Supplemental table 1. Definitions of exposure variables

|  |  |
| --- | --- |
| **Variable name** | **Definition** |
| Bacteriological confirmation of TB | Diagnosed by GeneXpert ® MTB/RIF |
| Clinical diagnosis of TB | Indicated if the participant was receiving combination therapy for active TB in the absence of bacteriological confirmation. |
| History of pulmonary TB | Any of the following WHO codes abstracted from the participant’s medical record: W38.1 (Positive Gene Expert), W36.1 (Smear +), or W50.0 prior to enrollment |
| Hyperglycemia | A fasting glucose >99 mg/dL, non-fasting glucose >199 mg/dL, or receipt of hypoglycemic medications. |
| Body Mass Index (BMI) | Calculated using participants’ height and weight and categorized as underweight (<18.5), normal (18.5–24.9), or overweight/obese (≥25) |

Supplemental table 2. Complete case analysis: Enrollment characteristics of PLWH by TB co-occurrence status

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Totaln=3,000 | No TBn=2,926 | TB casen=74 | p-value† |
| Age (years) |  |  |  | **<0.001** |
|  15-24 | 472 (15.7%) | 466 (15.9%) | 6 (8.1%) |  |
|  25-39 | 1,303 (43.4%) | 1,253 (42.8%) | 50 (67.6%) |  |
|  40-49 | 772 (25.7%) | 758 (25.9%) | 14 (18.9%) |  |
|  50+ | 453 (15.1%) | 449 (15.3%) | 4 (5.4%) |  |
| Age (years)\* | 37.6 (29.7-45.5) | 37.6 (29.7-45.6) | 35.0 (28.7-39.6) |  0.050 |
| Sex |  |  |  |  **0.042** |
|  Male | 1,237 (41.2%) | 1,198 (40.9%) | 39 (52.7%) |  |
|  Female | 1,763 (58.8%) | 1,728 (59.1%) | 35 (47.3%) |  |
| Clinical site |  |  |  |  0.19 |
|  Kayunga, Uganda | 537 (17.9%) | 524 (17.9%) | 13 (17.6%) |  |
|  South Rift Valley, Kenya | 1,048 (34.9%) | 1,023 (35.0%) | 25 (33.8%) |  |
|  Kisumu West, Kenya | 519 (17.3%) | 509 (17.4%) | 10 (13.5%) |  |
|  Mbeya, Tanzania | 555 (18.5%) | 534 (18.3%) | 21 (28.4%) |  |
|  Abuja & Lagos Nigeria | 341 (11.4%) | 336 (11.5%) | 5 (6.8%) |  |
| Marital status |  |  |  |  0.54 |
|  Not married | 1,403 (46.8%) | 1,371 (46.9%) | 32 (43.2%) |  |
|  Married | 1,597 (53.2%) | 1,555 (53.1%) | 42 (56.8%) |  |
| Education |  |  |  |  **0.004** |
|  None or some primary | 963 (32.1%) | 950 (32.5%) | 13 (17.6%) |  |
|  Primary or some secondary | 1,212 (40.4%) | 1,169 (40.0%) | 43 (58.1%) |  |
|  Secondary and above | 825 (27.5%) | 807 (27.6%) | 18 (24.3%) |  |
| Currently employed |  |  |  |  0.43 |
|  No | 1,854 (61.8%) | 1,805 (61.7%) | 49 (66.2%) |  |
|  Yes | 1,146 (38.2%) | 1,121 (38.3%) | 25 (33.8%) |  |
| Year enrolled |  |  |  |  0.94 |
|  2013-2017 | 2,667 (88.9%) | 2,601 (88.9%) | 66 (89.2%) |  |
|  2018-2020 | 333 (11.1%) | 325 (11.1%) | 8 (10.8%) |  |
| Total # People in household |  |  |  |  0.91 |
|  $\leq $3 | 947 (31.6%) | 923 (31.5%) | 24 (32.4%) |  |
|  >3-6 | 1,424 (47.5%) | 1,388 (47.4%) | 36 (48.6%) |  |
|  >6 | 629 (21.0%) | 615 (21.0%) | 14 (18.9%) |  |
| Consume alcohol |  |  |  |  0.98 |
|  No | 2,435 (81.2%) | 2,375 (81.2%) | 60 (81.1%) |  |
|  Yes | 565 (18.8%) | 551 (18.8%) | 14 (18.9%) |  |
| Smoker |  |  |  |  0.87 |
|  No | 2,867 (95.6%) | 2,796 (95.6%) | 71 (95.9%) |  |
|  Yes | 133 (4.4%) | 130 (4.4%) | 3 (4.1%) |  |
