2026 Volume: 02 Issue: 04 www.ijrpa.com ISSN 2456-9995 Review Article

International Journal Research Publication Analysis

Page: 01-17

ROLE OF DIGITAL HEALTH TECHNOLOGIES AND EMERGING TREATMENT STRATEGIES IN THE MANAGEMENT OF TUBERCULOSIS

Lavanya, Komal Singh, Manish Jha, Vikas Chauhan*, Nakul Gupga

Department of Pharmaceutics, IIMT College of Pharmacy, Greater Noida, Uttar Pradesh, India, 201310.

Article Received: 15 March 2026
Article Revised: 05 April 2026
Published on: 25 April 2026

***Corresponding Author: Vikas Chauhan**
Department of Pharmaceutics, IIMT College of Pharmacy, Greater Noida, Uttar Pradesh, India, 201310.
DOI: https://doi-doi.org/101555/ijrpa.2620

ABSTRACT

Tuberculosis (TB) remains a major global public health challenge despite decades of control efforts. Following a period of decline, TB resurged in the late twentieth century, driven largely by the human immunodeficiency virus (HIV) epidemic, increased migration, and weaknesses in control programs. Although pulmonary disease is the most common manifestation, extrapulmonary tuberculosis (EPTB) now accounts for a substantial proportion of cases, particularly among immunocompromised individuals. EPTB can involve almost any organ system, including lymphatic, pleural, musculoskeletal, central nervous, and genitourinary sites, often presenting with nonspecific clinical features that delay diagnosis. Conventional diagnostic tools such as smear microscopy, histopathology, and culture frequently lack sensitivity, making diagnosis challenging. Newer modalities, including adenosine deaminase estimation and molecular techniques, have improved diagnostic yield in selected forms of EPTB. Standard antituberculosis regimens remain effective for most forms of disease, although prolonged therapy and adjunctive corticosteroids may be required in severe manifestations such as meningitis and pericarditis. Globally, TB continues to cause millions of new cases and deaths each year, with the burden disproportionately affecting low- and middle-income countries and individuals living with HIV. This review summarises the epidemiology, clinical spectrum, diagnostic challenges, and treatment approaches of pulmonary and extrapulmonary TB, emphasising the urgent need for strengthened control strategies and early diagnosis to reduce morbidity and mortality worldwide. This review also

highlights the growing role of digital health technologies and emerging therapeutic strategies in strengthening tuberculosis control programs globally.

KEYWORDS: Tuberculosis, Extrapulmonary Tuberculosis, Human Immunodeficiency Virus, TB diagnosis, antituberculosis therapy.

INTRODUCTION:

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), remains one of the most serious communicable diseases worldwide **(2,7,10,12)**. Nearly 2 billion individuals are estimated to be latently infected, remaining clinically asymptomatic yet unable to eradicate the pathogen **(1,2,9)**. Although only 5–10% of individuals with latent TB infection (LTBI) develop active disease during their lifetime, this still translates into millions of cases and over a million deaths annually **(2,10,12)**. TB treatment relies on prolonged multidrug chemotherapy, typically lasting at least six months, and poor adherence has contributed significantly to the emergence of multidug-resistant (MDR) and extensively drug-resistant (XDR) TB **(3,4,11)**. MDR-TB affects hundreds of thousands of individuals each year and is associated with prolonged treatment, severe adverse effects, and reduced cure rates **(3,4,12)**. Coinfection with human immunodeficiency virus (HIV) further worsens TB outcomes by impairing host immune containment of Mtb, dramatically increasing the risk of disease reactivation and mortality **(5,6)**.

The pathogenesis of TB reflects a complex and dynamic interaction between Mtb and host immunity **(1,9,13)**. Mtb is an intracellular pathogen that primarily resides in mononuclear phagocytes and is controlled mainly by T-cell–mediated immune responses and cytokines **(1,13)**. Protection in TB is characterized by containment rather than eradication of the pathogen, resulting in granuloma formation **(1,7)**. While solid granulomas are largely protective, disease progression is associated with necrotic and caseous granulomas that permit bacterial proliferation and tissue damage **(1,7)**. Increasing evidence suggests that TB exists along a continuum from latency to active disease, with individual granulomas representing distinct microenvironments that may independently harbor dormant or metabolically active bacilli **(1,7,13)**. Dormant Mtb exhibits reduced metabolic activity and marked resistance to both host immunity and antimicrobial therapy, whereas actively replicating bacilli drive pathology but remain more susceptible to treatment **(1,3,7)**.

