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Nontuberculous mycobacterial lung disease: a blind spot in global lung health

Enfermedad pulmonar por micobacterias no tuberculosas: un punto ciego en la salud pulmonar global

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As clinicians, we frequently encounter patients experiencing years of persistent cough, repeated antibiotic courses, and misdiagnoses such as "recurrent bronchitis," resulting in delayed recognition of nontuberculous mycobacterial pulmonary disease (NTM-PD). After diagnosis is finally established, individuals face prolonged multidrug treatment regimens with poor tolerance and uncertain outcomes, including failure and relapse.

NTM-PD is a chronic, debilitating illness that is increasingly observed globally, particularly among older adults and people with structural lung disease (Prevots *et al.*, 2023). Globally, 86% percent of nontuberculous mycobacterial infection-associated deaths occurred in people aged ≥ 65 years (Harada *et al.*, 2025). In several high-income settings, NTM-PD incidence now exceeds that of tuberculosis (Bents *et al.*, 2024). However, in many South American countries, the disease remains undocumented and likely underdiagnosed due to limited diagnostic capacity and clinical overlap with tuberculosis (Carneiro *et al*., 2018; Mora *et al*., 2021). NTM-PD remains non-notifiable in most regions, unlike tuberculosis, leprosy, or Buruli ulcer. The absence of surveillance impedes accurate burden assessment, resource allocation, and service planning.

Where the diagnosis is made, care is often fragmented. In the absence of structured programs or an accountable clinical "home", NTM-PD is commonly managed through tuberculosis services, not due to suitability, but because these programs are the primary source of essential drugs such as rifamycins, ethambutol, or clofazimine. These already overburdened programs frequently provide medications to NTM-PD patients without formal mandate or budget, resulting in delays, operational challenges, and ethical dilemmas. Patients with chronic NTM-PD infection are thus left to navigate a system not designed for their needs.

Drug therapy is also deeply inadequate. Guideline-recommended regimens usually require at least 3 drugs for 18 months or longer, with significant toxicity, including ototoxicity, nephrotoxicity, visual disturbances, and cardiac effects (Daley *et al.,* 2020). Treatment success rates rarely exceeds 66% even in expert centers, and long-term mortality is substantial, reaching 19% at 1 year and 68% at 10 years in a recent nationwide Danish cohort (Dahl et al., 2025; Diel *et al.*, 2018). For some patients, surgical lung resection combined with antimicrobial therapy is the only potentially curative intervention; a sad reminder of the pre-antibiotic era of tuberculosis management (Kim *et al.*, 2023). A significant indicator of neglect

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is the lack of therapeutic innovation. The backbone drugs used in the most prevalent forms of NTM-PD, rifampicin, ethambutol, and macrolides, were not developed for this disease but were repurposed from tuberculosis therapy and lack formal approval for this indication. Over the past decades, only amikacin liposome inhalation suspension (ALIS, Arikayce®) has been approved for adults with refractory Mycobacterium avium complex-pulmonary disease (U.S. Food and Drug Administration, 2018). However, ALIS is not yet a first-line option, benefits only a subset of patients, and remains unaffordable for most low- and middle-income countries (LMICs). No other new agents have reached approval, and the drug-development pipeline remains limited, with several promising candidates abandoned or delayed (Conyers & Saunders, 2024).

This neglect is embedded within health systems. NTM-PD is largely absent from major WHO respiratory frameworks and The Union's global lung health agendas, and its non-notifiable status perpetuates underestimation of disease burden. In many regions, limited diagnostic capacity, particularly restricted access to species identification and susceptibility testing, further constrains care. Weak market incentives, driven by heterogeneous patient populations, prolonged treatment regimens, and regulatory complexity, discourage pharmaceutical investment. Care remains fragmented across specialties, with no integrated model comparable to tuberculosis or bronchiectasis programs. Collectively, these factors contribute to a widespread but underrecognized pandemic.

The respiratory health community has the capacity and the responsibility to change this trajectory. Progress will require recognizing NTM-PD as a notifiable disease, enabling robust surveillance and evidence-based resource allocation, and explicitly integrating it into the WHO and The Union agendas within global chronic respiratory disease strategies. Increased funding is required to develop new antimicrobials, host-directed therapies, and adjunctive interventions. In parallel, health systems should establish national NTM programs with dedicated centers and standardized care pathways to deliver coordinated, multidisciplinary, and longitudinal care, while ensuring equitable access to diagnostics, susceptibility testing, and existing therapies, including ALIS, particularly in LMICs where financial barriers are most significant. Finally, future clinical trials must move beyond microbiological endpoints alone and incorporate patient-centered outcomes such as quality of life and functional status.

NTM pulmonary disease is an increasingly important contributor to global chronic respiratory morbidity, yet it remains inadequately measured and under-prioritized. Addressing NTM-PD as a global health priority requires alignment between disease burden and research, regulatory, and clinical focus. Enhanced recognition is essential to achieving more effective and equitable care.

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