Advances, Challenges, and Emerging Therapies in Tuberculosis: A Comprehensive Review of Global Tuberculosis Control and Future Directions.

Abstract

Tuberculosis is a leading global cause of infectious morbidity and mortality, disproportionately affecting low- and middle-income countries with high population density and comorbidities like HIV and diabetes. The COVID-19 pandemic disrupted TB control efforts, halting declines in incidence and driving up mortality rates. MDR-TB and XDR-TB pose growing challenges worldwide, requiring prolonged, expensive, and toxic treatment regimens. Rapid assays such as Xpert MTB/RIF and line probe assays enable early detection and resistance profiling, augmented by novel biomarkers and AI for enhanced precision. Standard treatment for drug-sensitive TB remains a six-month regimen, while novel shorter regimens—including all-oral therapies with recently licensed drugs like bedaquiline, delamanid, and pretomanid—are redefining MDR/XDR-TB management. Innovations include host-directed therapies that modulate immunity, nanotechnology for targeted drug delivery, and bacteriophage therapy—in which phages selectively lyse drug-resistant strains, bypassing antibiotics while exhibiting low toxicity. Hurdles persist in standardization and access. Integrated diagnostics, phage-like innovations, public health initiatives, equity, and commitment are essential to reverse the epidemic and meet elimination targets.

Running Title

Advances and Emerging Therapies in Tuberculosis

Keywords

Tuberculosis (TB), Multidrug-resistant TB, Extensively drug-resistant TB, Emerging therapies, Bacteriophage therapy

1. Introduction

Tuberculosis (TB) is a major global health challenge, consistently ranking among the leading causes of morbidity and mortality due to infectious diseases worldwide, as confirmed by both the World Health Organization (WHO) and the U.S. Centers for Disease Control and Prevention (CDC)[1]. According to the WHO Global Tuberculosis Report 2023, an estimated 10.8 million people developed TB globally, with approximately 1.3 million deaths among HIV-negative individuals and an additional 214,000 deaths among HIV-positive individuals[2]. TB is a major public health concern in low- and middle-income nations, particularly in areas with high population density, socioeconomic dependency, and comorbidities like diabetes and HIV [3,4]. Its incidence rates have marginally increased following COVID-19 interruptions, reversing the previous decade's 2% yearly decline; a 3.6% increase is observed between 2020 and 2023[5]. Five nations account for 56% of global tuberculosis cases: India (26%), Indonesia (10%), China (6.8%), the Philippines (6.8%), and Pakistan (6.3%) [2]. India's yearly notification reached 26 lakh cases in 2024, with a 17.7% drop in incidence since 2015, however, elimination targets remain extremely challenging[6]. The CDC reiterates these concerns, underlining TB's continuation as a serious respiratory infectious illness in the U.S. and globally, with significant variance in disease burden linked to risk groups such as migrants, the immunocompromised, and senior citizens[1].

2. Transmission dynamics of Tuberculosis

Tuberculosis is caused by the bacterium *Mycobacterium tuberculosis* (MTB), an aerobic, non-spore-forming, non-motile bacillus with lipid-rich cell walls that confer acid-fast properties [7].This organism has a reproduction rate of approximately 20 hours and takes 3 to 8 weeks to manifest visually on solid media; therefore, laboratory identification is tedious. Airborne droplet nuclei are the primary mechanism of transmission and can remain suspended in the environment for an extended period of time [8].MTB infection leads to a spectrum of outcomes, ranging from active progressive disease to a clinically dormant, latent state. The specific host and bacterial factors that control the maintenance of latency and trigger reactivation are complex and remain an active area of investigation [9].