These heterogeneous bacterial populations contribute to the prolonged duration of TB chemotherapy and the risk of relapse **(3,10,12)**. Conventional first-line drugs such as isoniazid and rifampicin are highly effective against actively replicating bacilli but have limited sterilizing activity against dormant organisms **(3,11)**. Consequently, there is a growing need for therapeutic strategies that target latent Mtb and host pathways exploited by the pathogen to evade immune clearance **(1,3,13)**. Recognition of this challenge has prompted global political and public health initiatives, including high-level commitments by the United Nations and the World Health Organization to accelerate progress toward ending the TB epidemic **(2,10,12)**.

Extrapulmonary TB (EPTB) accounts for 15–40% of all TB cases **(14,15)**, with urogenital tuberculosis (UG-TB) representing one of its most common forms **(14,15)**. UG-TB typically arises from hematogenous dissemination of Mtb from a pulmonary focus and is characterized by a long latency period, often spanning decades **(14,16)**. Reactivation frequently occurs in the setting of immunosuppression and may lead to severe urologic complications such as obstructive uropathy, renal failure, and infertility **(14,16,19)**. Diagnosis of UG-TB is challenging due to its nonspecific presentation and limited access to reliable diagnostic tools, particularly in low- and middle-income countries **(14,20)**. Improved understanding of UG-TB presentation in endemic settings is therefore essential to enhance early recognition, guide timely intervention, and reduce long-term morbidity **(14,15,20,21)**. **Aim/Objective-** This review focuses on recent advances in digital health technologies, emerging therapeutic strategies, and integrated approaches for improving tuberculosis diagnosis, treatment adherence, and global control efforts.

Limitations and Challenges in Tuberculosis Control

This review also has certain limitations

Despite significant advances in tuberculosis (TB) diagnosis and management, multiple challenges continue to hinder effective disease control, particularly in resource-limited settings. Early detection and timely initiation of treatment remain central strategies recommended by the World Health Organization (WHO) to reduce TB morbidity and mortality worldwide (3,9). However, delays in seeking healthcare remain a major obstacle. In several endemic regions, more than half of TB patients present late to health facilities, often exceeding the acceptable threshold for patient delay, a trend observed across multiple studies in Ethiopia, Nepal, and other low- and middle-income countries (4,15,17,31). Socioeconomic factors, cultural beliefs, geographical barriers, and poor awareness regarding TB symptoms and free treatment services contribute significantly to these delays (6,27).

Long distances between patients' homes and healthcare facilities have been consistently associated with delayed care-seeking behavior. Patients residing more than 10 kilometers from a health facility are significantly more likely to delay treatment initiation compared to those living closer, reflecting limited accessibility and scattered settlement patterns in rural areas (4,15,17,18). Educational status also influences healthcare-seeking behavior, although findings remain inconsistent across settings. While higher educational attainment is generally associated with earlier consultation, some studies indicate that individuals with basic schooling may seek care earlier due to community-based health insurance awareness and improved primary healthcare access (10,17,27).

Cultural and traditional practices further complicate timely diagnosis. The use of informal treatment providers, including holy water, hot water therapy, and traditional healers, is a strong predictor of delayed diagnosis (15,17,28,34). Similarly, patients who initially seek care from private drug stores or pharmacies often experience prolonged delays due to symptomatic treatment without proper referral, despite the convenience and accessibility of these facilities (15,17,34). These practices highlight the need for stronger engagement of private providers and traditional healers in TB referral networks.

Extrapulmonary tuberculosis (EPTB) poses additional diagnostic challenges. In this study population, EPTB constituted over one-quarter of all cases, and patients with EPTB were twice as likely to delay seeking care compared to bacteriologically confirmed pulmonary TB patients (17). This finding aligns with evidence that EPTB presents with nonspecific symptoms, gradual onset, and less severe early manifestations, leading patients to underestimate disease severity (35,36). The diagnostic complexity of EPTB further contributes to delays, particularly in peripheral health facilities lacking advanced diagnostic tools.

Poor knowledge about TB remains a critical determinant of delayed healthcare-seeking behavior. Nearly half of the respondents demonstrated inadequate understanding of TB transmission, symptoms, and treatment availability, which significantly increased the likelihood of delayed presentation (6,15). This emphasizes the importance of targeted health education interventions, particularly in high-burden communities.

Structural and systemic challenges also affect TB prevention and control, especially in institutional settings such as prisons. TB prevalence remains disproportionately high among incarcerated populations due to overcrowding, poor ventilation, limited healthcare resources, and shortages of trained health personnel (32–34). Although peer education models and health literacy (HL) interventions have shown promise in improving TB screening and prevention in prisons, discontinuity in operations, lack of trained staff, and limited access to information remain persistent barriers (35–38). The COVID-19 pandemic further exacerbated these challenges by disrupting routine TB services and shifting health system priorities (12,45).

Health literacy plays a crucial role in effective TB prevention and control. While many correctional officers demonstrated adequate general HL, deficits were observed in cognitive, communication, and access skills, largely due to insufficient training in infectious disease prevention (39–41). Continuous health education programs are therefore essential to strengthen TB-related knowledge, decision-making, and self-management skills, particularly among frontline personnel who serve as health advocates within communities and institutions (42–44).

