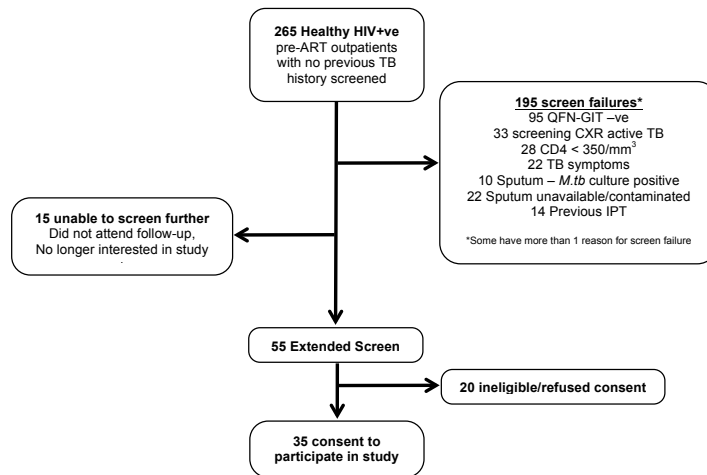


## Supplementary information

**a**



**b**

| Clinical characteristics of 265 screened participants  |               |                                                |        |
|--------------------------------------------------------|---------------|------------------------------------------------|--------|
| Parameter                                              | Result        | Parameter                                      | Result |
| Age med. – Med. (IQR)                                  | 32 (28–38)    | Sputum M.tb culture positive ( <i>n</i> = 244) | 4.1%   |
| Female                                                 | 85%           | TB symptom screen positive                     | 8.7%   |
| CD4 (/mm <sup>3</sup> ) – Med. (IQR) ( <i>n</i> = 259) | 520 (429–673) | CXR – Active TB                                | 13%    |
| CD4 > 350/mm <sup>3</sup>                              | 89%           | CXR – Inactive TB                              | 32%    |
| QFN-GIT Positive                                       | 64%           | Previous IPT – ( <i>n</i> = 262)               | 5.3%   |

### Supplementary Figure 1 – Screening approach and participant characteristics

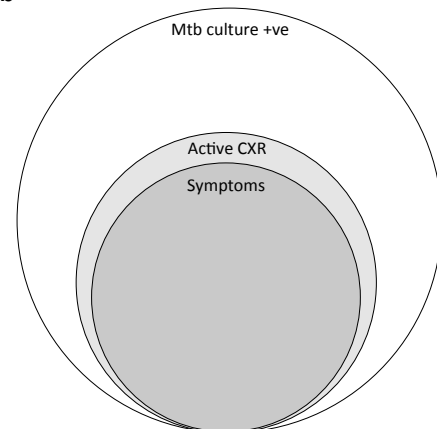
a. Screening approach and screen failures