3. Pathogenesis of Tuberculosis: Host-Pathogen Interactions and Disease Progression

The pathogenesis of tuberculosis is initiated upon inhalation. Bacilli that evade the mucociliary escalator reach the alveoli, where their phagocytosis by resident macrophages is a critical step that determines the outcome of the infection [10]. The dissemination of bacilli to regional lymph nodes triggers activation of T lymphocyte, which in turn orchestrates the recruitment of diverse immune cells to form granulomas [11]. While these organized structures are designed to contain the infection, the intricate mechanisms governing their function and ultimate fate remain subjects of ongoing research. Radiologically, a Ranke complex indicates healed primary tuberculosis which results from the fibrosis and calcification of an earlier Ghon complex; this late-stage finding is identified by the combination of a calcified parenchymal scar and calcified hilar or mediastinal lymph nodes [12]. Among individuals infected, approximately 5% progress to active disease within the first two years after primary infection, while an additional 5% experience reactivation and develop disease later in life [7]. Active tuberculosis results when host immune control is compromised, with granulomas undergoing caseous necrosis and airway rupture to form cavities [13]. These cavities facilitate high bacillary loads, transmission, foster drug resistance, promote fibrosis, and opportunistic secondary infections [14-16]. Notably, some granulomas do not cavitate and may heal by mechanisms that are not yet fully understood [17]. After an initial infection, an effective CD4+ and CD8+ T-cell response typically contains the bacteria within three to eight weeks, establishing latent tuberculosis, which can fluctuate between true dormancy and subclinical disease[18]. In adults, most active tuberculosis cases arise from reactivation of latent infection rather than new primary infection. Although prior infection provides partial protection against reinfection, exogenous reinfection can occur, especially in immunocompromised individuals or those with significant exposure [19].

4. TB Disease Burden and Risk Determinants in the COVID-19 Era

TB remains a major global health challenge [20,21], with approximately 90% of infected individuals harbouring latent infection and around 5% progressing to active disease during their lifetime [7]. In 2022, TB caused an estimated 1.3 million deaths worldwide, marking a slight decline from previous years[21]. The COVID-19 pandemic severely disrupted TB management globally [22], resulting in increased TB mortality due to healthcare system interruptions and the diversion of resources to COVID-19 care, which delayed TB diagnosis and escalated case burdens in subsequent years [23]. Despite decades of advances in prevention and treatment, tuberculosis remains the second leading infectious cause of mortality worldwide, trailing COVID-19 [24]. Surveillance data from 2023 indicated a resurgence of tuberculosis in the United States (US), with 9615 reported new cases[25]. Additionally, TB remains the leading cause of death among people living with HIV, accounting for 167,000 deaths in 2022 alone [26]. Several risk factors predispose individuals to TB progression, including advanced age with immune senescence, genetic immunodeficiencies, HIV infection, organ transplantation, prolonged corticosteroid therapy, cytotoxic chemotherapy, TNF antagonist use, malnutrition, diabetes, smoking, and heavy alcohol consumption [27,28].

Another major challenge is MDR-TB, defined as resistance to at least isoniazid and rifampicin[29]. MDR-TB is particularly prevalent in high-burden regions such as India, China, Russia, and parts of Africa [30]. The most severe type of TB, extensively drug-resistant tuberculosis (XDR-TB), is characterised by additional resistance to fluoroquinolones and second-line injectable drugs such as capreomycin, amikacin, or kanamycin [30].A study on the prevalence and geographic distribution of certain genotypes found that the Beijing genotype accounted for 31.78% of drug-resistant pulmonary *M. tuberculosis* isolates, primarily affecting younger patients in China [31]. In Luoyang, an MDR-TB prevalence of 11.4% was reported, with males, urban inhabitants, and retreatment cases identified as categories at higher risk [32]. Meanwhile, Western Siberia exhibits some of the highest MDR-TB rates globally, with an increase from 19.2% to 26.4%, constituting 67.9% of MDR-TB cases [33]. Comparatively, the US reported a much lower MDR-TB prevalence of 1.4% in 2023 [34]. Table 1 further details the prevalence of MDR-TB in selected high-burden countries [21].

These epidemiological patterns are further reflected in demographic inequalities, where MDR-TB preferentially affects males [35]. Multiple studies consistently indicate that males have approximately 2 to 3 times higher prevalence drug-resistant TB compared to females, especially in productive age groups under 50 years [36]. A systematic review concluded that males have a higher prevalence of MDR-TB (over 20%) than females (approximately 13%), indicating a higher susceptibility to drug-resistant TB[37].At the global level, in 2023, an estimated 10.8 million people developed tuberculosis, with multidrug-resistant and rifampicin-resistant TB accounting for about 150,000 deaths worldwide [38]. The management of drug-resistant TB remains highly complex, costly, and is associated with poorer treatment outcomes, posing a significant barrier to its control and elimination efforts [39]. Furthermore, the simultaneous problems of HIV coinfection and drug-resistant tuberculosis, as well as health-care system disruptions induced by the COVID-19 pandemic, have reaffirmed its status as an urgent global health priority. This underscores the significance of continuous surveillance, increased access to suitable treatment, and enhanced public health initiatives.

