

Drug-Resistant Tuberculosis Combat- A Multilayered and Multidisciplinary Approach to Avoid a Grim Future

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There has been an emergence of one of the most lethal diseases due to Tuberculosis (TB) infection, that result in a quarter of all mortalities pertaining to TB. This deadly disease is caused by drug-resistant TB ^{1,2}. It was estimated in the 2024 Global TB Reports that in the year 2023, the incidence of cases of TB globally was 10.8 million, and mortality due to the infection was about 1.20 million. Of these cases, about 0.4 million were due to multidrug-resistant or rifampicin-resistant TB. The report sought to highlight the severity of the challenges posed by the resistant variant of the bacteria upon the global efforts to control this disease ^{3,4}. This resistant disease is one of the front-runners for all-cause mortality and morbidity throughout the world. There is a profound economic impact due to drug-resistant TB, with eighty-one percent of households facing financially ruinous healthcare expenses while seeking treatment ³.

Disparities have been observed both globally and regionally in the impact of this variant. In Ukraine, due to the ongoing crisis, the country is experiencing a breakdown of its healthcare infrastructure and, consequently, a surge in drug-resistant TB. In Europe, Ukraine's neighboring nations are seeing the expansion of cases of TB that are resistant to existing drugs due to population displacement. Such an incidence only amplifies the global TB threat ^{3,4}.

An association has been noted between drug-resistant TB and prolonged regimen of treatment, low success rates of treatment, severe adverse effects that are severe, and extensive societal and healthcare costs. There is, therefore, massive pressure on the national public health system, communities, families, and on the suffering individuals ^{5,6}.

The Global Trend of Drug-Resistant Tuberculosis

The age-standardized incidence rate (ASIR) for multidrug-resistant TB remains high worldwide. In the last thirty years, there has been a rise in rifampicin-resistant TB across all regions globally, notably in South Asian and Sub-Saharan nations. Inadequate investment in resources and weak policies further contribute to the gaps in control of this variant of TB in such disadvantaged regions that are already burdened by high disease prevalence ⁷. One of the main factors driving drug-resistant TB is the mismanagement of anti-tubercular drug treatment, such as failure to adhere to

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the medication regimen, improper use of drugs, and misuse. This issue is especially prevalent in resource-strained Sub-Saharan African and South Asian nations, which are mostly economically disadvantaged, having a deficiency in regulatory bodies and standardized treatment protocols. Consequently, the spread of TB of a resistant variant is worsened^{8,9}. Additionally, many low-and middle-income countries lack timely detection and proper management, aggravating the uncontrolled transmission of this malicious disease^{10,11}. Furthermore, with continued exposure to anti-tubercular treatment, resistant strains of *Mycobacterium tuberculosis* transform to become variants that are more complex as well as more lethal.

Addressing the Growing Challenge of Drug-Resistant Tuberculosis

To curb the rising trend of TB variant which are resistant to drugs, several comprehensive steps are necessary (Figure 1). There should be a focus on improving coordinated worldwide coordinated actions to advance the transfer of technology and financial aid, strengthening timely diagnostic capacities, optimizing management guidelines, and improving infrastructure related to the health of the general population¹²⁻¹⁴.

In low-income regions, the developed nations, non-government organizations (NGOs) and international bodies should help by sharing expertise and technology. Low-income countries should have easy access to technologies and treatments, such as advanced methods for detecting drug resistance and cutting-edge, standardized treatment protocols, developed by organizations like the World Health Organization (WHO) and platforms such as the Global Fund^{16,17}.

Similarly, improving the ability to detect drug resistance early is essential. GeneXpert is one such technology that enhances the accuracy and speed of identifying drug-resistant TB. This allows for timely detection and treatment¹⁸⁻²⁰. Screening needs to be ensured for high-risk groups, such as those with human immunodeficiency virus infection, as well as those suffering from TB relapse^{21,22}.

Improvement in adherence to treatment and ensuring the management as per the protocol of treatment are essential. The supply of anti-tubercular drugs should be consistent, and standardized treatment regimens, like therapy under direct observation, must be maintained. To prevent the development of resistance,

comprehensive psychological and social support should be provided alongside treatment, which significantly boosts adherence and minimizes interruptions^{23,24}.

Global Initiative to Combat Drug-Resistant Tuberculosis

WHO has recently launched initiatives to eradicate TB, sparking global clinical trials to develop new anti-tubercular drugs, optimizing short-course therapies, and advancing vaccine production. However, these trials encounter many obstacles, including limited generalizability of results, lack of comprehensive reviews, and fragmented research designs.

