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# PrimeView
# Multidrug-resistant tuberculosis

Multidrug-resistant tuberculosis (MDR-TB) is a public health issue in several regions of the world, especially Eastern Europe, Russia, Asia and sub-Saharan Africa. MDR-TB is more difficult to diagnose and is associated with higher mortality and morbidity and higher rates of post-TB lung damage than drug-susceptible TB.

## Mechanisms

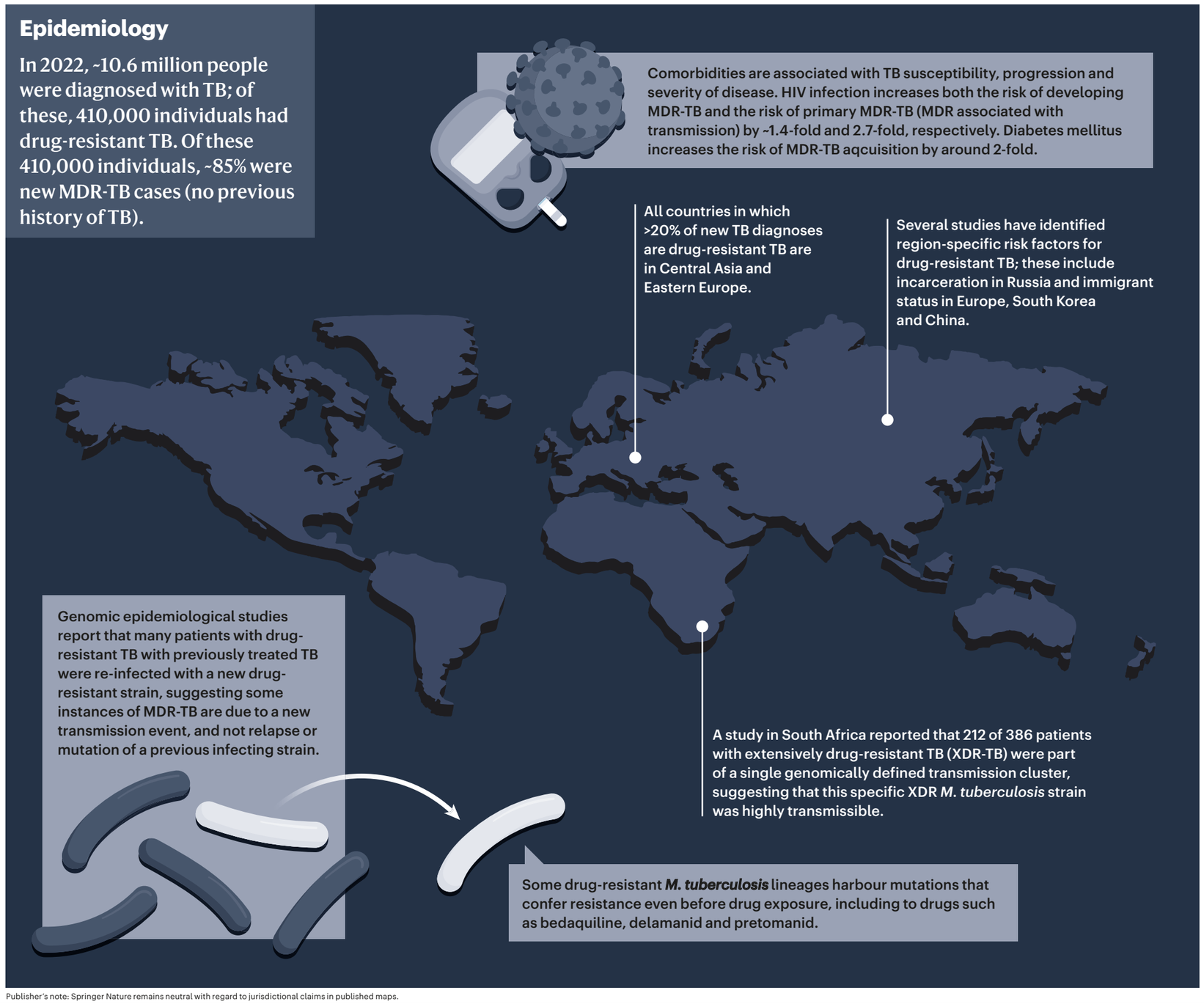
Tuberculosis (TB) is a respiratory disease caused by the bacterium *Mycobacterium tuberculosis*. The mechanisms of drug resistance in TB are complex and multifactorial. *De novo* resistance occurs through spontaneous and random chance genomic mutations. *M. tuberculosis* fitness may be increased through these mutations, for example efflux pump efficiency may be increased by mutations over time leading to more efficient expulsion of the drugs from the *M. tuberculosis* organisms. *M. tuberculosis* organisms with drug resistance can proliferate with inappropriate or sub-optimal drug exposure or interruption of therapy. Sub-optimal drug delivery at the site of disease can result from pharmacokinetic variability (variability in metabolism, absorption and/or elimination of drugs) or from heterogeneity in drug penetration of TB lesions such as cavities, or from factors such as suboptimal dosing or treatment interruptions.

## Diagnosis

Symptoms include fever, loss of weight and appetite, night sweats, coughing (sometimes with blood) and chest pain. The current global public health strategy lies mostly in passive case finding (the patient self-reports with symptoms to a health-care facility). However, ~50% of the total TB case-load within a community is relatively asymptomatic, and approximately one-third of patients with MDR-TB remain undetected. Passive case finding enables uninterrupted transmission of the disease before diagnosis. Community-based active case finding (screening) should be prioritized to avoid further transmission events. Methods for screening could include X-ray screening, sputum-based molecular testing or smear microscopy. Unfortunately, there is debate about the optimal strategy, and availability of effective screening tests is low.

## Epidemiology

In 2022, ~10.6 million people were diagnosed with TB; of these, 410,000 individuals had drug-resistant TB. Of these 410,000 individuals, ~85% were new MDR-TB cases (no previous history of TB).




## Management

First-line TB drugs include isoniazid, rifampicin, ethambutol and pyrazinamide. Second-line drugs have been classified as group A drugs (levofloxacin or moxifloxacin, bedaquiline and linezolid), group B drugs (clofazimine and cycloserine orterizidone) and group C drugs, which are useful treatment adjuncts. The 2022 WHO guidelines on drug-resistant TB recommend the BPaLM regimen (24-week course of bedaquiline, pretomanid, linezolid and moxifloxacin) for patients with MDR-TB when fluoroquinolone susceptibility is presumed or documented. A longer regimen is indicated for patients with poor prognostic features such as high mycobacterial burden, extensive disease or complicated extra-pulmonary disease. Injectable anti-TB drugs are no longer indicated to treat MDR-TB but can still be considered in rescue regimens for XDR-TB, for which limited treatment options exist. Notably, there is increasing resistance to group A drugs, including bedaquiline, in TB-endemic countries that may complicate management strategies.

## Outlook

One of the targets of the Sustainable Development Goals between 2015 and 2030 is to end the global TB epidemic, and the WHO end TB strategy calls for a 90% reduction in TB deaths and an 80% decrease in TB incidence by 2030. Intensified research and innovation is a major focus of these strategies. Future diagnostic efforts must focus on community-based active case finding, thus preventing transmission and amplification of the epidemic. New tools and biomarkers are required to improve screening methods and identify the most infectious patients to provide early treatment initiation and halt transmission.





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