Journal Reading

A Longitudinal Study on Latent TB Infection Screening and Its Association With TB Incidence in HIV Patients

Ngai Sze Wong, Chi Chiu Leung, Kenny Chi Wai Chan, Wai Kit Chan, Ada Wai Chi Lin, & Shui Shan Lee

SCIENTIFIC REPORTS

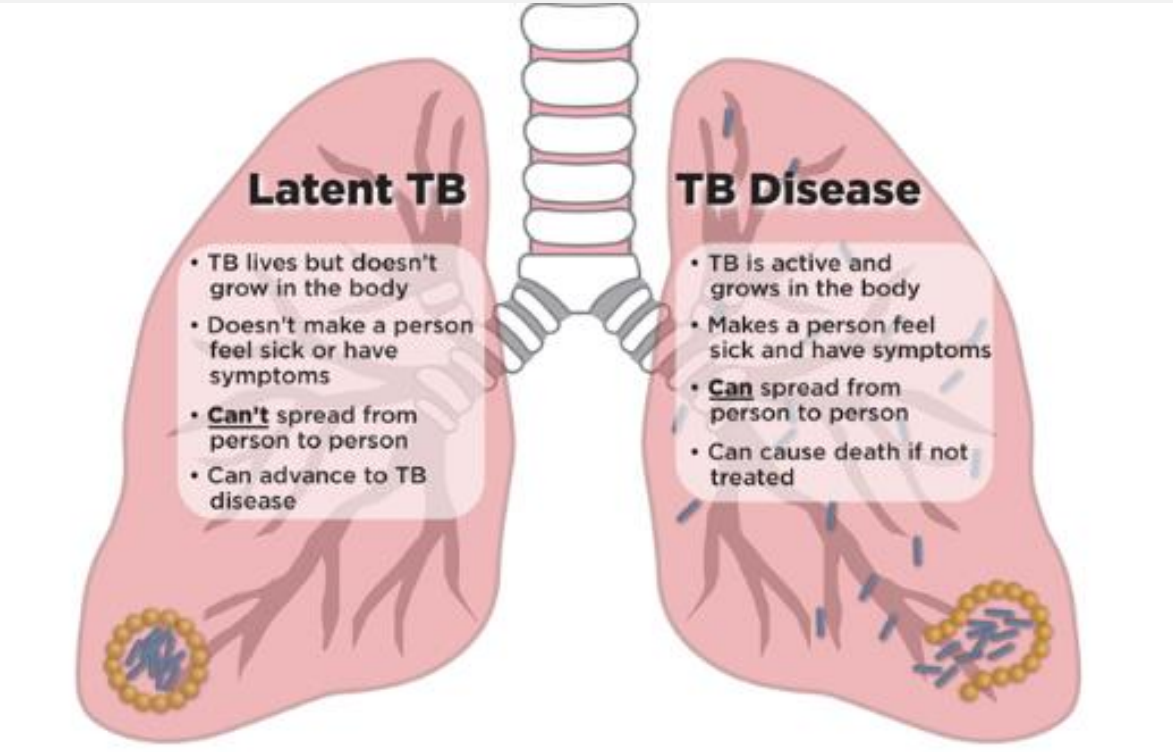
Received: 30 January 2019
Accepted: 27 June 2019
Published online: 12 July 2019

Penyaji
Marcella – 1820221175

Pembimbing
Dr.dr. Soroy Lardo, Sp.PD,KPTI FINASIM

Kepaniteraan Klinik Ilmu Penyakit Dalam
Fakultas Kedokteran UPN "Veteran" Jakarta
2020

INTRODUCTION



- Latent TB infection (LTBI) in HIV patients, its treatment, and immunological recovery following highly active antiretroviral therapy (HAART) could interact and impact TB disease progression.
- Aim: to examine the factors associated with LTBI and TB disease development among HIV patients.

