Overall, Twitter is an efficient channel for information sharing among health-care professionals, policymakers, and the general public who can actively participate with leaders and experts worldwide, at any time, at no cost. Encouraging more health-care professionals to tweet on antimicrobial resistance can bring us closer to achieving WHO's goal of improving awareness and understanding of antimicrobial resistance.

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Latent tuberculosis infection: diagnostic tests and when to treat

Latent *Mycobacterium tuberculosis* infection is defined by WHO as "a state of persistent immune response to *M tuberculosis* antigens with no evidence of clinically active tuberculosis disease".[1] An estimated 1·7 billion people worldwide have latent tuberculosis infection, of whom up to 10% are at risk of reactivating into active tuberculosis during their lifetime.[2] Latent tuberculosis infection can be effectively treated and this can prevent progression to active tuberculosis, benefitting both the individual and the community. Treatment regimens for latent tuberculosis infection[1] reduce the risk of developing active tuberculosis by at least 60%.[1,3] To achieve the 2035 and 2050 End TB Strategy goals,[4] the very challenging and arduous task of screening and treating this huge latent tuberculosis infection reservoir needs to be addressed.

The 2018 WHO latent tuberculosis infection guidelines[1] recommend latent tuberculosis infection screening and treatment should focus on people at a high risk of latent tuberculosis infection reactivation regardless of background epidemiology, particularly people living with HIV and children younger than 5 years who are household contacts of pulmonary tuberculosis patients in all settings. Other groups recommended for latent tuberculosis screening include anyone initiating anti-tumour necrosis factor treatment, receiving dialysis, preparing for organ or haematological transplantation, or with silicosis. In countries with a low prevalence of tuberculosis, such as the USA, a large proportion of people who are diagnosed with active tuberculosis appear to have developed the disease from untreated latent tuberculosis infection.[5] Thus, all high-income countries now have proactive latent tuberculosis infection screening and treatment programs for all new migrants and refugees.

Despite two decades of research, no gold standard diagnostic tests exist for latent tuberculosis infection. Currently three latent tuberculosis infection tests are recommended by WHO:[1] the tuberculin skin test (TST) and two interferon-γ release assays (IGRAs), QuantiFERON-TB Gold In-Tube and T-SPOT TB. False negative IGRA tests have been reported in 12% of active tuberculosis cases[6] and in 28·8% of patients with extrapulmonary tuberculosis.[7] The effects of latent tuberculosis infection tests on patient management outcomes or on tuberculosis control programmes

in high tuberculosis endemic countries remain to be defined. Cohort studies in low tuberculosis endemic countries indicate that IGRAs might predict progression of latent tuberculosis infection to active tuberculosis disease,[8,9] although they raise more questions than they answer. In contacts of active tuberculosis cases who progressed to active tuberculosis, 39% had a negative QuantiFERON-TB Gold test and 32% had a negative T-SPOT TB test.[8]

Of note, TST and IGRAs cannot differentiate between latent tuberculosis infection and active disease and they should not be used as diagnostic tests for active tuberculosis. In those apparently healthy individuals with a positive IGRA or TST, the decision to treat latent tuberculosis infection using one of several treatment regimens recommended by WHO[1] should not be taken lightly. Before latent tuberculosis infection treatment is commenced on the basis of a positive IGRA or TST test, it is crucial that active tuberculosis is ruled out by taking a thorough history and doing a physical examination and the relevant investigations. Those with weight loss, night sweats, elevated erythrocyte sedimentation rate or C-reactive protein, and abnormal imaging should be investigated further. People suspected of having active tuberculosis should receive the recommended quadruple therapy, and not latent tuberculosis infection treatment regimens. This therapy is particularly important in cases of extrapulmonary tuberculosis[7] and children[10] where the lack of access to clinical samples makes it difficult to accurately exclude active tuberculosis. Another difficult issue is that the preventive treatment regimens might not be suitable for individuals with latent tuberculosis infection who have been exposed to multidrug-resistant tuberculosis or extensively drug-resistant tuberculosis.[11]