There are factors related to science, politics, and strategies that influence the conduct of research in this field. The first United Nations High-level Meeting on TB held in 2018 led to a significant rise in clinical trials from the year 2018 to 2023²⁵⁻²⁷. Phase IV trials increased after the year 2017 for drugs like Bedaquiline, which shows the global demand for safe and effective anti-tubercular drugs aiming at drug-resistant TB. Now, the focus is on maximizing current therapies, accessibility, and medication, and promoting treatment management rather than finding new drugs. The updated WHO guidelines and the End TB Strategy in 2019 helped increase investment on development of drugs against resistant TB²⁸. Bedaquiline has been approved and included in the WHO treatment guidelines, reflecting the urgency to find a way against resistant TB²⁹⁻³¹. Research continues to find shorter treatment duration and minimize the adverse drug effects of already existing drugs like rifampicin and isoniazid to meet public and clinical demands.

A greater number of TB clinical trials are observed in China and South Africa, as in those countries' disease burden is high, they have more research capacity, and supportive environments. The 'Healthy China 2030' strategy promotes TB prevention and treatment and encourages collaboration between different sectors. China includes TB management. The country therefore advances the "TB-Free Community" model, which alleviates patients' financial burdens and improves access to diagnosis at the community level. They also launched 'Action Plan to stop TB (2019-2022)'. There exists a high-level policy framework that supports the planned TB trials and underscores the seriousness of their continued research agenda. The country also uses AI-powered diagnostic tools and tongue swab tests to screen for TB and improve clinical trial enrollment³²⁻³⁴.