Image from: AIDSinfo. HIV and Opportunistic Infections, Coinfections, and Conditions. 2019

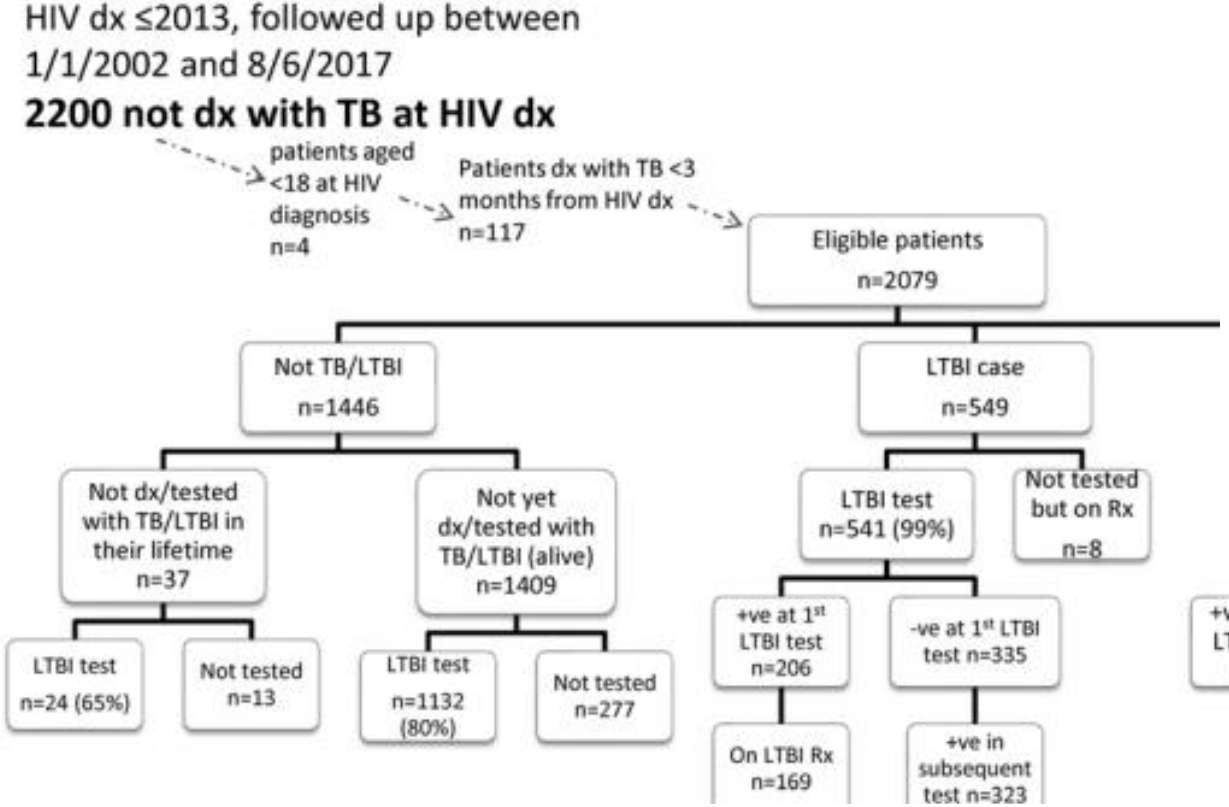
METHODS

Data Sources and Variables

- Demographics, clinical and LTBI screening and treatment were accessed **retrospectively**.
- The collected data included demographics (date of birth, gender, ethnicity, residence), HIV diagnosis date, HIV transmission route, date and specificity of ADI, baseline body mass index (BMI), diagnosis date of diabetes mellitus (DM), HAART initiation date, date of death, TB diagnosis date, date of TB or LTBI treatment initiation with regimen, baseline and pre-HAART viral load, and longitudinal measurements of CD4, CD8, CD4/CD8 ratio, and LTBI testing results (TST or IGRA).

Outcome Variables

- The **main outcome: TB disease development** → obtained from records showing **clinical and/or microbiological TB** diagnosis with date of treatment initiation.
- **Time to TB disease** was **the interval (months) from HIV diagnosis date to either TB diagnosis date or TB treatment initiation date**, whichever earlier.
- The data **end point** for patients without TB was either date of **death** or the **latest in-care date** (CD4 measurement date or LTBI testing date), whichever later.
- **Positive LTBI** was defined as either an **induration of ≥5 mm within 48 to 72 hours** with TST or positive IGRA results.



