

# Tuberculosis at a crossroads: rethinking detection, management, and innovation

Maria L. de Souza-Galvão

*Unitat de Tuberculosi Vall d'Hebron-Drassanes, Servei de Pneumologia, Hospital Universitari de la Vall d'Hebron, Barcelona, Spain*

Despite being a preventable and treatable disease, tuberculosis (TB) remains one of the world's deadliest infectious threats. According to the WHO's 2025 global report, an estimated 10.7 million people developed TB and 1.23 million died from it in 2024. These figures highlight persistent inequalities, rising drug resistance, and the limits of current diagnostic and therapeutic strategies.

As global health systems struggle to recover from the post-pandemic landscape, TB demands renewed attention and a more integrated, forward-looking approach. In this monographic series of *Barcelona Respiratory Network Reviews* (BRN), several authors contribute to the following topics:

The first article, titled *Screening for tuberculosis in vulnerable populations* (Jiménez-Fuentes et al.<sup>1</sup>) underscores the critical importance of active screening strategies in high-risk groups such as migrants from high-incidence countries, homeless individuals, people who use

drugs, and the incarcerated. The article describes the tools available for screening (symptoms, plain radiography or with CAD, rapid molecular tests, TST, IGRA, and the new C-Tb test) and analyzes different screening algorithms according to the combination of tests. Evidence from multidisciplinary local programs shows that combining outreach work, rapid diagnostics, and social support improves case detection and treatment adherence. Screening, the authors argue, is not only a public health intervention but also a measure of social justice.

A recurring clinical challenge is managing patients with strong clinical and radiological suspicion of TB but lacking microbiological confirmation. The second article: *Tuberculosis without microbiological confirmation*, by Bellido-Calduch et al.<sup>2</sup>, reviews the diagnostic and therapeutic approach to tuberculosis without microbiological confirmation, a frequent situation in early stages or paucibacillary forms, where patients usually present milder

**Correspondence to:**

Maria L. de Souza-Galvão

E-mail: malu.desouza@vallhebron.cat

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symptoms and less specific radiological images, compatible with an initial disease state and low bacillary load. This review proposes a structured clinical approach that integrates diagnostic probabilities, imaging patterns, molecular tests, temporal evolution, and exclusion of alternative diagnoses. When the suspicion is high, timely empirical treatment remains essential to prevent progression, transmission, and poor outcomes.

Drug-resistant TB continues to impose a substantial burden, with long and toxic regimens and major psychosocial consequences. In the third article: *A holistic approach to drug-resistant tuberculosis*, Casas et al.<sup>3</sup> review the evolution of therapeutic regimens, from the old 18 to 24-month treatments to the current 6 to 9-month oral regimens with bedaquiline, pretomanid, linezolid, and moxifloxacin (BPaLM), pointing out the global difficulties in accessing drugs and resistance testing. This article highlights the impact of multidisciplinary, patient-centred care, combining medical therapy with psychological, nutritional, and social support. New all-oral regimens, including BPaLM, are transforming outcomes, but the authors emphasize that biomedicine alone is not enough – holistic care is vital to achieving sustained cure.

Although TB contributes significantly to the global challenge of antimicrobial resistance, it has often been excluded from antimicrobial stewardship (AMS) frameworks. In the review titled: *Antimicrobial stewardship in the management of TB*, Brehm et al.<sup>4</sup> argue for fully integrating TB into stewardship programs to optimise diagnostic pathways, ensure appropriate use of key agents such as bedaquiline and linezolid, incorporate therapeutic drug

monitoring and genomic tools, and strengthen surveillance systems. Stewardship, the authors contend, is essential to safeguarding current and future TB treatments.

In countries where tuberculosis is steadily declining, non-tuberculous mycobacterial infections are emerging as a growing challenge, with treatments that remain difficult, far less standardized than those for TB, and with few therapeutic advances in recent years. The final article: *Phage therapy in mycobacterial disease*, by Cumplí-Gargallo et al.<sup>5</sup>, explores the emerging field of bacteriophage therapy for *Mycobacterium abscessus* and other mycobacterial infections. Although clinical evidence stems mostly from compassionate-use cases, early results are encouraging, with reductions in bacterial burden, radiological improvement, and good tolerability. Preclinical studies also suggest potential synergy with antibiotics.

For *M. tuberculosis*, research is at an earlier phase, yet the development of targeted phage cocktails marks a promising step toward future clinical trials. Phage therapy is unlikely to replace conventional regimens soon, but it may become an essential adjunct for highly resistant or complex infections.

Together, these contributions illustrate how the fight against TB requires integration rather than fragmentation: combining social interventions with better diagnostics, holistic care for resistant disease, stewardship-driven prescribing, and innovative therapeutic strategies. As TB remains a global challenge, the insights from this BRN monographic series reinforce the urgency – and the opportunity – to rethink our collective approach.

## REFERENCES

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