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A Comprehensive Review of Tuberculosis: Epidemiology, Diagnosis, Treatment, Prevention, and Research

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ABSTRACT

Tuberculosis (TB), which is triggered by Mycobacterium tuberculosis, continues to be a prominent contributor to infectious disease-related deaths worldwide, even after many years of attempts to manage it. Exceeding 10 million instances and surpassing a million fatalities each year, tuberculosis predominantly impacts nations with low to middle income. This is fuelled by elements like poverty, dense living conditions, inadequate nutrition, and co-infection with HIV. The rise of multidrug-resistant and extensively drug-resistant tuberculosis has added complexity to control measures. This evaluation delves into the comprehensive range of tuberculosis—covering aspects such as transmission, pathogenesis, worldwide epidemiology, diagnostic methods, treatment protocols, drug resistance, preventive measures, and current research endeavours. Focus is directed towards innovative molecular diagnostics, the incorporation of artificial intelligence, therapies aimed at the host, and the relationship between tuberculosis and comorbid conditions such as HIV and diabetes. An approach that encompasses multiple sectors and is fuelled by innovation is essential for achieving worldwide tuberculosis elimination goals.

Keywords: Tuberculosis, MDR-TB, Diagnosis, Host-Directed Therapies, Epidemiology, BCG Vaccine, Drug Resistance

INTRODUCTION

Tuberculosis (TB), instigated by the bacterium Mycobacterium tuberculosis, continues to be one of the most persistent and catastrophic infectious ailments throughout human history. Even though it is avoidable and manageable, tuberculosis remains one of the leading causes of mortality globally, taking the lives of more than 1.3 million individuals each year and impacting approximately 10.6 million in 2022, as reported by the World Health Organisation (WHO,

2023). The ongoing worldwide challenge of tuberculosis, especially in nations with limited resources, showcases a multifaceted interaction of biological, societal, financial, and systemic factors, demanding a unified and collaborative strategy for its management and ultimate elimination.

The spread of tuberculosis occurs mainly through the air, rendering it extremely infectious in densely populated or inadequately ventilated environments. The inhalation of contaminated droplets resulting from coughing, sneezing, or verbal communication facilitates the entry of M. tuberculosis into the alveoli of the lungs, where it is subsequently engulfed by alveolar macrophages. The microorganism's capacity to obstruct the fusion of phagosomes and lysosomes enables its survival and proliferation within host cells, resulting in the development of granulomas—structured immune formations designed to confine the infection. Although a majority of infected persons transition into a latent TB infection (LTBI) phase, characterised by the presence of dormant bacteria that are neither active nor contagious, around 5–10% may advance to active TB disease. This progression is particularly prevalent among individuals with weakened immune systems, including those affected by HIV/AIDS, diabetes, malnutrition, or those receiving immunosuppressive treatments. The worldwide spread of tuberculosis is markedly imbalanced. The regions of South-East Asia and Africa carry the most substantial loads, with nations like India, China, Indonesia, and the Philippines playing a major role in the worldwide tally of cases (WHO, 2023). In these nations, disparities in socioeconomic status, insufficient healthcare systems, nutritional deficiencies, substandard living conditions, and restricted access to prompt diagnosis and treatment intensify the proliferation and consequences of tuberculosis. The co-occurrence of HIV and tuberculosis remains a significant concern for public health; in the year 2022, 8% of all tuberculosis instances worldwide were found in individuals living with HIV, with the African region representing an unequal portion (UNAIDS, 2020). The interplay between these co-epidemics amplifies their impact, as HIV markedly heightens the likelihood of TB reactivation and advancement, whereas TB continues to be the foremost cause of mortality among individuals living with HIV.

A significant challenge in the battle against tuberculosis is the rise of drug-resistant variants, especially multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB). MDR-TB, characterised by resistance to at least isoniazid and rifampicin, impacted more than 465,000 individuals worldwide in 2019. Meanwhile, XDR-TB presents an even more significant danger owing to its resistance against fluoroquinolones and second-line injectable medications (Falzon et al., 2017). These resilient variants pose greater challenges and costs for treatment, frequently necessitating extended therapies accompanied by significant adverse effects, consequently deteriorating patient prognoses and elevating mortality rates. Although the BPaLM treatment protocol (bedaquiline, pretomanid, linezolid, and moxifloxacin) has demonstrated potential in shortening the treatment period to 6 months, issues related to availability and expense continue to pose considerable challenges in numerous high-burden areas (Conradie et al., 2022). The COVID-19 outbreak has added layers of complexity to worldwide tuberculosis management initiatives. Healthcare systems faced immense strain, leading to interruptions in diagnostic and therapeutic services, while resources were reallocated, causing notable declines in tuberculosis detection and reporting. The Global TB Report 2021 recorded a decline in newly identified TB cases for the first time in more than ten years—a regression directly linked to the pandemic. This decline presents significant challenges for realising the WHO's End TB Strategy, which targets a 90% decrease in TB fatalities and an 80% reduction in TB cases by the year 2030 (WHO, 2021).

From a medical perspective, tuberculosis presents in various manifestations. The prevalent form, pulmonary tuberculosis, manifests through a continual cough (extending beyond two weeks), discomfort in the chest, coughing up blood, elevated temperature, nocturnal sweating, loss of weight, and exhaustion. Nonetheless, extrapulmonary tuberculosis—impacting organs like the lymphatic system, cerebral region, renal system, and skeletal structure—is gaining recognition, particularly among those with weakened immune systems. Tuberculous meningitis, for instance, represents one of the most critical extrapulmonary manifestations, frequently resulting in permanent neurological impairment or fatality if not addressed (Seddon et al., 2019). Childhood tuberculosis necessitates unique attention, as young patients frequently exhibit vague symptoms, resulting in postponed diagnoses and increased mortality rates within this demographic.

Initiatives aimed at enhancing tuberculosis diagnosis have progressed significantly over the last ten years. Conventional methods such as sputum smear microscopy are being supplanted by advanced molecular diagnostic approaches like GeneXpert MTB/RIF, which facilitates swift identification of tuberculosis and rifampicin resistance in just a matter of hours. Moreover, the incorporation of artificial intelligence (AI) in the analysis of chest radiographs, especially in environments with limited resources, has the capacity to enhance diagnostic precision and alleviate the workload on radiologists (Qin et al., 2021). Interferon-Gamma Release Assays (IGRAs) and tuberculin skin tests (TST) are commonly employed to identify latent tuberculosis infection (LTBI), particularly in healthcare professionals and individuals with HIV. However, these methods are unable to distinguish between latent and active tuberculosis disease. Regarding preventive measures, the Bacillus Calmette-Guérin (BCG) vaccine remains in use for infants in regions where tuberculosis is prevalent, providing defence against serious paediatric manifestations of the illness, including miliary tuberculosis and tuberculosis meningitis. Nonetheless, its restricted effectiveness in averting pulmonary tuberculosis in adults has sparked continuous investigation into advanced TB vaccines, like M72/AS01E, which exhibited a 50% success rate in a phase IIb trial (Schrager et al., 2020). Moreover, public health initiatives such as contact tracing, proactive case identification, and community involvement play a crucial role in managing the transmission of tuberculosis. Mobile health innovations, educational initiatives, and digital compliance tracking systems are demonstrating significant effectiveness in lowering treatment abandonment rates, especially in resource-limited regions (Masini et al., 2016). In addition to medical treatments, the societal factors influencing tuberculosis—such as economic hardship, cramped living conditions, inadequate nutrition, social stigma, and restricted healthcare access—need to be tackled to achieve sustainable advancements. Tuberculosis is not merely a health condition; it is also a manifestation of social disparity, significantly impacting underprivileged groups including migrants, incarcerated individuals, and those without stable housing (Davidson et al., 2024). Consequently, a successful tuberculosis control approach must encompass collaboration across various sectors, implementation of social protection initiatives, and enhancement of health systems to address systemic obstacles to care.

Epidemiology and Pathogenesis

2.1 Understanding TB Transmission

Tuberculosis (TB) predominantly affects the respiratory system, spreading via airborne droplets that harbour Mycobacterium tuberculosis (M.tb) bacilli. When a person with active pulmonary tuberculosis coughs, sneezes, laughs, or even converses, they emit infectious droplet nuclei into the atmosphere, which can linger for hours—particularly

in enclosed, inadequately ventilated spaces. Breathing in just a few bacilli could be enough to trigger an infection, especially in individuals with weakened immune systems or those who have been exposed for extended periods (Davidson et al., 2024).