Subjects: HIV-infected patients attending the Integrated Treatment Centre (ITC), the largest HIV clinical service with a caseload of >3000 in Hong Kong, are **tested for LTBI annually** until a positive result or TB diagnosis.

Inclusion criteria: 1. patients diagnosed with HIV between 2002 (when LTBI testing became fully implemented) and 2013, 2. aged ≥18 at HIV diagnosis were selected.

Exclusion: with past history of TB or concurrent active TB disease (TB diagnosis within three months of HIV diagnosis)

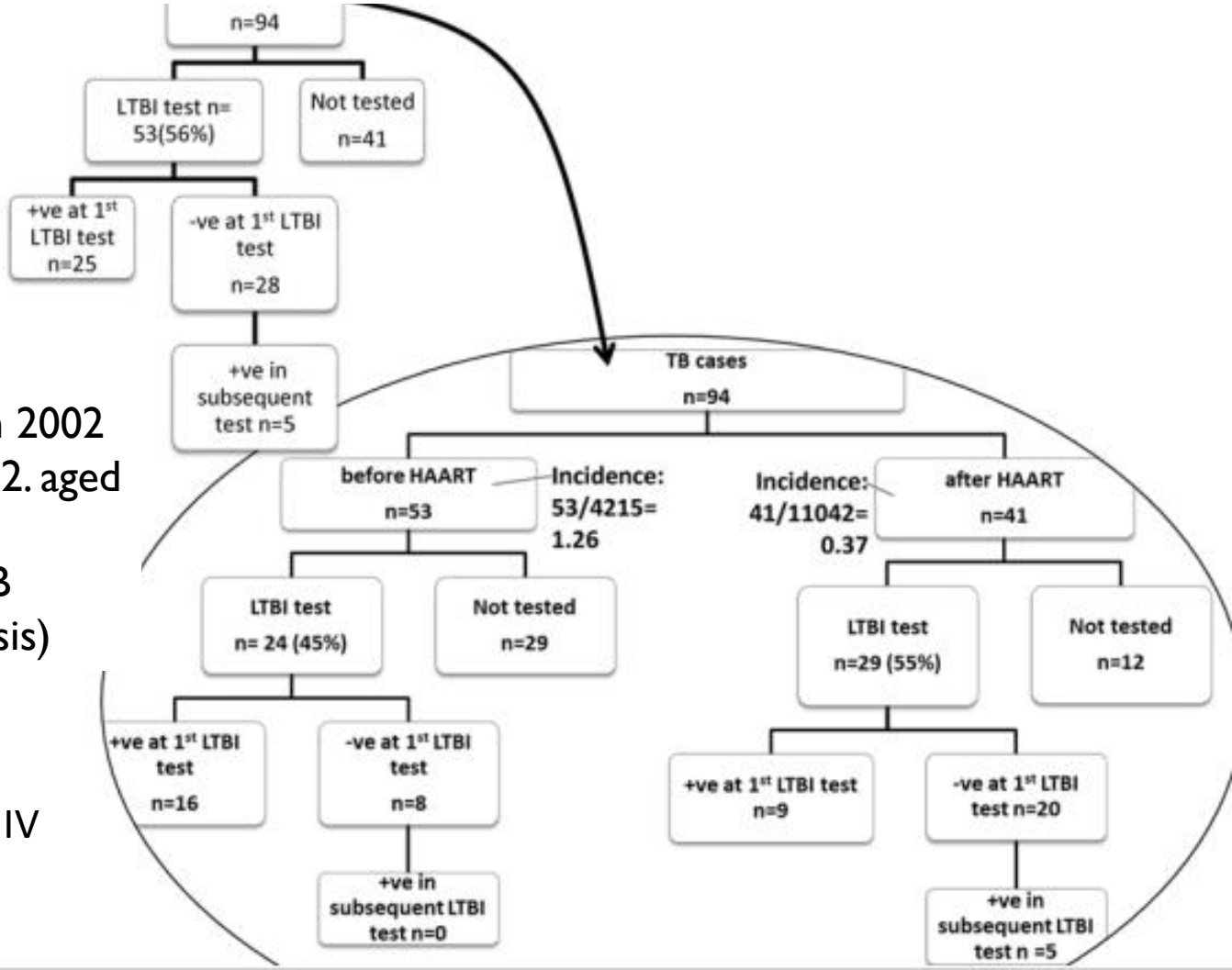


Figure 1. Flow chart of LTBI testing and treatment among HIV patients.

