Review Article

Recent Advances in Tuberculosis Diagnosis and Treatment: Clinical and Translational Progress (2020–2025)

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Received: 08-04-2026; **Revised:** 23-06-2026; **Accepted:** 29-06-2026; **Published online:** 20-07-2026.

ABSTRACT

More than a decade of global control efforts has ended with Tuberculosis (TB) being a top contagious cause of morbidity and mortality all over the world. Even though the most basic principles of TB pathogenesis and epidemiology have been firmly defined before the year 2020, the following five-year period is characterised by rapid progress in diagnostic tools, therapeutic regimes, and digital health interventions. These technologies have enhanced early detection, treatment results, and patient-centred care significantly, especially in high-burden settings. This review will provide a summary of recent clinical and translational developments in the field of tuberculosis testing and treatment but will focus on the developments considered in line with the contemporary global priorities in the control of tuberculosis. Among the crucial improvements in diagnostics, there are quick molecular tests that can help identify drug resistance and artificial intelligence-related chest radiography that can be used to conduct massive screening of the population, and finally, biomarker-based testing that promotes diagnosis in vulnerable groups, including individuals living with HIV. Regarding treatment, the application of shorter rifapentine regimens of drug-susceptible TB and entirely oral and short-course regimens of multidrug-resistant and extensively drug-resistant TB are significant paradigm shifts in the management of the disease. Parallel to that, digital adherence technologies have become useful to facilitate patient engagement and treatment completion. It is the case, however, despite such advancements, that there are continued issues that involve equitable access, cost, capacity in health systems, and new resistance to newer agents. It will be necessary to deal with these hurdles to bring innovation to the population level. Altogether, the current advances in TB diagnostics and treatment are giving a new push towards eradicating TB, assuming the appropriate incorporation of such innovations into the national TB programs.

Keywords: Tuberculosis; Molecular diagnostics; Drug-resistant tuberculosis; Artificial intelligence; TB treatment; Digital health.

INTRODUCTION

Tuberculosis is a significant worldwide social health issue, being one of the foremost causes of fatalities by a single infectious agent in the world[1,2]. Although effective anti-tuberculosis drugs have been available for several decades, TB still seems to have a huge burden, especially in low- and middle-income countries [3,4]. Recurrent transmission, late diagnosis, protracted treatment, and poor adherence have hindered gains that can be made towards the eradication of TB [5,6].

The outbreak and transmission of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB have made disease control activities even more difficult [3,4]. Traditional methods of diagnosis, including the use of microscopy of sputum, are not sensitive, particularly in paucibacillary disease, extrapulmonary TB, children, and individuals with HIV [15,18]. Equally, long treatment plans have in the past been linked to high turnover and toxicity rates of treatment, which are the causes of poor outcomes and emergence of drug resistance [26,27].

The period of accelerated innovation in TB control between 2020 and 2025 presupposes innovations in molecular biology, artificial intelligence (AI), and the creation of new drugs, as well as digital health [7-9]. Although the COVID-19 pandemic has disrupted TB services in the majority of countries, it has also led to the rapid increase of molecular capacity, decentralisation of diagnostics, and digital health platforms, which are now applied to TB care [7,10-12].

Quick molecular diagnosis tests that can identify Mycobacterium tuberculosis and drug resistance in a few hours have revolutionised the process of early case identification and early treatment [13-16]. AI-supported chest radiography has increased screening capacity in the locations that have less access to certified radiologists, supporting active case-finding programs on massive scales [19-23]. Parallel to this, biomarker-based diagnostic tests have enhanced TB diagnosis in the vulnerable populations, especially those living with HIV [38-40].

Innovation in therapy at this time has been no exception. Regimens of shorter rifapentine-containing treatments have shortened the treatment period and have not affected the effectiveness against TB that is susceptible to the drug [24,25]. The development of fully oral regimens (bedaquiline, prelatamivir, linezolid) is changing the MDR- and XDR-TB treatment approaches, which had been previously based on

the injectable arm, which was linked with high toxicity and noncompliance [27-31].

The given review addresses the use of recent developments in TB diagnosis and treatment reported between 2020 and 2025, in particular, with the primary emphasis on clinically relevant and translational breakthroughs in line with the current global priorities of the fight against TB [9,50]. The long historical discourse has been reduced to the bare minimum in the name of staying focused on innovation, implementation, and future directions.

