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TB-HAART trial

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We read with interest Sayoki Mfinanga and colleagues' recent TB-HAART randomised trial in sub-Saharan Africa.[1] Initiation of antiretroviral therapy (ART) within 2 weeks of the start of pulmonary tuberculosis treatment for patients with CD4 cell counts more than 220 cells per μL did not confer any advantage over delayed ART initiation on a composite outcome of tuberculosis treatment failure, recurrence, and death. The authors concluded that comanagement of HIV infection and tuberculosis in sub-Saharan Africa remains challenging because of toxic effects, drug inter-actions, risk of antiretroviral drug resistance, pill burden, immune reconstitution inflammatory syndrome, and cost. Thus, they argued that WHO guidelines should be updated to recommend the delay of ART initiation until completion of tuberculosis treatment for patients with HIV and CD4 cell counts more than 220 cells per μL.

Although the authors noted concern about potential toxic effects of early ART initiation, their study showed no harm in terms of mortality, grade 3 and 4 adverse events, and immune reconstitution inflammatory syndrome. However, several studies have shown that even a short deferral of ART comes at the expense of recovery of CD4-positive T cells. Deferment of ART until the completion of tuberculosis treatment could also lead to loss to follow-up and subsequent morbidity and mortality.[2] Initiation of ART during tuberculosis treatment enables linkage between HIV and tuberculosis treatment programmes and could improve adherence. ART integration into tuberculosis treatment settings could help to improve ART uptake among patients with tuberculosis who also have HIV.[3]

Additionally, the ART regimen used in TB-HAART was a combination of zidovudine, lamivudine, and efavirenz. WHO guidelines recommend the use of tenofovir-based regimens, which are generally better tolerated than zidovudine.[4] The WHO guidelines published in 2013 recommend initiation of ART for all people living with HIV with CD4 counts 500 cells per μL. The guidelines have further promoted increased uptake of ART among HIV-positive patients with tuberculosis by removing the CD4 cell count requirement. Revision of the WHO guidelines could undo these gains by adding an additional barrier to ART initiation.

We applaud Mfinanga and colleagues for doing a strong study that responds to a gap in the scientific literature. However, we believe that the benefi ts of early ART are convincing,

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from the patient-level, to the broader programmatic perspective. We argue that evidence is insufficient to change WHO guidelines. Although more operational research is being done, the worldwide health community should focus on strengthening of health systems by integration of tuberculosis and HIV clinical services.

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