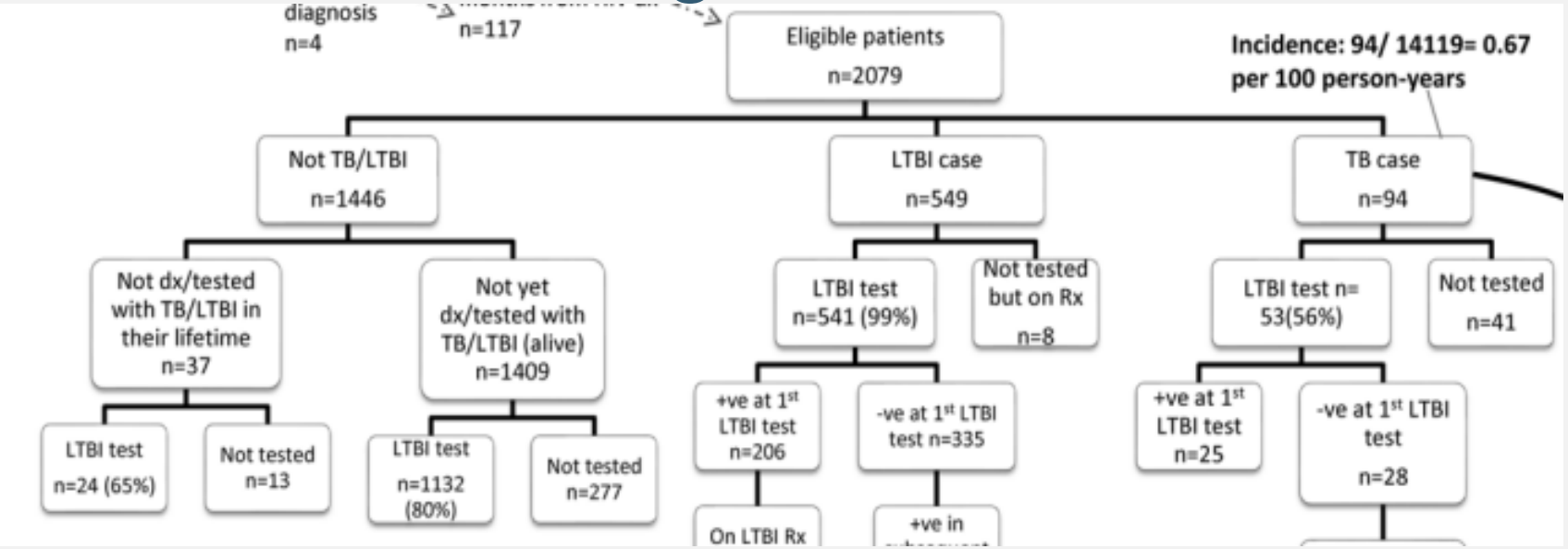
METHODS

Statistical Analysis

- We calculated: the **crude incidence rates** of TB (events/100 PY) and 95% C.I. assuming Poisson distribution. *PY was the sum of follow-up years with either CD4 measurement or LTBI testing records.
- **Factors with significantly ($p < 0.05$) higher risk** of developing TB disease identified in Cox proportional hazards regression analyses. .
- In light of the significant **association of HAART coverage with TB** incidence, we included HAART status (time dependent) and LTBI treatment status as confounders in multivariable Cox regression models.
- Separately, **characteristics of patients ever tested and never tested** for LTBI were compared, and the **associated factors** of the positive LTBI testing results were explored in logistic regression models.