High-transmission environments include:

- Overcrowded homes and urban slums
- Prisons and detention centers
- Homeless shelters
- Hospitals and healthcare facilities, especially with poor infection control (Masini et al., 2016; Kaur et al., 2024)

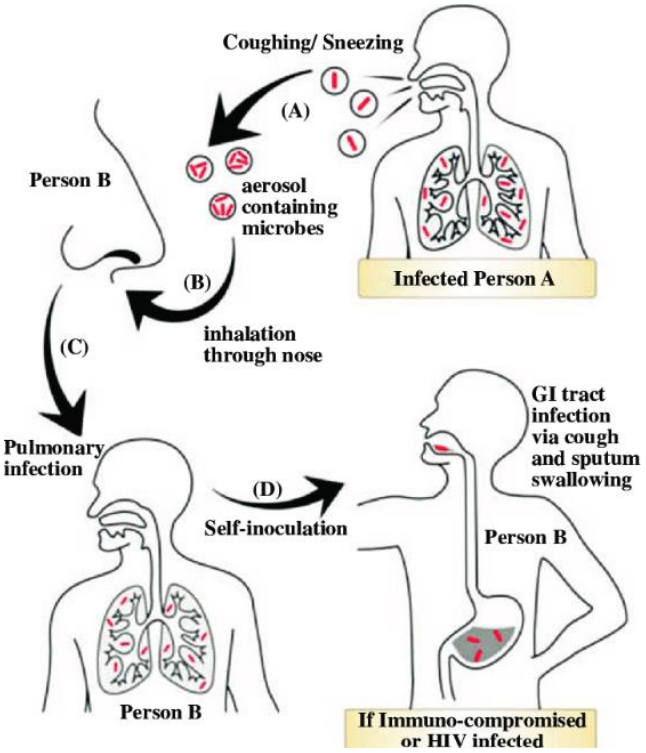

Fig. 1: Modes of Tuberculosis Transmission and Progression in the Human Body

Source: https://www.researchgate.net/profile/Asesh-Banerjee/publication/281781720/figure/fig3/AS:666768956848131@1536196092371/The-overall-picture-of-the-common-modes-of-infection-caused-by-Mycobacterium.png

The spread of disease is significantly shaped by various social factors affecting health, including economic hardship, malnutrition, high population density, and restricted availability of healthcare services. People with latent tuberculosis infection (LTBI) carry the bacteria in an inactive form, exhibiting no symptoms and posing no risk of spreading the disease. Nonetheless, around 5–10% of people with latent tuberculosis infection (LTBI) may advance to active disease during their lifetime, with this risk significantly heightened in situations of immune compromise (Esmail et al., 2018; Bruchfeld et al., 2015).

Groups that are particularly vulnerable to advancing from latent tuberculosis infection (LTBI) to active tuberculosis (TB) encompass: • Persons affected by HIV/AIDS (the co-occurrence heightens the risk by 18 to 20-fold) (Gelaw et al., 2019; Bruchfeld et al., 2015)

- Individuals diagnosed with diabetes mellitus (Alemu et al., 2021; Yorke et al., 2017)
- Under-nourished persons
- Individuals receiving immunosuppressive therapies like TNF-α blockers (Zhang & Yew, 2015; Nahid et al., 2016)

Factors such as gender, age, and profession significantly influence the dynamics of transmission. Men have a greater likelihood of developing tuberculosis compared to women, which can be attributed to elevated levels of smoking, alcohol consumption, and exposure in the workplace (Zumla et al., 2015). The demographic of individuals aged 15 to 44 years continues to be the most frequently impacted group, frequently as a result of heightened exposure within the community and restricted access to healthcare services (Furin, Cox, & Pai, 2019).

While pulmonary tuberculosis is the most contagious variant, extrapulmonary tuberculosis (EPTB) is gaining recognition, especially among those with weakened immune systems. Types of extrapulmonary tuberculosis (EPTB) encompass tuberculous meningitis, lymph node infection, skeletal tuberculosis (known as Pott's disease), pleural fluid accumulation, and genitourinary tuberculosis. These conditions present greater diagnostic challenges

owing to their vague or specific symptoms related to particular organs (McShane, 2015; Seddon et al., 2019).

2.2 TB Pathogenesis

The development of tuberculosis involves a complex interplay between the bacterium M. tuberculosis and the immune defences of the host. The adventure commences as aerosolised bacilli are breathed in and arrive at the alveoli within the lungs. In that location, they are engulfed by local alveolar macrophages, serving as the initial line of immune defence. In contrast to numerous other bacterial species, M. tuberculosis has developed intricate strategies to avoid annihilation within macrophages. It obstructs the fusion of phagosomes and lysosomes, hinders the acidification process within the phagosome, and alters the signalling pathways of host cells to establish a favourable intracellular environment that allows for undetected replication (Flynn & Chan, 2001; Gygli et al., 2017).

The immune system of the host identifies the infection and triggers a T-helper 1 (Th1)-driven response, marked by the generation of interferon-gamma (IFN-γ), which stimulates macrophages to eliminate intracellular bacteria. This results in the development of granulomas—a defining characteristic of tuberculosis. Granulomas are structured formations made up of infected macrophages, Langhans giant cells, epithelioid cells, and lymphocytes, encased within a fibrous capsule. Their objective is to "isolate" the infection and hinder its spread (Schrager et al., 2020; Esmail et al., 2018). In the majority of immunocompetent persons, this leads to a latent tuberculosis infection, during which the bacilli stay inactive yet alive, occasionally for many years.

As host immunity diminishes—whether from HIV co-infection, nutritional deficiencies, malignancies, or medically induced immunosuppression—the integrity of the granuloma may decline, resulting in the reactivation of tuberculosis. The caseous core of granulomas undergoes liquefaction, resulting in the creation of necrotic spaces within lung tissue. These spaces create an oxygen-abundant setting perfect for bacterial proliferation and allow bacteria to infiltrate the airways, greatly enhancing their ability to spread (McShane, 2015; Nahid et al., 2016). Pulmonary tuberculosis, particularly in its cavitary variant, poses a significant challenge both clinically and epidemiologically.

Extrapulmonary manifestations occur when bacilli leave the pulmonary setting through lymphatic or haematogenous dissemination. Miliary tuberculosis, for example, is marked by the existence of tiny, millet-seed-shaped lesions dispersed across the lungs and various other organs. It frequently manifests in individuals with weakened immune systems and is linked to elevated mortality rates (Seddon et al., 2019). Tuberculous meningitis, a serious form of the disease, entails the infection of the protective membranes surrounding the brain and is particularly prevalent among young children and those living with HIV. In the absence of prompt identification and intervention, it can result in permanent neurological harm or fatality (McShane, 2015; Gopalaswamy et al., 2020).

Additionally, contemporary research has redirected attention to host-directed therapies (HDTs), which aim to adjust the immune response instead of directly eliminating the bacteria. The reasoning behind this is that managing inflammatory harm and re-establishing immune equilibrium can avert tissue degradation and improve the elimination of bacteria. Instances encompass the reapplication of medications such as metformin, statins, and immune checkpoint blockers for the treatment of tuberculosis (Tiberi et al., 2022; Schrager et al., 2020).

2.3 Global TB Trends

In spite of over a hundred years of progress in medicine, tuberculosis remains a prominent contributor to infectious disease fatalities across the globe. According to the WHO Global TB Report (2023), approximately 10.6 million individuals were

diagnosed with TB in 2022, resulting in 1.5 million fatalities, among which were 167,000 individuals living with HIV. Tuberculosis has now overtaken HIV/AIDS as the primary cause of mortality attributed to a single infectious agent (WHO, 2023). These disheartening figures highlight not just the enduring nature of TB but also the worldwide inadequacy in executing fair healthcare and public health measures.

The geographical distribution of tuberculosis is markedly uneven. Almost 70% of all tuberculosis cases are found in the South-East Asian and African regions. Nations such as India, China, Indonesia, Pakistan, Nigeria, and the Philippines persist in documenting the most elevated incidence rates, influenced by high population densities, restricted healthcare access, nutritional deficiencies, and inadequately financed tuberculosis control initiatives (WHO, 2023; Floyd et al., 2018). Disparities between rural and urban areas continue to exist, with urban slums and rural backlands acting as breeding grounds for tuberculosis, attributed to factors such as overcrowding, inadequate ventilation, and insufficient monitoring systems (Chatterjee & Pramanik, 2015).

