate tuberculosis by 2035 is to be met. To achieve this ambitious target, increased investment is needed to scale up existing technologies and interventions to locate, diagnose, and treat everyone who has tuberculosis, and to facilitate the development of new diagnostics, drugs, innovative treatments and vaccines.[6] However there are major gaps in funding for implementation of existing interventions (US$1·4 billion)[1] and research and development (estimated at $1·3 billion),[7] which will need to be addressed. Failure to close these funding gaps will put the substantial advances made in tuberculosis control over the past 15 years in jeopardy and will enhance the spread of multidrug-resistant tuberculosis (MDR tuberculosis), further increasing the economic burden on developing countries.[8] Funding gaps need to be addressed urgently, with the involvement of bilateral and multilateral donors, the private sector, and affected countries.[7]

For more on **World TB Day** see http://www.who.int/campaigns/tb-day/2016/event/en/

Traditional approaches to anti-tuberculosis drug development have produced only small incremental improvements in tuberculosis therapy, and these have had no major effect on tuberculosis transmission globally. With few new tuberculosis drugs to work with clinically available, and in view of the growing epidemic of MDR tuberculosis, tuberculosis service providers and researchers worldwide are in the difficult position of trying to do more with less. Tuberculosis services currently face two major unmet clinical needs: first is the crucial need for shorter tuberculosis treatment regimens (shorter than 6 months for drug-sensitive tuberculosis and shorter than 18 months for MDR tuberculosis) to improve patient adherence, improve treatment outcomes, and reduce cost. Second is the neglected but very important issue of prevention of long-term, permanent lung damage, which occurs in up to 50% of patients with pulmonary tuberculosis, even if they have completed a course of

	Achievements since global emergency declared	Areas in need of improvement
Effects of tuberculosis	Deaths from tuberculosis have fallen by 47% since 1990 and an estimated 43 million lives have been saved Global tuberculosis incidence fell by an average of 1·5%, and tuberculosis prevalence in 2015 was 42% lower than in 1990 The number of people dying from HIV-associated tuberculosis declined by 32%	Tuberculosis caused 1·5 million deaths in 2014 About 9·6 million people worldwide developed active tuberculosis and half a million people developed MDR tuberculosis, of which a large percentage remain undiagnosed and untreated XDR tuberculosis was identified in 105 countries Only a third of the estimated 1·2 million people living with HIV who developed tuberculosis in 2014 were on antiretroviral therapy
Treatment and prevention	Eight new or repurposed anti-tuberculosis drugs are in development and several new tuberculosis treatment regimens are being trialled An anti-tuberculosis drug candidate (TBA-354) is in phase 1 testing Bedaquiline and delamanid are available to treat MDR tuberculosis Fifteen tuberculosis vaccine candidates are undergoing clinical trials	Treatment regimens that can shorten duration of therapy and can cure most patients with MDR or XDR tuberculosis Treatments that can reduce permanent lung damage and prevent long-term functional disability in patients who recover from pulmonary tuberculosis Assessment and further development of host-directed therapies High cost of treating patients with MDR tuberculosis
Diagnostics	Xpert MTB/RIF has been rolled out in 116 low-income and middle-income countries The new diagnostics pipeline is healthy	37% of the 9·6 million new cases in 2014 of tuberculosis were undiagnosed Of roughly 480 000 cases of MDR tuberculosis only 123 000 were diagnosed
MDG targets	Global implementation of the DOTS strategy together with advances in socioeconomic development have meant that MDG targets to halt and reverse tuberculosis incidence in most WHO regions during 2014 were achieved	Political advocacy and support Increased donor/funder and pharmaceutical investments into rollout of existing interventions, newly licensed drugs, and rapid diagnostics
Funding	Funding for tuberculosis prevention, diagnosis and treatment reached US$6·6 billion in 2015, up from $6·2 billion in 2014 International donor funding increased since 2006, reaching $0·8 billion in 2015 Most of the funding that was provided from 2004 to 2013 came from the Global Fund (72%), USA (14%), Canada (4%), and the UK (3%)	Many national tuberculosis programmes are unable to raise the funding required for full implementation of strategic plans The African region has by far the largest funding gap ($0·4 billion in 2015)

MDG=Millennium Development Goals. MDR=multidrug resistant. XDR=extensively drug resistant. DOTS=directly observed treatment, short-course

Table: Key message from the WHO global tuberculosis report

tuberculosis treatment.[9] This damage results in chronic cough, breathlessness, impaired lung function, inability to return to work to earn a living, and reduced lifespan.[10] The WHO 2015 tuberculosis report[2] does not mention recent innovative developments in host-directed therapies (HDTs),[11] which might meet both clinical and programmatic needs. Various HDTs are now available, which have the potential to modulate anti-*M tuberculosis* immune responses, reduce excess inflammation, repair lung tissue, prevent lung damage, and enhance the effectiveness of tuberculosis drug therapy, reduce the lengthy duration of tuberculosis therapy, and improve treatment outcomes.[12] These HDTs should be prioritised and funding made available urgently to assess their use as adjuncts to conventional therapy.

Meanwhile, increased investments are needed to increase the use of existing drugs, rapid diagnostic tests and drug susceptibility assays, and surveillance activities,for tuberculosis. Use of bedaquiline and delamanid (the only two new tuberculosis drugs to be licensed in the past decade) should be expanded and development of associated drug susceptibility testing platforms will be needed to ensure optimised use of these drugs. Encouragingly, for the first time in decades, political and pharmaceutical groups are uniting to tackle the tuberculosis pandemic. 90 community-based, non-governmental, and other civil society organisations from 35 countries met in Addis Ababa, Ethiopia, on November 11–13, 2015, and issued a statement of action[13] to define the next steps to implement the *End TB Strategy*. The US Government announced the *National action plan for combating multidrug-resistant tuberculosis*,[14] The Global TB Caucus, is a rapidly growing international network of parliamentarians from across the world and is generating greater finances to help to tackle tuberculosis. On Jan 22, 2016, at the World Economic Forum in Davos (Switzerland), more than 80 leading international pharmaceutical, and biotechnology,called on governments to work closely with them to address the rising threat of antimicrobial resistance, including MDR tuberculosis.[15] These collective actions provide a much-needed boost and optimism for the global fight against tuberculosis.

For the **Global TB Caucus website** see www.globaltbcaucus.org

For the **Host-Directed Therapies Network Consortium website** see http://www.unza-uclms.org/hdt-net

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