Studies focused on host gene expression and blood RNA signatures symmetry during progression from latent tuberculosis infection to active disease show promise, although further development of easy-to-use, affordable point-of-care tests is needed.[12,13] For consistency of comparison of existing IGRAs and TST with newer tests, it would be prudent to use the evaluation framework[14] for new tests, which predict progression from latent tuberculosis infection to active clinical disease. More specific latent tuberculosis infection screening tests are urgently needed that reliably identify latent tuberculosis infection and predict the likelihood of latent tuberculosis infection progressing to active disease. That would be the most important contribution to programmatic management of latent tuberculosis infection, allowing accurate identification of latent infection, distinguish latent infection from active disease, and enable treatment specific to latent tuberculosis infection.

World leaders at the unprecedented United Nations General Assembly High Level meeting on tuberculosis,[15] in September, 2018, unanimously adopted a political declaration in which they committed to identify and treat 30 million people with latent tuberculosis infection, highlighting the importance of proactive screening of contacts of active tuberculosis cases and those most at risk of re-activating latent tuberculosis infection. For all their imperfections, the TST and IGRAs are the only WHO-approved latent tuberculosis infection screening tests that we have at present, and they must be used prudently and optimally following the latest WHO programmatic guidelines.[1]

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Revolutionary new treatment regimens for multidrug-resistant tuberculosis

Multidrug-resistant tuberculosis continues to be a major global public health crisis. WHO estimated that, in 2017, there were 458 000 cases of multidrug-resistant tuberculosis, defined as resistance to the two frontline drugs for tuberculosis, rifampicin and isoniazid.[1] A huge global burden of multidrug-resistant tuberculosis remains undiagnosed and untreated, with only one in four cases detected. Furthermore, just over half of those patients who are diagnosed with multidrug-resistant tuberculosis are being cured using WHO-approved treatment regimens.

Apart from inadequate facilities to diagnose multidrug-resistant tuberculosis, health services and patients in areas highly endemic for multidrug-resistant tuberculosis face major challenges. The treatment regimens are lengthy and involve expensive injectable agents, with considerable adverse effects, that require substantial patient support and follow-up to minimise toxicity, ensure cure, and reduce further emergence of resistance. The relative contributions of new and well established drugs to treat multidrug-resistant tuberculosis have informed the design of optimal multidrug-resistant tuberculosis regimens and their duration of treatment, and they serve as the basis for development of WHO multidrug-resistant tuberculosis therapeutic guidelines. In 2011, treatment for multidrug-resistant tuberculosis constituted 20 months, requiring an injectable drug for 8 months and inclusion of a fluoroquinolone. The pressure to reduce the long duration and high cost of treatment for multidrug-resistant tuberculosis led to shorter regimens being used under programmatic and trial conditions. In 2016 WHO endorsed, in select cases, on the basis of very low certainty in the evidence, a conditional recommendation for a shorter 9–12-month regimen that included injectables to treat multidrug-resistant tuberculosis.[2] Although intuitively appealing, the stringent criteria for its use meant that it was applicable to only a small proportion of individuals requiring treatment.[3]

A rapid WHO communication[4] published in August, 2018, made key changes to the recommended treatment for multidrug-resistant tuberculosis, prioritising oral drugs over injectables. For the first time ever, a new all-oral 20-month treatment regimen is now proposed, which is anticipated to be less toxic and more efficacious and to reduce hospitalisation rates.[5] The regimen recommends bedaquiline and linezolid together with levofloxacin or moxifloxacin and cycloserine or clofazimine. Injectable kanamycin and capreomycin are no longer required. Full WHO guidelines will follow soon. This revolutionary all oral regimen has the potential to radically change treatment delivery for multidrug-resistant tuberculosis.

The success of this WHO recommendation will depend on political and donor momentum, which needs to accelerate if the global multidrug-resistant tuberculosis crisis is to be curtailed and controlled. At the current slow rate of investment and progress this acceleration remains unrealistic. Implementation of the new recommendations must happen quickly with minimal disruption to health systems and