b. Clinical characteristics of 265 screened participants

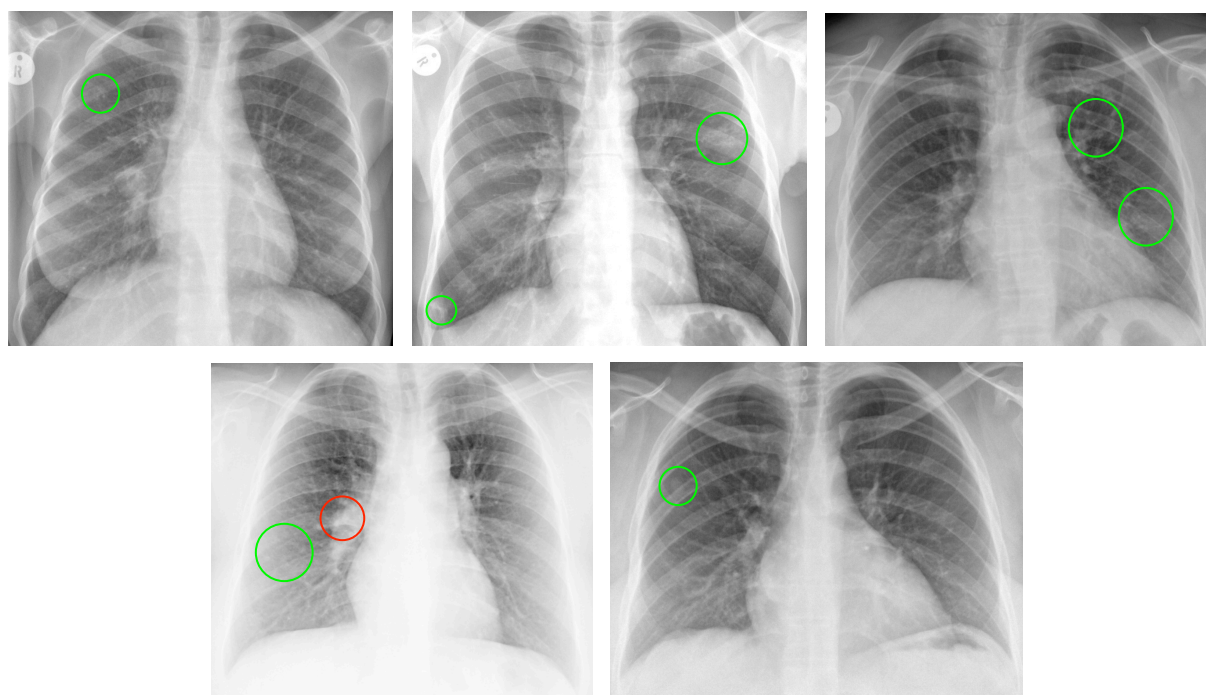
a

| Clinical characteristics of participants excluded at screening with prevalent TB from 244 participants with sputum culture results |                  |                  |         |
|------------------------------------------------------------------------------------------------------------------------------------|------------------|------------------|---------|
| Parameter                                                                                                                          | Culture positive | Culture negative | p value |
| Number                                                                                                                             | 10               | 234              | NA      |
| Age – Med. (IQR)                                                                                                                   | 30.5 (26–38)     | 33 (28–38)       | 0.39    |
| Female                                                                                                                             | 90%              | 85.9%            | 1.00    |
| CD4 (/mm <sup>3</sup> ) – Med. (IQR)                                                                                               | 502 (448–605)    | 527 (432–685)    | 0.58    |
| QFN-GIT Positive                                                                                                                   | 90%              | 64.1%            | 0.172   |
| TB symptoms                                                                                                                        | 40%              | 7.2%             | 0.007   |
| CXR – Active TB                                                                                                                    | 50%              | 11.5%            | 0.026   |
| Previous IPT                                                                                                                       | 0%               | 6.0%             | 1.0     |

b



c



**Supplementary Figure 2 – Screened participants excluded with prevalent TB (sputum culture positive for M.tb)**

a. Comparison of clinical characteristics between those screened with and without prevalent TB. The gaussian distribution of the data was determined by Shapiro-Wilk test and variance compared by F-test. Non-parametric data then compared using Mann-Whitney *U* test and parametric data compared using t-test. Proportions were compared by  $\chi^2$  test or Fisher's exact test (if the contingency included a number  $\leq 5$ ).

b. Area proportional Venn diagram showing overlap of symptoms and CXR with evidence of active TB.

c. Screening CXR for 5 participants with prevalent TB with evidence of active TB on CXR. Green circle outlines parenchymal lesions and red circle hilar lymphadenopathy.