Table 1: Recent MDR-TB epidemiology country-wise

Country	% Global MDR-TB Cases	MDR-TB in New Cases (%)	MDR-TB in Retreatment Cases (%)	References
India	27%	3.2%	16%	[40]
Russia	7.4%	24%	54%	[41]
China	7.3%	3.2%	16%	[42]
Philippines	7.2%	3%	20%	[41]
Indonesia	7.4%	3.2%	16%	[43]
Namibia	—	5–6%	15–20%	[21]
Pakistan	—	4.2%	18%	[44]

5. Molecular Characterization and Clinical Relevance of MDR-TB Resistance Mechanisms

Molecular characterisation of circulating MDR-TB strains has revealed significant global variability, highlighting the complex genetic landscape that underpins resistance [45,46]. Certain genotypes, particularly the Beijing strain prevalent in northern India and several other high-burden regions, have been closely linked with enhanced virulence and strong association with MDR [47,48]. Molecular analyses indicate that resistance is primarily driven by mutations in specific loci—most notably the *katG* gene, responsible for isoniazid resistance, and the *rpoB* gene, conferring rifampicin resistance [49]. Across distinct geographical populations, these resistance determinants tend to aggregate within predictable hotspot regions of the genome, pointing to a consistent global pattern of resistance evolution [50]. Multiple studies have demonstrated a recognizable sequence in the acquisition of resistance, wherein isoniazid, resistance typically emerges before rifampicin, suggesting a stepwise process in the genetic adaptation of MTB under selective drug pressure [51,52]. Genotyping data further reinforce the association between particular strain lineages and MDR-TB, with the Beijing genotype frequently identified as a dominant lineage in northern India and East Asia[53,54]. Among the most common resistance-conferring mutations, *katG* S315T is strongly linked to isoniazid resistance, while mutations at *rpoB* codons 516, 526, and 531 are typically associated with rifampicin resistance[55-57]. Despite this, a small but clinically significant set of MDR isolates lack these typical resistance mutations, as reported in a study from Uganda, limiting the detection rate of molecular diagnostic tools such as GeneXpert and line probe assays(LPAs)[58,59].

The implications of such molecular diversity extend beyond basic microbiology to patient outcomes. The accuracy of drug susceptibility testing (DST) plays a pivotal role in successful treatment and survival. Zürcher et al. [60] observed that patients with discordant DST results, meaning that molecular and phenotypic DST outcomes were inconsistent, had twice the risk of mortality as those with concordant test results.This finding underscores the critical importance of reliable, comprehensive genotypic characterization in guiding effective MDR-TB diagnosis, drug selection, and global control strategies.

6. Advances in Tuberculosis Diagnostics: Molecular, Biomarker, and AI Innovations

Recent years have seen substantial progress in TB diagnostics, greatly enhancing the speed and accuracy of disease detection and drug resistance identification. Highly sensitive molecular tests, such as the WHO-endorsed Xpert MTB/RIF assay, enable rapid detection of *M. tuberculosis* and simultaneous identification of rifampicin resistance directly from clinical samples, typically sputum, with sensitivity and specificity of 80-85% and 95–98%[61,62]. This technology has become a critical tool for early and accurate diagnosis, allowing early treatment initiation compared to the weeks required by traditional culture methods [63]. LPAs, based on polymerase chain reaction (PCR) technology, are now recommended for upfront detection of resistance against isoniazid and rifampicin by identifying specific genetic mutations in MTB directly from specimens[64]. Although culture remains the gold standard for tuberculosis diagnosis because of its high specificity and capacity for comprehensive drug susceptibility testing, molecular diagnostics have revolutionized TB detection by providing rapid, sensitive, and user-friendly alternatives suitable for resource-limited settings[65-67]. These assays complement traditional methods by enabling quick screening and early resistance detection, and WHO guidelines recommend their integration as frontline diagnostics to reduce delays and improve treatment outcomes[68]. Recent innovations include the second-generation Xpert Ultra with enhanced sensitivity for detecting paucibacillary and extrapulmonary TB, loop-mediated isothermal amplification (LAMP) assays for simple and rapid point-of-care testing, and next-generation sequencing for comprehensive resistance profiling[69-71]. Additionally, emerging technologies that detect TB antigens offer improved diagnostic accuracy in challenging cases such as extrapulmonary TB[72]. Although higher costs and equipment requirements limit widespread implementation, these advances collectively represent a major step forward in global TB control through earlier detection and effective management of both drug-sensitive and drug-resistant diseases.