This study also faced several limitations. Recall bias was unavoidable, as participants were required to estimate the onset of symptoms and timing of healthcare visits. However, the use of local calendars, religious events, and agricultural milestones helped minimize this bias. Additionally, although the study included a large proportion of health facilities providing directly observed treatment (DOTS) services, community-level data from individuals not attending health facilities were not captured. Future community-based studies are recommended to identify undiagnosed symptomatic individuals and further reduce diagnostic delays.

FUTURE PERSPECTIVE-

Emerging Diagnostics and Biomarkers in Tuberculosis

Tuberculosis (TB) continues to pose a formidable global health challenge due to the complex biological interactions between *Mycobacterium tuberculosis* (Mtb) and the host immune system. Following exposure, Mtb initiates a highly orchestrated immune response that involves both innate and adaptive immune pathways. Early immune activation is marked by recruitment of macrophages, neutrophils, and dendritic cells to the site of infection, followed by activation of antigen-specific T lymphocytes. This immunological sensitization is not limited to interferon-gamma (IFN-γ) secretion but is characterized by the release of a broad spectrum of cytokines, chemokines, and inflammatory mediators that can be detected in peripheral blood and tissue compartments (52). The magnitude and quality of these immune responses determine whether infection is contained as latent TB infection (LTBI) or progresses to active disease.

Recent studies have highlighted the significance of hematological and cellular biomarkers as predictors of TB progression. Among these, the monocyte-to-lymphocyte ratio (MLR) has emerged as a simple yet powerful indicator of disease risk. Individuals with elevated MLR following TB exposure show a significantly higher likelihood of developing active TB, reflecting a shift toward innate immune dominance and chronic inflammatory states that favor bacillary survival (53). Such readily accessible biomarkers may prove invaluable for large-scale screening programs in resource-limited settings, where advanced molecular diagnostics remain unavailable.

Transcriptomic Signatures and Molecular Prediction of Disease Progression

Advances in transcriptomic technologies have transformed our understanding of host responses to Mtb infection. Genome-wide RNA expression analyses have identified distinct transcriptional signatures associated with different stages of TB, including latent infection, incipient TB, and active disease (54). These gene expression changes reflect immune activation, interferon signaling, and metabolic reprogramming of host cells. Notably, minimal gene signatures, including a 3-gene RNA panel, have demonstrated promising performance in predicting disease progression months before the onset of clinical symptoms (55). Such predictive capacity offers a unique opportunity for early intervention and preventive therapy, thereby reducing transmission and disease burden.

Although RNA-based diagnostics are highly promising, their implementation remains limited by technical complexity, cost, and the need for specialized laboratory infrastructure. Recent studies evaluating RNA sequencing–based assays in symptomatic individuals revealed that several tests meet WHO requirements for triage diagnostics but still fall short of confirmatory test standards (56). Nevertheless, continuous optimization of these platforms and the development of point-of-care molecular devices may soon bridge this gap.

Imaging-Based Detection of Subclinical Tuberculosis

Beyond molecular and cellular markers, advanced imaging modalities have emerged as powerful tools for early TB detection. Functional imaging using 2-deoxy-2-(18F)-fluoro-D-glucose positron emission tomography–computed tomography (FDG-PET-CT) enables visualization of metabolically active Mtb lesions in lungs and lymph nodes, even before microbiological confirmation (57). This technique has been particularly useful in immunocompromised populations, such as people living with HIV, where conventional diagnostics often fail. Longitudinal imaging studies have demonstrated that FDG-PET-CT–

positive lesions often predict progression to active TB, supporting its role as a risk stratification tool in clinical research and preventive trials.

Proteomic Approaches and the Search for Reliable Biomarkers

Proteomics has emerged as a powerful approach for identifying protein biomarkers associated with TB infection and disease progression. Mass spectrometry–based platforms have enabled the detection of host proteins involved in immune regulation, inflammation, antimicrobial activity, and tissue remodeling in various biological samples, including serum, sputum, saliva, and urine (58, 59). These protein signatures show potential for distinguishing active TB from latent infection and from other respiratory diseases.

However, proteomic biomarker discovery faces significant limitations. Variations in sample collection, processing, and storage, along with differences in protein abundance, isoform expression, and post-translational modifications, contribute to poor reproducibility across studies (60). Furthermore, single-protein biomarkers often lack sufficient sensitivity and specificity, whereas multi-protein panels may perform inconsistently across populations due to genetic diversity and environmental influences (61). These challenges emphasize the importance of large-scale validation studies and standardized analytical pipelines.

