Tuberculosis: current challenges and beyond

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Although preventable and curable, TB is still a major global health threat. The recent #COVID19 pandemic and other conflicts have left an unsettling scenario for #TB. We need urgent, united and effective multi-sectoral responses to #EndTB. https://bit.ly/40gpBrG

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Abstract

Despite being a preventable and curable disease, tuberculosis (TB) is still a major global health threat and the second leading cause of death due to an infectious agent worldwide. All the efforts invested to end TB have resulted overall in rather slow decreases in TB incidence and mortality rates, which have been further negatively affected by the ongoing coronavirus disease 2019 (COVID-19) pandemic. While the majority of targets of the End TB Strategy remain off track, and we have not yet overcome the disruptions caused by the COVID-19 pandemic, recent conflicts such as the ongoing war in Ukraine are threatening the decrease of the burden of TB even further. To get back on track and get closer to ending TB, we need urgent, global, well-structured and committed multi-sectoral actions that go beyond national and global TB programmes with the support of deep investments in research and facilitation of equitable and rapid implementation of innovation worldwide.

Introduction

Tuberculosis (TB) represents a major global health threat that, despite being preventable and treatable, is the 13th leading cause of death worldwide and the second leading infectious killer after coronavirus disease 2019 (COVID-19) [1, 2]. In the past decades, the TB burden has been slowly decreasing; however, with the emergence of COVID-19 and the current political conflicts, including the war in Ukraine, proper functioning of healthcare services and TB control programmes are threatened, and the milestones set by the international health community to end TB remain unreached. In this viewpoint article, we discuss some of the challenges faced when tackling TB and the proposed strategy to end it.

Global TB burden

With 10.6 million estimated new cases, 1.6 million deaths and 1.7 billion latently infected in 2021, TB remains a major global health concern [1]. Although able to affect anyone anywhere, in low- and middle-income countries TB stands as the eighth and seventh most common cause of death, respectively, and these countries bear the burden of 80% of all TB cases [2]. In 2020, the World Health Organization (WHO) regions of South-East Asia and Africa accounted for more than two-thirds of all new TB cases (43% and 25%, respectively), with 46% of deaths estimated in South-East Asia and 39% in Africa [2]. Furthermore, ~450 000 new cases worldwide are multidrug-resistant TB (MDR-TB)/rifampicin-resistant TB, 78% being MDR-TB. The highest MDR-TB rates are detected in Belarus, Russia and Moldova, with

38%, 35% and 33% of new TB cases, respectively, followed by Kyrgyzstan and Tajikistan with 29% and Kazakhstan and Ukraine with 27%, meaning that one out of three new TB cases are MDR-TB [3]. Although still a major concern, MDR-TB has remained stable in the past years, representing <5% of TB cases. Finally, 8% of TB cases globally are HIV-associated; three-quarters of these are found in Africa, with a high incidence also in Russia and Ukraine [3].

Challenges

During the past years, the TB burden has been slowly decreasing at a rate of 1.5–2% per year [2]. Such low speed is due to many factors. Firstly, there is a large TB (latent) infection pool, which, together with risk factors for active disease, global ageing, slow and insufficient case detection, low cure rates and drug resistance, favours the slow incidence decline. Furthermore, TB is tightly linked to social-economic determinants. The main vulnerable people are those living in poor, crowded and poorly ventilated conditions; those living with HIV, diabetes, malnutrition, alcohol abuse, and drug and tobacco use; and migrants, refugees, prisoners, ethnic minorities and marginalised populations. The higher the gross domestic product (GDP) the lower the TB incidence, whilst the higher the level of undernutrition, the higher the incidence [1]. Moreover, other major disruptive events like the current pandemic and political conflicts greatly slow down the decline of TB burden.

The three layers

The determinants affecting TB burden may be classified into three layers of challenges that can be addressed within national TB programmes, the general health sector and beyond health; the latter are faced through good performance of sectors addressing undernutrition, poor living conditions, discrimination and marginalisation (figure 1). To end TB, a multi-sectoral approach involving all stakeholders, all government