| Clinical characteristics of 35 participants by PET/CT status |                             |                          |                                                   |         |
|--------------------------------------------------------------|-----------------------------|--------------------------|---------------------------------------------------|---------|
| Parameter                                                    | Undergoing PET/CT<br>(n=35) | Subclinical TB<br>(n=10) | Latent TB – no<br>subclinical pathology<br>(n=25) | p value |
| Age years – Med. (IQR)                                       | 31 (27–38)                  | 29.5 (27–35)             | 32 (27–39)                                        | 0.17    |
| Female                                                       | 91%                         | 90%                      | 92%                                               | 1.00    |
| CD4 (/mm <sup>3</sup> ) – Med. (IQR)                         | 517 (393–658)               | 406 (384–548)            | 517 (435–724)                                     | 0.14    |
| Viral load (copies/ml) – Med. (IQR)                          | 10,800 (1,982–26,052)       | 18,949 (6,878–51,166)    | 9,958 (625–20,702)                                | 0.07    |
| WHO clinical – stage 1 (%) : stage 2 (%)                     | 80 : 20                     | 70 : 30                  | 84 : 16                                           | 0.38    |
| Years HIV positive – Med. (IQR)                              | 2.1 (0.8–5.2)               | 4.5 (0.8–7.5)            | 1.7 (0.9–3.5)                                     | 0.32    |
| CRP (mg/L) Med(IQR)                                          | 1.9 (1–4)                   | 2.1 (1–4)                | 1.9 (1–3.9)                                       | 0.95    |
| WCC (x10 <sup>9</sup> /L) – Med. (IQR)                       | 5.34 (4.49–6.53)            | 5.59 (4.24–7.38)         | 5.34 (4.92–6.42)                                  | 0.97    |
| ESR (mm/hr) – Med. (IQR)*                                    | 37.5 (27–50)                | 41 (28–83)               | 36 (26–46.5)                                      | 0.39    |
| Pulse (bpm) – Med. (IQR)                                     | 71 (67–75)                  | 74 (68–75)               | 70 (67–75)                                        | 0.23    |
| Respiratory rate (brpm) – Med. (IQR)                         | 16 (16–19)                  | 16 (16–18)               | 16 (16–20)                                        | 0.95    |
| Temperature (°C) – Med. (IQR)                                | 35.9 (35.5–36.4)            | 36.0 (35.5–36.6)         | 35.8 (35.6–36.5)                                  | 1.00    |
| Systolic Blood Pressure (mmHg) – Med. (IQR)                  | 119 (108–129)               | 107 (104–118)            | 123 (116–129)                                     | 0.08    |
| QFN-GIT TBAg-Nil (IU/ml) – Med. (IQR)                        | 1.76 (0.59–7.52)            | 4.57 (0.69–9.1)          | 1.76 (0.59–4.11)                                  | 0.53    |
| Screening CXR – Inactive TB                                  | 40%                         | 60%                      | 32%                                               | 0.23    |
| Screening CXR – Active TB                                    | 0%                          | 0%                       | 0%                                                | 1.00    |
| BMI (kg/m <sup>2</sup> ) – Med. (IQR)                        | 28.7 (24.5–33.3)            | 24.8 (23.3–29.5)         | 28.8 (26.8–34.1)                                  | 0.09    |
| % weight change/28 days – Med. (IQR)                         | –0.60% (–1.09–+0.42)        | –0.84% (–1.38– –0.50)    | –0.24% (–1.03–+0.93)                              | 0.10    |
| History of household contact **                              | 46%                         | 40%                      | 48%                                               | 0.72    |
| History of TB treatment or IPT                               | 0%                          | 0%                       | 0%                                                | 1.00    |
| BCG scar (n=34)                                              | 37%                         | 33%                      | 40%                                               | 0.72    |
| Never smoked                                                 | 89%                         | 90%                      | 88%                                               | 1.00    |
| Current Biomass exposure (n=34)                              | 2.9%                        | 0%                       | 4.2%                                              | 1.00    |
| Never drunk alcohol                                          | 80%                         | 80%                      | 80%                                               | 1.00    |
| Unemployed                                                   | 63%                         | 40%                      | 72%                                               | 0.12    |