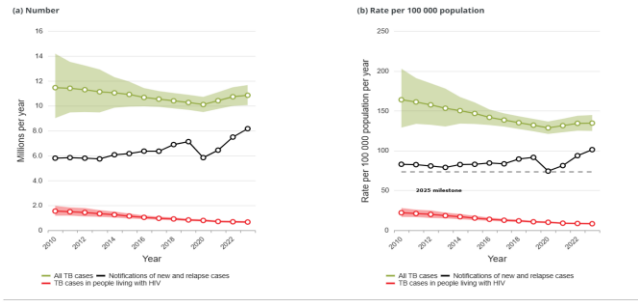

Fig. 2 Global trends in the estimated number of incident TB cases (a) and the incidence rate (b), 2010–2023

Source: https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/tb-reports/global-tuberculosis-report-2024/tb-disease-burden/1-1-tb-incidence

The COVID-19 outbreak has exacerbated tuberculosis management results on a worldwide scale. The interruption of standard health services, a decline in tuberculosis notifications, postponed diagnoses, and breaks in treatment compliance have undone almost ten years of advancements (Chakaya et al., 2020; WHO, 2023). In numerous nations, the outbreak redirected both personnel and monetary assets from tuberculosis initiatives, leading to heightened transmission rates and fatalities.

Equally concerning is the escalating dilemma of drug-resistant tuberculosis (DR-TB). In 2019, over 450,000 individuals were impacted by multidrug-resistant tuberculosis (MDR-TB), characterised by its resistance to isoniazid and rifampicin. Extensively drug-resistant tuberculosis (XDR-TB), characterised by resistance to fluoroquinolones and second-line injectable medications, presents an even greater challenge for treatment and has now been documented in more than 120 nations (Falzon et al., 2017; Tiberi et al., 2022). Even though recent medications such as bedaquiline and pretomanid have enhanced treatment results, worldwide cure rates for MDR/XDR-TB remain under 60% (Conradie et al., 2022).

In the meantime, initiatives aimed at managing tuberculosis have broadened to encompass more than just therapeutic measures. The advancement of vaccine development is accelerating, with hopeful contenders like M72/AS01E demonstrating a 50% effectiveness in thwarting active TB in adults who are latently infected (McShane, 2015). Digital health innovations, including AI-driven X-ray analysis, telemedicine for remote diagnostics, and smartphone-based adherence monitoring, are being incorporated into national tuberculosis initiatives, especially in areas with limited resources (Boehme et al., 2010; WHO, 2021).

Newly arising issues also encompass post-TB lung disease (PTLD)—a condition that impacts survivors, leading to enduring respiratory challenges. PTLD

encompasses bronchiectasis, fibrosis, airflow limitation, and persistent respiratory manifestations, which further intensify the healthcare challenges in nations where tuberculosis is prevalent (Yadav & Rawal, 2024).

Table 1: Overview of Epidemiology and Pathogenesis of Tuberculosis

Aspect	Details	Implications
Mode of Transmission	Airborne droplets from cough, sneeze, or speech of individuals with active pulmonary TB	High potential for rapid spread, especially in crowded, poorly ventilated settings
Infectious Dose	As few as 1–10 bacilli can cause infection	Extremely contagious; control requires early diagnosis and respiratory precautions
High-Risk Environments	Urban slums, prisons, refugee camps, healthcare settings	Prioritization of ventilation, screening, and surveillance in these areas
Latent TB Infection (LTBI)	Dormant bacilli within granulomas; 25% of global population affected	Serves as a reservoir; reactivation risk increases with immune compromise
Reactivation Risk Factors	HIV, diabetes, malnutrition, corticosteroid therapy	Tailored screening and preventive therapy essential in these populations
Demographic Vulnerabilities	Men, young adults (15–44), people in low- and middle-income countries	Gender-sensitive and age-targeted TB programs required
Granuloma Formation	Immune response involving macrophages, T-cells, and fibroblasts encapsulating bacilli	Central to latent TB control; breakdown leads to reactivation
Pulmonary vs. Extrapulmonary TB	Pulmonary TB is more contagious; EPTB affects CNS, lymph nodes, bones, and other organs	EPTB harder to diagnose, especially in immunocompromised individuals
Miliary TB and TB Meningitis	Disseminated TB forms due to hematogenous spread	Require prompt diagnosis and aggressive treatment; high mortality risk
Immune Evasion by M. tuberculosis	Inhibits phagosome-lysosome fusion in macrophages	Promotes intracellular survival and persistence
Global Burden (2022)	10.6 million new cases; 1.3 million deaths (HIV-negative); 167,000 deaths (HIV-positive)	TB remains a top infectious killer; health systems must refocus post-COVID
Regions Most Affected	South-East Asia, Africa, Western Pacific	Need for international cooperation, funding, and equitable healthcare access
Impact of COVID-19 on TB	Reduced notifications, delayed diagnoses, disrupted treatment	Urgent need for resilient, integrated infectious disease programs
Drug Resistance (MDR/XDR-TB)	MDR: resistant to isoniazid & rifampicin; XDR: includes fluoroquinolones and second-line injectables	Threatens global TB control; necessitates new regimens and better diagnostics

Aspect	Details	Implications
Post-TB Lung Disease (PTLD)	Chronic respiratory conditions post-cure, e.g., fibrosis, bronchiectasis	Long-term care and rehabilitation programs needed for TB survivors
Emerging Research Areas	Host-directed therapies, digital diagnostics, vaccine candidates (e.g., M72/AS01E)	Potential game-changers in TB prevention and personalized treatment

Diagnosis and Screening

The identification of tuberculosis (TB) is fundamental to successful management approaches, but it continues to be laden with practical difficulties, particularly in environments with limited resources. Timely and precise identification is essential not just for the care of individual patients but also for interrupting the transmission cycle within the community (World Health Organisation, 2023; Floyd et al., 2018). The traditional method has depended on sputum smear microscopy, a technique that was established over a hundred years ago. While being cost-effective and fairly straightforward to execute, it is hindered by limited sensitivity—especially in individuals co-infected with HIV, young children, and those with extrapulmonary tuberculosis (Pai et al., 2017; Chatterjee & Pramanik, 2015). Furthermore, smear microscopy is unable to differentiate between Mycobacterium tuberculosis and non-tuberculous mycobacteria (Sharma & Upadhyay, 2020).

In order to overcome these constraints, cultural techniques like Löwenstein-Jensen (solid medium) and MGIT (liquid medium) are regarded as more sensitive, albeit requiring a considerable amount of time, often taking several weeks to yield results (Boehme et al., 2010; Gygli et al., 2017). These techniques continue to be the benchmark for validating diagnoses and assessing drug resistance. Nonetheless, in areas with significant burdens where time is of the essence and laboratory facilities are insufficient, the lag can result in fatal outcomes (Masini et al., 2016; Tiberi et al., 2022).

The emergence of molecular diagnostics has been revolutionary. The GeneXpert MTB/RIF test, supported by the WHO, transformed tuberculosis diagnosis by providing outcomes in less than two hours while concurrently identifying rifampicin resistance (Boehme et al., 2010; World Health Organisation, 2021). This real-time PCR assay proves to be particularly beneficial in identifying smear-negative and extrapulmonary instances, which frequently elude traditional detection methods. The latest Ultra iteration enhances sensitivity to an even greater extent, detecting TB in paediatric patients and those infected with HIV who present with paucibacillary disease (Fox et al., 2013; Bruchfeld et al., 2015).

Additional molecular techniques like Line Probe Assays (LPAs) are being utilised more frequently to identify drug resistance. LPAs examine alterations in genes such as rpoB, katG, and inhA to identify resistance to both first- and second-line medications (Zhang & Yew, 2015; Falzon et al., 2017). Their function is crucial in steering tailored therapeutic strategies for multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB), particularly in nations experiencing an increase in resistance (Tiberi et al., 2022; Arslan et al., 2025).

Recent advancements encompass TrueNat and LAMP assays, which are compact and powered by batteries—ideal for conducting tests in remote regions. The outcomes of these assessments indicate encouraging findings regarding sensitivity, response duration, and user-friendliness (Al-Karawi et al., 2023; Floyd et al., 2018).