Brief Overview of Tuberculosis Pathogenesis

Mycobacterium tuberculosis is the aerobic, acid-fast bacillus that causes TB, and which is spread mainly via aerosolised droplets inhaled [5]. After inhalation, alveolar macrophages phagocytise bacilli, activating a complicated immune response of the host that defines the fate of the infection[36.42].

The formation of granuloma is a characteristic of TB pathogenesis and the indication of an effort of the host to limit infection. Nevertheless, M. tuberculosis may also remain in granulomas over long periods of time, causing latent TB infection and reactivation [42,48]. Recent research has stressed that TB is on a continuum between latent and incipient infection to subclinical and active disease, as opposed to a dichotomy [35,41].

Recent progress in immunology and systems biology has uncovered extensive heterogeneity of host immune responses, in both inflammatory pathways, immune regulation, and metabolic adaptation [36,37]. Such lessons have been used mainly in translational applications, including biomarker discovery, host-directed treatments, and predictive diagnostics [35,37,49].

Since the current review is dedicated to recent advances in the domain of diagnostics and therapeutics, it is not devoted to a particular immunopathological mechanism. Rather, it is viewed through the prism of pathogenesis, as far as it has contributed to the design of modern diagnostic methods and treatment programs.

Recent Advances in Tuberculosis Diagnosis (2020–2025)

1. Molecular Diagnostic Platforms

Rapid molecular diagnostics are one of the most significant advances in TB control, with substantial growth between 2020 and 2025 [13,14]. WHO-endorsed tests such as Xpert MTB/RIF Ultra, Xpert MTB/XDR, and Truenat MTB allow for the simultaneous detection of M. tuberculosis and resistance to key anti-TB drugs [15, 18].

Xpert MTB/RIF Ultra shows better sensitivity compared to earlier versions, especially in cases with low bacterial counts, extrapulmonary TB, and pediatric TB [15,47]. Xpert MTB/XDR expands resistance detection to isoniazid, fluoroquinolones, and second-line injectable drugs. This helps healthcare providers start the right treatments for drug-resistant TB sooner [16].

Truenat MTB tests are designed to be portable and battery-operated. They have made it possible to perform molecular testing in remote healthcare facilities, improving early case detection in areas with a high burden of disease [17,18] (Fig.1).

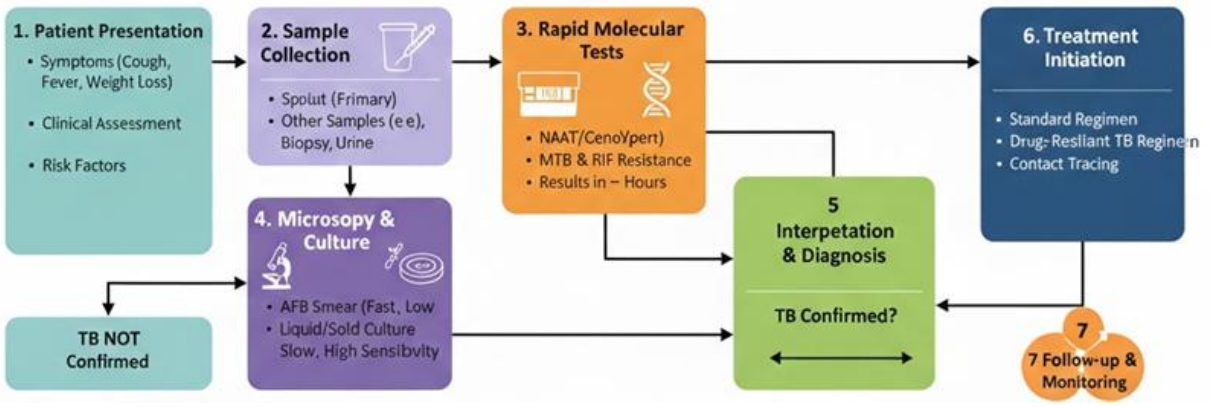

Figure 1: Workflow of Modern TB Diagnosis

2. Artificial Intelligence–Assisted Chest Imaging

Chest radiography remains an important screening tool for TB, but historically, it has been limited by the number of trained radiologists [21]. AI-based computer-aided detection systems like CAD4TB and qXR use deep learning algorithms to analyse digital chest X-rays and provide probability scores for TB [19,20].