Major advances in tuberculosis diagnostics encompass novel biomarkers, molecular tests, artificial intelligence (AI) platforms, and next-generation point-of-care tools that collectively enhance accuracy, speed, and accessibility. Host- and pathogen-derived biomarkers such as *IFN-γ*, *IP-10*, *ferritin*, and *Ag85B* are being developed to differentiate latent from active disease, predict progression risk, and monitor treatment response, while proteomic and transcriptomic studies have identified high-performing protein panels including *FCGR3B*, *FETUB*, *LRG1*, *ADA2*, *CD14*, and *SELL*[73-75]. Blood-based markers, such as specific microRNAs (*miR-143*, *miR-139*, *miR-454*) and circRNAs, are also under investigation to simplify testing and reduce invasiveness[76,77]. AI algorithms are automating chest X-ray interpretation to detect nodules, consolidations, and cavities with high accuracy, supporting objective screening and diagnosis[78-80]. Deep learning and machine learning models integrate genomic, biomarker, and clinical data to predict TB, drug resistance, and outcomes, often surpassing traditional methods in early detection and reducing misdiagnosis[81-83]. Clinical decision support systems integrate patient history, imaging, and molecular results to guide treatment, particularly in complex MDR and extrapulmonary cases, while AI-driven telemedicine platforms extend diagnostic abilities to resource-limited locations [84,85]. Emerging approaches such as recombinase-aided amplification (RAA) and thermal imaging protocols are being explored for lymph node and extrapulmonary TB to address gaps where conventional testing is limited[86]. The integration of rapid molecular methods with AI analysis streamlines turnaround time and boosts point-of-care performance, enabling timely treatment and strengthening case detection, thus accelerating progress toward global TB elimination goals.

7. Treatment Strategies and Advances in Tuberculosis Management

Standard treatment for drug-susceptible TB involves a six-month regimen, beginning with an intensive two-month phase of four primary drugs: isoniazid, rifampicin, ethambutol, and pyrazinamide, followed by a continuation phase of four months with isoniazid and rifampicin to eliminate residual bacilli and reduce relapse risk. Treatment duration significantly increases and effectiveness decreases for MDR and XDR TB, necessitating prolonged use of second-line agents, which are often associated with adverse side-effects and higher toxicity[29]. The WHOs End TB Strategy aims to reduce TB incidence by 90% and deaths by 95% by 2035[87]; however, ongoing challenges such as drug resistance, TB/HIV coinfection, and the impacts of the COVID-19 pandemic threaten these ambitious goals[88]. These factors underscore the continued urgency for enhanced diagnostics, optimized treatment regimens, and robust public health interventions to control TB globally.

Treatment strategies for TB in 2025 include standardized and novel shortened regimens, newly approved drugs for drug-resistant TB, and advanced therapeutic drug monitoring (TDM) protocols to optimize individual care. The traditional first-line therapy remains the six-month course of isoniazid, rifampicin, ethambutol, and pyrazinamide, while shortened four-month regimens of high-dose rifapentine and moxifloxacin are advised for suitable adults and children with non-severe, drug-sensitive tuberculosis [89,90]. For MDR or rifampicin-resistant TB, WHO recommends all-oral, six-month regimens such as BPaLM (bedaquiline, pretomanid, linezolid, moxifloxacin) and BDLLfxC (bedaquiline, delamanid, linezolid, levofloxacin, clofazimine) based on molecular susceptibility testing[91,92]. Recently approved drugs like bedaquiline, delamanid, and pretomanid form the backbone of all-oral regimens for MDR and XDR TB[93,94]. Linezolid remains essential but is associated with side effects; newer oxazolidinones (sutezolid, tedizolid) are currently in trials showing promising safety and efficacy[95,96]. Meropenem-clavulanate and novel carbapenems such as tebipenem and faropenem are being explored for XDR-TB cases[97,98]. The shift to all-oral regimens reduces risk and improves outcomes compared to previous protocols involving injectables [99,100].

Therapeutic drug monitoring tailors TB therapy by measuring drug levels in plasma, dried blood spots, urine, or hair to account for metabolic variability, organ dysfunction, drug interactions, and adherence[101]. Techniques such as LC-MS/MS, HPLC, and UPLC enable precise, real-time quantification of drugs including rifampicin, isoniazid, bedaquiline, and linezolid, especially for complex cases and vulnerable populations such as MDR/XDR TB patients, those with poor clinical response, HIV coinfection, or liver/kidney dysfunction, and when drugs with narrow therapeutic windows are used[101]. TB guidelines encourage TDM to minimize toxicity and adverse events while maximizing efficacy. This strategic integration of shorter regimens, new drugs, and TDM is reshaping TB treatment outcomes and supporting progress toward global elimination.