3.1 Screening High-Risk Groups

Screening methodologies are crucial for detecting both latent tuberculosis infection (LTBI) and active tuberculosis in individuals who are at heightened risk. Latent tuberculosis infection (LTBI) impacts almost

one-fourth of the world's population and acts as a significant reservoir for potential future cases, especially if not properly managed within at-risk groups (Esmail et al., 2018; Schrager et al., 2020). Targeted screening should focus on specific groups such as individuals affected by HIV/AIDS, those diagnosed with diabetes mellitus, healthcare professionals, close associates of tuberculosis patients, incarcerated individuals, migrants, and those suffering from malnutrition (Gelaw et al., 2019; Alebel et al., 2019; WHO, 2023).

Individuals living with HIV are particularly vulnerable, as tuberculosis is responsible for nearly one-third of deaths associated with AIDS globally (UNAIDS, 2020; Gelaw et al., 2019). Combined TB-HIV services that offer simultaneous screening and treatment have demonstrated efficacy in enhancing detection rates and patient results (WHO, 2013; Zeru, 2021). The World Health Organisation advises that for these groups, it is essential to implement symptom screening alongside either the Tuberculin Skin Test (TST) or Interferon-Gamma Release Assays (IGRAs), including options like QuantiFERON-TB Gold and T-SPOT.TB (Bruchfeld et al., 2015; Nahid et al., 2016). Although TST continues to be extensively utilised because of its affordability, it exhibits restricted specificity in populations vaccinated with BCG (Yorke et al., 2017). IGRAs provide enhanced specificity; however, they are more expensive and necessitate laboratory facilities (Schrager et al., 2020).

A further group at elevated risk comprises individuals with diabetes, who face a threefold increase in the likelihood of developing active tuberculosis. Elevated blood sugar levels hinder both the innate and adaptive immune responses, fostering conditions that promote the reactivation of tuberculosis (Alemu et al., 2021; Yorke et al., 2017). In nations such as India and China—where the prevalence of diabetes and tuberculosis is significantly elevated—there is a growing endorsement for integrated screening initiatives.

Correctional facilities serve as a significant focal point for epidemiological concerns. Prisoners frequently reside in cramped and inadequately ventilated environments, promoting the transmission of tuberculosis. In certain environments, the occurrence of tuberculosis within correctional facilities exceeds that of the broader community by more than 30-fold (Lönnroth et al., 2015; Masini et al., 2016). Consistent evaluation through symptom checklists, chest radiographs, and GeneXpert in correctional environments has proven effective in the prompt identification and management of cases (Chakaya et al., 2020; Enos et al., 2018).

3.2 New Diagnostic Tools and AI Integration

In the past few years, artificial intelligence (AI) and digital technologies have surfaced as formidable partners in the battle against tuberculosis (TB). A highly promising application is the utilisation of AI-driven computer-aided detection (CAD) software for the interpretation of chest radiographs. In regions facing a deficit of radiologists, artificial intelligence systems are capable of examining chest X-ray images to identify irregularities indicative of tuberculosis with impressive precision (Qin et al., 2021; Tiberi et al., 2022). These instruments have demonstrated sensitivities surpassing 90% and can be utilised through cloud-based systems or even mobile gadgets.

Computer-aided design instruments are currently incorporated into digital tuberculosis initiatives in nations such as South Africa, India, and Kenya—where immediate screening in remote regions has significantly enhanced the rates of case identification. They prove to be especially beneficial in large-scale screening initiatives, where a multitude of X-rays needs to be assessed rapidly. In addition, the integration of AI evaluation with symptom assessment and molecular testing facilitates a layered diagnostic strategy, enhancing both sensitivity and specificity.

Further advancements encompass digital adherence technologies (DATs), including mobile applications

and electronic pill dispensers, which guarantee that patients fulfil the entire regimen of tuberculosis treatment. Lack of adherence significantly contributes to the failure of treatment and the development of drug resistance. Technological solutions such as 99DOTS and evriMED have demonstrated a notable enhancement in treatment compliance across India, Kenya, and Bangladesh (WHO, 2021; Masini et al., 2016).

Table 2: Summary of TB Diagnosis and Screening Approaches and Innovations

Topic	Description	Diagnostic/Screening Tools	Advantages/Challenges	Key References
Traditional Diagnosis	Initial TB diagnosis based on sputum smear microscopy, widely used for decades	Ziehl-Neelsen stain microscopy	Inexpensive and quick; low sensitivity; ineffective in HIV-positive and pediatric cases	Pai et al., 2017; Chatterjee & Pramanik, 2015; Sharma & Upadhyay, 2020
Culture Methods	Used to confirm TB diagnosis and assess drug resistance	Löwenstein-Jensen medium, MGIT culture systems	High sensitivity and specificity; long turnaround time (2–6 weeks)	Boehme et al., 2010; Gygli et al., 2017; Tiberi et al., 2022
Molecular Testing	Modern approach offering rapid and sensitive results, including drug resistance	GeneXpert MTB/RIF, GeneXpert Ultra, Line Probe Assays (LPAs)	Detects rifampicin resistance in <2 hours; improved case detection in smear-negative TB	Boehme et al., 2010; Nahid et al., 2016; Zhang & Yew, 2015; Falzon et al., 2017
Emerging Portable Devices	Next-gen diagnostics designed for decentralized or low-resource settings	TrueNat, LAMP	Battery-operated, field-friendly; good sensitivity; useful in rural areas	Floyd et al., 2018; Al-Karawi et al., 2023
Latent TB Screening	Detection of TB infection in high-risk but asymptomatic individuals	Tuberculin Skin Test (TST), Interferon-Gamma Release Assays (IGRA)	TST cheap but nonspecific in BCG-vaccinated; IGRAs are more specific but expensive	Bruchfeld et al., 2015; Nahid et al., 2016; Schrager et al., 2020; Yorke et al., 2017
High-Risk Group Identification	Targeted testing improves detection and reduces risk of community spread	Contact tracing, symptom screening, chest X-rays, GeneXpert	Essential for HIV patients, diabetics, prisoners, malnourished, healthcare workers	Gelaw et al., 2019; Alebel et al., 2019; WHO, 2023; Lönnroth et al., 2015; Enos et al., 2018

Topic	Description	Diagnostic/Screening Tools	Advantages/Challenges	Key References
TB-HIV Co-infection Screening	Co-management programs detect and treat both infections effectively	Combined TB and HIV screening protocols	Integrated care improves outcomes; essential in high-burden countries	UNAIDS, 2020; WHO, 2013; Zeru, 2021; Bruchfeld et al., 2015
TB in Diabetic Patients	Immunosuppression from hyperglycemia increases TB susceptibility	Dual screening protocols for TB and diabetes	Emerging public health concern in LMICs with high diabetes prevalence	Alemu et al., 2021; Falzon et al., 2017; Yorke et al., 2017; World Health Organization, 2021
TB in Prisons and Closed Spaces	High transmission due to overcrowding and poor ventilation	Routine symptom checklists, CXR, GeneXpert	Very high TB burden; targeted screening programs are effective	Lönnroth et al., 2015; Masini et al., 2016; Chakaya et al., 2020; Enos et al., 2018
AI-Based Diagnostics	CAD software analyzes CXR images to detect TB-related abnormalities	AI-CAD platforms trained on large datasets	Effective in mass screening and rural outreach; minimizes human error	Qin et al., 2021; Tiberi et al., 2022; Masini et al., 2016; Ngari et al., 2023
Digital Adherence Technologies	Tools to track medication use and reduce treatment interruption	99DOTS, evriMED, smartphone-based alerts	Increases treatment success; mitigates MDR/XDR-TB risk	WHO, 2021; Masini et al., 2016; Tiberi et al., 2022
Diagnostic Gaps and Equity	Technology adoption must consider infrastructure limitations	Deployment plans for underserved populations	Requires funding, training, and maintenance	Schrager et al., 2020; Furin et al., 2019; Floyd et al., 2018; Davidson et al., 2024

The identification and assessment of tuberculosis have advanced significantly in the last twenty years. Although traditional methods such as sputum microscopy continue to be relevant, the path ahead is paved with molecular diagnostics, AI-enhanced radiography, and digital adherence innovations. Identifying high-risk groups and uncovering latent TB is crucial for reducing transmission and reaching

tuberculosis eradication objectives. Nonetheless, technology by itself is insufficient to address the issue. Fair access, advancement of infrastructure, and integration across various sectors must work in tandem with innovative diagnostics to guarantee that everyone is included in the battle against TB.