Studies conducted between 2020 and 2025 show that AI-assisted systems achieve diagnostic accuracy similar to that of expert radiologists [19,22]. These tools are increasingly used for mass screening, triage, and active case-finding campaigns, especially in areas with limited resources [22,23] (Table 1).

Table 1: Recent advances in tuberculosis diagnosis

Diagnostic method	Key feature	Clinical benefit
Xpert MTB/XDR	Molecular PCR	Rapid resistance detection
Truenat MTB	Portable PCR	Point-of-care testing
CAD4TB	AI imaging	Mass screening
FujiLAM	Biomarker assay	Improved sensitivity in HIV

3. Biomarker-Based Diagnostics

Biomarker research has focused on overcoming the limitations of sputum-based diagnostics. This is particularly important for children, people living with HIV, and patients with extrapulmonary TB [38–40]. The Fujifilm SILVAMP TB-LAM (FujiLAM) assay marks a significant improvement, showing better sensitivity than earlier urine LAM assays [38,40].

Additionally, host blood transcriptomic signatures like RISK6 have shown potential for detecting early TB and predicting disease progression, which could lead to targeted preventive therapy [35,37,49].

Recent Advances in Tuberculosis Treatment and Management

1. Drug-Susceptible Tuberculosis

The traditional six-month treatment for drug-susceptible TB has often created issues with adherence and completing the treatment [26]. Recent clinical trials have shown that rifapentine-based regimens can shorten the treatment time to four months while keeping similar effectiveness [24,25].

These shorter regimens help patients stick to their treatment, lower healthcare costs, and assist in program implementation. This has led to their approval by the WHO and adoption in national TB programs [24–26].

2. Drug-Resistant Tuberculosis

The way we manage MDR- and XDR-TB has changed with the introduction of fully oral treatments [27–31]. The bedaquiline, pretomanid, and linezolid (BPaL) regimen has shown high cure rates in patients with severe drug-resistant TB [27].

Recent improvements, like BPaLM, have enhanced safety and tolerability while keeping effectiveness [28–30]. These regimens remove injectable medications, shorten treatment to about six months, and greatly enhance patients' quality of life [29–31] (Table 2) (Fig.2).

Table 2: Recent tuberculosis treatment regimens

Regimen	Indication	Duration
Rifapentine-based	Drug-susceptible TB	4 months
BPaL	MDR/XDR-TB	6 months
BPaLM	MDR-TB	6 months

