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# HIV a culprit in more than one million TB deaths in South Africa, study finds

HIV has dramatically increased tuberculosis (TB) incidence and mortality in South Africa, according to the first study to assess the impact of HIV and multiple TB interventions on the country's TB burden at a national level.

Between 1990 and 2019, the team behind the study found that 8.8 million people developed TB, and 2.1 million died. They also found that HIV was responsible for 4.8 million TB cases and 1.4 million deaths.

Published in the September issue of the *International Journal of Infectious Diseases*, the study used a dynamic TB transmission model to analyse TB incidence and deaths caused by HIV between 1990 and 2019. The study then estimated the reduction in TB incidence due to directly observed therapy (DOTS), antiretroviral therapy (ART), isoniazid preventive therapy (IPT), increased TB screening, and Xpert MTB/RIF.

According to the findings, interventions implemented by the South African TB program have led to notable reductions in TB incidence, with ART and increased screening contributing to most of the decline.

"Our model also showed that the other interventions — DOTS, IPT, and Xpert MTB/RIF — had modest impacts on TB incidence. For most of the interventions (increased screening, ART, and Xpert MTB/RIF), the impact on TB deaths was proportionately greater than the impact on TB incidence," said Mmamapudi Kubjane, researcher in the School of Public Health and Family Medicine at the University of Cape Town and lead author of the study.

South Africa is ranked among the top 20 high TB burden countries. The TB epidemic grew rapidly in the early 1990s, primarily driven by HIV. HIV infection is the strongest individual-level TB risk factor, increasing the risk of progression to TB disease and reactivation of latent TB infection, worsening treatment outcomes and increasing mortality.

With HIV being the strongest driver of the TB epidemic, Kubjane said the model estimated that even in the absence of HIV, TB incidence in South Africa would remain high. "This was demonstrated in the no-HIV counterfactual scenario, in which there were an estimated 235 cases per 100,000 population in 2019. This rate is much higher than the estimated TB incidence for industrialized regions, such as Europe and America. The high TB burden in the

HIV-negative population indicates other underlying factors that drive the epidemic - low rates of diagnosis and risk factors that increase susceptibility to TB disease," she said.

In 2019, the study found that the provision of ART led to a 20% reduction in TB incidence. "The benefits of ART in reducing incidence depend on CD4 count and duration of ART. HIV-positive individuals who initiate ART earlier at higher CD4 counts and stay on ART for longer experience the greatest benefits of ART," said Kubjane.

She noted that the effect of ART on reducing TB incidence increased during the mid-2000s when access to ART expanded in South Africa. Over time, the CD4 count threshold at which individuals can start ART has increased, and average ART durations have increased, consequently contributing to the substantial reduction in the population-level TB incidence.

Intensified TB screening also led to significant declines in TB incidence. Between 2005 and 2012, South Africa scaled-up efforts to identify TB cases and testing rates doubled. As a result, there were rapid reductions in TB incidence owing to increased TB screening during this period. In 2019, increased screening led to a 28% reduction in TB incidence.

The study found that reductions in TB incidence due to DOTS and IPT were less than 3% in all years.

Kubjane said the reasons for DOTS having minimal impact on TB may include high ongoing *Mycobacterium tuberculosis* transmission rates, high prevalence of substantial risk factors, such as HIV, which increase progression to disease, and the emergence of resistant TB. "Our findings of the minimal impact of DOTS align with studies that suggested that DOTS would have minimal impact in settings with a high HIV burden."

"The small population-level impact of IPT on TB incidence in HIV-positive individuals is consistent with other epidemiologic analyses, attributing the limited impact to the low implementation of IPT in South Africa. Other reasons may be because this HIV-positive population has a high risk of progression to disease or because IPT does not necessarily cure latent *Mycobacterium tuberculosis* infection in HIV-positive individuals," she said.

Study lead author, Mmamapudi Kubjane

Photo: Supplied

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