Treatment and Management

4.1 Current Treatment Guidelines

The management of tuberculosis has experienced a hundred years of transformation, but the fundamental tenet persists: extended combination therapy is crucial to avert resistance and recurrence. The World Health Organisation (WHO) presently advises a six-month treatment plan for drug-susceptible tuberculosis, which is segmented into an intensive phase followed by a continuation phase (WHO, 2023). The rigorous phase encompasses a duration of two months during which isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E) are administered—commonly referred to as HRZE. This is succeeded by a four-month extension phase utilising isoniazid and rifampicin (HR). This protocol has demonstrated efficacy in the majority of patients and is grounded in years of clinical studies and empirical data (Nahid et al., 2016; WHO, 2021).

The effectiveness of the conventional treatment protocol, nonetheless, relies on rigorous compliance, sufficient nutritional assistance, and prompt identification. Irregular or insufficient therapy frequently results in unsuccessful treatment, recurrence, or the emergence of drug-resistant tuberculosis (DR-TB) (Floyd et al., 2018; Davidson et al., 2024). The directly monitored treatment, abbreviated as DOTS, approach—where individuals receive oversight while taking their medications—has been crucial in enhancing compliance, particularly in resource-limited environments (Masini et al., 2016; WHO, 2021). In the case of extrapulmonary tuberculosis (EPTB), the therapeutic approach is akin to that of pulmonary TB but can be prolonged to a duration of 9 to 12 months, especially in instances of severe manifestations like tuberculous meningitis or osteomyelitis. This is due to the slower rate of bacterial eradication and the intricacies involved in tissue damage. In cases involving children, medication dosages are determined by weight and frequently modified to enhance tolerability and avert toxicity (Kaur et al., 2024).

- The conventional HRZE regimen lasting 6 months continues to serve as the worldwide standard for managing drug-susceptible tuberculosis (WHO, 2023).
- Extrapulmonary tuberculosis frequently necessitates extended treatment periods—lasting as long as 12 months in critical instances (Seddon et al., 2019).
- The oversight of DOTS enhances compliance and mitigates the risk of resistance (Masini et al., 2016).

4.2 New Treatment Regimens and Innovations

The therapeutic environment has undergone a significant transformation with the emergence of abbreviated, more potent treatment protocols for multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant TB (XDR-TB). A highly promising novel treatment regimen is BPaLM, which includes bedaquiline, pretomanid, linezolid, and moxifloxacin. Research endeavours, including the Nix-TB and ZeNix investigations, have demonstrated that this half-year entirely oral treatment protocol can reach success rates exceeding 85%, in contrast to merely 50–60% for traditional regimens that extended over 18–24 months (Conradie et al., 2022; Tiberi et al., 2022).

These advancements not only shorten the length of treatment but also eliminate the need for injectable medications, which were once infamous for their adverse effects, such as kidney damage and permanent hearing impairment (Lange et al., 2018; Zumla et al., 2015). The emergence of bedaquiline—a diarylquinoline that specifically targets the

mycobacterial ATP synthase—and pretomanid, which interferes with cell wall synthesis and respiration, signifies a transformative change in tuberculosis pharmacology (Zhang & Yew, 2015; Gygli et al., 2017).

In the interim, linezolid, a member of the oxazolidinone class, plays a vital role due to its bactericidal properties; however, it necessitates careful administration owing to potential risks of bone marrow suppression and neuropathy. These concerns have led to investigations focused on optimising dosing strategies (Conradie et al., 2022; Falzon et al., 2017).

Alongside BPaLM, abbreviated treatment courses for drug-susceptible tuberculosis, like the 4-month combination of HRZE and moxifloxacin, have demonstrated potential, especially among adolescents and adults exhibiting mild pulmonary disease (Nahid et al., 2016; WHO, 2021).

- BPaLM reduces the duration of MDR-TB therapy from 24 months to just 6 months, demonstrating significant effectiveness (Conradie et al., 2022).
- Completely oral treatment plans enhance comfort and compliance, eliminating the need for injections (Lange et al., 2018).
- The toxicity associated with Linezolid raises significant concerns—dosing requires meticulous management (Falzon et al., 2017).

4.3 Managing Drug-Resistant Tuberculosis (DR-TB)

Drug-resistant tuberculosis continues to pose the greatest challenge in the worldwide effort to manage and control TB. MDR-TB, characterised by resistance to at least isoniazid and rifampicin, along with XDR-TB, which includes resistance to fluoroquinolones and second-line injectable medications, are being reported more frequently across the globe (Falzon et al., 2017; Tiberi et al., 2022). As per the estimates from the World Health Organisation, more than 465,000 fresh instances of multidrug-resistant tuberculosis (MDR-TB) were documented worldwide in 2019, while extensively drug-resistant tuberculosis (XDR-TB) was recognised in over 120 nations (WHO, 2023; Floyd et al., 2018).

Effectively addressing DR-TB requires a tailored, data-driven strategy. Testing for drug susceptibility (DST) through molecular techniques such as Line Probe Assays (LPA) and whole-genome sequencing (WGS) is crucial for informing treatment regimen choices (Gygli et al., 2017; Pai et al., 2017). These instruments assist in circumventing empirical therapy, which poses a danger of exacerbating resistance.

Second-line treatments, such as fluoroquinolones (for instance, levofloxacin and moxifloxacin) and injectable options (like amikacin and capreomycin), have historically been utilised but are now being gradually replaced by regimens that include bedaquiline, owing to their enhanced effectiveness and safety profiles (Zumla et al., 2015; Al-Karawi et al., 2023).

It is crucial to observe for negative reactions, such as cardiac irregularities (associated with bedaquiline), peripheral nerve damage (linked to linezolid), and liver harm. Educating patients and providing psychosocial assistance are essential, as noncompliance continues to be a significant obstacle, frequently intensified by the length of treatment, the number of medications, and adverse effects (Masini et al., 2016; Enos et al., 2018).

Innovative digital adherence technologies (DATs) like 99DOTS and evriMED smart pillboxes are being utilised to guarantee that patients fulfil their treatment regimens, particularly in nations with significant health challenges (WHO, 2021; Qin et al., 2021). These instruments leverage mobile technology to dispatch notifications and monitor adherence, assisting healthcare providers in taking prompt action when doses are overlooked.

- MDR/XDR-TB necessitates individualised, DST-informed treatment (Gygli et al., 2017).

- Regimens centred around Bedaquiline are taking the place of injectable treatments (Tiberi et al., 2022).
- Intelligent compliance instruments enhance results in settings with limited resources (WHO, 2021).

4.4 Addressing TB-HIV and TB-Diabetes Comorbidities

The management of tuberculosis escalates significantly in complexity when there are concurrent infections or additional health conditions present. The co-occurrence of HIV and TB, for instance, not only hastens the advancement of TB but also alters the metabolism of medications and heightens the vulnerability to adverse effects (Bruchfeld et al., 2015; Gelaw et al., 2019). In these situations, antiretroviral treatment (ART) ought to commence within the initial two weeks of tuberculosis therapy, especially for individuals with CD4 counts below 50 cells/mm³ (WHO, 2013; Davidson et al., 2024).

Nonetheless, interactions between medications, especially involving rifampicin and specific antiretroviral therapies, require meticulous management to prevent toxicity or the risk of therapeutic failure (Yorke et al., 2017; Chakaya et al., 2020). Integrated care frameworks and combined TB-HIV services are crucial for enhancing compliance and lowering death rates (UNAIDS, 2020; Zeru, 2021).

In a similar vein, diabetes mellitus, currently acknowledged as a significant risk factor for tuberculosis, compromises both innate and adaptive immune responses, leading to poorer outcomes in tuberculosis treatment (Alemu et al., 2021; Falzon et al., 2017). Managing blood glucose levels is essential, and metformin, in addition to its role in glycaemic management, is currently under investigation for its effects on host-directed immunomodulation in tuberculosis (Schrager et al., 2020; Tiberi et al., 2022).

