

New classification of tuberculosis to support efforts to eliminate the disease

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Scanning electron micrograph of *Mycobacterium tuberculosis* bacteria, which cause TB. Credit: NIAID

A new way to classify tuberculosis (TB) that aims to improve focus on the early stages of the disease has been presented by an international team involving researchers at UCL.

The new framework, published in *The Lancet Respiratory Medicine*, seeks to replace the approach of the last half century of defining TB as either active (i.e., causing illness and potentially infectious to others) or latent (being infected with the bacterium that causes TB [M tuberculosis] but feeling well and not infectious to others)—an approach researchers say is limiting progress in eradicating the disease.

Of note, large surveys conducted in over 20 countries recently have shown that many people with infectious TB feel well.

Under the new classification, there are four disease states: clinical (with symptoms) and subclinical (without symptoms), with each of these classed as either infectious or non-infectious. The fifth state is M. tuberculosis infection that has not progressed to disease—that is, M. tuberculosis may be present in the body and alive, but there are no signs of the disease that are visible to the naked eye, for example with imaging.

The researchers say they hope the International Consensus for Early TB (ICE-TB) framework, developed by a diverse group of 64 experts, will help lead to better diagnosis and treatment of the early stages of TB which have historically been overlooked in research.

TB remains the world's most deadly infectious disease currently and has caused over one billion deaths in the last 200 years. An estimated three million cases a year are not reported to [health systems](#) and more than half of these cases will be asymptomatic.

The international team was led by researchers at UCL, London School of

Hygiene & Tropical Medicine, The Walter and Eliza Hall Institute (WEHI), University of Cape Town, Imperial College London and the South African Medical Research Council.

Dr. Hanif Esmail, co-lead author at the UCL Institute for Global Health and MRC Clinical Trials Unit at UCL, said, "The binary paradigm of active disease versus latent infection has resulted in a one-size-fits-all antibiotic treatment for disease, but designed for those with the most severe form of disease. This leads to potential over-treatment of individuals with subclinical TB.

"A key research priority now is to identify the best combination, dosage and duration of antibiotics to treat each TB state, as well as the benefits of treating the subclinical states."

Professor Rein Houben (London School of Hygiene and Tropical Medicine), co-lead author of the paper, said, "While providing treatment to people who become very sick with TB has saved millions of lives we are not stopping transmission of the disease."

"To prevent transmission of TB, we need to move away from focusing just on the very sick and look at earlier disease states, identifying people who may be infectious for months or years before they develop TB symptoms.

"Our consensus framework replaces the old binary concept of 'active' versus 'latent' TB with a more detailed classification system that we hope, if widely adopted, could help to improve treatment for those with early-stage TB and drive forward efforts to eradicate the disease."

The framework was developed via a Delphi process designed to reach a consensus among a diverse group. The process began with a scoping review of papers and online surveys of experts and culminated in a two-

day meeting in Cape Town, South Africa, of researchers from a range of disciplines as well as policymakers, clinicians, and TB survivors.

Dr. Anna Coussens, co-lead author from WEHI, said, "One key finding in the consensus is moving the disease threshold and acknowledging that disease does not just start with symptoms or transmission, but when tissue is damaged.

"In time we hope our framework can contribute to TB elimination by leading to improved early diagnosis and treatment, optimizing patient outcomes and minimizing transmission."

The researchers noted that the disease process was non-linear—that people may fluctuate between infectious and non-infectious states, and between the presence and absence of symptoms or signs.

They also said that better diagnostic tools were needed to identify many of the TB states. For instance, there is currently no test to detect a viable *M. tuberculosis* infection (i.e., one where the bacteria are physiologically active), as opposed to a non-viable infection or recent infection that has cleared.

The international team involved stakeholders from 19 countries including International Union Against TB and Lung Disease, The StopTB partnership, World Health Organization, FIND, National TB Programs, TB Proof, and researchers from a number of universities and medical research institutes.

More information: International consensus classification of early tuberculosis states to guide research for improved care and prevention: A Delphi exercise, *The Lancet Respiratory Medicine* (2024). [DOI: 10.1016/S2213-2600\(24\)00028-6](https://doi.org/10.1016/S2213-2600(24)00028-6)

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