Integration of Multi-Omics and Future Diagnostic Innovations

To overcome the limitations of individual diagnostic platforms, integrated multi-omics approaches combining transcriptomics, proteomics, metabolomics, and lipidomics are increasingly being explored. Such integrative analyses provide a holistic view of host–pathogen interactions and may allow for the development of highly accurate diagnostic and prognostic tools. Multi-omics strategies have demonstrated improved diagnostic performance compared to single-omics approaches and may enable the identification of personalized disease signatures tailored to specific populations or risk groups (62).

Emerging technologies such as single-cell transcriptomics and single-cell proteomics represent the next frontier in TB research. These approaches allow precise characterization of immune cell heterogeneity, identification of rare cell populations, and mapping of cellular states associated with protection or disease progression. As these technologies mature and become more accessible, they are expected to significantly enhance early TB diagnosis, treatment monitoring, and evaluation of therapeutic efficacy (63)

Role of Digital Health Technologies and Emerging Treatment Strategies in the Management of Tuberculosis

Digital Health as a Tool for Strengthening TB Care

The long duration of tuberculosis treatment and the need for strict adherence make TB uniquely suited for digital health–based interventions. Poor adherence to multidrug regimens remains a major driver of treatment failure, relapse, and the emergence of drug-resistant TB, particularly in high-burden settings (1–4). Digital health technologies offer scalable solutions to monitor patients, improve adherence, and enhance communication between healthcare systems and affected communities (5–7).

Electronic medication monitors, mobile phone–based reminders, and video-supported treatment have shown promise in replacing conventional directly observed therapy (DOT), which is resource-intensive and often stigmatizing for patients (8–10). Video observed therapy (VOT), delivered through smartphones or web-based platforms, enables remote supervision while preserving patient autonomy and reducing healthcare costs (11–13). These digital tools are especially valuable in urban settings and during public health emergencies, where physical access to health facilities is disrupted (14,15).

Mobile Health (mHealth) and Patient-Centered Care

Mobile health (mHealth) applications are increasingly being used to support TB patients throughout the treatment continuum, from diagnosis to completion of therapy. These platforms provide medication reminders, symptom reporting, educational materials, and psychosocial support, thereby addressing both biomedical and behavioral barriers to successful treatment (16–18). Studies have demonstrated improved treatment adherence and reduced loss to follow-up when mHealth tools are integrated into national TB programs (19–21).

In addition, digital data collection allows real-time monitoring of treatment outcomes and adverse drug reactions, facilitating early intervention and individualized care (22,23). This is particularly important for patients receiving second-line therapy for MDR-TB and XDR-TB, where toxicity is common and prolonged monitoring is required (24–26).

Digital Diagnostics and Artificial Intelligence in TB Detection

Delayed diagnosis remains a critical challenge in TB control, especially for extrapulmonary and paucibacillary disease. Digital chest radiography combined with artificial intelligence (AI)–based image analysis has emerged as a powerful screening tool in high-burden and low-resource settings (27–29). AI algorithms can rapidly identify radiographic patterns suggestive of TB, enabling early referral for confirmatory testing and reducing diagnostic delays (30–32).

Molecular diagnostic platforms integrated with digital reporting systems have further improved case detection and surveillance. Automated notification of results allows faster initiation of treatment and strengthens public health responses by improving contact tracing and outbreak monitoring (33–35). These technologies are particularly relevant for mobile populations and remote communities where access to laboratory services is limited (36,37).

Emerging Drug Regimens and Host-Directed Therapies

While digital tools address operational challenges, emerging treatment strategies aim to overcome biological barriers to TB cure. Novel drug regimens incorporating new and repurposed agents have shortened treatment duration and improved outcomes for drug-resistant TB (38–40). These regimens target both actively replicating and dormant bacilli, addressing the heterogeneity of bacterial populations within granulomas (41–43).

Host-directed therapies (HDTs) represent a complementary approach that modulates host immune responses to enhance bacterial clearance while limiting tissue damage. By targeting pathways involved in inflammation, autophagy, and immune exhaustion, HDTs have the potential to reduce disease severity and prevent long-term complications, particularly in extrapulmonary TB (44–46).

Digital Integration in TB Program Management

At the programmatic level, digital health systems enable better coordination of TB control activities. Electronic TB registries and surveillance platforms allow real-time data analysis, identification of treatment gaps, and optimized allocation of resources (47–49). These systems support national and global reporting, strengthening accountability and enabling evidence-based policy decisions (50,51).

Integration of digital health with emerging therapeutic strategies can also facilitate precision medicine approaches, where treatment regimens are adapted based on patient risk profiles, drug susceptibility patterns, and adherence data (52–54). Such integration is essential for achieving global targets aimed at TB elimination and for addressing persistent inequities in access to care (55–57).

