

# Is prophylaxis against tuberculosis required for HIV infected individuals in settings with low incidence of tuberculosis?

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## Background

Association of HIV and tuberculosis (TB) is well recognised.

HIV infected patients, particularly those with low CD4 count, are at high risk of reactivation of latent TB.

Identification of patients with latent TB and treating them with isoniazide preventive treatment (IPT) may prevent development of active TB.

Current data suggest combined antiretroviral therapy (cART) can reduce the rate of incident TB among HIV infected patients (1).

The UK has one of the highest incidences of tuberculosis in Western European countries; 12.3 per 100,000 population in 2013 (2).

The UK guidelines recommend screening of HIV infected patients with the following criteria for latent TB:

- From Sub-Saharan African countries on cART for less than two years
- From countries with medium incidence of TB (Eastern Europe, Central Asia, North Africa, the Middle East, South Asia, East Asia, and the Caribbean)

The guidelines recommend offer of IPT to those with positive interferon gamma reactive assays (IGRA)(3).

Data on the impact of TB prophylaxis on prevention of new cases of TB in settings with low TB incidence are scant.

We investigated the incidence of TB and the effectiveness of TB prophylaxis in a HIV cohort in the UK.

## Methods

This was an observational study on HIV infected patients attending University Hospitals Birmingham followed between 1st April 2011 and the 31st October 2013.

Patients with culture proven TB after HIV diagnosis were classified as having "active TB".

For each patient attending the clinic during this period, data for the country of birth, start of cART treatment and CD4 count at the time of the first clinic visit were collected.

Patients' countries of origin were classified in high and low risk groups according to the guidelines.

Data were collected for every clinic visit between the 1st April 2011 and the 31st October 2013.

Patients were classed as high risk of TB if they met any of the criteria set in the national guidelines.

	Country of Origin	On cART?	CD4 count (cells/mm <sup>3</sup> )
<b>Criterion 1</b>	Sub-Saharan Africa	No or <2 months	Any
<b>Criterion 2</b>	Medium incidence of TB (Eastern Europe, Central Asia, North Africa, the Middle East, South Asia, East Asia, and the Caribbean)	No or <2 months	<500
<b>Criterion 3</b>	Others	No or <6 months	<350

Because of their modest predictive value and sub-optimal sensitivity in HIV infected patients, we did not consider a role for IGRA in our calculations.

## Results

Data for 1,442 patients were reviewed; 112 patients without information on their country of origin were excluded from analysis. The remaining 1,330 HIV infected patients were followed up for a median of 27 (quartiles: 14, 29) months; 2,385 patient-years (PY) of follow up.

Heterosexual sex and sex between men accounted for 56 and 40% of HIV transmissions respectively.

There were 16 cases of active TB in the period; an incidence of 6.7/1000 PY.