| Recreational drug use |  |  |  |  0.48 |
| No | 2,920 (97.3%) | 2,847 (97.3%) | 73 (98.6%) |  |
| Yes | 80 (2.7%) | 79 (2.7%) | 1 (1.4%) |  |
| Ever been incarcerated |  |  |  |  **0.038** |
|  No | 2,690 (89.7%) | 2,629 (89.8%) | 61 (82.4%) |  |
|  Yes | 310 (10.3%) | 297 (10.2%) | 13 (17.6%) |  |
| Hyperglycemiaa |  |  |  |  0.67 |
|  No | 2,713 (90.4%) | 2,645 (90.4%) | 68 (91.9%) |  |
|  Yes | 287 (9.6%) | 281 (9.6%) | 6 (8.1%) |  |
| Time since HIV diagnosis |  |  |  | **<0.001** |
|  <1 year | 1,140 (38.0%) | 1,097 (37.5%) | 43 (58.1%) |  |
|  1-5 years | 763 (25.4%) | 742 (25.4%) | 21 (28.4%) |  |
|  >5 years | 1,097 (36.6%) | 1,087 (37.1%) | 10 (13.5%) |  |
| Time since HIV diagnosis (years)\* | 2.9 (0.2-6.7) | 3.0 (0.2-6.8) | 0.4 (0.1-3.3) | **<0.001** |
| Duration in HIV care |  |  |  | **<0.001** |
|  <6 months | 1,023 (34.1%) | 976 (33.4%) | 47 (63.5%) |  |
|  6 months to <2 years | 406 (13.5%) | 401 (13.7%) | 5 (6.8%) |  |
|  >2 years | 1,571 (52.4%) | 1,549 (52.9%) | 22 (29.7%) |  |
| Time since HIV diagnosis (years)\* | 2.4 (0.1-6.4) | 2.6 (0.2-6.4) | 0.1 (0.0-2.9) | **<0.001** |
| Duration on ART |  |  |  | **<0.001** |
|  ART naive | 875 (29.2%) | 841 (28.7%) | 34 (45.9%) |  |
|  <6 months | 420 (14.0%) | 404 (13.8%) | 16 (21.6%) |  |
|  6 months to <2 years | 410 (13.7%) | 404 (13.8%) | 6 (8.1%) |  |
|  2 years to <4 years | 334 (11.1%) | 327 (11.2%) | 7 (9.5%) |  |
|  >4 years | 961 (32.0%) | 950 (32.5%) | 11 (14.9%) |  |
| Duration on ART (years)\* | 3.3 (0.7-6.3) | 3.4 (0.7-6.3) | 1.1 (0.1-4.0) | **<0.001** |
| ART regimen |  |  |  |  **0.033** |
|  AZT/NVP/3TC | 477 (15.9%) | 472 (16.1%) | 5 (6.8%) |  |
|  AZT/EFV/3TC | 163 (5.4%) | 160 (5.5%) | 3 (4.1%) |  |
|  TDF/NVP/3TC | 168 (5.6%) | 166 (5.7%) | 2 (2.7%) |  |
|  PI-based | 174 (5.8%) | 170 (5.8%) | 4 (5.4%) |  |
|  TLE | 933 (31.1%) | 910 (31.1%) | 23 (31.1%) |  |
|  Other | 210 (7.0%) | 207 (7.1%) | 3 (4.1%) |  |
|  ART naïve | 875 (29.2%) | 841 (28.7%) | 34 (45.9%) |  |
| Missed doses ART (past month) |  |  |  |  **0.002** |
|  Not on ART | 875 (29.2%) | 841 (28.7%) | 34 (45.9%) |  |
|  No missed doses ART | 1,814 (60.5%) | 1,776 (60.7%) | 38 (51.4%) |  |
|  Missed 1+ doses ART | 311 (10.4%) | 309 (10.6%) | 2 (2.7%) |  |
| Body mass index (BMI) |  |  |  | **<0.001** |
|  Underweight | 339 (11.3%) | 319 (10.9%) | 20 (27.0%) |  |
|  Normal | 1,915 (63.8%) | 1,869 (63.9%) | 46 (62.2%) |  |
|  Overweight/obese | 746 (24.9%) | 738 (25.2%) | 8 (10.8%) |  |
| CD4 count |  |  |  | **<0.001** |
|  <200 cells/mm3 | 567 (18.9%) | 538 (18.4%) | 29 (39.2%) |  |
|  >200 cells/mm3 | 2,433 (81.1%) | 2,388 (81.6%) | 45 (60.8%) |  |
| Viral load |  |  |  | **<0.001** |
|  <6 months on ART | 1,291 (43.0%) | 1,241 (42.4%) | 50 (67.6%) |  |
|  <1000 copies/mL | 1,506 (50.2%) | 1,487 (50.8%) | 19 (25.7%) |  |
|  >1000 copies/mL | 203 (6.8%) | 198 (6.8%) | 5 (6.8%) |  |
| History of pulmonary TBb |  |  |  | **<0.001** |
|  No | 2,800 (93.3%) | 2,749 (94.0%) | 51 (68.9%) |  |
|  Yes | 200 (6.7%) | 177 (6.0%) | 23 (31.1%) |  |
| TB diagnosis methodc |  |  |  | *-* |
| Bacteriological |  |  | 58 (%) |  |
| Clinical |  |  | 16 (%) |  |