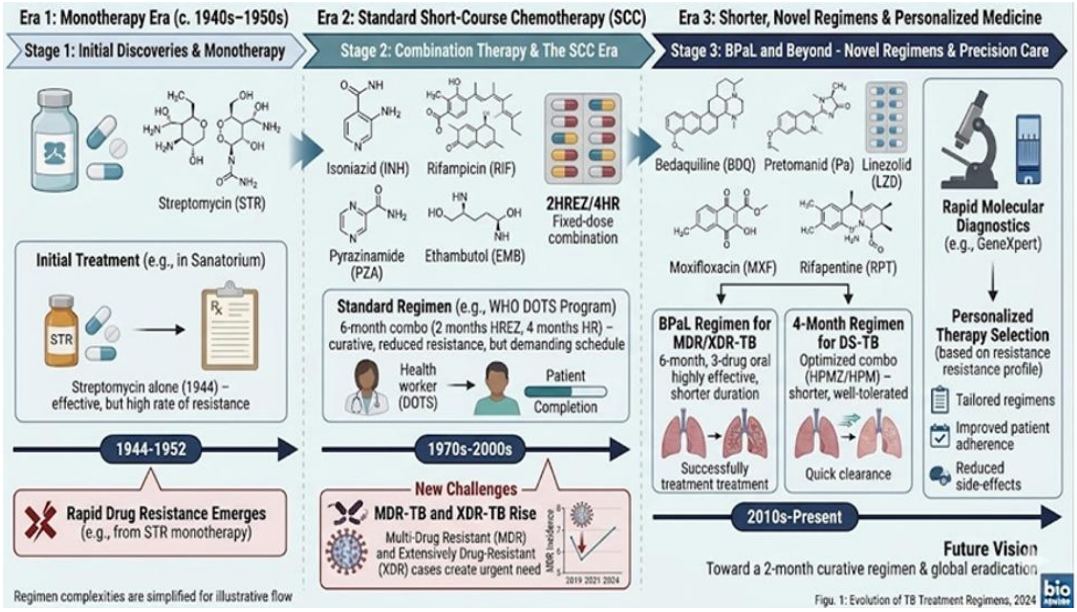

Figure 2: Evolution of TB Treatment Regimens

3. Digital Adherence Technologies

Digital adherence technologies like video-observed therapy, electronic medication monitors, and mobile health apps have become useful additions to TB treatment [23,32]. These tools help patients stay engaged, increase adherence, and lessen the strain on healthcare systems, especially in areas with high TB rates [32,33].

Challenges and Future Perspectives

Despite significant progress, several challenges limit the impact of recent advances on the general population. Access to modern diagnostics and newer drugs is still uneven, especially in low- and middle-income countries [32,33]. Issues like infrastructure, high costs, and supply-chain problems continue to slow down widespread implementation [34].

The rise of resistance to newer medications shows how crucial it is to promote responsible use of antimicrobials, maintain ongoing surveillance, and use new treatment plans wisely [34,36]. Furthermore, to successfully implement digital health technologies, health systems must be ready, ensure data security, and gain patient acceptance [23,32].

Future strategies for controlling TB must combine technological innovation with strengthening health

systems, fair financing, and ongoing political commitment to meet the goals of the End TB Strategy [9,50].

DISCUSSION

Recent advances in tuberculosis (TB) diagnosis and treatment mark a significant shift from traditional methods to a focus on patient-centred care. The time frame from 2020 to 2025 is particularly important. It involves the merging of molecular diagnostics, artificial intelligence (AI), and shorter, effective treatment plans that match global TB control priorities [1,2,9,50]. These changes tackle ongoing issues like delayed diagnosis, inadequate detection of drug resistance, and poor treatment adherence.

Rapid molecular diagnostic tools like Xpert MTB/RIF Ultra, Xpert MTB/XDR, and Truenat MTB have changed the landscape of early TB detection. They provide accurate results in just a few hours, allowing for quick identification of drug resistance [13–18]. The growth of resistance profiling beyond rifampicin is crucial for guiding the right treatment in multidrug-resistant TB. This improvement leads to better treatment results and helps prevent further resistance [3,16]. At the same time, AI-assisted chest X-rays have increased screening capacity in areas with high TB rates and limited resources. They reduce the need for specialised radiologists and help with large-scale case-finding efforts [19–23].

Biomarker-based diagnostics, especially urine lipoarabinomannan tests and host transcriptomic signatures, have also improved TB diagnosis for vulnerable groups, including people living with HIV and those with low levels of bacteria [38–40,35]. These tools show potential for earlier detection and targeted intervention, such as identifying early-stage TB, which is vital for prevention efforts [41,49].

On the treatment side, shorter rifapentine-based regimens for drug-susceptible TB and fully oral regimens like BPaL and BPaLM for drug-resistant TB have greatly improved how tolerable treatments are, leading to better adherence and higher cure rates [24–31]. Digital tools for monitoring adherence have further supported these regimens by boosting patient engagement, especially in decentralised care settings [23,32].

Despite these improvements, major challenges still exist. Unequal access to diagnostics and new medications, infrastructure problems, and the potential for drug resistance remain. These factors highlight the need for continual investment, responsible use of antibiotics, and strengthening health systems [33–36]. Successfully incorporating these innovations into national TB programs is crucial for achieving global TB elimination goals.

CONCLUSION

Recent progress in TB diagnosis and treatment from 2020 to 2025 marks a crucial time in TB control. Rapid molecular tests, AI-assisted imaging, biomarker tests, and shorter all-oral treatment plans have greatly improved how we detect and manage the disease, leading to better results for patients. Making sure everyone can access and effectively use these innovations is vital for meeting global TB elimination goals.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Acknowledgements

The authors acknowledge the Department of Pharmaceutical Chemistry, JSS College of Pharmacy, JSS Academy of Higher Education and Research, Mysuru, India.

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