Does Long-Term ART Reduce TB Rates to Background Population Levels? Data from a National HIV cohort

RK Gupta[1,2], AE Brown[2], B Rice[2], HL Thomas[3], D Zenner[3,4], A Pozniak[5], I Abubakar[3], V Delpech[2]*, M Lipman[1]*

1. Division of Medicine, University College London, London, UK
2. HIV / STI Department, Centre for Infectious Disease Surveillance and Control, Public Health England, London, UK
3. TB Section, Centre for Infectious Disease Surveillance and Control, Public Health England, London, UK
4. Research Department of Infection and Population Health, University College London, London, UK
5. Chelsea & Westminster Hospitals NHS Foundation Trust, London, UK

**VD and ML contributed equally to this work*

Background:

- Anti-retroviral therapy (ART) is associated with a time-dependent decrease in HIV-associated tuberculosis (TB) incidence.
- However, it remains unclear whether TB rates in people receiving long-term ART remain above those in the background population.

Methods:

- This study used data from the national HIV & AIDS Reporting System (HARS) linked to the Enhanced TB Surveillance (ETS) system for England, Wales & Northern Ireland, using probabilistic matching.
- TB incidence in the HIV-positive cohort was calculated (2007-11) and compared to HIV-negative population rates in 2009 (middle year of HIV positive cohort), calculated using Office for National Statistics denominators (minus those seen for HIV care in 2009). TB cases were assumed to be HIV-negative if they did not match to a HIV record by 31/12/2011.
- Data on ART use, most recent CD4 count and ethnicity were available for 99%, 92% and 100% of person-years (PY) respectively.

Results:

- The HIV positive cohort included 79,919 adults with 231,664 PY of follow-up;. Of these, 33.8% were female, median age was 39 years, 50% were white, and 36% were black-African.
- 1,550 individuals (1.9%) in the HIV-positive cohort were diagnosed with TB during follow-up; there were 7,598 HIV-negative TB cases in 2009.

Figure 1: *TB incidence by months on ART, stratified by ethnicity. Error bars represent 95% confidence intervals*

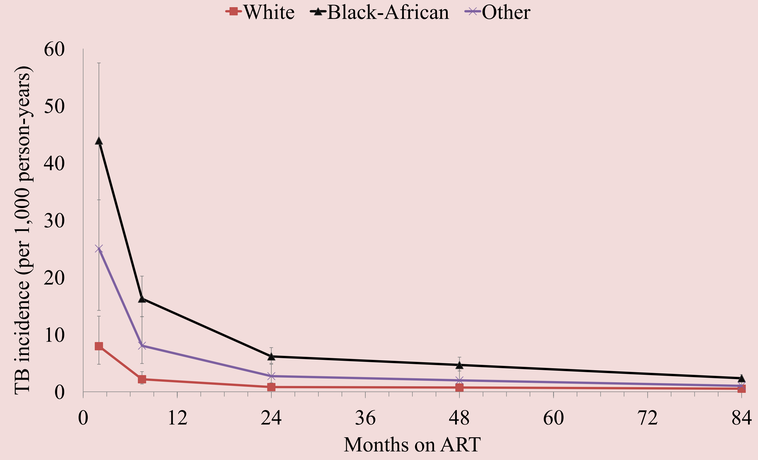
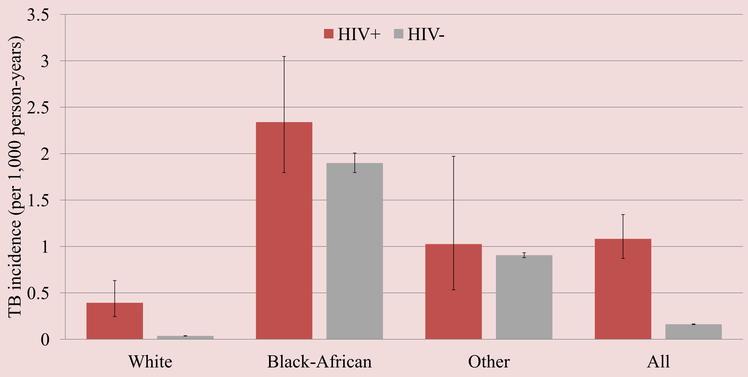


Figure 2: *TB incidence among adults in the HIV-positive cohort receiving ART with a most recent CD4 cell count of ≥500 cells/μL, compared to the background HIV-negative population, stratified by ethnicity.*



- Overall TB incidence in the HIV-positive cohort was 6.7/1,000 PY; this was significantly higher in black-Africans than white individuals (13.6/1,000 vs. 1.7/1,000; p<0.001) and declined as time on ART increased [**Figure 1**].
- TB rates among HIV-positive individuals during long-term ART (≥5 years) were similar to the background population in the black-African and other ethnic groups, but remained considerably higher than the background population in the white ethnic group. This elevated incidence in the white ethnic group persisted when analysis was restricted to person-time on ART with CD4 count ≥500 cells/μL [**Figure 2**].
- Among white individuals diagnosed with incident TB while receiving ART with CD4 ≥500 cells/μL (n=17) and for whom data were available, 3/13 had a social risk factor for TB, 16/16 had a suppressed viral load, and 13/16 were UK-born.
- TB incidence was also computed over a longer time period in the HIV-positive cohort (2002-2011) to test the findings of the main analysis; this made little difference to the results..

Conclusions:

- TB incidence in HIV-positive individuals receiving long-term ART is similar to background population rates in black-Africans, but remains high regardless of HIV status in this ethnic group.
- In the white ethnic group, while TB rates are lower overall, HIV infection is associated with elevated TB incidence despite effective ART, compared to the background population. Underlying explanations for this require further evaluation.