Data are presented as n (column %).

\*Data presented as median (Interquartile range)

†P-values were calculated using Pearson’s chi-squared tests; Bold indicates significance at p<0.05.

Abbreviations: PLWH, people living with HIV; TB, tuberculosis; ABC, abacavir; 3TC, lamivudine; AZT, azidothymidine (zidovudine); TDF, tenofovir; TLE, tenofovir/lamivudine/efavirenz

aHyperglycemia was defined as a fasting glucose >99 mg/dL, non-fasting glucose >199 mg/dL, or receipt of hypoglycemic medications.

bHistory of pulmonary TB was defined as any of the following WHO codes abstracted from the participant’s medical record: W38.1 (Positive Gene Expert), W36.1 (Smear +), or W50.0.

c Bacteriological confirmation of TB was diagnosed by GeneXpert ® MTB/RIF; Clinical diagnosis of TB was indicated if the participant was receiving combination therapy for active TB in the absence of bacteriological confirmation.

Supplemental Table 3. Complete case analysis: Factors associated with prevalent TB at enrollment among PLWH

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | OR (95% CI) | p-value | aOR (95% CI) † | p-value |
| Age (years) |  |  |  |  |
|  15-24 | Ref |  | - |  |
|  25-39 | **3.10 (1.32-72.7)** | 0.009 | **3.12 (1.21-8.01)** | **0.01** |
|  40-49 | 1.43 (0.54-3.75) | 0.46 | 1.64 (0.57-4.73) | 0.35 |
|  50+ | 0.69 (0.19-2.46) | 0.57 | 0.78 (0.20-3.04) | 0.72 |
| Sex |  |  |  |  |
|  Female | Ref |  | - |  |
|  Male | **1.61 (1.01-2.55)** | 0.04 | 1.35 (0.81-2.27) | 0.25 |
| Clinical site |  |  |  |  |
|  Kayunga, Uganda | Ref |  | - |  |
|  South Rift Valley, Kenya | 0.98 (0.50-1.94) | 0.97 | 1.12 (0.51-2.46) | 0.76 |
|  Kisumu West, Kenya | 0.79 (0.34-1.82) | 0.58 | 0.92 (0.36-2.3) | 0.86 |
|  Mbeya, Tanzania | 1.59(0.79-3.20) | 0.20 | 1.70 (0.76-3.78) | 0.19 |
|  Abuja & Lagos Nigeria | 0.60 (0.21-1.69) | 0.33 | 0.63 (0.19-2.10) | 0.45 |
| Education |  |  |  |  |
|  None or some primary | Ref |  | - |  |
|  Primary or some secondary | **2.68 (1.43-5.02)** | **0.002** | **2.65 (1.36-5.19)** | **0.004** |
|  Secondary and above | 1.63 (0.79-3.35) | 0.183 | **2.32 (1.02-5.27)** | **0.04** |
| Ever been incarcerated |  |  |  |  |
|  No | Ref |  | - |  |
|  Yes | **1.88 (1.02-3.47)** | **0.042** | 1.67 (0.81-3.40) | 0.15 |
| Time since HIV diagnosis |  |  |  |  |
| >5 years | Ref |  | - |  |
| 1-5 years | **3.08 (1.44-6.57)** | **0.004** | **2.61 (1.15-5.92)** | **0.021** |
| <1 year  | **4.26 (2.13-8.52)** | **<0.001** | 1.69 (0.64-4.48) | 0.28 |
| Duration in HIV care |  |  |  |  |
| >2 years | Ref |  | - |  |
| 6 months to <2 years | 0.87 (0.33-2.33) | 0.79 |  |  |
| <6 months  | **3.39 (2.03-5.66)** | **<0.001** |  |  |
| ART regimen |  |  |  |  |
|  TLE | Ref |  | - |  |
|  AZT/NVP/3TC | 0.42 (0.16-1.11) | 0.08 | 0.94 (0.31-2.86) | 0.92 |
|  AZT/EFV/3TC | 0.74 (0.22-2.49) | 0.63 | 1.16 (0.31-4.31) | 0.82 |
|  TDF/NVP/3TC | 0.48 (0.11-2.04) | 0.32 | 0.97 (0.20-4.70) | 0.97 |
|  PI-based | 0.93 (0.32-2.73) | 0.89 | 1.94 (0.578-6.63) | 0.28 |
|  Other | 0.57 (0.17-1.92) | 0.36 | 1.23 (0.32-4.72) | 0.31 |
|  ART naïve | 1.59 (0.93-2.74) | 0.08 | 1.04 (0.54-2.00) | 0.88 |
| Body mass index (BMI) |  |  |  |  |
|  Normal | Ref |  | - |  |
|  Underweight | **2.55 (1.48-4.36)** | **0.001** | **2.44 (1.36-4.35)** | **0.002** |
|  Overweight/obese | **0.44 (0.21-0.94)** | **0.03** | 0.46 (0.21-1.01) | 0.05 |
| CD4 count |  |  |  |  |
|  >200 cells/mm3 | Ref |  | - |  |
|  <200 cells/mm3  | **2.86 (1.77-4.60)** | **<0.001** | 1.54 (0.91-2.64) | 0.11 |
| Viral load |  |  |  |  |
|  <1000 copies/mL | Ref |  | - |  |
|  <6 months on ART | **3.15 (1.84-5.37)** | **<0.001** | 2.06 (0.81-5.20) | 0.12 |
|  >1000 copies/mL | 1.97(0.73-5.35) | 0.18 | 1.49 (0.52-4.29) | 0.45 |

