

# ELIMINACIJA TUBERKULOZE - DOSTIGNUĆA I IZAZOVI

## TUBERCULOSIS ELIMINATION - ACHIEVEMENTS AND CHALLENGES

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### SAŽETAK

U 2023. godini, 7,8 miliona ljudi širom sveta novodijagnostikovano je sa tuberkulozom (TB), čime je TB ponovo postala vodeći uzrok smrti među zaraznim bolestima - nadmašivši COVID-19. Uprkos napretku u dijagnostici i lečenju, globalno opterećenje TB i dalje opada sporo, 1,5-2% godišnje. Na to utiču brojni faktori: velika baza osoba latentno inficiranih bacilom tuberkuloze bez manifestne aktivne bolesti, sve češći faktori rizika za endogenu reaktivaciju bolesti, globalno starenje populacije, sporo i nedovoljno otkrivanje slučajeva, niske stope izlečenja, rastuća otpornost na lekove i ko-infekcija sa HIV-om. Da bi se ostvario dalji napredak i eliminisala TB, neophodno je ubrzano ulaganje u inovacije. Prioriteti uključuju razvoj brzih dijagnostičkih testova koji se mogu koristiti na licu mesta, širu primenu digitalnih alata i veštačke inteligencije, stvaranje bezbednijih i efikasnijih lekova i kraćih režima lečenja, primenu vakcina za pre- i post-ekspoziciju, kao i povećanje dostupnosti novih alata i tehnologija u regionima sa najvećim opterećenjem.

Ključne reči: tuberkuloza; opterećenje bolesti; dijagnostika; inovacije u lečenju; strategije eliminacije

### ABSTRACT

The reported global number of people newly diagnosed with TB was 7.8 million in 2023. Despite the progress in diagnosis and treatment, TB has returned to being the world's leading cause of death from a single infectious agent (replacing COVID-19).

During the past years, the TB burden has been slowly decreasing at a rate of 1.5-2% per year, due to many reasons: large TB infection pool, increasing risk factors for active disease, global ageing, slow and insufficient case detection, low cure rates, drug resistance and TB/HIV co-infection. To move towards further achievements and TB elimination, we need to accelerate development of new diagnostics, including new point-of-care tests for infection and disease, explore global digital health approaches, enhance artificial intelligence use, develop new drugs that are safer and easier to use, shorter treatment regimens, and effective pre- and post-exposure vaccines as well as transfer tools and technologies widely to the most affected.

Keywords: tuberculosis; achievements; challenges; elimination

### INTRODUCTION

Even in the 21st century of dizzying growth and technology development, tuberculosis (TB) as an old disease still represent a major global health challenge, despite all the possibilities for prevention and management. Based on the latest data, it is the 13th leading cause of death worldwide. TB was the second leading infectious killer after coronavirus disease 2019 (COVID-19). However, despite this progress, TB has returned to being the world's leading cause of death from a single infectious agent (replacing COVID-19) [1,2].

The reported global number of people newly diagnosed with TB was 7.8 million in 2023. This is the highest number since WHO began global TB monitoring, above the pre-COVID baseline (and previous historical peak) of 7.6 million in 2022. The numbers in 2022 and 2023 probably includes a sizeable backlog of people who developed TB in previous years, but whose diagnosis and treatment was delayed by COVID-related disruptions that affected access to and provision of health services. India, Indonesia and the Philippines, which collectively accounted ≥60% of the global reductions in the number of people newly diagnosed with TB in 2020 and 2021, all recovered to above 2019 levels in 2022. Globally in 2023, TB caused an estimated 1.25 deaths, which is decline from the previous year when 1.3 million people died of TB.

Around 450 000 new cases worldwide are reported as multidrug-resistant TB (MDR-TB)/rifampicin-resistant 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 [2]. 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 [2].

TB is caused by the bacillus *Mycobacterium tuberculosis*, which spread when people affected with TB expel bacteria into the air (by coughing, sneezing, singing or speaking loudly). As TB incidence declined globally over the years, the recent estimates showed that the quarter instead a third of the global population have been infected with TB [3]. Following infection, the risk of developing TB disease is highest in the first 2 years (approximately 5%), after which it is much lower [4]. Some people will clear the infection. The risk is higher among adults and adolescents living with HIV, household contacts (regardless of HIV status), people who are initiating anti-TNF treatment, receiving dialysis, preparing for an organ or haematological transplant, people who have silicosis, people with diabetes, engaged in the harmful use of alcohol, tobacco smokers and underweight people unless they also belong to other risk groups, prisoners, health workers, immigrants from countries with a high TB burden, homeless people and people who use drugs [3, 5, 6]. Of the total number of people who develop TB disease each year, about 90% are adults, with more cases among men than women. The disease typically affects the lungs (pulmonary TB) but can affect other sites as well [2].

Without treatment, the death rate from TB disease is high (about 50%) [7]. With treatments currently recommended by WHO (a 4-6 months course of anti-TB drugs), about 85% of people with TB can be cured. [8]. Regimens of 1-6 months are available to treat TB infection [3] but they are not widely used.

During the past years, the TB burden has been slowly decreasing at a rate of 1.5-2% per year [2], due to many reasons: large TB infection pool, increasing risk factors for active disease, global ageing, slow and insufficient case detection, low cure rates, drug resistance and TB/HIV co-infection. In addition, TB is closely linked to the 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 [1,2]. Furthermore, major disruptive events like the pandemic and political conflicts greatly slow down the decline of TB burden [9].

The determinants affecting TB burden can be classified into three layers of challenges (figure 1) 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 [10].

Figure 1. Factors influencing vulnerabilities to illness



Source: Adapted from Bates I et al. Vulnerability to malaria, tuberculosis, and HIV/ AIDS infection and disease. Part I: Determinants operating at individual and household level. *Lancet Infectious Diseases*, 2004, 4:267-277

To end TB, a multi-sectoral approach involving all stakeholders, all government departments, the private sector, community engagement and survivor groups is necessary.

To decrease TB burden, global targets have been set within the End TB Strategy of the WHO, in line with the United Nations (UN) Sustainable Development Goals. Approved by the WHO's World Health Assembly in 2014, the Strategy aims to "end TB" by 2030/2035 [11], 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.

Certain milestones are set to evaluate the progress towards the targets [11]. However they are far from being achieved [2]. Due to the disruptions caused by COVID-19, the situation has worsened, mortality increased in 2020-2022 compared to 2019. All targets to end TB are off track, except for that regarding people living with TB/HIV receiving TB preventive treatment [2].

## CONCLUSION

To get back and move towards further achievements and elimination, we need to accelerate development of new diagnostics, including new point-of-care tests for infection and disease, explore global digital health approaches, enhance artificial intelligence use, develop new drugs that are safer and easier to use, shorter treatment regimens, and effective pre- and post-exposure vaccines as well as transfer tools and technologies widely to the most affected.

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