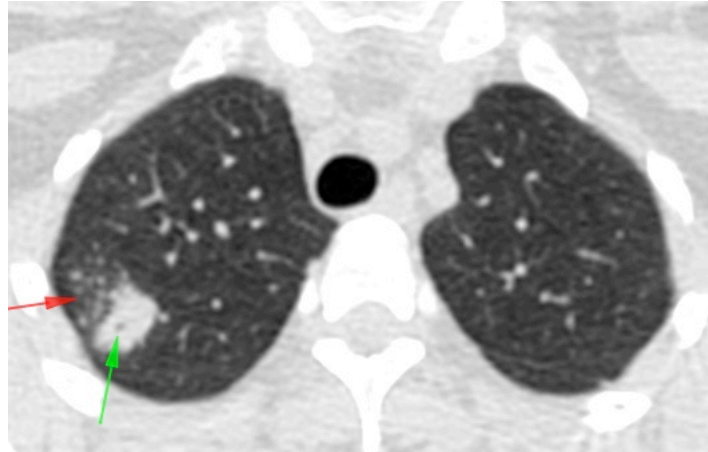
**Supplementary Table 1 – Participant characteristics in those with and without subclinical pathology**

Clinical characteristic of the 35 recruited participants on day of screening. The gaussian distribution of the data was determined by Shapiro – Wilk test and variance compared by *F* – test. Non-parametric data then compared using Mann – Whitney *U* test and parametric data compared using *t* – test. Proportions were compared by  $\chi^2$  test or Fisher’s exact test (if the contingency included a number  $\leq 5$ ).

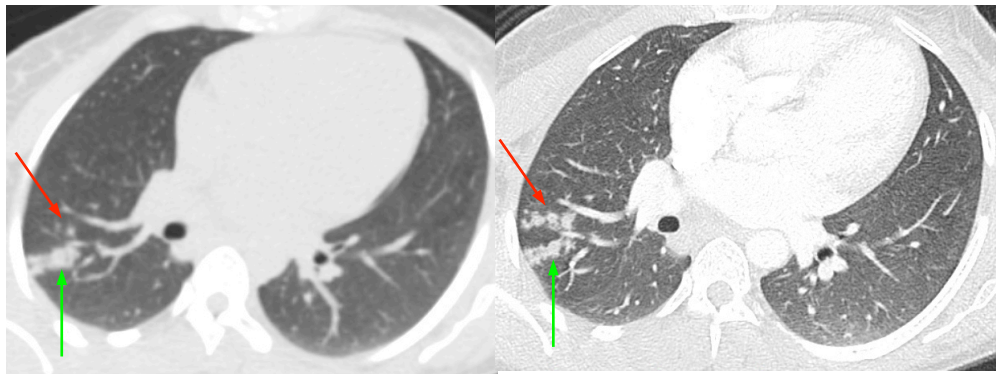
\* ESR commonly raised in health HIV infected persons. \*\* = TB contact median of 7 years previously (IQR 2.5 – 17 years).

CRP = C – reactive protein, WCC = White cell count, ESR = Erythrocyte Sedimentation Rate, WHO = World Health Organization, BMI = Body Mass Index, BCG = Bacillus Calmette-Guérin vaccine, % weight change/28 days = change in weight over screening period as a percentage (standardized as per 28 days)

**a**



**b**



**Supplementary Figure 3 – Radiographic images showing disease extent and progression**

a. Coronal section of CT component of initial FDG-PET/CT in participant (labelled “6” in **Fig. 1e**) who developed symptoms seven days following scan and was culture positive (smear negative). Green arrow shows small area of cavitation within dense consolidation surrounded by area of tree-in-bud opacification (red arrow)

b. Multi-planar reconstructions (MPR) of CT images of same participant (labelled “5” in **Fig. 1e**) 4 weeks apart (2<sup>nd</sup> CT scan (with intravenous contrast) clinically indicated). Left panel from initial FDG-PET/CT scan shows area of infiltration, which has progressed down adjacent lobule in 2<sup>nd</sup> scan in right panel 4 weeks later. Patient developed TB symptoms 30 days after initial scan but was sputum culture negative. Symptoms and radiographic changes improved with introduction of standard TB therapy (2HRZE/4HR).