- Initiate antiretroviral therapy promptly in cases of HIV-TB co-infection—ideally within a fortnight for individuals with low CD4 counts (WHO, 2013).
- Oversee the interactions between rifampicin and antiretroviral therapy to guarantee a secure and efficient treatment process (Yorke et al., 2017).
- The presence of diabetes exacerbates the results of tuberculosis—maintaining glycaemic control is essential (Alemu et al., 2021).

4.5 Host-Directed Therapies (HDTs) and Future Horizons

Conventional tuberculosis treatment focusses on the bacillus, whereas host-directed therapies (HDTs) seek to adjust the immune response, minimise tissue injury, and enhance the elimination of bacteria (Schrager et al., 2020). HDTs hold significant potential for addressing drug-resistant or treatment-resistant tuberculosis, incorporating repurposed medications like metformin, statins, immune checkpoint inhibitors, and vitamin D derivatives (Tiberi et al., 2022; McShane, 2015).

While still in the preliminary phases, HDTs present the possibility of minimising treatment length, alleviating post-TB lung complications (PTLD), and lowering the chances of relapse. Current experiments are in progress, with certain HDTs exhibiting complementary effects when paired with conventional TB treatment protocols (Schrager et al., 2020).

- HDTs influence immune mechanisms rather than directly attacking M. tuberculosis (Tiberi et al., 2022).
- Reimagined medications such as metformin and statins exhibit potential (Schrager et al., 2020).
- Upcoming treatment protocols might integrate antimicrobials alongside agents that modulate host responses.

Table 3: Overview of TB Treatment and Management Strategies

Strategy	Description	Duration / Regimen	Key Drugs	Supporting References
Standard HRZE Therapy	6-month regimen for drug-susceptible TB, divided into 2-month intensive and 4-month continuation phases.	6 months	Isoniazid, Rifampicin, Pyrazinamide, Ethambutol	WHO (2023); Nahid et al. (2016); McShane (2015)
DOTS Strategy	Directly Observed Treatment, short-course—enhances adherence, prevents resistance.	Full duration	Same as above	Masini et al. (2016); WHO (2021)
Extrapulmonary TB Management	Longer regimens used for TB meningitis, bone TB, etc.	9–12 months	HRZE + extension	Seddon et al. (2019); WHO (2021)
BPaLM Regimen for MDR-TB	All-oral 6-month regimen with high cure rates (>85%); avoids injectables.	6 months	Bedaquiline, Pretomanid, Linezolid, Moxifloxacin	Conradie et al. (2022); Tiberi et al. (2022)
Drug-Resistant TB Management	Requires DST-guided therapy; second-line drugs used carefully with toxicity monitoring.	6–20 months	Levofloxacin, Linezolid, Bedaquiline	Gygli et al. (2017); Falzon et al. (2017); Al-Karawi et al. (2023)
Digital Adherence Tools	Mobile reminders and smart pillboxes (e.g., 99DOTS, evriMED) to ensure completion of therapy.	Ongoing during treatment	N/A	WHO (2021); Qin et al. (2021); Masini et al. (2016)
Comorbidity Management (HIV/TB)	ART must begin within 2 weeks of TB therapy in patients with CD4 < 50. Drug-drug interaction monitoring is crucial.	Concurrent	Rifampicin + ART	Bruchfeld et al. (2015); WHO (2013); Yorke et al. (2017)
TB and Diabetes Management	Dual screening and glycemic control improve outcomes; metformin studied for host-directed effects.	Throughout treatment	Anti-TB + anti-diabetics	Alemu et al. (2021); Falzon et al. (2017); Schrager et al. (2020)

The current approach to TB treatment lies at the convergence of long-established understanding and state-of-the-art advancements. Although conventional HRZE protocols remain effective for the majority of individuals with drug-sensitive TB, the swiftly changing environment of MDR/XDR-TB

therapy underscores the significance of tailored medicine, technological advancements, and innovative pharmaceutical progress. Addressing tuberculosis in individuals with concurrent conditions such as HIV and diabetes necessitates customised strategies and collaborative healthcare efforts. In the meantime, therapies aimed at the host could potentially transform tuberculosis treatment by focussing on the interaction between the host and the pathogen instead of solely targeting the pathogen itself. In order to achieve the objectives set forth by the End TB Strategy 2035, worldwide initiatives must guarantee comprehensive access to these advancements, diminish inequalities within health systems, and incorporate social and digital solutions that extend beyond the use of antibiotics. Tuberculosis is no longer merely an ailment of the respiratory system—it has evolved into a condition influenced by disparities, biological factors, and access to opportunities.

Prevention and Control

Tuberculosis, although treatable, continues to be one of the most lethal infectious ailments globally. Although diagnosis and treatment serve as fundamental components of tuberculosis management, prevention—encompassing both medical and social aspects—is just as vital. Prevention includes a range of activities: from immunisation, to measures for controlling infections, to community-oriented public health initiatives that tackle social determinants. The World Health Organization's End TB Strategy highlights the significance of cohesive preventive actions focused on eradicating tuberculosis by the year 2035 (WHO, 2021; Chakaya et al., 2020).

5.1 TB Vaccines

The Bacille Calmette–Guérin (BCG) vaccine, which was launched in the 1920s, remains the sole authorised tuberculosis vaccine globally. Every year, more than 100 million infants receive this treatment, mainly in nations where tuberculosis is widespread (McShane, 2015; WHO, 2023). The BCG vaccine provides significant defence against serious types of tuberculosis in young individuals, including miliary tuberculosis and tuberculosis meningitis. However, its effectiveness in preventing adult pulmonary tuberculosis—the most contagious variant—tends to be inconsistent and frequently limited (Seddon et al., 2019; Schrager et al., 2020). As a result of this constraint, international health investigators have focused their efforts on creating advanced TB vaccines for the future. The leading contender is M72/AS01E, a recombinant fusion protein vaccine created by GSK in collaboration with the Bill & Melinda Gates Foundation. In a Phase IIb study, it demonstrated a 50% effectiveness in halting the advancement from latent TB infection (LTBI) to active pulmonary TB in adults (Schrager et al., 2020; McShane, 2015). This signifies a remarkable advancement, particularly for those residing in nations heavily impacted by the prevalence of LTBI. A further encouraging approach is the revaccination tactic—delivering BCG to older youth or teenagers. Recent studies have demonstrated that revaccination using BCG can decrease persistent TB infection rates by almost 45% (McShane, 2015; WHO, 2021). Furthermore, candidates such as VPM1002 and ID93+GLA-SE are currently in the midst of clinical trials, aiming to improve immunity and possibly supplant BCG entirely.

- BCG safeguards against severe tuberculosis in paediatric populations, yet its efficacy diminishes when addressing pulmonary tuberculosis in adults (McShane, 2015).
- M72/AS01E demonstrates a 50% effectiveness in preventing the advancement of active tuberculosis in adults who are latently infected (Schrager et al., 2020).
- Strategies for revaccination with BCG and innovative candidates such as VPM1002 are currently in the development phase (WHO, 2021).

5.2 Infection Control Measures

Controlling infections is an essential, frequently neglected component of tuberculosis prevention—particularly in medical facilities, correctional institutions, refugee shelters, and densely populated areas where the risk of transmission is elevated. Tuberculosis is a respiratory illness transmitted through airborne droplets when an individual with active pulmonary TB coughs, sneezes, or talks. Due to the ability of these droplets to linger in the atmosphere for extended periods, it is crucial to implement effective infection control measures to safeguard both patients and healthcare personnel.

The World Health Organisation advocates for a structured infection control system that consists of three tiers:

1. Management measures – Prompt assessment, cough evaluation, expedited processing of TB candidates, and isolation of contagious individuals.
2. Environmental regulations – Adequate ventilation mechanisms, natural air circulation, ultraviolet germicidal light, and air purification in medical facilities.
3. Individual safeguarding strategies – Employment of N95 respirators by medical personnel and surgical masks by patients with infectious conditions (Floyd et al., 2018; WHO, 2021).

Swift diagnostic methods, especially GeneXpert and AI-enhanced chest X-rays, significantly reduce the duration required for diagnosis, facilitating prompt isolation and treatment (Boehme et al., 2010; Qin et al., 2021). These instruments minimise the duration patients occupy ambiguous environments, where they may inadvertently transmit infections to others. Beyond healthcare establishments, initiatives rooted in the community are essential. Informing communities regarding proper cough practices, air circulation, and the significance of adhering to treatment protocols contributes to minimising transmission within homes and workplaces.