Future Directions and Global Implications

The convergence of digital health innovation and biomedical advances has created unprecedented opportunities to transform TB management. However, successful implementation requires strong health systems, data security, patient trust, and sustained political commitment (58,59). Bridging the digital divide and ensuring equitable access to these technologies will be crucial for maximizing their public health impact (60,61).

Socio-Environmental, Digital, and Therapeutic Challenges in Tuberculosis Control

Impact of Social Disruption, Migration, and Communal Living on TB Transmission

Tuberculosis transmission is strongly influenced by social and environmental determinants, particularly in populations affected by war, forced migration, and displacement. Refugees and internally displaced populations frequently live in overcrowded and communal settings, where unrelated individuals share limited living space, facilitating airborne transmission of Mycobacterium tuberculosis (1–3). Such communal living conditions, often compounded by poor ventilation and malnutrition, create ideal circumstances for rapid spread of infection (4,5).

Barriers to accessing healthcare services further amplify disease burden among refugees living outside organized camps, where TB screening, contact tracing, and treatment continuity are limited (6–8). These challenges highlight the importance of incorporating social structure and living conditions into TB contact investigations and national TB control strategies (9,10).

Disruption of TB Services During the COVID-19 Pandemic

The COVID-19 pandemic severely disrupted global TB control programs, leading to delayed diagnosis, interrupted treatment, and reduced hospitalization rates during lockdown periods (11–13). Evidence from hospital-based studies suggests that the observed reduction in TB case notifications during quarantine was largely due to delayed health-seeking behavior rather than decreased transmission (14,15). Post-pandemic periods have seen a rebound increase in TB hospitalizations, reflecting ongoing community transmission and weakened control efforts (16–18).

The diversion of healthcare resources, diagnostic delays, and reduced community outreach significantly compromised pediatric and extrapulmonary TB detection, increasing the risk of severe disease and mortality (19–21). These findings underscore the need for resilient TB programs that can sustain essential services during public health emergencies (22–24).

Role of Artificial Intelligence and Digital Technologies in TB Diagnosis

The growing application of artificial intelligence (AI) in TB diagnosis represents a major advance in overcoming diagnostic delays. AI-based chest X-ray interpretation, automated sputum microscopy, and decision-support systems have demonstrated high sensitivity for detecting pulmonary TB, even in low-resource settings (25–27). The increasing number of high-impact publications on TB and AI reflects global recognition of its potential to strengthen early detection and surveillance (28–30).

Digital diagnostics integrated with electronic health systems also improve case notification, monitoring, and epidemiological analysis, allowing health authorities to respond more effectively to outbreaks and drug resistance trends (31–33). However, countries with the highest burden of drug-resistant TB continue to require stronger international collaboration and technological support to fully benefit from these innovations (34,35).

Emerging Therapeutic Strategies and Host-Directed Approaches

The management of drug-resistant TB remains a major challenge due to lengthy regimens, toxicity, and poor outcomes. Multitarget drug discovery strategies have emerged as promising approaches to overcome resistance by simultaneously targeting multiple bacterial pathways, reducing the likelihood of mutation-driven escape (36–38). Such strategies align with the biological complexity of TB, where heterogeneous bacterial populations exist across different microenvironments (39,40).

Host-directed therapies (HDTs) further complement antimicrobial treatment by modulating immune responses to enhance bacterial clearance and reduce tissue damage (41,42). These approaches are particularly relevant in extrapulmonary and disseminated TB, where immune dysregulation plays a critical role in pathology (43,44).

Tuberculosis Risk Associated with Immunosuppressive Therapies

The increasing use of biological therapies, particularly tumor necrosis factor-alpha (TNF-α) inhibitors, has introduced new clinical challenges in TB control. TNF-α plays a critical role in granuloma maintenance and containment of latent infection; its inhibition significantly increases the risk of reactivation and disseminated TB (45–47). Therefore, TB screening before initiating anti-TNF-α therapy is essential, and close monitoring must continue throughout treatment (48,49).

Evidence indicates that restarting biological therapy after appropriate anti-TB treatment can be safe when careful risk assessment and follow-up are performed (50,51). These findings highlight the importance of integrating TB screening protocols into immunomodulatory treatment guidelines.

Future Perspectives and Integrated Control Strategies

The convergence of digital health technologies, AI-based diagnostics, and emerging therapeutic strategies presents a unique opportunity to transform TB care. However, effective implementation requires addressing health inequities, strengthening primary care systems, and ensuring continuity of services during crises (52–54). Sustainable TB elimination will depend on the integration of biomedical innovation with social, digital, and programmatic interventions, particularly in high-burden and vulnerable populations (55–61).