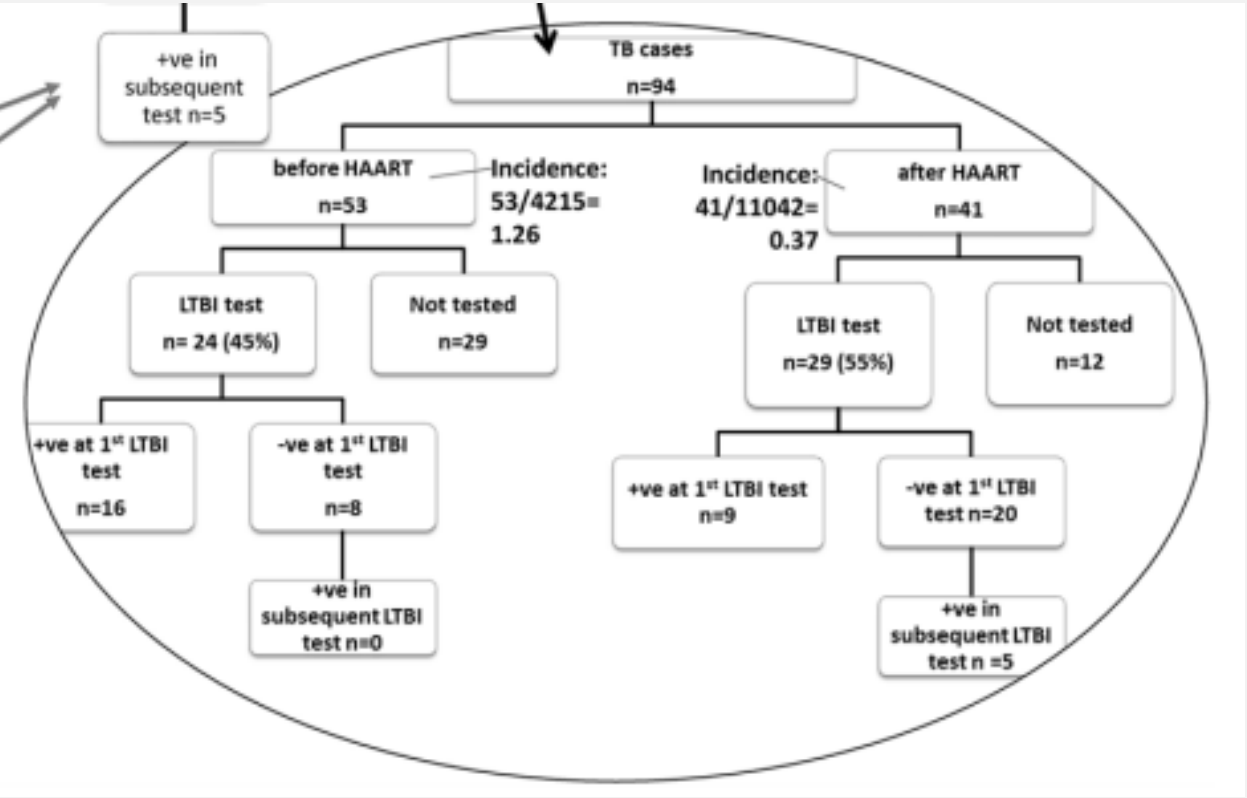
RESULTS

LTBI Screening and Identification



- **Eighty-four percent** (1740/2079) of patients have been tested for LTBI at least once.
- Compared to never-tested patients, a **higher proportion of those tested** at least once were **male** (85% for ever tested vs 78% for never-tested), **Chinese** (78% vs 51%), **local residents** (92% vs 62%), have been diagnosed with **DM** (5% vs 1%), **initiated HAART** (91% vs 46%), and diagnosed with **ADI** (15% vs 10%)
- Among HIV patients who had been **screened for LTBI, 32%** (549/1740) were **tested positive**
  Around **40% of the LTBI positive** cases (224/549) were identified **at the first test,** with non-Chinese, non-local residents, previous testing in earlier calendar year, a higher CD4 level, not on HAART, longer interval before HAART initiation, and no diagnosis with any ADI were associated with a positive result
- Patients tested **positive at the first** LTBI test were **more likely to develop TB** disease, compared to those tested negative (OR=6.68, 95% C.I.=3.82 to 11.68)