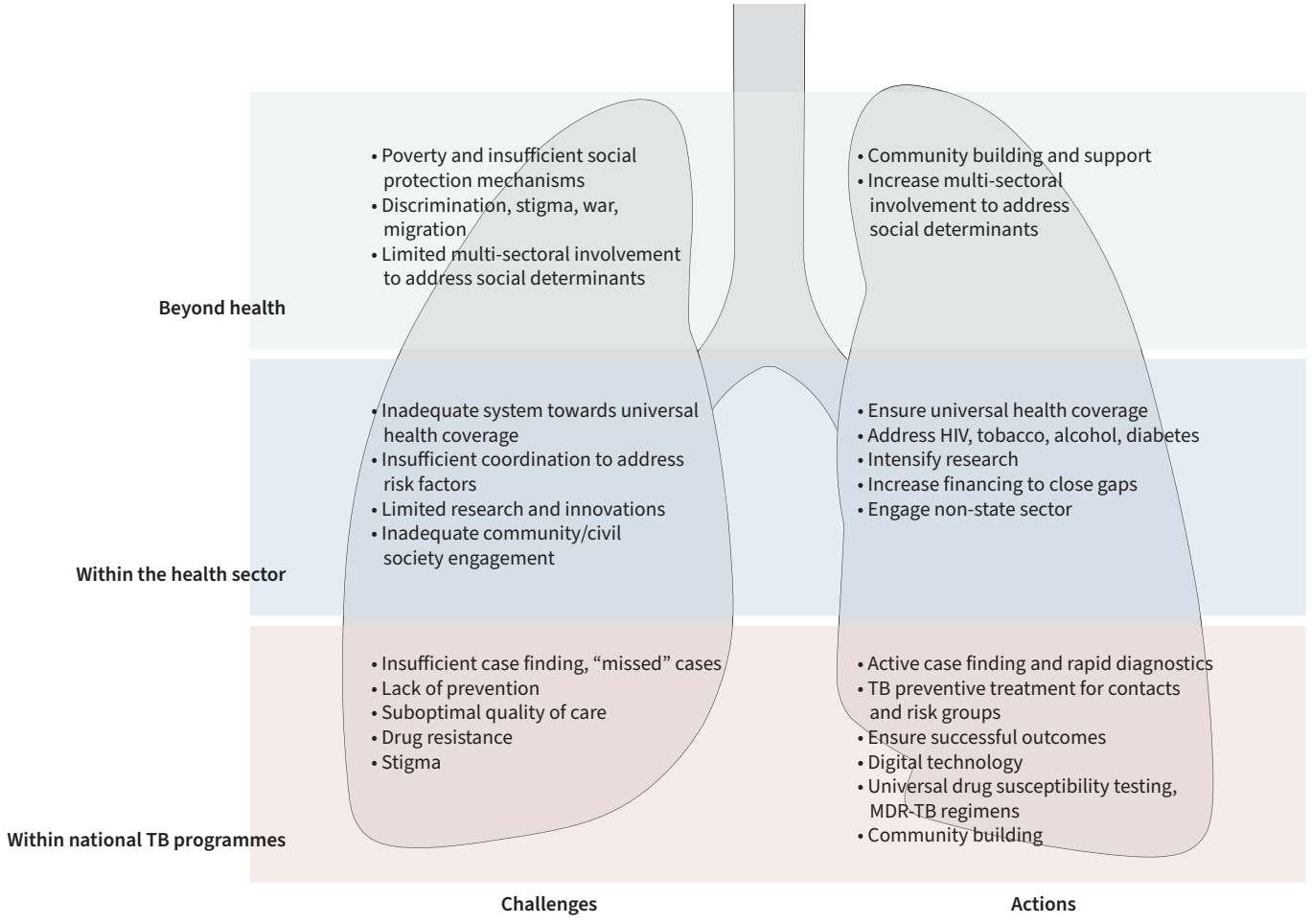

FIGURE 1 The three layers of tuberculosis (TB) challenges and actions. MDR: multidrug-resistant. Adapted from [4].

departments, the private sector, community engagement and survivor groups is required. This approach should consider good health and well-being secured by national TB programmes and the general health system, together with different sectors of development within the framework of the Sustainable Development Goals (SDGs) addressing the variety of determinants affecting TB. In this regard, the Western Pacific Regional Framework to End TB has classified TB interventions into three layers: essential TB functions, health system foundation (bold policies), and health beyond health [4]. This classification reflects the global health approach that foresees the engagement of sectors beyond health to reach a health outcome such as TB burden decline.

The COVID-19 pandemic and war

Besides general challenges, certain unforeseen events greatly disrupt TB burden control actions. Since the end of 2019, COVID-19 has severely hit the global healthcare system and, subsequently, national and global TB programmes [5, 6]. By reducing healthcare facilities and services, and reallocating human resources, diagnostic platforms and budgets, by the end of 2020 the pandemic had already caused a 20% decrease in TB detection and proper treatment, an 18% drop in case notifications, and an increase in TB deaths for the first time since the early 2000s [2]. According to the latest Global TB Report, there was a partial recovery in case notifications to 6.4 million in 2021, similar to that recorded in 2016–2017 [1].