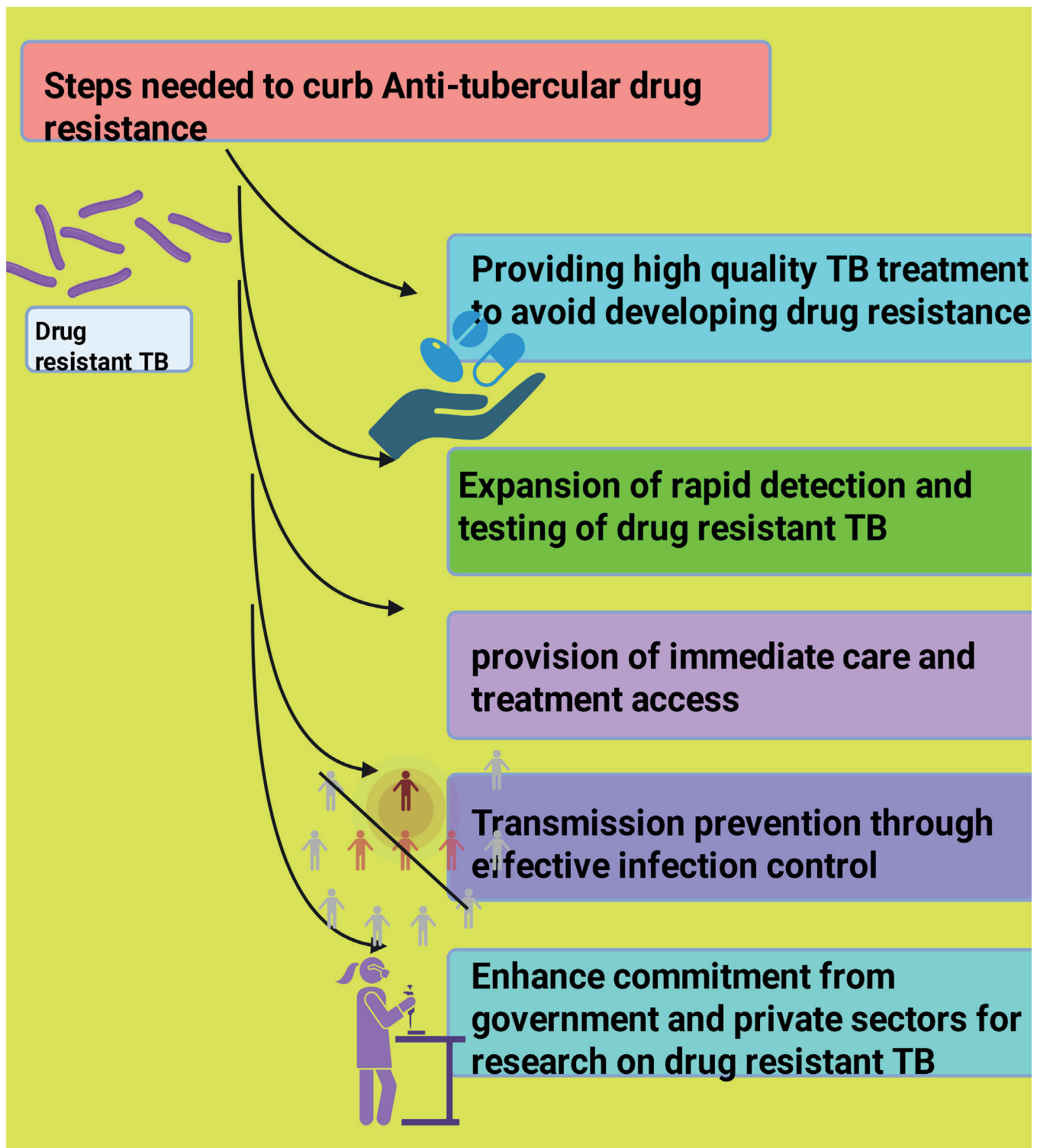


Figure 1: Shows the various steps needed to curb Anti-tubercular drug resistance. TB: Tuberculosis. This figure was created with the premium version of BioRender¹⁵ (<https://biorender.com/> Accessed March 3, 2026) with license number LN29FGTQ7C.

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Similarly, South Africa includes TB control within its National Health Insurance system. They coordinate healthcare resources across sectors using their clinical practice guidelines as the key. Their Ministry of Health promotes evidence-based treatment for infectious diseases, like TB³⁵. Such integration of policy and technology models in South Africa and China can be adapted by other regions with high disease burden. This would promote research efficiency and alignment of resources with the needs of the public.

While academic institutions are the main funders, indicating the critical role of basic research in TB therapy development, funding from pharmaceutical companies remains limited. This reflects their preference for more profitable medications over public health concerns.

Therefore, partnerships between public and private organizations need to be strengthened to attract industry investment in research funding for drug-resistant TB. Non-profit organizations' active participation and collaboration with others help bridge these gaps. Notably, the major players in global health include the Bill & Melinda Gates Foundation and the Global Fund, which provide aid and support for innovation in TB drugs, offering strategic and financial backing for impactful initiatives.

Bedaquiline, pretomanid, and delamanid are the main drugs used to treat this resistant disease. In 2018, the WHO's guideline on multidrug-resistant TB directed that clinical trials of drugs should include vulnerable groups like those with HIV co-infection, women of childbearing age, and children. This helped promote gender-specific trials after 2021. Additionally, the United Nations Children's Fund (UNICEF) 2013 "Roadmap for Childhood TB: Toward Zero Deaths," the 2018 "Roadmap towards ending TB in children and adolescents," and the Global Fund's targeted financing and administrative actions paved the way for developing pediatric dosages.³⁹

Key Players in Advancing Tuberculosis Control and Prevention

Improving TB management and control infrastructure remains the key to effectively preventing and controlling the disease. The infrastructure of primary healthcare in remote and rural areas needs to be strengthened; also,

the TB health records management system and overall control capabilities need to be enhanced.⁴⁰ In addition to that, strict medical surveillance and treatment for prevention in case of those who come in close contact with patients having the resistant strain are needed to decrease the incidence and spread of drug-resistant TB. This will help prevent transmission in the community, limit the spread of disease, and significantly enhance the public health system's capacity to address TB⁴¹. Finally, the public health policies should be reinforced, and the importance of health education cannot be overstated. Treatment and prevention of drug-resistant TB need to be promoted to improve public understanding of TB, which will also help reduce disease spread⁴². A combined multi-dimensional and multi-layered approach is required to combat the drug-resistant TB challenges in low to middle-income countries. These steps will eventually help achieve global TB control goals.

Consent for Publication

The author has reviewed and approved the final version and agrees to be responsible for all aspects of the work, including any issues related to accuracy or integrity.

Disclosure

Mainul Haque serves on the editorial board of the Bangladesh Journal of Medical Science (BJMS). The authors declare that they have no financial ties or affiliations with any organization, association, or entity directly or indirectly related to the topic or materials discussed in this review paper.

Data Availability

The information for this review paper is sourced from publicly available sources.

Authorship Contribution

All authors contributed significantly to the work, whether in the conception, design, utilization, collection, analysis, or interpretation of data, or all these areas. They also participated in drafting, revising, or critically reviewing the paper, gave their final approval for the published version, decided on the journal to which the article would be submitted, and took responsibility for all aspects of the work.

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