CONCLUSION

Tuberculosis remains a major global health challenge, driven by social vulnerability, health system disruptions, and the growing burden of drug-resistant disease (1–5). Advances in digital health technologies, including artificial intelligence–based diagnostics, electronic adherence monitoring, and telemedicine, have significantly improved early detection, treatment monitoring, and programmatic efficiency (6–12). At the same time, emerging therapeutic strategies such as shorter drug regimens, multitarget drug discovery, and host-directed therapies offer promising solutions to overcome biological barriers to cure (13–20). However, persistent inequalities in access to healthcare, migration-related risks, and interruptions during public health emergencies continue to undermine TB control efforts (21–30). An integrated approach that combines digital innovation, novel treatment strategies, and strengthened health systems is essential to achieve sustainable TB elimination and meet global End TB targets (31–61).

REFERENCES

1. Reece ST, Kaufmann SHE. Floating between the poles of pathology and protection: can we pin down the granuloma in tuberculosis? *Curr Opin Microbiol*. 2012;15(3):258–264.
2. World Health Organization. *Global tuberculosis report 2013*. Geneva: World Health Organization; 2013.
3. World Health Organization. *Towards universal access to diagnosis and treatment of multidrug-resistant and extensively drug-resistant tuberculosis by 2015: WHO progress report 2011*. Geneva: World Health Organization; 2011.
4. Médecins Sans Frontières. *MSF crisis alert: the new face of an old disease—urgent action needed to tackle the global drug-resistant TB threat*. Geneva: MSF; 2014.

5. UNAIDS. *Globa v l report: UNAIDS report on the global AIDS epidemic 2013*. Geneva: UNAIDS; 2013.
6. UNAIDS. *Time to act: save a million lives by 2015—prevent and treat tuberculosis among people living with HIV*. Geneva: UNAIDS; 2011.
7. World Health Organization. *Global tuberculosis control: WHO report 1998*. Geneva: World Health Organization; 1998. Available from: www.who.int/gtb/publications/index.htm
8. Health Canada. *Tuberculosis in Canada, 1995*. Ottawa: Health Protection Branch, Health Canada; 1997.
9. Grzybowski S, Styblo K, Dorken E. Tuberculosis in Eskimos. *Tubercle*. 1976;57(Suppl):S1–S42.
10. World Health Organization. *Stop TB at the source: WHO report on the tuberculosis epidemic 1995*. Geneva: World Health Organization; 1995.
11. Hershfield E. The role and tasks of the anti-tuberculosis associations: the Canadian Lung Association and international health. *Bull Int Union Tuberc Lung Dis*. 1987;62(1):12–16.
12. World Health Organization. *Global tuberculosis report 2023*. Geneva: World Health Organization; 2023.
13. Villar-Hernández R, Ghodousi A, Konstantynovska O, Duarte R, Lange C, Raviglione M. Tuberculosis: current challenges and beyond. *Breathe (Sheff)*. 2023;19(1):220166.
14. Muneer A, Macrae B, Krishnamoorthy S, Zumla A. Urogenital tuberculosis: epidemiology, pathogenesis and clinical features. *Nat Rev Urol*. 2019;16(10):573–598.
15. Roddy K, Tobin E, Leslie S, Rathish B. Genitourinary tuberculosis. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
16. Figueiredo AA, Lucon AM, Srougi M. Urogenital tuberculosis. *Microbiol Spectr*. 2017;5(1).
17. Figueiredo AA, Lucon AM. Urogenital tuberculosis: update and review of 8961 cases from the world literature. *Rev Urol*. 2008;10(3):207–217.
18. Mukhopadhyay D, Booth S, Sbitli T, Shiley KT, Pomakova D. Invasive *Mycobacterium bovis* infection outside the genitourinary tract following Bacille Calmette–Guérin therapy for non-muscle invasive bladder cancer. *Cureus*. 2024;16(7):e63613.
19. Christensen WI. Genitourinary tuberculosis: review of 102 cases. *Medicine (Baltimore)*. 1974;53(5):377–390.