While still struggling with COVID-19 consequences, the Russian invasion of Ukraine on 24 February 2022 put this situation at greater risk, especially given the severity of TB burden in both countries. Besides the terrible losses of lives due to their direct effects, wars and conflicts disrupt basic pillars of society such as education, economy, nutrition and access to social and healthcare services, resulting in devastating and long-lasting consequences. Since the invasion began, hundreds of buildings have been destroyed, thousands of civilians have died, and >7.7 million refugees have left Ukraine for neighbouring countries (according to the United Nations (UN) and UN Refugee Agency), causing Europe's largest refugee crisis since World War (WW) II. Looking back, during WWI, TB deaths increased greatly [7], and TB was considered the major health disaster of WWII [8], where malnutrition, overcrowding and health services disruption, among others, caused a major increase in TB deaths [9]. Although anti-TB drugs were not available until the end of WWII, the negative effects of these conflicts on TB have also been seen in later historical warfare events. During the civil war in Guinea-Bissau (June 1998 to May 1999), a three-fold increase in TB mortality during the first 6 months of war was attributed to treatment interruption [10]. Due to the Syrian crisis, starting in 2011, a sharp increase in TB cases was registered in neighbouring countries, attributed to the mass movement of refugees [11]. Additionally, with respect to the previous conflict in 2014 in Ukraine, one of the countries with the highest MDR-TB rates worldwide (>7000 new cases per year [3]), an almost two-fold increase of MDR-TB cases was documented in 2016 (post-war) *versus* 2014 (pre-war) (25% *versus* 14% of total TB cases, respectively) [12, 13]. At the moment, according to official statistics [14, 15], the numbers of newly diagnosed TB cases and patients on treatment are similar to those in the same time span, when comparing 2021 with 2022 data. This may be evidence for the hidden epidemic of TB in Ukraine due to undiagnosed and/or delayed diagnosed cases and the lack of data in the military conflict and occupied territory zones, respectively [14, 15]. Therefore, the current war in Ukraine will undoubtedly have negative consequences for TB control and require additional efforts from neighbouring countries on refugee patient follow-ups.

The End TB Strategy

To decrease TB burden, global targets have been established in the context of the End TB Strategy of the WHO, the UN's SDGs, and the High-Level Meeting at the UN General Assembly in 2018. Approved by the WHO's World Health Assembly in 2014, the Strategy aims to "end TB" by 2030/2035 [16], ensuring equitable access to high-quality diagnosis, treatment, care and prevention for everyone affected by TB, without the risk of incurring catastrophic expenditure or social repercussions. The Strategy is based on three pillars: 1) integrated, patient-centred care and prevention; 2) bold policies and supportive systems; and 3) intensified research and innovation. These pillars are built upon four fundamental principles to be respected by all countries adopting the Strategy: 1) government stewardship and accountability, with monitoring and evaluation; 2) building a strong coalition with civil society and communities; 3) protecting and promoting human rights, ethics and equity; and 4) adaptation of the strategy and targets at country level, with global collaboration.

To evaluate the progression of the Strategy, certain milestones are set [16], which unfortunately are far from reached [1, 2]. Although TB incidence has been falling by 2% per year since 2015, the overall decrease by 2020 was 11% instead of the intended 20% [2]. Importantly, due to the disruptions caused by COVID-19, the situation has worsened, with only 5.8 of the 9.9 million estimated cases in 2020 being reported and treated, resulting in a gap of 4.1 million missing TB cases [2]. Additionally, mortality

increased by 5.6% in 2020 compared to 2019, leaving an overall 9.2% mortality decrease by 2020, far from the intended 35%. Thus, all targets to end TB are off track, except for that regarding people living with TB/HIV receiving TB preventive treatment [1, 2]. To get back on track we need to accelerate development of new diagnostics, including new point-of-care tests for infection and disease, and explore further global digital health initiatives and artificial intelligence approaches, new drugs that are safer and easier to use, shorter treatment regimens, and effective pre- and post-exposure vaccines. Moreover, implementation capacity and urgency in transferring tools and technology to the most affected countries must be built. Taking the direction of enhanced collaboration within the health sector and beyond, policy makers and healthcare providers should further focus their efforts towards a system approach and universal health coverage to ensure that vertical, disease-specific efforts are progressively evolving towards harmonised, comprehensive and integrated methods while preserving the essential elements of an effective TB prevention, care and control strategy [17]. An example of an integrated approach is the adoption of a multi-disease diagnostic platform to detect several diseases through a single tool, thus facilitating detection, increasing the chances of successful screening, and perhaps avoiding the consequences of unidirectional reallocation of resources when facing pandemics such as COVID-19 [6]. Coupling more research investments with facilitation of equitable and rapid implementation of innovations is therefore a paradigm to advance TB response.

Conclusions

Despite the efforts to end TB, incidence and mortality rates are decreasing rather slowly, leaving TB as a major global health threat. This situation has been further affected by COVID-19 and other conflicts including the war in Ukraine, leaving an unsettling scenario for TB worldwide. Once again, we will be reminded that "war is the enemy of health" [18], that TB is tightly linked to social determinants and poverty, and that strong reliable multi-sectoral interventions are needed urgently to address it. Besides sound health practices and good performance of TB services, bold policies need to be a key focus in combating TB. Without adequate nutrition, universal health coverage and social protection, we will be unable to improve TB outcomes. In the absence of a global health approach that engages sectors devoted to poverty alleviation, social protection, nutrition, clean energy, sustainable cities, gender equality, equity in societies, *etc*., we will not reach any target. Although a great part of the success in eliminating TB will depend on the immediate action taken by South-East Asian and African countries, global action is necessary as TB does not respect borders: "TB anywhere is TB everywhere", as an old slogan used to say. To reach the set targets and end TB, having united, well-structured, reliable, accountable and effective multi-sectoral responses is crucial. Additionally, going beyond TB programmes and the healthcare sector, addressing the lack of social protection while mitigating crucial social determinants is also pivotal to end TB.

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