- Tuberculosis transmits through airborne particles—adequate airflow and effective triage diminish the risk (Lawn & Zumla, 2011).
- Infection management encompasses administrative, environmental, and individual strategies (WHO, 2021).

Swift diagnostic measures and effective isolation strategies hinder the transmission of nosocomial tuberculosis (Boehme et al., 2010).

5.3 Public Health Approaches

Biomedical instruments by themselves are insufficient to eradicate TB. The societal factors influencing tuberculosis—economic hardship, inadequate nutrition, high population density, social stigma, and restricted healthcare access—need to be tackled via holistic public health initiatives (Davidson et al., 2024; Lönnroth et al., 2015). A highly efficient approach for early identification involves contact tracing, which entails screening all individuals who have been in close proximity to an infectious TB case for symptoms and conducting tests for both latent and active TB (WHO, 2023; Enos et al., 2018). Proactive case identification (PCI), involving mobile health units and community health personnel who actively assess at-risk groups, has demonstrated significant effectiveness in nations with high disease prevalence like Kenya, India, and South Africa (Ngari et al., 2023; Chakaya et al., 2020). These initiatives concentrate on perilous settings such as city slums, mining areas, correctional facilities, and refugee shelters, where the prevalence of undetected tuberculosis is frequently considerable. Technological innovations are transforming public health engagement. Mobile apps and SMS-driven platforms serve as tools for symptom reporting, ensuring treatment compliance, and providing health education in remote and underserved regions (Masini et al., 2016; WHO, 2021). Applications such as 99DOTS, evriMED, and TB REACH leverage straightforward technology to enhance patient involvement and minimise the risk of loss to follow-up. A vital component is the function of

community health workers (CHWs)—skilled local personnel who connect the divide between established health systems and underserved communities. They engage in door-to-door tuberculosis awareness initiatives, provide medication distribution, and assist in ensuring treatment adherence, particularly for individuals encountering financial or logistical challenges (Fox et al., 2013; WHO, 2021). Furthermore, social safety net programs—like food aid, travel allowances, and accommodation support—have demonstrated effectiveness in enhancing tuberculosis outcomes by tackling fundamental obstacles to accessing care.

- The processes of contact tracing and proactive case identification are crucial for the prompt detection of tuberculosis (WHO, 2023).
- Mobile applications and text messaging services enhance compliance with treatment protocols (Masini et al., 2016).
- Community health advocates improve engagement and diminish stigma (Fox et al., 2013).
- Policies for social protection enhance tuberculosis results in at-risk groups (Lönnroth et al., 2015).

Table 4: TB Prevention and Control Measures

Intervention Type	Approach	Target Group/Setting	Tools Used	Supporting References
Vaccination (BCG)	Prevents severe TB in children, but efficacy wanes in adulthood.	Infants, neonates	BCG vaccine	McShane (2015); WHO (2023); Seddon et al. (2019)
M72/AS01E Vaccine	New candidate with 50% efficacy in LTBI cases; in late-stage trials.	Adults with latent TB	M72/AS01E recombinant protein	Schrager et al. (2020); McShane (2015)
Infection Control (Hospitals)	3-level approach: administrative, environmental (e.g., ventilation), and personal protection (e.g., masks).	Healthcare settings	N95 masks, triage protocols	WHO (2021); Lawn & Zumla (2011); Floyd et al. (2018)
Rapid Diagnostic Isolation	Use of AI-based CXR and GeneXpert to quickly identify infectious cases and isolate them early.	High-burden clinics, prisons	GeneXpert, AI radiography	Boehme et al. (2010); Qin et al. (2021); WHO (2021)
Public Health Campaigns	Education about cough hygiene, early symptoms, nutrition, and stigma reduction through CHWs and media outreach.	General public, rural areas	Community outreach, mobile health teams	Fox et al. (2013); Lönnroth et al. (2015); Masini et al. (2016)
Active Case Finding (ACF)	Proactive screening in prisons, slums, and camps	At-risk populations	Mobile clinics, digital X-rays, symptom	Chakaya et al. (2020); Ngari et

Intervention Type	Approach	Target Group/Setting	Tools Used	Supporting References
	using mobile vans and AI tools.		checks	al. (2023); WHO (2023)
Social Protection	Housing support, food aid, and transport subsidies to improve treatment adherence.	Economically vulnerable TB patients	Government/NPO programs	Floyd et al. (2018); Lönnroth et al. (2015); WHO (2021)

The safeguarding and management of tuberculosis should reach far beyond the confines of medical facilities and research centres. Although scientific advancements—like the M72 vaccine and AI-enhanced diagnostics—are transformative, the triumph of public health fundamentally relies on fairness, accessibility, and cohesive integration. An effective tuberculosis management approach should integrate medical resources with community involvement, infection prevention methods, and social policy initiatives. The battle against TB is becoming progressively multifaceted, encompassing BCG vaccinations, digital adherence tracking, AI-driven radiology, and community health workers conducting door-to-door outreach. The objective of the WHO to eradicate TB by 2035 is both bold and attainable—provided that countries dedicate themselves to thorough, inclusive, and evidence-based prevention approaches that ensure no individual is overlooked.

Research and Development

The exploration and advancement of tuberculosis (TB) have embarked on a revolutionary phase characterised by a significant transition from reactive management to proactive, precision-focused methodologies. Despite tuberculosis being one of the most lethal infectious ailments globally, progress in pharmaceutical innovation, host-immunology, and systems biology has started to bridge longstanding deficiencies in therapy, prevention, and diagnostic methods (World Health Organisation, 2023; Esmail et al., 2018). Current investigations are progressively centred on creating innovative pharmaceutical strategies aimed at tackling multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB). This includes the examination of host-directed therapies (HDTs) that influence the immune system, as well as the formulation of comprehensive care frameworks that cater to the increasing prevalence of tuberculosis in communities afflicted by additional health challenges such as HIV, diabetes, and malnutrition. Every one of these pathways signifies not just a pursuit of scientific knowledge but also a moral obligation: neglecting to innovate threatens to permit tuberculosis to sustain its status as a predominant global killer for many years ahead.

6.1 New TB Drugs and Regimens

A significant domain of advancement in tuberculosis research is the creation of more concise, safer, and highly effective treatment protocols for both drug-susceptible tuberculosis (DS-TB) and drug-resistant tuberculosis. Traditionally, the management of drug-susceptible tuberculosis (DS-TB) has necessitated a duration of six months for therapy, whereas the treatment protocols for multidrug-resistant tuberculosis (MDR-TB) have spanned 18 to 24 months and included painful injections accompanied by significant adverse effects (Nahid et al., 2016; WHO, 2021). In light of these constraints, the identification of novel agents like bedaquiline, pretomanid, and delamanid has resulted in considerable transformations in therapeutic

approaches. Bedaquiline specifically focusses on the mycobacterial ATP synthase and has shown notable efficacy against multidrug-resistant tuberculosis (MDR-TB), offering enhanced safety profiles in comparison to conventional injectable medications (Gygli et al., 2017; Arslan et al., 2025). Pretomanid and delamanid, which belong to the nitroimidazole category, interfere with cell wall formation and exhibit strong bactericidal effects in both aerobic and anaerobic environments (Tiberi et al., 2022; McShane, 2015).

This research culminates in the BPaLM protocol—a half-year oral therapy that integrates bedaquiline, pretomanid, linezolid, and moxifloxacin. This entirely oral, abbreviated treatment plan has shown an impressive 89% success rate among individuals suffering from MDR-TB and XDR-TB, providing optimism to countless patients who once endured lengthy and harmful therapies (Conradie et al., 2022; WHO, 2023). Significantly, BPaLM enhances treatment results while also promoting patient compliance and lowering the expenses of the healthcare system linked to extended hospital stays. Clinical studies persist in evaluating its effectiveness among varied demographics, while initiatives are in progress to enhance its accessibility in resource-limited, high-burden areas (Falzon et al., 2017; Floyd et al., 2018).

In conjunction with these advancements, scientists are exploring comprehensive TB treatment protocols that would be effective against every strain of tuberculosis, irrespective of any drug resistance. This may streamline the commencement of treatment and lessen the requirement for comprehensive drug susceptibility assessments, especially in regions with inadequate laboratory facilities. This advancement signifies a transition towards individualised therapy in tuberculosis management—an aspect previously deemed unattainable in the realm of worldwide infectious disease care.

