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Early HIV treatment improves survival in some patients with newly diagnosed TB

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Starting anti-HIV treatment within two weeks of the diagnosis of tuberculosis, or TB, improved survival among patients with both infections who had very low immune-cell counts, according to an analysis by researchers at the University of Pittsburgh Graduate School of Health. Those with strong immune systems, however, might benefit from waiting until after the end of the six-month TB treatment before initiating anti-HIV therapy, they found.

In a study published in the current issue of *Annals of Internal Medicine*, the team recommended updating physician guidelines to take the findings into account.

Infection with HIV can promote progression and re-infection to active TB after initial exposure to Mycobacterium tuberculosis, the organism that causes TB, explained senior author Jean B. Nachega, M.D., Ph.D., M.P.H., associate professor of infectious diseases and microbiology and of epidemiology, Pitt Public Health. Treating HIV and TB simultaneously is challenging for many reasons, including the requirement for patients to take multiple pills several times daily for each infection, drug-drug interactions and overlapping side effects.

"Current World Health Organization guidelines recommend starting TB treatment first, followed by HIV treatment as soon as possible within two to eight weeks for patients who have moderately to severely compromised immune systems, but there was not conclusive evidence to guide treatment in other levels of immune suppression," Dr. Nachega

said. "We aimed to investigate the optimal timing of HIV initiation in light of recent published randomized clinical trials on this topic."

The team systematically reviewed data from more than 4,500 people participating in eight randomized clinical trials of early initiation of HIV anti-retroviral therapy (ART) conducted in Asia, Africa and the United States. They found that survival rates were better among patients who started ART within two weeks of the initiation of TB treatment and who also had very low CD4 T-cell counts of less than 0.050 x 109cells/liter, as measured by a blood test which reflects severe immune system suppression due to HIV infection. Of note, early initiation also was associated with a two-fold increase in the frequency of a complication called TB-Immune Reconstitution Inflammatory Syndrome, which can be fatal in rare occasions. There was no evidence to support or refute a survival benefit for patients with CD4 counts between 0.050 and 0.220 x 109cells/liter.

"Our findings support guidelines recommending early initiation of ART in patients with a high degree of immune system compromise," Dr. Nachega said. "But delaying ART might be possible until the end of TB treatment with patients with CD4 counts greater than 0.220 x 109cells/liter, which could reduce the burden of taking two complex drug regimens at the same time."

However, Dr. Nachega noted that there is other emerging evidence showing the clinical and public health benefits associated with early initiation of HIV treatment, other than survival. Indeed, early treatment may be beneficial by decreasing comorbidities due to ongoing inflammation caused by HIV and decreasing HIV sexual transmission.

"Clinicians will need to weigh these benefits against the burden of co-administration of TB and HIV treatment on a case-by-case basis, but the overarching goal is likely to be a move toward treating all HIV-positive

people as early as possible," said Dr. Nachega.

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