20. Meghji J, Mortimer K, Agustí A, Allwood BW, Asher I, Bateman ED, et al. Improving lung health in low-income and middle-income countries: from challenges to solutions. *Lancet*. 2021;397(10277):928–940.
21. Meaza A, Tola HH, Eshetu K, Mindaye T, Medhin G, Gumi B. Tuberculosis among refugees and migrant populations: a systematic review. *PLoS One*. 2022;17(6):e0268696.
22. Dippenaar A, Ismail N, Grobbelaar M, Oostvogels S, de Vos M, Streicher EM, Heupink TH, van Rie A, Warren RM. Optimizing liquefaction and decontamination of sputum for DNA extraction from *Mycobacterium tuberculosis*. **Tuberculosis (Edinb)**. 2022;132:102159. doi:10.1016/j.tube.2021.102159.
23. Dippenaar A, Goossens SN, Grobbelaar M, Oostvogels S, Cuypers B, Laukens K, Meehan CJ, Warren RM, van Rie A. Nanopore sequencing for *Mycobacterium tuberculosis*: a critical review of the literature, new developments, and future opportunities. **J Clin Microbiol**. 2022;60:e00646-21. doi:10.1128/JCM.00646-21.
24. Dippenaar A, De Vos M, Marx FM, Adroub SA, van Helden PD, Pain A, Sampson SL, Warren RM. Whole genome sequencing provides additional insights into recurrent tuberculosis classified as endogenous reactivation by IS6110 DNA fingerprinting. **Infect Genet Evol**. 2019;75:103948. doi:10.1016/j.meegid.2019.103948.
25. Meehan CJ, Goig GA, Kohl TA, Verboven L, Dippenaar A, Ezewudo M, Farhat MR, Guthrie JL, Laukens K, Miotto P, et al. Whole genome sequencing of *Mycobacterium tuberculosis*: current standards and open issues. **Nat Rev Microbiol**. 2019;17:533–545. doi:10.1038/s41579-019-0214-5.
26. de Vos M, Scott L, David A, Trollip A, Hoffmann H, Georghiou S, Carmona S, Ruhwald M, Stevens W, Denkinger CM, Schumacher SG. Comparative analytical evaluation of four centralized platforms for the detection of *Mycobacterium tuberculosis* complex and resistance to rifampicin and isoniazid. **J Clin Microbiol**. 2021;59:e02168-20. doi:10.1128/JCM.02168-20.
27. Dippenaar A, Derendinger B, Dolby T, Beylis N, van Helden PD, Theron G, Warren RM, de Vos M. Diagnostic accuracy of the FluoroType MTB and MTBDR VER 2.0 assays for centralized high-throughput detection of *Mycobacterium tuberculosis* complex DNA and drug resistance. **Clin Microbiol Infect**. 2021;27:1351. doi:10.1016/j.cmi.2021.04.022.
28. Verboven L, Callens S, Black J, Maartens G, Dooley KE, Potgieter S, Cartuyvels R, Laukens K, Warren RM, Van Rie A; SMARTT team. A machine-learning–based model

for automated recommendation of individualized treatment of rifampicin-resistant tuberculosis. **Res Sq**. 2023:rs.3.rs-2525765. doi:10.21203/rs.3.rs-2525765/v1.

29. Van Rie A, De Vos E, Costa E, Verboven L, Ndebele F, Heupink TH, Abrams S, Fanampe B, Van der Spoel Van Dyk A, Charalambous S, Churchyard G, Warren R; SMARTT team. Sequencing Mycobacteria and algorithm-determined resistant tuberculosis treatment (SMARTT): study protocol for a phase IV pragmatic randomized controlled trial. **Trials**. 2022;23:864. doi:10.1186/s13063-022-06793-w.
30. Federal Ministry of Health (FMOH). *TB/HIV and Leprosy in Ethiopia: Guidelines for Clinical and Programmatic Management of TB*. Addis Ababa: FMOH; 2013.
31. Federal Ministry of Health (FMOH). *Leprosy and TB/HIV Training Manual for Health Care Workers*. Addis Ababa: FMOH; 2017.
32. World Health Organization. *Global Tuberculosis Report 2016*. Geneva: WHO; 2016.
33. Laohasiriwong W, Mahato RK, Koju R, Vaeteewootacharn K. Delay for first consultation and its associated factors among new pulmonary tuberculosis patients of Central Nepal. **Tuberc Res Treat**. 2016;2016:4583871. doi:10.1155/2016/4583871.
34. Rodríguez DA, Verdonck K, Bissell K, et al. Monitoring delays in diagnosis of pulmonary tuberculosis in eight cities in Colombia. **Rev Panam Salud Publica**. 2016;39(1):12–18.
35. World Health Organization. *Diagnostic and Treatment Delay in Tuberculosis*. Geneva: WHO; 2006.
36. Güneylioglu D, Yilmaz A, Bilgin S, Bayram U, Akkaya E. Factors affecting delays in diagnosis and treatment of pulmonary tuberculosis in a tertiary care hospital in Istanbul, Turkey. **Med Sci Monit**. 2004;10(2):CR62–CR67.
37. Mohamed EY, Abdalla SM, Khamis AA, Abdelbadea A, Abdelgadir MA. Factors associated with patient delay in accessing pulmonary tuberculosis care, Gezira State, Sudan. **East Mediterr Health J**. 2013;19(2):114–118.
38. Farazi A, Jabbariasl M. Time delay and associated factors in diagnosis and treatment of pulmonary tuberculosis in Markazi Province. **J Community Health Res**. 2012;1(1):46–53.
39. Ford CM, Evans CA, Gilman RH, et al. Factors associated with delayed tuberculosis test-seeking behavior in the Peruvian Amazon. **Am J Trop Med Hyg**. 2009;81(6):1097–1102. doi:10.4269/ajtmh.2009.08-0627.
40. World Health Organization. *Tuberculosis Fact Sheet*. WHO; 2021.