8. Comprehensive Strategies for Tuberculosis Prevention and Control

Prevention and control of TB in 2025 involves a combination of vaccination, immunoprophylaxis, comprehensive public health strategies, and integrated care models, especially targeting TB-HIV co-infection[26]. Core prevention focuses on early detection, prompt treatment, and interrupting transmission chains through infection control measures in community and healthcare settings[2]. Preventive treatment for latent TB infection remains vital for high-risk groups such as close contacts, people living with HIV, and immunocompromised individuals[102]. Infection control includes respiratory hygiene, environmental measures such as ventilation and UV light, and personal protective equipment in healthcare environments.

Integrated TB-HIV diagnosis, offer screeningand treatment for both conditions at a single site by coordinated teams thereby enhancing outcomes and reduce mortality. WHO guidelines recommend systematic, integrated screening in primary healthcare with operational manuals to support implementation. This integration enhances adherence, reduces loss to follow-up, and facilitates comprehensive care of co-infected patients[2].The Bacillus Calmette-Guérin (BCG) vaccine remains widely used but offers limited protection against adult pulmonary TB. Novel vaccines, such as M72/AS01E, are under development aiming to prevent infection, disease progression, and transmission[103]. Immunoprophylaxis includes post-exposure vaccination to prevent relapse and therapeutic vaccines that may improve treatment outcomes[104]. Expanding access and coverage of effective vaccines in high-burden regions remains critical to accelerating TB elimination.

Public health strategies emphasize the "Detect - Treat - Prevent - Build" framework, integrating rapid diagnostics and effective treatment through national programs like India’s National Tuberculosis Elimination Programme (NTEP), supported by digital monitoring and social support. Active case finding, contact tracing, community engagement, and private sector inclusion are vital to reduce missed cases and improved adherence[105,106]. Addressing social determinants such as nutrition, housing, and poverty through multisectoral collaboration strengthens TB control efforts. Together, these approaches form the foundation of modern TB prevention and control, enhancing care and reducing TB burden and transmission globally

9. Innovative Research and Emerging Therapies Transforming Tuberculosis Treatment

Research innovations in TB in 2025 are cantered on novel host-directed therapies (HDTs), advances in nanotechnology for drug delivery, telemedicine and digital health platforms, and emerging bacteriophage therapies[107-111]. HDTs modulate the host immune response rather than directly targeting *M. tuberculosis*, potentially enhancing treatment efficacy, reducing tissue damage, and limiting drug resistance[111]. Repurposed drugs like azithromycin exemplify HDTs by reducing harmful inflammation, promoting autophagy, and improving bacterial clearance, which may shorten treatment duration and improve outcomes, particularly in multidrug-resistant TB[112,113].

Nanoparticles (NPs) serve as targeted, controlled-release drug delivery systems that improve bioavailability, reduce dosages, and minimize toxicity of anti-TB drugs. Biocompatible polymers and carbon nanotubes enable sustained release and enhance cellular uptake, optimizing therapy effectiveness[107,114]. Nanotechnology also holds promise for vaccine delivery and diagnostics.Telemedicine facilitates remote diagnosis, treatment monitoring, and adherence support through video directly observed therapy (DOT) and SMS reminders, enhancing patient compliance and outcomes, particularly in resource-limited settings[115]. Digital health interventions offer scalable, cost-effective tools for real-time data capture, personalized patient engagement, and support, crucial for continuity of care and addressing underprivileged populations[116].