RESULTS

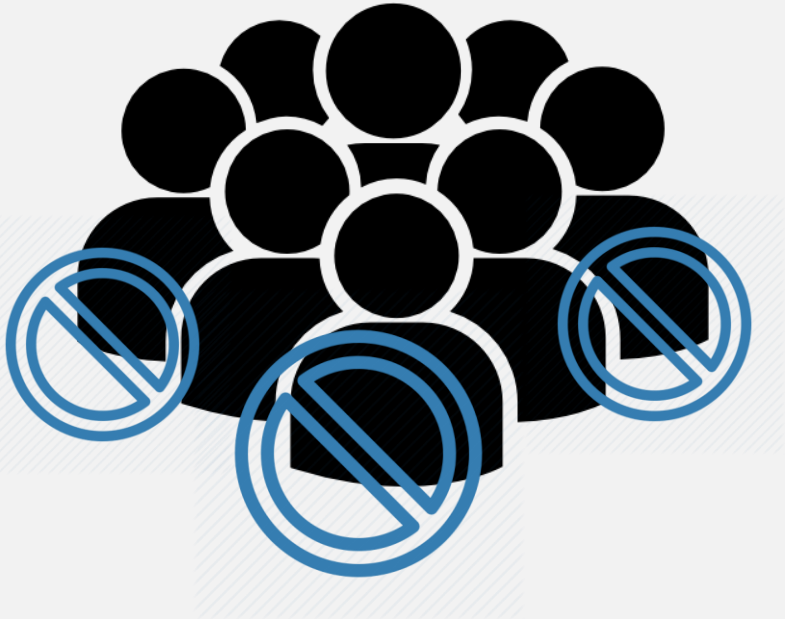


TB Incidence

- With 14119 PY of follow-up, the **TB incidence was 0.67 /100 PY** (94/14119, 95% C.I. =0.54 to 0.81/100 PY).
- Around half (53/94) of the TB cases were diagnosed **before HAART** initiation, giving a TB incidence of **1.26/100 PY** (53/4215, 95% C.I. = 0.95 to 1.63/100 PY).
- **After HAART** initiation, TB incidence dropped by 70% (41/11042= **0.37 /100 PY**, 95% C.I.=0.27 to 0.50/100 PY).
- Adjusted by HAART status, the **adjusted hazard ratio (aHR)** of TB disease development among patients tested **positive at the first** LTBI test (aHR=6.18, 95% C.I.= 3.57 to 10.73) was much **higher than** those **ever tested LTBI positive** (aHR=2.54, 95% C.I.=1.47 to 4.37)

DISCUSSION

Limitations



- 1. Study **population was relatively young** (98% aged below 65)
- 2. **False-positive LTBI testing** could occur
- 3. Study was conducted in an **intermediate TB burden city**. Extrapolation of the results to high burden developing countries would require further studies for validation.
- 4. In addition, 95% of LTBI test results were based on TST instead of IGRA. The association **between CD4 and test results might not be applicable** when IGRA is the main testing method

DISCUSSION

- Our results suggested that baseline LTBI screening for all HIV patients is an **important step** for reducing TB incidence.
- Results showed that HIV patients **never tested** for LTBI and those **tested positive at the first** instance were at **higher risk of TB** disease development, consistent with the results of a study in Spain.
- In our study, there was a **drop** of TB incidence (in HIV care) by three-folds **following HAART initiation**.
- Patients with higher CD4 and/or CD4/CD8 ratio were at lower risk of TB disease development, as observed in our and previous studies, as a result of immune recovery.

CONCLUSION

- Baseline **LTBI screening is important** for all HIV patients for minimising occurrence of clinical TB diseases and for reducing TB incidence in the population.
- However, with early HAART initiation among HIV patients**, re-evaluation** of the strategy of annual LTBI screening is needed.
- The **risk factors** identified in this study might provide useful references for the re-evaluation.