Bold indicates significance at p<0.05. Abbreviations: TB, tuberculosis; PLWH, people living with HIV; OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; ART, antiretroviral therapy, ABC, abacavir; 3TC, lamivudine; AZT, azidothymidine (zidovudine); TDF, tenofovir; TLE, tenofovir/lamivudine/efavirenz

†Model building: includes age, sex, site plus all predictors with a p-value of <0.2 in the bivariate analyses; Dropped duration in HIV care due to collinearity; Removed missed doses and duration on ART as analysis was not restricted to PLWH on ART

Supplemental Table 4. Complete case analysis-Crude incidence rate of TB among PLWH per 100,000 person-years

|  |  |
| --- | --- |
|  | TB incidence rate (95% CI) |
| Overall | 482 (377-616) |
| Program |  |
|  Kayunga, Uganda | 397 (213-738) |
| South Rift Valley, Kenya | 590 (407-854) |
| Kisumu West, Kenya | 577 (348-958) |
| Mbeya, Tanzania | 339 (161-711) |
| Abuja & Lagos, Nigeria | 295 (111-786) |

Abbreviations: TB, tuberculosis; PLWH, people living with HIV; CI, confidence interval

Supplemental Table 5. Complete case analysis-Factors associated with incident TB among PLWH (n=45)~