Bacteriophages, viruses that specifically infect bacteria, are being explored as novel treatments for drug-resistant TB. Early experimental work demonstrates that phage therapy can complement or substitute antibiotics in difficult-to-treat TB cases under ongoing clinical trials. Phages such as *D29* and *DS6A* have shown efficacy against drug-resistant strains in vitro and in infection models[1]. Intravenous administration of phage *DS6A* in humanized mice infected with aerosolized *M. tuberculosis*showed improved pulmonary function and reduced bacterial load[1]. Bacteriophages offer advantages including specificity to bacteria, replication at infection sites, and ability to overcome antibiotic resistance mechanisms[117,118]. Multiple mycobacteriophages, including *DS-6A*, *TM4*, *D29*, *T7*, *P4*, *PDRPv*, *BTCU-1*, *Bo4*, *SWU1*, *GR-21/T*, *My-327*, *Ms6*, and *Bxz2*, have been studied for their therapeutic potential against tuberculosis [119]. These phages target various *Mycobacterium* species, with mechanisms ranging from lysing bacterial cell walls via lysins (e.g., *D29*, *Ms6*, *BTCU-1*), interfering with transcription critical to bacterial survival (*T7*, *P4*), to inhibiting bacterial metabolism (*SWU1*) [120-127].Their actions result in significant reduction or complete elimination of *M. tuberculosis* and related infections in vitro and in animal models, highlighting their promise as alternatives or adjuncts to conventional TB therapy, especially against drug-resistant strains.Dedrick et al., reported the compassionate use of phages in 20 patients with drug-resistant mycobacterial infections and observed favourable outcomes without adverse effects[128]. Inhalable spray-dried phage powders are being developed to deliver phages directly to the lungs, providing a targeted, patient-friendly approach for pulmonary TB[128]. Clinical case series and on-going trials have demonstrated the safety and efficacy of phage therapy, often showing a synergistic effect with antibiotics that enhances bacterial eradication and may potentially resensitize bacteria[129]. Despite progress, challenges include standardizing clinical trials, understanding phage resistance, and optimizing phage cocktails to maximize efficacy and minimizing bacterial escape. Integration of bacteriophage therapy into TB treatment presents a promising strategy against MDR and XDR TB, warranting further controlled trials to confirm long-term safety and efficacy.

10. Tuberculosis Elimination: Progress, Challenges, and Policy Imperatives for Achieving Global Targets

TB elimination depends on coordinated global and national strategies; however, progress remains uneven due to entrench socioeconomic and health system barriers. The Global Plan to End TB (2023–2030) prioritizes accelerating progress through expanded case detection, investment in new diagnostics, drugs, and vaccines, and integration of TB care within broader health systems[130]. India’s NTEP aims to eliminate TB by 2025, five years ahead of global targets. Its four strategic pillars “Detect, Treat, Prevent, and Build” are realized through active case finding, real-time digital surveillance, private sector engagement, rapid molecular diagnostics, adherence support via SMS, and direct benefit transfers for nutritional supplementation[105]. These interventions have significantly reduced TB incidence, mortality, and the number of undiagnosed cases. However, the COVID-19 pandemic disrupted this progress both nationally and internationally, delaying elimination efforts. Globally, countries such as Oman, Qatar, and Saudi Arabia have reported substantial progress, with treatment success rates of 90%, 100%, and 87%, respectively[131]. These successes reflect robust health systems, universal access to rapid molecular diagnostics, and comprehensive management of drug-resistant TB. Central Asian countries—including Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, and Uzbekistan, benefit from the WHO-supported TB-Free Central Asia Initiative, which promotes rapid diagnostics, integration of TB care into primary health systems, and shorter all-oral regimens for drug-resistant TB[91].

Common drivers of success for TB management include strong political commitment, multisectoral collaboration, universal access to WHO-recommended molecular diagnostics, and introduction of shorter all-oral regimens for drug-resistant TB, robust surveillance systems, digital case reporting, and integration of TB services with primary healthcare. Despite these advances, major barriers threaten the achievement of the End TB 2030 targets. Critical challenges include funding gaps, health system inadequacies, persistent socioeconomic inequities, disruptions caused by the COVID-19 pandemic, the growing burden of drug-resistant TB, gaps in preventive measures and innovation, and barriers faced by vulnerable populations such as migrants, children, and the urban poor[132,133]. Achieving TB elimination requires policy innovation to strengthen multisectoral collaboration alongside increased investment in research and development of new drugs, vaccines, and diagnostics. Ultimately, progress toward elimination depends on equitable access, resilient health systems, and sustained political will at both national and global levels.

11. Conclusion

Tuberculosis continues to pose a formidable global health challenge despite significant advances in diagnostics, treatment regimens, and prevention strategies. The emergence of multidrug-resistant and extensively drug-resistant strains underscores the urgent need for innovative therapeutic approaches and expanded access to rapid molecular diagnostics. Recent progress in host-directed therapies, nanotechnology-based drug delivery, and bacteriophage therapy offers promising avenues to overcome current limitations, especially in managing resistant infections. Integrating these scientific advances with strengthened public health infrastructures, comprehensive surveillance, and multisectoral policy initiatives is critical to achieving the global End TB targets. Continued investment in research, equitable healthcare access, and addressing social determinants of health remain pivotal for sustainable TB control and eventual global elimination

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