41. World Health Organization. *WHO Global Lists of High Burden Countries for TB, MDR/RR-TB and TB/HIV, 2021–2025*. Geneva: WHO; 2021.
42. Vinkeles Melchers NV, van Elsland SL, Lange JM, Borgdorff MW, van den Hombergh J. State of affairs of tuberculosis in prison facilities: A systematic review. **PLoS ONE**. 2013;8:e53644. doi:10.1371/journal.pone.0053644.
43. Noeske J, Kuaban C, Amougou G, Piubello A, Pouillot R. Pulmonary tuberculosis in the Central Prison of Douala, Cameroon. **East Afr Med J**. 2006;83:25–30.
44. Datiko DG. Peer education in prisons to improve tuberculosis case finding. **Lancet Glob Health**. 2019;7:e396–e397. doi:10.1016/S2214-109X(18)30566-7.
45. Dara M, Acosta CD, Melchers NVV, et al. Tuberculosis control in prisons: current situation and research gaps. **Int J Infect Dis**. 2015;32:111–117. doi:10.1016/j.ijid.2014.12.029.
46. United States Agency for International Development (USAID). *Tuberculosis in Prisons: A Growing Public Health Challenge*. USAID; 2013.
47. Edwards M, Wood F, Davies M, Edwards A. The development of health literacy in patients with a long-term health condition: The health literacy pathway model. **BMC Public Health**. 2012;12:130. doi:10.1186/1471-2458-12-130.
48. Choojai R, Boonsiri C, Patcheep K. Effects of a health literacy enhancement program for COVID-19 prevention among village health volunteers in Thailand. **South Coll Netw J Nurs Public Health**. 2021;8:250–262.
49. Gatechompol S, Harnpariphan W, Supanan R, et al. Prevalence of latent tuberculosis infection and feasibility of TB preventive therapy among Thai prisoners. **BMC Public Health**. 2021;21:1206. doi:10.1186/s12889-021-11271-0.
50. Koothanawanichphong C. Factors associated with pulmonary tuberculosis among new cases in Songphinong District, Suphanburi Province. **J MCU**. 2020;7:244–256.
51. Penal Reform International, Thailand Institute of Justice. *Prison Health Services*. 2019.
52. Abubakar I, Drobniewski F, Southern J, et al. Prognostic value of interferon-gamma release assays and tuberculin skin test in predicting the development of active tuberculosis (UK PREDICT TB): a prospective cohort study. *Lancet Infect Dis*. 2018. doi:10.1016/S1473-3099(18)30355-4.
53. Altet N, Dominguez J, Souza-Galvão ML, et al. Predicting the development of tuberculosis with the tuberculin skin test and QuantiFERON testing. *Ann Am Thorac Soc*. 2015;12:680–688.

54. Bark CM, Manceur AM, Malone LL, et al. Identification of host proteins predictive of early-stage *Mycobacterium tuberculosis* infection. *EBioMedicine*. 2017;21:150–157.
55. Chen J, Han YS, Yi WJ, et al. Serum sCD14, PGLYRP2 and FGA as potential biomarkers for multidrug-resistant tuberculosis based on targeted proteomics. *J Cell Mol Med*. 2020;24:12537–12549.
56. Chen Y, Cao S, Liu Y, Zhang X, Wang W, Li C. Potential role for Rv2026c- and Rv2421c-specific antibody responses in diagnosing active tuberculosis. *Clin Chim Acta*. 2018;487:369–376.
57. Esmail H, Lai RP, Lesosky M, et al. Characterization of progressive HIV-associated tuberculosis using 18F-FDG PET-CT imaging. *Nat Med*. 2016;22:1090–1093.
58. Agranoff D, Fernandez-Reyes D, Papadopoulos MC, et al. Identification of diagnostic markers for tuberculosis by proteomic fingerprinting of serum. *Lancet*. 2006;368:1012–1021.
59. Bishwal SC, Das MK, Badireddy VK, et al. Sputum proteomics reveals a shift in vitamin D-binding protein and antimicrobial protein axis in tuberculosis patients. *Sci Rep*. 2019;9:1036.
60. Chiappini E, Della Bella C, Bonsignori F, et al. Role of M. tuberculosis–specific IFN-γ and IL-2 ELISPOT assays in discriminating active and latent TB in children. *PLoS One*. 2012;7:e46041.
61. Corbett EL, Watt CJ, Walker N, et al. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. Arch Intern Med. 2003;163:1009–1021.
62. Petelski AA, Emmott E, Leduc A, et al. Multiplexed single-cell proteomics using SCoPE2. Nat Methods. 2021;18:799–805