6.2 Host-Directed Therapies (HDTs)

Conventional tuberculosis medications focus on directly attacking the mycobacterium, yet new findings advocate for the advancement of host-directed therapies (HDTs) designed to boost the immune system's capacity to manage or eradicate TB infections. The development of tuberculosis is influenced not only by the virulence of the bacteria but also by the inflammatory response of the host. When this response is out of balance, it can lead to tissue damage, cavitation, and pulmonary fibrosis (Flynn & Chan, 2001; Yadav & Rawal, 2024). HDTs provide a method to alter this equilibrium by adjusting immune mechanisms, enhancing lung recovery, and shortening treatment time when utilised in conjunction with antimicrobial interventions.

One of the most promising HDTs is metformin, a widely recognised medication for diabetes management. In addition to regulating blood sugar levels, metformin stimulates AMP-activated protein kinase (AMPK) and boosts autophagy within macrophages, facilitating the destruction of intracellular M. tuberculosis (Esmail et al., 2018; Gopalaswamy et al., 2020). Research indicates that tuberculosis patients who have diabetes and are treated with metformin experience improved treatment results and reduced relapse rates in comparison to individuals receiving conventional diabetes management (Alemu et al., 2021). Statins, frequently prescribed for hyperlipidaemia, additionally influence the immune system by diminishing pro-inflammatory cytokines, improving phagolysosomal fusion, and lessening lung damage in animal studies of tuberculosis (Sheikhpour et al., 2023; Tiberi et al., 2022).

Additional experimental HDTs encompass checkpoint inhibitors that amplify T-cell activation by obstructing the PD-1/PD-L1 pathway; vitamin D supplementation, which elevates antimicrobial peptide expression; and matrix metalloproteinase

(MMP) inhibitors, which could avert lung tissue deterioration linked to TB-induced inflammation (Schrager et al., 2020; Gygli et al., 2017). While a majority of HDTs remain in the preclinical or initial clinical stages, their potential to shorten treatment timelines, avert relapses, and enhance lung recovery may profoundly transform the landscape of tuberculosis treatment.

6.3 TB and Comorbidities

The interconnected reality of tuberculosis—where it exists alongside various chronic and infectious ailments—requires that investigators and healthcare frameworks merge tuberculosis treatment with comprehensive management of comorbidities. The co-occurrence of HIV and tuberculosis continues to pose a major challenge to global health. The presence of HIV diminishes the levels of CD4+ T cells, which hampers the immune system's ability to manage tuberculosis infections and elevates the likelihood of TB reactivation by more than 20 times (Gelaw et al., 2019; Bruchfeld et al., 2015). Indeed, tuberculosis stands as the foremost cause of mortality for individuals living with HIV, particularly in sub-Saharan Africa, where the availability of prompt TB and antiretroviral treatment (ART) continues to be irregular (UNAIDS, 2020; WHO, 2023).

The prevailing guideline suggests commencing ART at the earliest opportunity while undergoing TB therapy. Nonetheless, this method is not devoid of obstacles. The immune reconstitution inflammatory syndrome (IRIS), the interplay of drug toxicities, and the intricate pharmacokinetics associated with tuberculosis and HIV treatments require meticulous clinical oversight (Zeru, 2021; WHO, 2013). Models of integrated care, such as co-located TB-HIV clinics and synchronised medication protocols (for instance, dolutegravir-based ART), have demonstrated enhancements in outcomes and a decrease in mortality rates (Ngari et al., 2023; CDC, 2021).

The connection between diabetes and tuberculosis has attracted growing interest, especially in nations with a high prevalence where there are simultaneous increases in both tuberculosis and type 2 diabetes. Individuals with diabetes exhibit compromised neutrophil activity, diminished cytokine synthesis, and lowered T-cell stimulation, resulting in a threefold increase in their susceptibility to tuberculosis (Alemu et al., 2021; Yorke et al., 2017). In nations like India, Ethiopia, and China, programs featuring dual-screening have surfaced, and the World Health Organisation currently advocates for bidirectional surveillance of tuberculosis and diabetes in regions where these diseases are prevalent (Alebel et al., 2019; Falzon et al., 2017). In addition to HIV and diabetes, the results related to tuberculosis are significantly affected by factors like undernutrition, mental health issues, and persistent respiratory conditions, including COPD and post-TB lung disease (PTLD) (Yadav & Rawal, 2024; Davidson et al., 2024).

Table 5: Innovations in TB Research and Development

Innovation Area	Description	Stage of Development	Impact Potential	References
BPaLM Regimen	New 4-drug combination with 89% success in MDR-TB/XDR-TB cases.	Phase III trials	Shortens treatment, improves adherence	Conradie et al. (2022); WHO (2023)
Pan-TB Regimens	Universal regimens under research to eliminate need for	Ongoing trials	Could simplify and accelerate	Dheda et al. (2019); McShane (2015)

Innovation Area	Description	Stage of Development	Impact Potential	References
	DST before treatment.		treatment decisions	
Host-Directed Therapies	Repurposed drugs like metformin and statins modulate immune pathways to control inflammation and enhance bacterial clearance.	Preclinical/Phase II	May shorten duration, improve recovery, reduce relapse	Schrager et al. (2020); Gopalaswamy et al. (2020)
Checkpoint Inhibitors	Immune enhancement via PD-1/PD-L1 modulation.	Experimental	Improves T-cell response in chronic TB	Flynn & Chan (2001); Tiberi et al. (2022)
TB-HIV Integrated Care	Combined clinics and early ART reduce mortality in co-infected patients.	Scaled in high-burden countries	Reduces complexity, improves survival	Zeru (2021); UNAIDS (2020); WHO (2013)
TB-Diabetes Integration	Dual screening and glycemic control reduce complications.	WHO-endorsed	Key in countries with high prevalence of both diseases	Alemu et al. (2021); Alebel et al. (2019); Falzon et al. (2017)
Vitamin D and MMP Inhibitors	Supportive HDTs aiming at lung protection and inflammation control.	Early-stage trials	May reduce post-TB lung damage	Gygli et al. (2017); Schrager et al. (2020)

The exploration and advancement of tuberculosis are reaching a pivotal and optimistic phase. Innovative protocols such as BPaLM are optimising the treatment of MDR-TB, while host-directed therapies (HDTs) present a fresh perspective centred on the host. Additionally, comprehensive care models are confronting the intricate relationships between tuberculosis and accompanying health conditions, allowing for a multifaceted approach to combat the disease. Nonetheless, unlocking the complete capabilities of these advancements necessitates ongoing funding for research frameworks, fair access to novel treatments, and resilient healthcare systems that can adjust to evolving epidemiological conditions. Tuberculosis is no longer merely a germ to be eradicated—it serves as a perspective through which we must reassess public health fairness, scientific advancement, and the entitlement to health in the modern era.

Conclusion

Tuberculosis remains a formidable obstacle to worldwide health, even though it is both preventable and manageable. The enduring presence of tuberculosis is anchored in a multifaceted interaction of biological, environmental, socioeconomic, and political elements that go beyond the confines of medicine itself. Although progress in molecular diagnostics like GeneXpert, AI-enhanced radiography, and drug susceptibility assessments has expedited case identification and tailored treatment, significant inequalities in access to these resources persist worldwide. Forms of tuberculosis that resist treatment—particularly multidrug-resistant TB and

extensively drug-resistant TB—present significant obstacles, necessitating extended and frequently harmful treatment protocols that still do not ensure recovery in numerous circumstances. The emergence of innovative medications such as bedaquiline and pretomanid has provided optimism; however, logistical challenges and financial constraints hinder their broad adoption. Proactive approaches, encompassing enhanced immunisation (for instance, M72/AS01E), infection management, and treatment for latent TB, present considerable potential, particularly when paired with strong public health measures such as contact tracing and digital adherence assistance. Host-targeted treatments signify an innovative realm, with the potential to diminish disease severity and enhance results by focussing on the human immune system instead of the pathogen itself. Above all, tuberculosis represents a condition of disparity. To eradicate tuberculosis, it is insufficient to merely create improved medications or diagnostic tools—we must also deconstruct the societal and economic frameworks that enable its persistence. This necessitates a collective commitment across various sectors, ongoing financial support, strong political determination, and international collaboration. It is only at that point that we can progress towards the WHO's End TB Strategy and ultimately eradicate this age-old affliction.

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