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | HR (95% CI) | p-value | aHR (95% CI) † | p-value |
| Age (years) \*\*‡ |  |  |  |  |
|  15-39\* | Ref |  | **-** |  |
|  40-49 | **2.35 (1.16-4.78)** | **0.02** | **2.57 (01.25-5.30)** | **0.01** |
|  50+ | 1.75 (0.76-4.01) | 0.18 | 1.90 (0.79-4.53) | 0.14 |
| Sex |  |  |  |  |
|  Female | Ref |  | - |  |
|  Male | 1.49 (0.82-2.66) | 0.18 | 1.24 (0.66-2.34) | 0.48 |
| Clinical site |  |  |  |  |
|  Kayunga, Uganda | Ref |  | - |  |
|  South Rift Valley, Kenya | 1.13 (0.51-2.46) | 0.31 | 1.11 (0.488-2.53) | 0.80 |
|  Kisumu West, Kenya | 0.55 (0.21-1.43) | 0.22 | 0.50 (0.17-1.40) | 0.19 |
|  Mbeya, Tanzania | 0.14 (0.01-1.11) | 0.06 | 0.15 (0.01-1.24) | 0.80 |
|  Abuja & Lagos Nigeria | **0.26 (0.08-0.89)** | **0.03** | **0.26 (0.07-0.92)** | **0.03** |
| Marital status‡ |  |  |  |  |
| Married\* | Ref |  |  |  |
| Not Married | 0.76 (0.41-1.41) | 0.38 |  |  |
| Highest level of education‡ |  |  |  |  |
|  None or some primary\* | Ref |  |  |  |
|  Primary or some secondary | 1.17 (0.57-2.39) | 0.66 |  |  |
|  Secondary and above | 0.94 (0.43-2.01) | 0.87 |  |  |
| Employment status‡ |  |  |  |  |
| Unemployed | Ref |  |  |  |
| Employed | 0.92 (0.51-1.67) | 0.78 |  |  |
| Total no. people in household‡ |  |  |  |  |
| <3\* | Ref |  |  |  |
| 4-6 | 0.88 (0.43-1.77) | 0.72 |  |  |
| >6 | 1.53 (0.71-3.26) | 0.27 |  |  |
| Alcohol use‡ |  |  |  |  |
| No\* | Ref |  |  |  |
| Yes | 1.13 (0.50-2.54) | 0.75 |  |  |
| Cigarette use‡ |  |  |  |  |
| No\* | Ref |  |  |  |
| Yes | 0.95 (0.13-6.88) | 0.95 |  |  |
| Time since HIV diagnosis\*\*‡ |  |  |  |  |
| >5 years\* | Ref |  | - |  |
| <5 years | 1.71 (0.87-3.32) | 0.11 | 2.06 (0.95-4.45) | 0.06 |
| Duration in HIV care\*\*‡ |  |  |  |  |
| >2 years\* | Ref |  |  |  |
| <2 years | 0.69 (0.25-1.89) | 0.47 |  |  |
| ART regimen‡ |  |  |  |  |
|  TLE | Ref |  | - |  |
|  AZT/NVP/3TC | 0.69 (0.26-1.84) | 0.47 | 0.96 (0.33-2.78) | 0.95 |
|  AZT/EFV/3TC | 0.51 (0.06-3.84) | 0.52 | 0.44 (0.05-3.47) | 0.43 |
|  TDF/NVP/3TC | 1.62 (0.61-4.32) | 0.33 | 2.01 (0.66-6.09) | 0.21 |
|  PI-based | 0.80 (0.32-1.97) | 0.63 | 0.81 (0.31-2.11) | 0.66 |
|  Other | **0.122 (0.03-0.46)** | **0.002** | **0.13 (0.03-0.53)** | **0.004** |
|  ART naïve | 1.49 (0.34-6.44) | 0.59 | 0.65 (0.09-4.61) | 0.66 |
| Body mass index (BMI) ‡ |  |  |  |  |
|  Normal\* | Ref |  | - |  |
|  Underweight | 1.40 (0.54-3.61) | 0.48 | 1.31 (0.49-3.41) | 0.58 |
|  Overweight/obese | 0.52 (0.24-1.09) | 0.08 | 0.64 (0.29-1.39) | 0.26 |
| CD4 count‡ |  |  |  |  |
|  >200 cells/mm3\* | Ref |  | - |  |
|  <200 cells/mm3  | **3.25 (1.59-6.64)** | **0.001** | 2.19 (0.96-4.99) | 0.06 |
| Viral load‡ |  |  |  |  |
|  <1000 copies/mL\* | Ref |  | - |  |
|  <6 months on ART | 1.92 (0.56-6.55) | 0.29 | 2.25 (0.41-12.3) | 0.34 |
|  >1000 copies/mL | **2.86 (1.31-6.25)** | **0.008** | 2.17 (0.91-5.23) | 0.08 |

Bold indicates significance at p<0.05. Abbreviations: TB, tuberculosis; PLWH, people living with HIV; HR, hazard ratio; aHR, adjusted hazard ratio; CI, confidence interval; ABC, abacavir; 3TC, lamivudine; AZT, azidothymidine (zidovudine); TDF, tenofovir; TLE, tenofovir/lamivudine/efavirenz; TLD, tenofovir/lamivudine/dolutegravir.

~Participants with TB at enrollment visit did not contribute to time to event models.

\* Missing data were folded into reference category.

†Model building: includes age, sex, site plus all predictors with a p-value of <0.2 in the bivariate analyses; Removed missed doses and duration on ART as analysis was not restricted to PLWH on ART; History of TB was dropped as we did not collect information on the outcome that would distinguish between latent reinfection or a new episode of post primary infection which is beyond the scope of this paper.

‡Time varying covariates included in the model

\*\*Categories collapsed due to small cell sizes