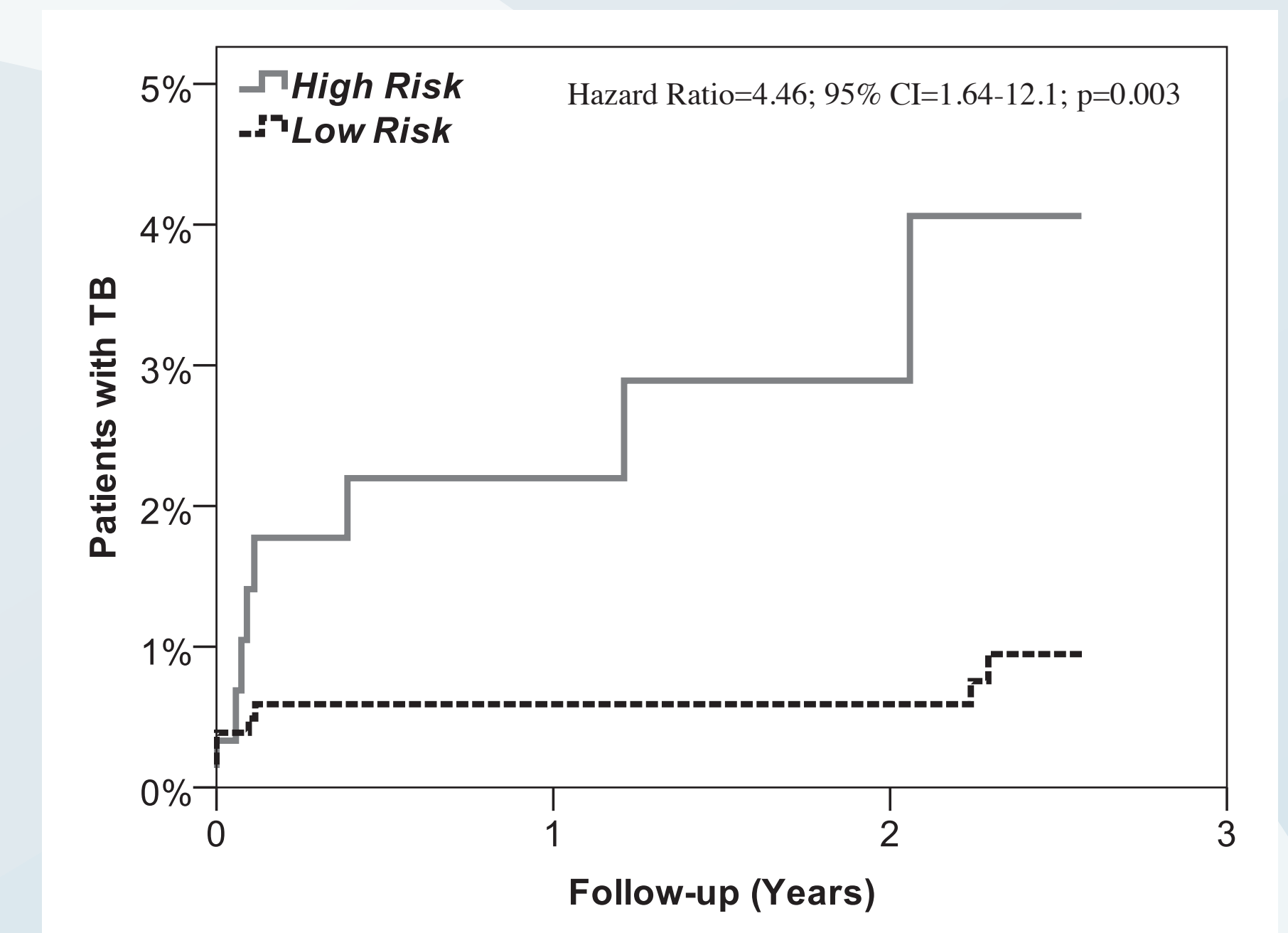
There were 301 (22%) patients who met the UK guidelines' criteria for being at risk of latent TB infection.

Demography summary of study patients	Number of Patients (n=1330)
<b>Age*</b>	<b>41.6 (10.4)*</b>
<b>Gender</b>	
Male	848 (63.8%)
Female	482 (36.2%)
<b>Ethnicity</b>	
White	530 (39.8%)
Black	670 (50.4%)
Asian	66 (5.0%)
Mixed	51 (3.8%)
Not Specified	13 (1.0%)
<b>Country of Origin</b>	
Sub-Saharan Africa	584 (43.9%)
Other High Risk Countries	74 (5.6%)
<b>cART status</b>	
Not on or <2 Months	537 (40.4%)
Not on or <6 Months	575 (43.2%)
<b>CD4 count (cells/mm<sup>3</sup>)</b>	
<350	312 (23.5%)
<500	657 (49.4%)
<b>Risk Criteria</b>	
Criterion 1	189 (14.2%)
Criterion 2#	19 (1.4%)
Criterion 3#	93 (7.0%)
<b>Total High Risk Patients</b>	<b>301 (22.6%)</b>

\*Data reported as: "Mean (SD)"

#Total does not include those patients deemed high risk by previous criteria

## Kaplan-Meier plot on survival of HIV infected patients to active TB.



The patients classified as high risk by the UK guidelines were significantly more likely to develop active TB than those that were low risk (Hazard Ratio=4.46; 95% CI=1.64-12.1; p=0.003).

IPT for every high risk patient at the time of HIV diagnosis would prevent one case of TB for every 62 patients treated, within one year.

## Discussion

In our centre the incidence of active TB was lower than the national rate. We identified 301 patients who met the criteria for start of IPT with a positive IGRA according to the UK guidelines. Current data however suggest that IPT should be recommended to all patients receiving cART in moderate to high risk incidence areas of TB irrespective of IGRA results (4).

Applying this criteria to our cohort would have resulted in prevention of one case of active TB for every 62 patients treated in one year. It is important to note that at best IPT confers a 60% reduction in the risk of active TB (5). The effectiveness of IPT in our cohort may therefore be less than what we calculated.

UK criteria for identifying patients at risk of latent TB should be utilised for screening patients for active TB when clinically symptomatic.

IPT for asymptomatic at-risk patients in cohorts with low incidence of active TB may not be necessary.

Patients meeting the criteria set by UK guidelines should be offered to start cART at any CD4 count.

## References

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